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Barcelona 2017

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25th UEG Week 2017

Barcelona, Spain, October 2017

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Dear Colleagues,

On behalf of the UEG Scientific Committee, I would like to take this opportunity to thank you most sincerely for your contribution as an abstract reviewer for the original programme of the 25th UEG Week Barcelona 2017.

The abstract reviewing process has been again very important this year, with a number of innovations introduced to improve especially the poster abstract presentations.

I know just how much time and effort reviewing abstracts takes, but without your expertise we would not have the quality that I believe we have achieved in the free paper and poster sessions, and UEG Week would not be the top international digestive diseases meeting that it has become today. Thank you!

We received a total of 3438 abstracts for UEG Week Barcelona 2017. In total, 2341 abstracts were accepted, giving an acceptance rate of 68.13%. Of these, 378 abstracts will be delivered as oral presentations and 1963 as posters. I am even more pleased to tell you that standards have again reached a very high level, and we can expect to be exposed to most interesting research and great presentations.

This high volume and high standard confirm that UEG Week is the most important forum at which to present your best research. We have received 95 video cases which were formally evaluated by the Scientific Committee for presentation in Barcelona. As in previous years, late-breaking abstracts have been scored by the Scientific Committee for presentation in Barcelona.

The quality of reviewing this year was excellent, but if you have any further (positive or negative) comments, please do let us know!

Finally, but most importantly, thanks to all investigators both within and outside Europe who have submitted their research to the meeting, and who are clearly contributing to making the 25th UEG Week Barcelona 2017 such a great success!

Professor Magnus Simrén
Chair, UEG Scientific Committee, Barcelona 2017
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Introduction: Computer-aided diagnosis (CAD) powered by artificial intelligence is attracting increased attention as an option to improve the performance of optical biopsy for evaluating colorectal polyps [1]. Although positive preliminary data have been shown for applying CAD to endoscopy (EC) (500-fold ultra-magnifying endoscopy; Olympus Corp., Tokyo, Japan) [2, 3], no prospective data have been shown for applying CAD to endocytoscopy.

Aims & Methods: The present study is an initial prospective trial to validate the feasibility of applying CAD to endocytoscopy in a routine colonoscopy practice. A total of 88 patients (38 women, 50 men; mean age 64 years) in whom colorectal polyps had been detected using EC for colonoscopy were prospectively enrolled in the study between January and March 2017. When a polyp was detected, an on-site endocytoscopist predicted the polyp pathology using the CAD system [2], which was designed to output the predicted pathology of the target lesion—whether neoplastic or non-neoplastic—based on the probability of the diagnosis (0–100%) immediately after obtaining a methylene blue-stained EC image. The endocytoscopist obtained as many images as he thought were needed, each of which was evaluated using image-based analysis. The diagnostic ability of the CAD for each image was assessed with reference to the final pathology of the resected specimen. The main outcome measures were diagnostic sensitivity specificity, accuracy, positive predictive value, and negative predictive value of the CAD system for identifying neoplastic change with high confidence (probability >90%). Prior to initiating the trial, 13,861 EC images were used for machine-learning the CAD model.

Results: Overall, 126 lesions (62 neoplastic lesions, 64 non-neoplastic lesions; mean size 6 mm) were detected, all of which were successfully analyzed using the CAD system. A total of 1014 EC images of neoplastic lesions and 1480 EC images of non-neoplastic lesions were obtained during the colonoscopies of these patients. Among them, 55% (1378/2494) were diagnosed with high confidence (CAD probability was >90%). The sensitivity, specificity, accuracy, positive predictive value, and negative predictive value of the CAD system in identifying neoplastic change with high confidence were 97%, 67%, 83%, 78%, and 95%, respectively (Table). No complications occurred during the study.

Conclusion: This prospective trial revealed that applying CAD to EC was feasible, with a negative predictive value of >90%, which is likely to meet the threshold required for optical biopsy of colorectal polyps. Our next goal is to increase the proportion of high confidence diagnoses, which is currently limited to 55%.

Disclosure of Interest: All authors have declared no conflicts of interest.
A2 United European Gastroenterology Journal 5(5S)

MONDAY, OCTOBER 30, 2017
10:30:12:00
OPENING SESSION: PART II - HALL 6

OP003 DIFFERENTIALLY O-GLYCOSYLATED CARBOXYL ESTER LIPASE CAUSES A MODY8-LIKE PHENOTYPE IN MICE
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Introduction: Maturity-onset diabetes of the young type 8 (MODY8) is a mono- genotype syndrome of diabetes and a pancreatic exocrine dysfunction caused by mutations in exon 11 of the Carboxyl Ester Lipase (CEL) gene where clustered O-GalNAc glycosylation sites are encoded.1 C-terminal truncated CEL reduces the viability of pancreatic acinar and beta cell models, indicating the induction of apoptosis in pancreatic cells.2 Aims & Methods: The aim of the present study was to establish a mouse model that allow for the investigation of the pathophysiological mechanisms in MODY8. Therefore, we hypothesized that truncated O-glycosylation of Cel (Cel-Tn) is responsible for the MODY8 phenotype and investigated the pathogenicity of differentially glycosylated Cel. For this purpose, we generated a transgenic mouse model with a conditional Cosmc knockout mediated by the pancreas specific translocation factor 1α (Pstf1α) mouse strain to induce Tn antigen expression in pancreatic acinar cells and thereby truncated O-glycan formation. Results: In accordance with the reported cluster of symptoms in MODY8 patients, characterization of Cosmc-deficient mice revealed symptoms of exocrine pancreatitis, a condition with autodigestion, altered exocrine function, impaired amylase granule release and decreased enzymatic elastase and lipase activity. Moreover, examination of fasting serum glucose and HbA1c displayed elevated levels and reduced amount of fasting serum C-peptide conformable with diabetes based on both clinical and biochemical measures. In addition, we observed reduced numbers of pancreatic acinar cells in Cosmc knockout mice indicating cytotoxicity of Cel-Tn. Our results indicate that the impairment of O-glycosylation on Cel was responsible for the observed MODY8-related phenotype, similar to mutation induced C-terminal truncation. Conclusion: This study demonstrates that deletion of Cosmc in pancreatic acinar cells leads to the loss of O-glycosylation, with consecutive expression of Tn-modified Cel, thus resulting in a MODY8 phenotype. These findings demonstrate the first generation of a MODY8-like phenotype in a mouse model and implicates the relevance of O-glycan formation.
Disclosure of Interest: All authors have declared no conflicts of interest.
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OP004 BENEFITS OF H. PYLORI ERADICATION IN PREVENTING GASTRIC CANCER IN THE OLDER POPULATION: RESULTS FROM A POPULATION-STUDY
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4Department Of Medicine, The University of Hong Kong, Hong Kong/Hong Kong PRC
5UCL School Of Pharmacy, University College London, London/United Kingdom
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Introduction: Helicobacter pylori (HP) eradication has been shown to reduce the risk of gastric cancer development, it remains elusive whether there is a point of no return on the HP-associated gastric carcinogenesis cascade. In particular, there are limited data on the benefits of HP eradication on gastric cancer prevention in the older population (>60 years).
Aims & Methods: We aimed to compare the age-specific risk of gastric cancer development in a large cohort of HP infected subjects who had received HP eradication therapy with the local general population.
Methods: The results were based on a retrospective cohort study that included all HP-infected subjects who had received a 7-day course of clarithromycin-based triple therapy between 2003 and 2012 in Hong Kong. These subjects were identified from a territory-wide health database, which captured all patients’ clinical information in the local public health care system. We excluded subjects with history of gastronomy, were diagnosed to have gastric cancer prior to or within 12-month of HP therapy, and those who failed clarithromycin-based triple therapy. Person-years at risk were derived for each patient from the first date of HP therapy until the date of gastric cancer diagnosis, death or the date of censoring. Expected number of gastric cancer cases in the general population were estimated from the standardized incidence ratio (SIR) of the HP eradicated cohort as compared to the general population (SIR = 0.75; 95% CI, 0.61 to 0.92), corresponding to a 25% reduction in gastric cancer incidence. In contrast, the corresponding SIR was 1.37 (95% CI, 0.43 – 3.30) in the <40 years and 1.07 (95% CI, 0.82 – 1.38) in the 40-59.9 years groups.
Conclusion: In this large population-based study of HP-eradicated subjects, we found that the risk of gastric cancer was significantly lower among those who received HP eradication at ≥60 years than the age-matched general population. Our results suggest benefits of HP eradication on gastric cancer prevention even in the aged population.
Disclosure of Interest: All authors have declared no conflicts of interest.
References
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Introduction: Filgotinib is an oral, selective Janus kinase 1 (JAK1) inhibitor, with demonstrated efficacy in rheumatoid arthritis. This 20-week Phase 2 study evaluated the efficacy and safety of filgotinib in patients with active moderate-to-severely active CD. The primary endpoint (CDAI remission at Week 10) was met with an acceptable safety profile.
Aims & Methods: The effect of disease duration and location on response was assessed post hoc on the primary endpoint. 174 patients with moderate-to-severely active CD (the primary endpoint) (CDAI remission at Week 10) was analysed by disease duration (<5 years, 5–10 years and >10 years) and histological location (ileal, ileo-colonic, colonic).
Results: Baseline disease characteristics were similar in both initial treatment groups, showing a population of active Crohn’s patients (mean CDAI 293, mean SES-CD 14.6, mean CRP 15.6 mg/L, 41% >10 mg/L, oral corticosteroids use 51%, mean daily dose 21.6 mg). Most patients were anti-TNF naïve, 58% were anti-TNF non-responder. Forty-three percent were diagnosed for less than 5 yrs, 30% between 5 and 10 yrs and 27% for >10 yrs. Most anti-TNF naïve patients (63%) had <5 yrs CD, whereas 71% of anti-TNF non-responders were diagnosed >5 yrs. A total of 62% of patients had ileo-colonic disease, whereas 18% had ileal involvement only and 20% had only colonic involvement. The percentage of FIL-treated patients in clinical remission at W10 was not impacted by longer disease duration while for PBO-treated patients the percentage of remitters was lower with disease duration of >10 yrs. In FIL-treated patients, consistently high remission rates in both anti-TNF naïve and (to a lesser extent) anti-TNF non-responders were seen, independently of disease duration (anti-TNF naïve: 59%, 60%, 62%; anti-TNF non-responders: 42%, 37%, 32%, respectively for <5 yrs, 5–10 yrs and >10 yrs). FIL treatment effect was also shown independent of disease location, although a higher percentage of remitters was observed in the subgroup with colonic disease only (Table 1).
Table 1: CDAI remission at Week 10 by subgroup

<table>
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<th>Subgroup population</th>
<th>Filgotinib n = 128</th>
<th>placebo n = 44</th>
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<tr>
<td>Disease duration</td>
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<tr>
<td>&lt;5 years</td>
<td>28/53 (53%)</td>
<td>5/21 (24%)</td>
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<tr>
<td>5–10 years</td>
<td>17/40 (43%)</td>
<td>3/11 (27%)</td>
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<tr>
<td>&gt;10 years</td>
<td>15/35 (43%)</td>
<td>2/12 (17%)</td>
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<td>Disease location</td>
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<tr>
<td>Ileal</td>
<td>10/24 (42%)</td>
<td>1/7 (14%)</td>
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<tr>
<td>Ileo-colonic</td>
<td>31/46 (71%)</td>
<td>8/31 (26%)</td>
</tr>
<tr>
<td>Colonic</td>
<td>19/28 (68%)</td>
<td>1/6 (17%)</td>
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CDAI: Crohn’s Disease Activity Index.
Conclusion: This post-hoc analysis of the Phase 2 FITZROY study indicates that inhibition of JAK1 with filgotinib in Crohn’s patients is consistently associated with clinical remission, independently of disease duration and location.


Aims & Methods: Patients achieving clinical response after a single IV dose of UST in the UNITI-I&II induction studies were randomized 1:1:1 in IM-UNITI maintenance trial, but detailed exposure-response analyses using clinical efficacy, biomarkers of inflammation, and endoscopic substudy data have not yet been presented.

Results: Median ss troughs were approximately 3x greater with qw SC UST (2.11 g/mL and 0.62 g/mL for the qw and q12w regimen respectively). UST levels were lower in patients with higher baseline CRP (likely reflecting greater inflammatory burden), while oral AZA, 6-MP, or MTX use and weight did not have any notable effect. With qw and q12w regimens, higher proportions achieving clinical remission (eg >0.92 ml/g in qw Q8w), lower UST concentrations (in Qs > 0.5 ml/g), and endoscopic response and remission (in Qs > 0.5 ml/g) compared to PBO (Table). By ROC analyses, trough concentrations between 0.8 and 1.4 g/mL or greater were associated with greater maintenance of clinical remission.

Reference
Clinical Remission
Endoscopic Remission
Clinical Response
Modified Clinical Remission
Endoscopic Response
Endoscopic Improvement

Table 1: Efficacy Endpoints at Week 16

<table>
<thead>
<tr>
<th>Endpoints, n (%)</th>
<th>PBO N = 37</th>
<th>3 mg BID N = 39</th>
<th>6 mg BID N = 37</th>
<th>12 mg BID N = 36</th>
<th>24 mg BID N = 36</th>
<th>24 mg QD N = 35</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical Remission</td>
<td>4 (11) 5 (13)</td>
<td>12 (32) 17 (44)</td>
<td>16 (43)** 19 (51)**</td>
<td>21 (57)** 27 (72)**</td>
<td>22 (61)** 27 (72)**</td>
<td>23 (64)** 27 (72)**</td>
</tr>
<tr>
<td>Endoscopic Remission</td>
<td>0 (0) 4 (10)*</td>
<td>3 (8) 4 (8)*</td>
<td>3 (8)* 4 (8)*</td>
<td>6 (17) 6 (17)*</td>
<td>6 (17) 6 (17)*</td>
<td>6 (17) 6 (17)*</td>
</tr>
<tr>
<td>Clinical Response</td>
<td>12 (32) 17 (44)</td>
<td>16 (43)** 19 (51)**</td>
<td>21 (57)** 27 (72)**</td>
<td>22 (61)** 27 (72)**</td>
<td>23 (64)** 27 (72)**</td>
<td>24 (65)** 27 (72)**</td>
</tr>
<tr>
<td>Modified Clinical Remission</td>
<td>4 (12) 6 (16)</td>
<td>10 (30)* 16 (43)***</td>
<td>14 (39)** 18 (51)**</td>
<td>17 (47) 22 (61)**</td>
<td>17 (47) 22 (61)**</td>
<td>17 (47) 22 (61)**</td>
</tr>
<tr>
<td>Endoscopic Response</td>
<td>5 (14) 9 (23)</td>
<td>7 (21)** 10 (29)**</td>
<td>10 (29)** 13 (38)**</td>
<td>13 (38)** 16 (43)**</td>
<td>13 (38)** 16 (43)**</td>
<td>13 (38)** 16 (43)**</td>
</tr>
<tr>
<td>Endoscopic Improvement</td>
<td>1 (3) 5 (13)</td>
<td>7 (21)** 10 (29)**</td>
<td>10 (29)** 13 (38)**</td>
<td>13 (38)** 16 (43)**</td>
<td>13 (38)** 16 (43)**</td>
<td>13 (38)** 16 (43)**</td>
</tr>
</tbody>
</table>

Table: Clinical remission at Week 52 by outcome of Period 1 (Week 12) and Period 2 (Week 26) for patients who entered Period 3

<table>
<thead>
<tr>
<th>Original Period 1 treatment designation</th>
<th>Placebo</th>
<th>Risankizumab</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>200 mg</td>
<td>600 mg</td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td></td>
</tr>
<tr>
<td>Pts in clinical remission at Week 26, N</td>
<td>19</td>
<td>22</td>
</tr>
<tr>
<td>Pts in clinical remission at Week 52, n (%)</td>
<td>15 (78.9)</td>
<td>13 (59.1) 16 (76.2)</td>
</tr>
<tr>
<td>Pts in clinical remission at Weeks 12 and 26, N</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Pts in clinical remission at Week 52, n (%)</td>
<td>4 (80.0)</td>
<td>5 (100) 12 (85.7)</td>
</tr>
</tbody>
</table>
Introduction: Ozanimod, an oral, once-daily immunomodulator designed to selectively target S1P1 and S1P3, has demonstrated clinical efficacy in ulcerative colitis (UC) (Sandborn NEJM 2016) and is being evaluated in active Crohn’s Disease (CD). This Phase 2 open-label study in CD examined endoscopic and clinical efficacy.

Methods: Patients with active CD (Crohn’s Disease Activity Index [CDAI] score 220-450, total simple endoscopic score for CD [SES-CD] ≥6 or mean CDAI and SES-CD > 12) were dosed with ozanimod 1 mg daily. All subjects achieving the aforementioned endpoints based on the exposure-response quartile corresponding to 24 mg BID dose. The predicted percentage of endoscopic endpoints was achieved in subjects within upadacitinib plasma exposures.

Results: Sixty-nine patients were enrolled. At baseline, mean age was 37.7 years, mean SES-CD was 13.3, and mean CDAI was 320. Mean CD duration was 10.0 years, with less endoscopic disease (baseline SES-CD mean was 13.3, and mean CDAI was 320. Mean CD duration was 10.0 years). Daily electronic diary records were used to collect CD symptoms (including stool frequency, with neither worse than baseline.

Endoscopic Remission 0# 10 (6, 13) 15 (11, 19) 18 (15, 22) 20 (16, 24) 22 (18, 26)
Endoscopic Response 15 (11, 19) 34 (28, 39) 45 (39, 52) 52 (47, 58) 57 (50, 62)
Clinical Response 35 (29, 40) 52 (46, 57) 56 (50, 61) 58 (53, 63) 59 (53, 64)
Clinical Efficacy Endpoints at Week 12 or 16
CDAI Remission 20 (15, 24) 27 (23, 32) 32 (26, 38) 34 (29, 40) 36 (31, 42)
SES-CD Remission 0 9 (6, 12) 12 (8, 15) 15 (11, 20) 20 (16, 24) 24 (19, 28)
Table 1: Endoscopic Efficacy Endpoints at Week 12 or 16

Conclusion: Oral ozanimod demonstrated meaningful clinical improvements as early as Week 4 and endoscopic improvements at Week 12 in patients with moderate to severe CD. No new safety signals were identified.


Modified Clinical Remission: average daily SF ≥ 2.8 and average daily AP score ≤ 0.2. 2) NAFLD worse than baseline CESD index. Crohn’s disease activity index. < 150 Endoscopic Remission: SES-CD ≤ 4 and ≥ 2 point reduction from baseline, no subscore > 1. Endoscopic Response: ≥25% decrease in SES-CD from baseline. Endoscopic Improvement: >50% decrease in SES-CD from baseline or endoscopic remission.

Conclusions: Upadacitinib exposures associated with 18 mg BID to 24 mg BID are predicted to maximize the response for clinical and endoscopic endpoints.


In this study we evaluated the variability of the N-terminal (PS) [3]. Although much attention has been given to the possible role that the N-terminal may play in those domains that are localized in the C-terminal have been studied [2]. Nonetheless, little is known about how it could cause different degrees of pathology. The interaction of CagA with PS binding with proteins in host cells helps to have a better understanding on how it could cause different degrees of pathology. The interaction of CagA with PS requires a set of positively charged residues that is highly conserved among the different species. The most variable position naturally found was the K636N mutation, which generated a higher free energy change and a lower hydrogen bonding respect to the crystal structure 4DYV when evaluating the entire docking models. Nevertheless, the amount of hydrogen bonds increased when considering other mutations, specifically the K636N which was lysing towards a carboxylic bond generated two additional hydrogen bonds. This mutation was also associated with a severe pathology, which means that there could be other molecular forces involved in the CagA-PS complex interaction. Conclusion: The study of molecular forces involved in the CagA binding with proteins in host cells helps to have a better understanding on how it could cause different degrees of pathology. The interaction of CagA with PS requires a set of positively charged residues that is highly conserved among the different species. The most variable position naturally found was the K636N mutation, which generated a higher free energy change and a lower hydrogen bonding respect to the crystal structure 4DYV when evaluating the entire docking models. Nevertheless, the amount of hydrogen bonds increased when considering other mutations, specifically the K636N which was lysing towards a carboxylic bond generated two additional hydrogen bonds. This mutation was also associated with a severe pathology, which means that there could be other molecular forces involved in the CagA-PS complex interaction. Disclosure of Interest: All authors have declared no conflicts of interest.

References

Aims & Methods: In this study we evaluated the variability of the N-terminal CagA from 127 sequences. The major sites of conservation of the residues involved in the PS interaction were 617, 621 and 626, which had no amino acid position 636 had the lowest conservation score, so mutations in this position were evaluated in order to observe the differences in intermolecular forces of the CagA-PS complex. We evaluated the docking of 3 mutations: K636A, K636R and K636N. Results: The models of the crystal and mutations K636A, K636R and K636N presented a ΔG of −8.919907, −8.665261, −8.701923, −8.515097 kcal/mol, respectively. While, mutations K636A, K636R, K636N presented 0, 3, and 4 H-bonds, respectively, and the crystal structure had 1 H-bond. Likewise, the bulk effect of the ΔG and amount of H-bonds was estimated on the entire docking models. The type of mutation affected both, the ΔG (χ2(1)= 93.82, p-value <2.2×10−16) and the H-bonds (χ2(1)= 91.93, p-value <2.2×10−16). Of all the data, 76.9% of the strains that exhibit the K636N mutation produced a severe pathology. The average of the H-bond count diminished when comparing the mutations with the crystal structure of all the docking models. This means that other molecular forces are involved in the CagA-PS complex interaction.

Disclosure of Interest: All authors have declared no conflicts of interest.
Aims & Methods: Medline, Embase, CENTRAL, and grey literature sources were systematically searched to February 2017. We included randomized controlled trials in adults with moderate to severe UC that compared infliximab, adalimumab, golimumab, vedolizumab and tofacitinib to each other or placebo. Outcomes were change in mean difference in Inflammatory Bowel Disease Questionnaire (IBDQ) score, in Short Form-36 (SF-36) physical and mental component summary scores (PCS and MCS respectively), IBDQ response (≥ 16-point increase from baseline) and IBDQ remission (total IBDQ score of ≤ 170 points). We combined direct and indirect evidence through multivariate random-effects network meta-analyses and relative ranking of treatments was assessed using surface under the cumulative ranking (SUCRA) probabilities. We also estimated Predictive intervals (PrI), which indicate the interval within which the relative effect of a future study is expected to be, in order to facilitate interpretation of the results in the light of the magnitude of heterogeneity.

Results: We included 12 randomized, double-blind, placebo-controlled trials (3 with infliximab, 3 with adalimumab, 1 with golimumab, 1 with vedolizumab and 4 with tofacitinib). All interventions as induction therapy resulted in significantly improved mean IBDQ score compared to placebo (table). Table also had significantly higher mean SF-36 scores and higher rates of IBDQ remission and response than placebo. However, only infliximab (MD 18.58; 95%CI 13.19 to 23.97) and vedolizumab (MD 19.09; 95% CI 11.08 to 27.29) achieved a clinically meaningful improvement in HRQL, with an increase in IBDQ score of more than 16 points. Compared to each other, differences among agents did not remain significant when Predictive Intervals were included, since respective Predictive Intervals crossed the line of no effect. In terms of relative ranking, infliximab, vedolizumab and tofacitinib had comparable high probability of being the best treatment across all outcomes. Due to limited data on impact of maintenance therapy on quality of life a network meta-analysis for maintenance therapy could not be conducted with vedolizumab (MD 21.10; 95% CI 11.93 to 30.27) and tofacitinib (MD 20.80; 95% CI 13.55 to 28.05) resulted in substantially significant improvement in IBDQ score compared to placebo. Network meta-analysis results of mean difference in IBDQ score. Data indicate column-to-row mean difference (MD), 95% CI and 95% PrI for change in IBDQ score (i.e. a MD higher than 0.00 favours the column-defining treatment).

Conclusion: Short-term treatment with all pharmacological therapies improved quality of life. Evidence suggests that no single agent is superior to other although infliximab and vedolizumab seems to have greater impact on HRQL. More research is needed to assess the long-term effect of therapies on HRQL. Disclosure of Interest: All authors have declared no conflicts of interest.

**OP016 THE INCIDENCE OF MILD OPPORTUNISTIC SELF-REPORTED INFECTIONS IN PATIENTS WITH IMMUNE-MEDIATED INFLAMMATORY DISEASES**

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Introduction: Thiopurines and biologicals are important for maintenance of remission in immune-mediated inflammatory diseases (IMID). Since they modulate the immune system, the risk for opportunistic infections is theoretically increased. Several studies have reported an increased risk for severe infections associated with these drugs. However, few data are available on mild opportunistic infections in these patients. Since 2012, we use the telemedicine systems "myBiOCoch" (MIBD) for inflammatory bowel disease (IBD) patients and "myBiologicalcoach" (MBC) for all other IMID patients in our centre for monitoring and registration of medication (side-)effects and self-reported infections. We aimed to 1) validate the questionnaire on self-reported infections used in these systems and 2) describe the incidence of self-reported mild opportunistic infections in IMID patients.

Aims & Methods: Patients using MIBD or MBC were asked to fill out the questionnaire on self-reported infections every three months. For validation of the questionnaire, data on infectious events and their according therapy was collected from patients using MIBD from September 2014 through May 2016 and compared to pharmacy data and questionnaires of electronic patient records. Subsequently, data on infections reported by all patients using MIBD and MBC were included to calculate the incidence, nature, and severity of the infections. An infection was defined as mild if no antibiotic (AB) or antiviral medication (AV) was prescribed, as moderate if AB or AV was required and as severe in case of a hospitalisation.

Results: During the validation phase, 631 questionnaires were filled out by 86 patients. We found a 97% agreement between pharmacy data and questionnaires regarding infections and AB or AV use and a sensitivity and specificity of 58.3% (95% CI: 40.9–74.0) and 99.3% (95% CI: 98.1–99.8) respectively. In total, 425 IBD patients using MIBD and 197 IMD patients using MBC were included for evaluation of the incidence of self-reported infections. During a mean follow-up of 11.4 ± 4.9 months, 949 infections were reported, of which 75.8% were mild infections, 23.0% were moderate and 1.2% was severe (table 1).

Table 1: Number of infections in study population

<table>
<thead>
<tr>
<th>Infections</th>
<th>Mild (N)</th>
<th>Moderate (N)</th>
<th>Severe (N)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flu-like symptoms</td>
<td>137</td>
<td>7</td>
<td>1</td>
</tr>
<tr>
<td>Upper respiratory tract infection</td>
<td>205</td>
<td>51</td>
<td>0</td>
</tr>
<tr>
<td>Lower respiratory tract infection</td>
<td>16</td>
<td>29</td>
<td>1</td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td>25</td>
<td>74</td>
<td>1</td>
</tr>
<tr>
<td>Gastrointestinal tract infection</td>
<td>41</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Genital infection</td>
<td>12</td>
<td>7</td>
<td>0</td>
</tr>
<tr>
<td>Mouth/dental infection</td>
<td>62</td>
<td>10</td>
<td>0</td>
</tr>
<tr>
<td>Skin infection</td>
<td>48</td>
<td>22</td>
<td>2</td>
</tr>
<tr>
<td>Shingles</td>
<td>5</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>Herpes labialis</td>
<td>81</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Warts</td>
<td>50</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Fever e causa ignota</td>
<td>19</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Tuberculosis</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Meningitis</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Other infections</td>
<td>18</td>
<td>10</td>
<td>2</td>
</tr>
</tbody>
</table>

Conclusion: The patient-reported infectious diseases questionnaire used in the telemedicine tools MIBD and MBC is a valid method to monitor infections in IMID patients. The overall incidence of self-reported infections in IMID patients was 1.7 infections per patient-year. The mild and moderate infections are underreported in previously published post-marketing surveillance studies. Systematic registration of all infections in relation with therapy is important to optimise country specific screening and vaccination protocols. Disclosure of Interest: All authors have declared no conflicts of interest.

**OP017 TREAT TO TARGET FOR CROHN’S DISEASE WITH ADA LIMABUM TREATMENT IS COST EFFECTIVE OVER 48 WEEKS: AN ECONOMIC ASSESSMENT OF THE CALM TRIAL**


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6Hepato-Gastroentrologie HK, s.r.o., Hradec Králové/Czech Republic

7Beyzidem Vakif University, Istanbul/Turkey

8Medical University of Vienna, Vienna/Austria

9Presidio Columbus, Fondazione Policlinico Gemelli Universita Cattolica, Rome/Italy

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11AbbVie Inc., North Chicago/United States of America/IL

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Introduction: In an open-label, multicenter, 48-week randomized controlled trial of CDAI with moderate to severe Crohn’s disease (CALM), treat to target (T2T) approach, using biomarkers (Croative protein and fecal calprotectin) in addition to a response Activity Index (CDAI) and corticosteroid use was shown to improve the rate of mucosal healing compared to conventional clinical management (CM).1 As to whether favorable health economic effects associated with the clinical benefits have not been evaluated. Aims & Methods: A model was developed to evaluate the cost-effectiveness of T2T versus CM from the CALM trial using costs reflecting a United Kingdom (UK) setting. CDAI was used to map patients into four health states (remission: CDAI < 150, moderate: CDAI ≥ 150 to < 300, severe: CDAI ≥ 300 to < 450,
very severe: CDAI ≥450) weekly over the 48-week trial. Each health state was assigned a corresponding utility value to represent quality of life for a UK analysis.2 Average number of CD-related hospitalization was obtained from CALM. Hospital and health state cost data were derived from published UK-based research from the perspective of the National Health Service. Number of adalimumab (ADA) injections was estimated from CALM and current UK list prices were used for ADA costs. Proportion of patients in remission, CD-related hospitalizations, ADA injections, direct medical costs (including outpatient visits, lab tests, endoscopic procedures), quality-adjusted life years (QALYs), incremental cost-effectiveness ratio (ICER) and net monetary benefit (NMB) were calculated over 48 weeks. Deterministic and probabilistic sensitivity analyses (PSA) were conducted to assess uncertainty. Work productivity and activity impairment (WPAI) data from the CALM trial were also used in sensitivity analysis.

**Results:** At week 0, in the T2T cohort (n = 122), 73.0% were in moderate and 27.0% were in severe state; for the MC cohort (n = 122), 75.4%, 23.8%, and 0.8% were in moderate, severe, and very severe states, respectively. Over the 48 weeks, T2T was associated with higher remission rate (62.1% vs 47.3%), fewer CD-related hospitalizations (mean 0.13 vs 0.28), and more ADA injections (mean 30.87 vs 24.72) than CM. Total medical costs were £13, 296 in the T2T and £12, 627 in the CM treatment arms; 0.684 QALYs were observed for T2T and 0.652 for CM (table). T2T had 0.032 higher QALYs (95% confidence interval [CI] 0.024 to 0.025) and £669 higher total medical costs (95% CI £2, 529 to £3, 994). The ICER was £20, 913 per QALY (95% CI £94, 116 to -£61, 457 [TC dominant]), which was below the National Institute for Health and Care Excellence (NICE) threshold of £30,000.3 Analyses that included WPAI data from the trial also favored the T2T treatment algorithm. Results were robust in the sensitivity analyses.

**Table.** Economic outcomes and cost-effectiveness of treat to target versus clinical management using the CALM trial

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>T2T (n = 122)</th>
<th>CM (n = 122)</th>
<th>Incremental (T2T – CM)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment target</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hospitalizations*</td>
<td>0.13</td>
<td>0.28</td>
<td>-0.15</td>
</tr>
<tr>
<td>Remission rate**</td>
<td>62.1%</td>
<td>47.3%</td>
<td>14.8%</td>
</tr>
<tr>
<td>ADA doses</td>
<td>30.87</td>
<td>24.72</td>
<td>6.15</td>
</tr>
<tr>
<td>Hospitalization costs*</td>
<td>£1, 126</td>
<td>£2, 398</td>
<td>-£1, 270</td>
</tr>
<tr>
<td>Other direct medical costs</td>
<td>£1, 298</td>
<td>£1, 324</td>
<td>-£226</td>
</tr>
<tr>
<td>ADA dose costs</td>
<td>£10, 870</td>
<td>£8, 705</td>
<td>£2, 165</td>
</tr>
<tr>
<td>Total medical costs</td>
<td>£13, 296</td>
<td>£12, 627</td>
<td>£669</td>
</tr>
<tr>
<td>QALYs</td>
<td>0.684</td>
<td>0.652</td>
<td>0.032</td>
</tr>
<tr>
<td>ICER (per QALY)</td>
<td>£20, 913</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*CDC-related hospitalization

**Conclusion:** In an economic model using clinical data from the CALM trial, T2T appears cost-effective compared to CM even after considering higher drug costs, by providing increases in remission, decreases in CD-related hospitalization and improvements in quality of life for patients with CD.

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**References:**


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**Aims & Methods:** Adult pts with early UC (diagnosed ≤ 36 months) were enrolled in ICONIC irrespective of disease severity or treatment. For this analysis, we evaluated pts stratified by physician assessment of disease severity into severe, moderate, and remission groups. The following BL characteristics were described for the four groups: Simple Clinical Colitis Activity Index (SCCAI), UC-related HCRU measured during the 6 months prior to study enrollment (i.e., visits to treating physicians or other IBD-associated healthcare professionals, emergency room (ER) visits, hospitalizations and hospital admissions for surgeries); Health Related Quality of Life (HRQoL) (i.e., Short Inflammatory Bowel Disease Questionnaire (SIBDQ), pt-reported employment/ UC-related sick leave status and Work and Productivity Activity Index (WPAI:GH; including work time missed (absenteeism), impairment while working (presenteeism), overall work productivity impairment, and daily activity impairment domains). Data are presented as observed and summarized as means or proportions, as appropriate. Only available observed data are shown.

**Results:** A total of 1816 UC pts were enrolled in ICONIC; mean ± SD age was 38.5 ± 14.6 years and 833 (45.9%) were female. At BL, 230 pts (12.7%) were in remission, 672 pts (37.0%) had mild UC, 686 pts (36.8%) had moderate UC, and 234 (12.9%) had severe UC. SCCAI, HCRU, and SIBDQ measures at BL by UC severity are summarized in Table. Compared to pts in remission, pts with moderate to severe UC had 1.8 to 2.6-fold higher rates of hospitalizations and 1.6 to 2.5-fold higher rates of ER visits over the past 6 months. The total number of visits to the treating physician did not appear to differ across the disease severity groups. Pt with moderate and severe disease were associated with lower SIBDQ scores and higher WPAI:GH domain scores (i.e., greater impairment on work productivity) than pts with mild disease or those in remission. Of 172 (9.5%) pts, 1.8 to 2.6-fold higher rates of hospitalizations and 1.6 to 2.5-fold higher rates of ER visits over the past 6 months. The total number of visits to the treating physician did not appear to differ across the disease severity groups. Pt with moderate and severe disease were associated with lower SIBDQ scores and higher WPAI:GH domain scores (i.e., greater impairment on work productivity) than pts with mild disease or those in remission. Of 172 (9.5%) pts, who reported to be unemployed at BL. 24.4% (n = 42) considered their unemployment to be directly related to UC. Rates of unemployment due to UC were highest in severe UC (39.4%), followed by moderate (21.6%) and mild UC (18.4%) and lowest in pts in remission (16.7%). A total of 183 (10.1%) reported sick leave at BL. Sick leave time ranged from < 2 months (59.6%), 2-4 months (12.6%), > 4 months (22.4%). Among pts on sick leave, 81.4% (n = 149) indicated that it was UC-related, however for pts with severe UC in this group, 100% (n = 48) associated sick leave with UC. In pts with moderate UC, 43.6% (n = 65) reported UC-related sick leave. Table. Baseline SCCAI, HCRU, and HRQoL by UC severity.

**Table.** Baseline SCCAI, HCRU, and HRQoL by UC severity.

<table>
<thead>
<tr>
<th>Disease severity</th>
<th>In remission</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n = 230</td>
<td>n = 672</td>
<td>n = 668</td>
<td>n = 234</td>
</tr>
<tr>
<td>SCCAI, mean (SD)</td>
<td>0.8 (1.2)</td>
<td>1.7 (1.8)</td>
<td>3.8 (2.8)</td>
<td>6.3 (3.6)</td>
</tr>
<tr>
<td>HCRU during last 6 months:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Emergency room visits, n (%)</td>
<td>34 (14.8)</td>
<td>91 (13.5)</td>
<td>154 (23.1)</td>
<td>87 (37.2)</td>
</tr>
<tr>
<td>Hospitalizations, n (%)</td>
<td>42 (18.3)</td>
<td>118 (17.6)</td>
<td>216 (32.3)</td>
<td>113 (48.3)</td>
</tr>
<tr>
<td>Number of hospital days, mean (SD)</td>
<td>3.7 (1.5)</td>
<td>12.4 (10.3)</td>
<td>11.7 (11.1)</td>
<td>19.6 (19.7)</td>
</tr>
<tr>
<td>n = 39</td>
<td>n = 109</td>
<td>n = 191</td>
<td>n = 103</td>
<td></td>
</tr>
</tbody>
</table>

(continued)
Introduction: ICONIC is the largest ongoing, prospective, multi-country (n = 33) observational study, assessing cumulative burden in adult ulcerative colitis (UC) and Crohn’s disease (CD) patient population. The study population was adult UC and CD patients who underwent lower GI surgery defined as surgeries of the small intestine, colon, rectum and anus and categorized as resection, repair, bypass or drainage surgeries as defined by ICD-10-PCS. Patients were coded by relevant ICD-9-CM procedure codes, ICD-10-PCS codes and Current Procedural Terminology (CPT) codes after 1 September 2014 and had at least two diagnoses claims for UC or CD prior to surgery; were continuously enrolled for at least 6 months before and at least 30 days after surgery. Cases of postoperative infection within the study population were defined as postoperative wound infection, peritonitis, retroperitoneal infection, or sepsis occurring 2–30 days after the lower GI surgery [1]. Patient demographics, IBD characteristics, surgery-related variables, medical histories and medications use before surgery were assessed. Multivariate logistic regression analyses were used to identify risk factors for a postoperative infection.

Results: A total of 3360 IBD patients (mean age 51.2±17.9 years, women 52.5%, 1362.1/C00-2015 and 1998 CD, with mean age 55.1 and 48.2 years, respectively) had lower GI surgery during the study period and fulfilled the study criteria of being at risk of a postoperative infection. With 2 or more types of surgery, the index lower GI surgery lower period surgery was as follows: resection 60.8%, repair 17.5%, bypass 23.5%, postoperative infection incidence after the surgery was the 15.1% (95% confidence interval [CI]: 14.0%–16.4%) and was similar for UC (14.4%, 95% CI: 12.6%–16.4%) and CD (15.7%, 95% CI: 14.1%–17.3%) patients. Multivariable analysis in IBD patients identified the following as risk factors for a postoperative infection: prior history of postoperative infection (odds ratio(OR)=3.99, 95% CI: 3.11–5.12), open procedure (OR=2.33, 95% CI: 1.88–2.89), preoperative hospital stay at least 4 days (OR=1.90, 95% CI: 1.27–2.82), lower GI bypass surgery (OR=1.72, 95% CI: 1.39–2.13), lower GI resection (OR=1.61, 95% CI: 1.27–2.04), history of chronic obstructive pulmonary disease (OR=1.59, 95% CI: 1.14–2.23), use of systemic corticosteroids within 14 days before surgery (OR=1.53, 95% CI: 1.21–1.92), history of C. difficile infection (OR=1.53, 95% CI: 1.03–2.25), and anemia (OR=1.45, 95% CI: 1.17–1.80). The risk factor profile was similar for UC and for CD patients.

Conclusion: This study identified several risk factors for postoperative infection. Patients with these risk factors should be considered at an increased risk of postoperative infection.

Disclosure of Interest: H. Liang is an employee of Takeda Pharmaceuticals and receives stock or stock options from Takeda at the time of the study. T. Lissoos is an employee of Takeda Pharmaceuticals and receives stock or stock options from Takeda at the time of the study. S. Manne is an employee of Takeda Pharmaceuticals and receives stock or stock options from Takeda at the time of the study. P. Dolin is an employee of Takeda Pharmaceuticals and receives stock or stock options from Takeda at the time of the study.

Reference

OP020 DISEASE BURDEN AND FACTORS ASSOCIATED WITH ULCERATIVE COLITIS PROGRESSION IN SWEDEN
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Introduction: Ulcerative colitis (UC) is a systemic and debilitating disease; however, evidence regarding its progressive nature is limited. The objective of this study was to assess the disease burden associated with UC progression and to identify factors related to the progression in UC.

Aims & Methods: A retrospective cohort study was conducted using data obtained from electronic medical records in Uppsala County in Sweden and the Swedish longitudinal integration database for health insurance and labor market activities (LISA) between 1995 and 2014. Patients with UC aged ≥18 years with moderate disease activity (partial Mayo clinic score of 2–4 and treated with betamethasone or <40mg/day of other steroids) were identified and followed to observe the progression to severe UC. Severe UC was defined as having partial Mayo clinic score of 6 (or ≥6) and being treated with prednisone or ≥40mg/day of other steroids. Risk of all-cause hospitalization, UC-related hospitalization and UC-related surgery within one year were estimated among patients with progression vs non-progression using odds ratio (OR) estimated by logistic regression. Annual indirect costs were calculated and compared among patients who progressed and those who did not (age 18–65) based on the average number of sick leave days and the average annual Swedish salary (in 2014 SEK and Euro). Logistic regression models were used to examine the demographic and clinical factors associated with UC progression.

Results: Among 1361 patients with moderate UC identified, 321 (23.6%) progressed to severe UC in a median follow-up of 6.26 (interquartile range: 4.8) years. Use of biologic therapy was low (8.6%) during the follow-up.
 Compared to patients who did not progress, those who progressed to severe UC had a 1.45 times higher risk of a all-cause hospitalization (95% CI 1.12–1.87) and a 2.56 times higher risk of UC-related hospitalization (95% CI 1.86–3.52) within one year, adjusting for age and gender (table). A high but not statistically significant risk of UC-related surgery was observed (OR 1.78, 95% CI 0.36–3.59) in patients who progressed. Average sick leave days were significantly higher in patients who progress than those who did not (64.4 vs 38.6 days, p < 0.001), which translated to higher indirect costs of 141,574 SEK (or 15558 Euro) for progressed patients compared to 86,583 SEK (or 9153 Euro) for non-progressed patients (p = 0.001). Patients who were younger (OR 0.99, 95% CI 0.97–1.00, p = 0.005) and who used steroids (OR 11.84, 95% CI 4.74–29.59, p < 0.001) were more likely to progress from moderate to severe UC.

Table. Comparison of health care utilization and costs associated with sick leave days between UC patients with and without progression.

<table>
<thead>
<tr>
<th>Health care utilization, costs (mean SD)**</th>
<th>No Progress</th>
<th>Progress</th>
<th>Adjusted Odds (N = 1040)</th>
<th>Progress Adjusted Odds (N = 321)</th>
<th>Ratio (95% CI)*</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All-cause hospitalization</td>
<td>347</td>
<td>111</td>
<td>1.45</td>
<td>0.005</td>
<td>(33.37%)</td>
<td>(1.41–1.87)</td>
</tr>
<tr>
<td>UC-related hospitalization</td>
<td>117</td>
<td>80</td>
<td>2.56</td>
<td>&lt;0.001</td>
<td>(&lt;11.25%)</td>
<td>(2.49–3.52)</td>
</tr>
<tr>
<td>UC-related surgeries</td>
<td>23</td>
<td>12</td>
<td>1.76</td>
<td>0.120</td>
<td>(2.21%)</td>
<td>(0.86–3.59)</td>
</tr>
<tr>
<td>Sick leave days and Indirect costs, mean (SD)**</td>
<td>38.6</td>
<td>64.4</td>
<td>NA</td>
<td>0.0001</td>
<td>(106.7)</td>
<td>(141.3)</td>
</tr>
<tr>
<td>Sick leave days (SEK)</td>
<td>86</td>
<td>585</td>
<td>141,574</td>
<td>0.0001</td>
<td>(241,855)</td>
<td>(309,915)</td>
</tr>
<tr>
<td>Sick leave costs</td>
<td>9</td>
<td>515</td>
<td>15,558</td>
<td>0.0001</td>
<td>(26,577)</td>
<td>(34,057)</td>
</tr>
</tbody>
</table>

a adjusting for age and gender **measured within 1-year after index date

Conclusion: The disease burden associated with hospitalizations and sick leave days was significantly higher in patients who progressed to severe UC compared to those who did not. Younger age, longer disease duration and steroid use were significant factors associated with disease progression. Use of biologics was low in UC patients. Early identification of disease progression and intervention with appropriate treatment should be implemented to prevent considerable disease burden associated with UC progression.

Disclosure of Interest: J. Ståhlhammar: Consultant fees: AbbVie, P. Häusler: Consultant fees: AbbVie, L. Lång: Consultant fees: AbbVie, H. Beydogan: Employee: Qintiles IMS Health, Stockholm, Sweden, and received payment from AbbVie to assist the analyses of this study, L. Arnheim Dahlström: Employee: Quintiles IMS Health, Stockholm, Sweden, and received payment from AbbVie to assist the analyses of this study, M. Skup: Employee: AbbVie, W. Lee: Employee, stockholder: AbbVie

Reference


MONDAY, OCTOBER 30, 2017 10:30-12:00

IMAGING, SCREENING AND SURVEILLANCE OF COLORECTAL CANCER - 7.1

OP021 DIFFERENCES IN ADENOMA AND PROXIMAL SERRATED POLYP DETECTION AND ITS EFFECT ON THE LONG-TERM IMPACT OF A BIENNAI FIT-BASED COLORECTAL CANCER SCREENING PROGRAM – A MICROSIMULATION STUDY

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Introduction: Both adenoma detection rate (ADR) as well as the proximal serrated polyp detection rate (PSPDPR) are known to vary widely among endoscopy practices. However, little is known about the consequences of variances in both detection rates on the effectiveness of a screening program using biennial faecal immunochemical testing (FIT) as a triage modality. Using a microsimulation model, we aimed to evaluate the long-term CRC incidence and mortality, as well as the number of total colonscopies needed over 30 years after the implementation of a FIT-based CRC screening program. Overall ADR and PSPDPR levels of the participating endoscopists were varied in this model to evaluate its independent effect.

Methods: The ASCCA (Adenoma and Serrated pathway to Colorectal Cancer) model was set up to simulate the Dutch nationwide FIT-based screening program between 2014 and 2044. In this screening program, individuals aged 55–75 years are biennially invited, and FIT-positives referred for colonoscopy. The model predicted that the FIT-based screening program in the base-case scenario was associated with a long-term CRC incidence and mortality reduction 36.7% and 51.8% when compared to no screening. After 30 years of implementation of this screening program, an additional 102,862 colonoscopies per year were needed within the total Dutch population. At a fixed PSPDPR of 11.0%, an increase in ADR from 44.0% to 61.5% would result in a decrease in CRC incidence of 24.9% when comparing both scenarios. Similarly, long-term CRC mortality would decrease with 22.7%. For this increased in ADR, an additional 21,726 colonoscopies per year would be needed 30 years after the implementation of the FIT-based screening program using a fixed ADR of 59.0% and variable PSPDPR (from 3.0% to 14.5%) model outcomes did not substantially change; long-term CRC incidence reduction 35.7% to 37.4%, mortality reduction of 51.2 to 52.3%, number of additional colonoscopies needed per year of 120,834 to 120,872.

Conclusion: Based on the ASCCA model, an increase in ADR gradually reduces CRC incidence and mortality, whereas an increase of the PSPDPR does not decrease long-term CRC incidence and mortality on a population-level. This limited effect of the increase in the PSPDPR might be explained by the limited diagnostic accuracy of FIT for serrated polyps, only detected after a time delay in coexisting with adenomas. Other triage modalities, also aiming to detect advanced serrated polyps, should be further explored.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP022 HEAD-TO-HEAD COMPARISON OF DIAGNOSTIC PERFORMANCE OF NINE QUANTITATIVE FAECAL IMMUNOCHEMICAL TESTS FOR COLORECTAL CANCER SCREENING

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Introduction: Faecal immunochromatological tests (FITs) are increasingly used for colorectal cancer (CRC) screening. A variety of FIT brands are being used whose diagnostic performance has been evaluated in different study populations. It is therefore unclear to what extent differences in reported sensitivities and specificities reflect true differences in diagnostic performance or differences in study populations or study logistics. We therefore aimed to provide an evaluation and head-to-head comparison of the diagnostic performance of nine different quantitative FITs (qFITs) within a single screening study.

Methods: In the BLITZ study, conducted in Southern Germany, pre-colonoscopy native stool samples were obtained from participants of screening colonoscopy and stored frozen at –80 °C. Stool samples were thawed, homogenized and for every qFIT, a defined amount of stool was extracted and stored using each brand’s specific buffer-filled faecal sampling device. On the next day, blinded analyses were conducted. Four point-of-care and five laboratory-based tests were investigated. Sensitivities and specificities for CRC, advanced adenoma (AA) and their combination, advanced neoplasm (AN) were calculated. Comparative evaluations were performed at pre-set manufacturing cut-offs, at adjusted cut-offs yielding defined levels of specificity (97% and 93%) and at one uniform cut-off (15 µg haemoglobin (Hb)/g stool).

Results: Out of 1667 participants, recruited between 2005 and 2010, who fulfilled predefined inclusion criteria, 626 (38%) AN (case-n = 216) and 300 randomly selected controls without AN at screening colonoscopy were included in the study. Mean age was 63 years and 56% were male. At pre-set cut-offs the sensitivities for AN of the various qFITs ranged from 22% (95% confidence interval (CI), 16–28) to 46% (95% CI, 40–53) with specificities between 86% (95% CI, 81–89) and 30% (95% CI, 95–99) (Table). Adjusting cut-offs to yield a specificity of 97% for each test, the sensitivities for AN ranged from 21% (95% CI, 16–27) to 24% (95% CI, 18–30); with cut-offs between 6.11 µg/g and 29.54 µg/g. Adjusting cut-offs to yield a specificity of 93%, the sensitivities for AN ranged from 30% (95% CI, 24–36) to 35% (95% CI, 29–42); with cut-offs between 1.70 µg/g and 12.27 µg/g. Setting all cut-offs to 15 µg/g, the sensitivities for AN ranged from 16% (95% CI, 12–22) to 34% (95% CI, 28–41), with specificities between 94% (95% CI, 91–96) and...
Table: Comparison of sensitivity and specificity of qFITs at different cut-offs

<table>
<thead>
<tr>
<th>Cut-off (μg/g)</th>
<th>qFIT</th>
<th>Pre-set cut-off of manufacturer</th>
<th>Adjusted to 97% specificity</th>
<th>Adjusted to 95% specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.00</td>
<td>HB ELISA</td>
<td>81 (54–96) 44–37 (51) 46 (40–53) 86 (81–89)</td>
<td>96 (94–98)</td>
<td>81 (54–96) 44–37 (51) 46 (40–53) 86 (81–89)</td>
</tr>
<tr>
<td>3.70</td>
<td>QuantOn Hb</td>
<td>81 (54–96) 42–35 (49) 44 (38–51) 86 (81–89)</td>
<td>96 (94–98)</td>
<td>81 (54–96) 42–35 (49) 44 (38–51) 86 (81–89)</td>
</tr>
<tr>
<td>8.00</td>
<td>Eurolyser FOBT</td>
<td>63 (35–85) 20–14 (27) 25 (17–29) 97 (94–97)</td>
<td>96 (94–98)</td>
<td>63 (35–85) 20–14 (27) 25 (17–29) 97 (94–97)</td>
</tr>
<tr>
<td>10.00</td>
<td>OC Sensor</td>
<td>69 (41–89) 18–13 (24) 22 (16–28) 96 (94–98)</td>
<td>96 (94–98)</td>
<td>69 (41–89) 18–13 (24) 22 (16–28) 96 (94–98)</td>
</tr>
<tr>
<td>15.00</td>
<td>QuickRead go iFOBT</td>
<td>63 (35–85) 19–13 (25) 22 (16–28) 96 (94–97)</td>
<td>96 (94–98)</td>
<td>63 (35–85) 19–13 (25) 22 (16–28) 96 (94–97)</td>
</tr>
</tbody>
</table>

**Notes:**
- *MNP,* mean number of polyps; *ADR,* adenoma detection rate; *LPDR,* polyps of 1 cm or more; *NDR,* neoplasia detection rate.
- If rates of polyps and adenomas were higher than 35% and neoplasia higher than 5% after 50 years old (N = 4438), these rates remained higher than 26% and 29% and neoplasia approximately 4%, between 45 and 49 years old (N = 515), while they decrease strongly before 45 years old (N = 1076). Excluding patients with familial and personal history of polyps or cancer (irrespective of the age of the relative), detection rates were still significantly higher in patients from 45 to 49 years-old than in patients under 45 (N = 1076). Interestingly, we also found that ADR was negligible in patients between 30 and 39 years-old (N = 442) at 12.4 % with a low NDR at 1.1 %. As expected, in patients younger than 30, neoplasia is virtually absent and ADR very low (2.8 %).

### OP023: TAILORING COLONOSCOPY COLORECTAL CANCER SCREENING IN CHILDHOOD CANCER SURVIVORS: A MODELING STUDY

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**Introduction:** Childhood Cancer Survivors (CCS) develop colorectal cancer (CRC) more frequently than the general population. This increased risk varies according to the age of diagnosis of primary cancer and its treatment. The US Children’s Oncology Group has suggested tailoring CRC screening recommendations for those patients at highest risk of CRC (treated with abdominal, pelvic, and/or spinal radiation ≥30 Gray). In this study, we used a modeling-based method to evaluate cost-effectiveness of CRC screening in CSS.

### Table 1: MNP, ADR, LPDR and NDR upon age*

<table>
<thead>
<tr>
<th></th>
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<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>MNP</td>
<td>0.1</td>
<td>0.2</td>
<td>0.27</td>
<td>0.24</td>
<td>0.47</td>
<td>0.56</td>
<td>0.59</td>
<td>0.78</td>
<td>0.09</td>
<td>0.97</td>
<td>0.96</td>
</tr>
<tr>
<td>ADR</td>
<td>2.8</td>
<td>9.9</td>
<td>15.4</td>
<td>13.3</td>
<td>26</td>
<td>29</td>
<td>32.1</td>
<td>39.1</td>
<td>40.4</td>
<td>46.6</td>
<td>46</td>
</tr>
<tr>
<td>LPDR</td>
<td>0</td>
<td>2.7</td>
<td>3.1</td>
<td>2.9</td>
<td>4.5</td>
<td>7.7</td>
<td>7.4</td>
<td>9.9</td>
<td>11.6</td>
<td>11.7</td>
<td>13</td>
</tr>
<tr>
<td>NDR</td>
<td>0.3</td>
<td>1.1</td>
<td>1.5</td>
<td>0.78</td>
<td>3.9</td>
<td>3.6</td>
<td>4.1</td>
<td>5.7</td>
<td>5.7</td>
<td>6.5</td>
<td>6.2</td>
</tr>
</tbody>
</table>

* *MNP,* mean number of polyps; *ADR,* adenoma detection rate; *LPDR,* polyps of 1 cm or more; *NDR,* neoplasia detection rate. Rate of polyps and adenomas were higher than 35% and neoplasia higher than 5% after 50 years old (N = 4438), these rates remained higher than 26% and 29% and neoplasia approximately 4%, between 45 and 49 years old (N = 515), while they decrease strongly before 45 years old (N = 1076). Excluding patients with familial and personal history of polyps or cancer (irrespective of the age of the relative), detection rates were still significantly higher in patients from 45 to 49 years-old than in patients under 45 (N = 1076). Interestingly, we also found that ADR was negligible in patients between 30 and 39 years-old (N = 442) at 12.4 % with a low NDR at 1.1 %. As expected, in patients younger than 30, neoplasia is virtually absent and ADR very low (2.8 %).
Aims & Methods: We adjusted the existing Microsimulation Screening Analysis- Colon (MSAC) model for the US general population to reflect CRC and other-cancer mortality risk in CCS. CRC risks were based on epidemiologic studies investigating risk of secondary gastrointestinal cancer in CCS.1,2 Other-cancer mortality assumptions were informed by data from Surveillance, Epidemiology and End Results (SEER, 1973-2013). Costs and benefits of 75 colonoscopy screening strategies varying in screening intervals (3, 5, and 10 years), age to start (30, 35, 40, 45, 50), and age to stop screening (55, 60, 65, 70, 75) were separately evaluated for CCS with primary cancer diagnosis at age 5, 10, 15, 20, and 25 years. A willingness-to-pay threshold of $100,000 per life-year gained (LYG) was assumed to assess cost-effectiveness of CRC screening. Separate analyses were carried out to investigate optimal colonoscopy screening strategies in CCS at highest risk of CRC (Hodgkin Lymphoma, HL, or Wilms tumor, WT, survivors treated with abdominal and/or chest radiation).1,3

Results: Without screening, the number deaths due to CRC in CCS not at highest CRC risk varied according to age of primary cancer diagnosis: from 23 to 46 per 1000 CCS for primary cancers diagnosed at age 5 to 10 years. Screening with colonoscopy starting at age 50 could prevent more than 68% of all CRC deaths. Screening was most effective when started at age 40, preventing 74–80% of CRC deaths in CCS at acceptable costs (incremental cost-effectiveness ratios varied $67,000–99,000 per LYG according to age at primary cancer diagnosis). Fewer lower colorectal cancers may be considered in CCS at higher risk of CRC. 3-yearly colonoscopy starting at age 35 years was optimal in WT survivors, reducing 86% of CRC deaths; and, among HL survivors, 10-yearly colonoscopy screening starting at age 35 was optimal, averting 78% of CRC mortality.

Conclusion: In CCS, colonoscopy screening may be considered from earlier ages and with shorter screening intervals compared to the general population, due to their higher risk of CRC.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
3. Armstrong GT, Chen Y, Yasui Y, et al. Reduction in Late Mortality among CCS at highest risk of CRC (HL, or Wilms tumor, WT, survivors treated with abdominal and/or chest radiation).1,3

OP025 FOLLOW-UP OF COLORECTAL CANCER (CRC) PATIENTS INCLUDING 18FDG-PET-CT (PET-CT): AN OPEN-LABEL MULTICENTER RANDOMIZED TRIAL. (CLINICAL TRIAL: NCT 01504260)

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Aims & Methods: The aim of this study was [1] to quantify the effect of PET-CT on the chance of successful sphincter preservation in distal rectal cancer using MRI by comparing the height of tumours measured from the anorectal junction (AJR) on pre-and post-CRT MRI, which decreased to 27% after CRT. Area under the ROC-curve (AUC) to predict successfull sphincter preservation based on the confidence level score on post-CRT MRI was 0.81, sensitivity 91%, and specificity 61%. We assumed the post-CRT height measurements instead of the confidence level score, AUC was 0.86, sensitivity 70%, and specificity 90% (using a cut off of 28 mm).

Conclusion: The distance from the anorectal junction in distal rectal tumours increases as a result of CRT, thereby increasing the chance for successful sphincter preservation. Successful sphincter preservation can accurately be predicted using Receiver Operator Characteristics (ROC-curves) with the final surgical outcome as the standard of reference. Successful sphincter preservation was defined as a complete (R0) surgical resection of the rectum with preservation of the anal sphincter complex, without evidence of anastomotic tumour recurrence for a follow-up period of >2 years.

Disclosure of Interest: All authors have declared no conflicts of interest.

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Introduction: Curative surgery is the best therapy of CRC and related recurrences if detection early and small numbers. We have previously showed that 18F-FDG PET-Scan is a valuable tool in this field (1). Here, we assess whether adding semi-annual PET-CT to the usual surveillance would be cost-effective in high-risk recurrent CRC patients.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
short-term outcomes (Kato et al. Endosc Int Open 2016; 4: E521-E526). However, the long-term outcomes are not yet elucidated.

Aims & Methods: The purpose of this study is to evaluate the efficacy of ESD for elderly patients who are 75 years over recruited in a prospective study regarding the expanded indication of ESD for early gastric cancer (Soetikno et al. J Clin Oncol 2005; 23: 4490-4498). Subsequently, 57 primary cancers were found in 50 patients (SIR, 2.70; 95% confidence interval (CI), 2.03–3.51). The risk of head and neck cancers was markedly elevated (15 patients; SIR, 28.35; 95% CI, 16.87–43.07), followed by liver cancer (seven patients; SIR, 8.39; 95% CI, 2.85–13.23), lung cancer (nine patients; SIR, 3.13; 95% CI, 1.56–5.99), and gastric cancer (nine patients; SIR, 3.12; 95% CI, 1.59–5.65). Five of seven liver cancers were hepatocellular carcinomas. All patients with liver cancer were negative for hepatitis B and C. The histopathology types of nine lung cancers consisted of adenocarcinomas, two squamous cell carcinomas, two small cell carcinomas, and two with no diagnosis. The 5- and 10-year overall survival rates after ER were 88% and 78%, respectively. Five patients died of metastatic ESCCs. SPCs led to death (seven patients), two with head and neck cancer, one with pancreatic cancer and one with myelodysplastic syndrome.

Conclusion: Because patients have extremely high risks of head and neck cancers after ER for ESCCs, these regions should be carefully surveyed by oesophagogastroduodenoscopy. The liver, lungs, and stomach also have higher risks of the lungs and liver is recommended for such patients.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

OP028 INCIDENCE OF SUBSEQUENT PRIMARY CANCERS AFTER ENDOSCOPIC RESSECTION OF OESOPHAGEAL SQUAMOUS CELL CARCINOMAS
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Introduction: The incidence rate of a subsequent primary cancer (SPC) has been expected one. The incidence ratio (SIR) was obtained by dividing the observed incidence rate by the expected rate per 1000 person-years. The expected incidence rates in the general population and stomach were 5.5 and 1.4 per 1000 person-years. We retrospectively recommended surveillance for early detection of SPCs. We separated the elderly group into curative resection group; 273 cases, two according to JGCA Guideline, and non curative resection group; 16 cases. We compared the median observation period and 5-year overall survival rate. The survival rates were analyzed by Kaplan-Meier curves. Cox hazard model was used to evaluate their background.

Results: The median observation period and 5-year overall survival rate of elderly group 52.2±1.8 months and 90.0%, which is higher than the 75-year-old Japanese people’s general 5-year survival rate calculated by the national life tables. The non-elderly group and stomach were 96.3±1.3 months and 96.3%. The incidence rates of SPCs were measured after endoscopic resection for early cancers of the upper gastrointestinal tract. J Clin Oncol 2005; 23: 4490-4498.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

OP029 SHOULD TAKING BIOPSY SAMPLES FROM APPARENTLY NON-CANCEROUS TISSUES AROUND THE LESION BE PERFORMED TO DETERMINE RESECTION Margin BEFORE GASTRIC ENDOSCOPIC SUBMUCOSAL DISSECTION?
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Introduction: Endoscopic submucosal dissection (ESD) is widely performed for treating early gastric cancer (EGC) with little risk of lymph node metastasis. The preoperative identification of horizontal margin of EGC is important before ESD. There are some EGCs the margins of which cannot be determined by chromoendoscopy and magnifying endoscopy with narrow-band imaging (ME-NBI). Therefore, we performed biopsy samples from apparently non-cancerous tissues around the lesion (surrounding biopsy) to determine resection margins before ESD.

Aims & Methods: The aim of this study was to assess the predictors of cancer-positive results in surrounding biopsy before gastric ESD. From January 2015 through December 2016, EGCs which we performed more than two surrounding biopsies after the identification of the horizontal margin of EGC using by conventional endoscopy, chromoendoscopy and ME-NBI were enrolled in this study. To assess the predictors of cancer-positive results in surrounding biopsy, we performed univariate and multivariate analysis on the following factors; age (<75 vs. ≥75), sex (Male vs. Female), Helicobacter pylori (HP) infection (positive vs. negative vs. unknown), atrophy gastritis (positive vs. negative), macroscopic type (level type vs. depressed type vs. mixed type), location (Upper vs. Middle vs. Lower), color (reddish vs. discolored), lesion border by chromoendoscopy (clear vs. unclear), lesion size (<30 mm vs. ≥30 mm), ulceration (UL) (positive vs. negative), corkscrew vascular pattern (CVP) by ME-NBI (positive vs. negative), endoscopic diagnosis of invasion depth (cT1a vs. cT1b).

Results: A total of 811 EGCS in 768 patients (499 males, median age 72 years old, range 32–96 years old) were analyzed. Of these 60 lesions (7%) in 60 patients were cancer-positive results in the surrounding biopsies. Univariate analysis revealed that location, HP infection, macroscopic type, UL, lesion size and CVP were significant associated with cancer-positive results in the surrounding biopsy. Multivariate logistic regression analysis revealed that HP infection negative (OR 3.0 [95% CI 1.5–6.0], P=0.01), lesion size ≥30 mm (OR 3.1 [95% CI 1.3–6.8], P=0.01), UL positive (OR 2.7 [95% CI 1.2–5.7], P=0.01) and CVP positive (OR 4.0 [95% CI 1.4–10.4], P=0.007) were independent predictors for cancer-positive results in the surrounding biopsies. Four of 60 cases (7%) underwent surgery due to be out of ESD indications because of surrounding biopsies being cancer-positive. Among the 807 lesions in 764 patients who underwent ESD, only three (0.7%) were cancer-positive horizontal margin in ESD specimen.

Conclusion: This study successfully identified predictors of positive results in the surrounding biopsy. It can be useful to identify the horizontal margin of EGCs when lesions are ≥30 mm in size, negative for HP infection, UL positive and CVP by ME-NBI. When HP and CVP are negative, the evaluation of resection margins by surrounding biopsy would be necessary.

Disclosure of Interest: All authors have declared no conflicts of interest.
Aims & Methods: Endoscopic resection, including endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD), is widely used to treat early esophageal and gastric tumors in Japan, but is sometimes difficult to perform in high-risk patients who are elderly or who have difficult underlying diseases.

Aims & Methods: We aimed to clarify the local effectiveness and safety of endoscopic ampullectomy (CSP) for the curative treatment of early esophageal and gastric tumors in high-risk patients.

Subjects and Methods: We retrospectively studied high-risk patients with early esophageal and gastric tumors who met the inclusion criteria and underwent Ampullectomy (CSP) from October 2015 to February 2017. The inclusion criteria defining high-risk patients in whom endoscopic resection was difficult to perform were as follows: a) patients undergoing maintenance hemodialysis because of renal failure, b) patients in whom it was difficult to discontinue long-term anticoagulant or antiplatelet therapy, c) patients with a bleeding tendency due to factors such as liver cirrhosis and hematologic disease, d) patients in whom prolonged sedation was difficult, and e) patients in whom endoscopic resection was judged by their attending physicians to be difficult.

Results: CSP was performed in 208 patients with early esophageal or gastric tumors (esophageal tumors, 74 patients; gastric tumors, 134 patients). The median follow-up period was 33 months (range, 1 to 137) in patients with esophageal tumors and 31 months (range, 1 to 131) in patients with gastric tumors. CSP was completed in 97% (9/10) of patients with esophageal tumors and 78 years (range, 52 to 95) in patients with gastric tumors. The male:female ratio was 66:8 for esophageal tumors, and 103:31 for gastric tumors. The esophageal tumor diameter was 10 mm or less in 24 patients, 11 to 20 mm in 19 patients, and 21 mm or greater in 31 patients. The gastric tumor diameter was 10 mm or less in 63 patients, 11 to 20 mm in 51 patients, and 21 mm or greater in 20 patients. The histopathological diagnosis of the esophageal tumors was high-grade intraepithelial neoplasia in 23 patients, squamous-cell carcinoma in 44 patients, differentiated adenocarcinoma in 1 patient, and undetermined in 6 patients. The histopathological diagnosis of the gastric tumors was adenoma in 27 patients, differentiated adenocarcinoma in 96 patients, poorly differentiated carcinomia in 10 patients, and unknown in 1 patient. The preoperative depth of invasion of the gastric tumors was the submucosa or deeper layer in 67 patients, the muscularis mucosae or first layer of the submucosa in 6 patients, and the second layer of the submucosa in 1 patient. The preoperative extent of the lesion was classified as 0-IIa in 16 patients, 0-IIb in 12 patients, 0-III in 1 patient, and 0-IV in 1 patient. The vertical margins were negative in 77 patients, positive in 1 patient, and undetermined in 11 patients. The horizontal margins were negative in 9 patients, positive in 1 patient, and undetermined in 11 patients. The vertical margins were negative in all cases. In follow-up endoscopy at 3 months after CSP, all ulcers became scar and no recurrence was detected endoscopically. All biopsies from scar revealed non-neoplastic.

Conclusion: CSP could be performed safely for small SNADET. Efficacy of CSP should be evaluated at next phase III study.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP031 PHASE II STUDY OF COLD SNARE POLYPECTOMY FOR SUPERFICIAL NON-AMPULOID DUODENAL EPITHELIAL TUMOR (D- CSP TRIAL)


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Introduction: Small superficial non-ampullary duodenal epithelial tumor (SNADET) is often observed without any treatment in consideration of high complication rates in endoscopic treatment such as endoscopic submucosal dissection (ESD) and endoscopic mucosal resection (EMR). However, treatment is becoming more difficult to resect after tumor growth or many biopsies. Cold snare polypectomy (CSP) has been reported to minimize the risk of complications, and it has become a standard treatment for small colorectal polyps. We considered that CSP could also be suitable for small duodenal polyps.

Aims & Methods: The aim of this study was to evaluate the safety of CSP for SNADET. The major indication criteria were as follows: 1) endoscopically diagnosed SNADET (biopsy before treatment was not necessary, but definitive cancer was excluded), 2) <10 mm in size, 3) a single primary lesion. After registration, CSP was performed using an electrosurgical snare without electrocautery. Follow-up endoscopy and biopsy from scar was performed at 3 months after CSP. The primary endpoint was the rate of delayed complications (perforation and bleeding), secondary endpoints were the rate of spurring bleeding just after CSP, en bloc resection, residual tumor 3 months after CSP, adverse events. All patients provided written informed consent. This study was approved by the ethics committee of the University of Shizuoka. All data were collected and analyzed with University Hospital Medical Information Network Clinical Trials Registry(UMIN000019157).

Results: A total of 21 patients (pts) (male:female: 16:5, median age 71 years (range 60–85); 12 pts) had a history of at least one gastrointestinal surgery. The inclusion criteria were 66:8 for esophageal tumors, and 103:31 for gastric tumors. The esophageal tumor diameter was 10 mm or less in 24 patients, 11 to 20 mm in 19 patients, and 21 mm or greater in 31 patients. The gastric tumor diameter was 10 mm or less in 63 patients, 11 to 20 mm in 51 patients, and 21 mm or greater in 20 patients. The histopathological diagnosis of the esophageal tumors was high-grade intraepithelial neoplasia in 23 patients, squamous-cell carcinoma in 44 patients, differentiated adenocarcinoma in 1 patient, and undetermined in 6 patients. The histopathological diagnosis of the gastric tumors was adenoma in 27 patients, differentiated adenocarcinoma in 96 patients, poorly differentiated carcinomia in 10 patients, and unknown in 1 patient. The preoperative depth of invasion of the gastric tumors was the submucosa or deeper layer in 67 patients, the muscularis mucosae or first layer of the submucosa in 6 patients, and the second layer of the submucosa in 1 patient. The preoperative extent of the lesion was classified as 0-IIa in 16 patients, 0-IIb in 12 patients, 0-III in 1 patient, and 0-IV in 1 patient. The vertical margins were negative in 77 patients, positive in 1 patient, and undetermined in 11 patients. The horizontal margins were negative in 9 patients, positive in 1 patient, and undetermined in 11 patients. The vertical margins were negative in all cases. In follow-up endoscopy at 3 months after CSP, all ulcers became scar and no recurrence was detected endoscopically. All biopsies from scar revealed non-neoplastic.

Conclusion: CSP could be performed safely for small SNADET. Efficacy of CSP should be evaluated at next phase III study.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP032 ENDOSCOPIC AMPULLECTOMY FOR NON-INVASIVE AMPULLARY LESIONS: A SINGLE-CENTRE 10 YEAR RETROSPECTIVE COHORT STUDY

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Introduction: Benign tumours of the ampulla of Vater are rare, but the majority have malignant potential. Surgical resection was traditionally considered the standard of care; however, endoscopic ampullectomy is a minimally invasive alternative. Only a few case series have been published with relatively small sample sizes and short follow-up.

Aims & Methods: This study aims to retrospectively evaluate the safety and efficacy of endoscopic ampullectomy in a single tertiary referral centre over a 10-year period. All patients who underwent endoscopic ampullectomy were identified through the hospital endoscopy and pathology databases, and included in this study. The medical records were retrieved and reviewed with an extensive data analysis. The data points analysed included patient details, lesion characteristics, efficacy, adverse outcomes and recurrence rates.

Results: Fifty-three ampullectomies were performed on 26 female and 27 male patients with a mean age of 64 years (range 35–88 years). Patients with familial adenomatous polyposis (FAP) (n = 14) were significantly younger than those with sporadic lesions (n = 39) (51 vs. 69 years; P < 0.001). Ampullary tumours were most commonly detected during screening endoscopy in FAP patients (P < 0.001), followed by incidental discovery in patients without FAP who were investigated for abdominal pain (P = 0.001). Pre-ampullectomy assessments included a side-viewing endoscopic ultrasound (EUS) in all patients, endoscopic ultra sound (EUS) in 36% and magnetic resonance cholangiopancreatography (MRCP) in 19% of patients. The mean ampullary lesion size was 20 mm (range 6–50 mm) and in 37 patients confined to the ampulla. A lateral spreading tumour of the papilla (LST-P) was present in 16 patients. Lesions were resected en bloc when possible (57%), and the pancreatic duct was stented if feasible as prophylaxis against pancreatitis (83%). In addition, biliary sphincterotomy was performed in 28% of patients to mitigate the risk of cholangitis. Endoscopic
Conclusion: The study substantiates that endoscopic ampullectomy is a safe and highly efficacious procedure for managing non-invasive ampullary tumours. Aside from its therapeutic utility, endoscopic resection also confers the additional benefit of assessing the true histological diagnosis of the tumour which has implications to regard to prognosis and further management. A structured approach to initial lesion assessment, endoscopic treatment and surveillance is required to ensure the best outcomes in patient safety and lesion clearance.

Disclosure of Interest: All authors have declared no conflicts of interest.

MONDAY, OCTOBER 30, 2017 10:30-12:00

DIAGNOSIS AND MANAGEMENT OF CIRRHOSIS: UNMET NEEDS - ROOM E3

OP033 VON WILLEBRAND FACTOR ANTIGEN IS LINKED TO BACTERIAL TRANSLLOCATION, INFLAMMATION, AS WELL AS PROCOAGULANT IMBALANCE AND PREDICTS COMPLICATIONS OF CIRRHOSIS INDEPENDENTLY OF PORTAL HYPERTENSION SEVERITY

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Introduction: Von Willebrand factor (vWF) antigen has been shown to indicate the presence of clinically significant portal hypertension (CSPH), and thus precede the development of clinical events in patients with cirrhosis.

Aims & Methods: We aimed to investigate the impact of bacterial translocation and inflammation on vWF, as well as the association between vWF and procoagulant imbalance, and vWF antigen levels and complications of cirrhosis, independently of the severity of portal hypertension. Our study population comprised 225 patients with CSPH (hepatic venous pressure gradient [HVPG] ≥ 10 mmHg) without active bacterial infections or a history of hepatocellular carcinoma.

Results: Patient characteristics: Child-Turcotte-Pugh class [CTP]: A3:32%/B34%/C24%; median HVPG-19 (interquartile range [IQR]7) mmHg; median vWF antigen levels: 337(IQR:137)%. In addition to indicators of liver function and coagulation, vWF antigen levels were also independently associated with the presence of clinically significant portal hypertension (CSPH), and thus predicted the development of clinical events in patients with cirrhosis.

Conclusion: These study substantiates that endoscopic ampullectomy is a safe and highly efficacious procedure for managing non-invasive ampullary tumours. Aside from its therapeutic utility, endoscopic resection also confers the additional benefit of assessing the true histological diagnosis of the tumour which has implications to regard to prognosis and further management. A structured approach to initial lesion assessment, endoscopic treatment and surveillance is required to ensure the best outcomes in patient safety and lesion clearance.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP034 CLASS 1 OBESITY IS ASSOCIATED WITH INCREASED RISK FOR PORTAL VEIN THROMBOSIS IN HEPATITIS C PATIENTS WITH CIRRHOSIS: A NATIONWIDE ANALYSIS

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Introduction: Cirrhosis is a well-recognized risk factor for portal vein thrombosis (PVT). Obesity has been described to be a risk factor for thrombosis. However, limited information is available on how obesity impacts the development of PVT in patients with hepatitis C. As no large study has examined this relationship in cirrhotic patients, this study is to determine the impact of obesity on PVT development in cirrhotic patients.

Aims & Methods: This was a retrospective cohort study using the 2013 National Inpatient Sample, the largest publically available inpatient database in the US. Patients older than 18 years with an ICD-9 CM code for any diagnosis of liver cirrhosis (ICD-9 CM 571.2, 571.5, 571.6) were included. There were no exclusion criteria. The primary outcome was the impact of obesity on development of PVT (ICD 9 CM 452). Obesity was further sub-classified according to body-mass index (BMI) using ICD 9-CM codes. Secondary outcomes were in-hospital mortality, resource utilization measured by length of hospital stay (LOS) and total hospitalization charges. Odds ratios and means were adjusted for differences in morbidity, median income in the patient’s zip code, Charlson Comorbidity Index, hospital region, rural location, size and hospital teaching status on multivariate regression.

Results: 8842 patients with liver cirrhosis were included. 69.934 (12%) were obese, of which 1125 patients had PVT (mean age 59 years, 35.7% female). Overall in-hospital mortality rates were 9% (11% with PVT vs. 5% without PVT). On multivariate analysis for the primary outcome, cirrhotic obese patients did not have significantly different odds of OR of PVT compared to the non-obese. However, when stratifying by obesity subtype, obesity class 1 was associated with increased odds of PVT (OR:1.45, 95% CI 1.06–1.96, P = 0.02), while obesity class 3 was associated with a decreased odds of PVT (OR:0.72, 95% CI 0.58–0.88, P < 0.01) compared to the non-obese. For secondary outcomes, only increased odds of abdominal CT scan were evident (OR: 3.75, 95% CI 1.18–11.02, P = 0.02). PVT patients with PVT had longer lengths of stay and hospitalization charges compared to patients without PVT, though these were not significant on multivariate analysis. There were no significant differences in morbidity or in-hospital mortality when compared with patients without PVT.

Conclusion: Class 1 obesity is associated with increased odds of PVT, while class 3 obesity is associated with decreased odds of PVT in patients with cirrhosis. PVT is not associated with increased morbidity, mortality or resource utilization. A diagnosis of PVT in this population leads to an approximate four-fold increase in utilization of CT scan.

Disclosure of Interest: All authors have declared no conflicts of interest.

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Introduction: Non-alcoholic steatosis of the liver (NAFLD) has become the most common liver disease in industrialized western countries. NAFLD is the most common liver disease in industrialized western countries (1, 2). Patients with NAFLD are at increased risk for chronic liver disease (CLD), liver-related morbidity and mortality caused by complications of cirrhosis and hepatocellular carcinoma (HCC). The golden standard in evaluation of liver steatosis and inflammation is liver biopsy. With differentiated non-alcoholic fatty liver (NAFL) from non-alcoholic steatohapathies (NASL) is the liver biopsy. Unfortunately liver biopsy is invasive with some risk of complications, it’s costly and contains risk of sampling error. Therefore non-invasive steatosis measurement is preferred whenever biopsy is not mandatory. With Controlled Attenuation Parameter (CAP) integrated in the widely used Elastography tool Fibroscan a new tool was introduced for non-invasive quantitative and qualitative steatosis measurement recently. To date the CAP measurement had to be done within the same week as the biopsy and quality standards for CAP measurement were defined. Liver biopsies were classified according NAS Score: S0 ≤ 5%; S1 5–33%; S2 34–66%; S3 ≥ 66%. In addition data about fibrosis, inflammatory

Aims & Methods: The aim of this study was to analyse the accuracy of CAP values compared to the histologically quantified steatosis and to determine the CAP values in an unselected collective undergoing liver biopsy for any reason in a tertiary liver centre in Switzerland. Method: Between March 2015 and August 2016, all patients who underwent liver biopsy for any reason were screened to meet the inclusion criteria. The CAP measurement had to be done within the same week as the biopsy and quality standards for CAP measurement were defined. Liver biopsies were classified according NAS Score: S0 ≤ 5%; S1 5–33%; S2 34–66%; S3 ≥ 66%. In addition data about fibrosis, inflammatory

Disclosure of Interest: All authors have declared no conflicts of interest.
activity, body mass index (BMI) and liver disease were recorded. For diagnosis of NAFLD, the STE-Fire score was used. Results: From 3,2015 to 8,2016 290 subjects were screened and 224 were included. 146 (65%) were male. Steatosis grades were S0 (0–5%) n = 85 (38%), S1 (6–33%) n = 82 (37%), S2 (34–66%) n = 33 (15%) and S3 (>66%) n = 24 (11%). BMI mean was 26.8 kg/m² (SD 5.0). Mean BMI for the S0: 24.9 kg/m² (SD 3.3), for S1: 26.5 kg/m² (SD 4.2), for S2: 27.3 kg/m² (SD 4.9) and for S3: 32.5 kg/m² (SD 7.1). 114 patients had BMI ≥ 25 kg/m². Median CAP values for S0: 227 dB/m (IQR 199–249), S1: 265 dB/m (IQR 228–295), S2: 307 dB/m (IQR 283–336), S3: 335 dB/m (IQR 319–351), p < 0.0001. Steatosis groups compared separately to the next high or lower group showed the following p values: S0 vs S1: p < 0.0001, S1 vs S2: p = 0.00012 and S2 vs S3: p = 0.03. The group BMI ≥ 25 kg/m² had median CAP 229 dB/m (IQR 206–267) and for BMI < 25 kg/m²: 280 dB/m (IQR 232–321), p < 0.0001. In the subgroup NAFLD and NASH (n = 52) median CAP was 324.5 dB/m (IQR 297–352.25), the group including all the other diagnoses (n = 172) median CAP was 239.5 dB/m (IQR 214.75–280), p < 0.0001. Median CAP of the NASH group (n = 38) vs NAFLD group (n = 14) were not significantly different, 330 dB/m (IQR 300–358) vs CAP 310 dB/m (IQR 276–324), p = 0.506. Optimal cut-off values using the maximum Youden index were: 258 dB/m for S0 vs S1, 2, 3; 282.5 dB/m for S0, 1 vs S2, 3; and 307.5 dB/m for S0, 1, 2 vs S3. AUROC see table.

Conclusion: CAP shows strong association to steatosis grading also in an unselected population. Especially the groups NAFLD/NASH vs other liver diseases and the groups BMI < vs. > 25 kg/m² showed highly significant different CAP values. Comparing CAP for NAFLD vs NASH showed no significant difference.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

**OP036 A RANDOMIZED CONTROLLED TRIAL COMPARING NITAZOXANIDE PLUS LACTULOSE VERSUS LACTULOSE ALONE IN TREATMENT OF OVERT HEPATIC ENCEPHALOPATHY**

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**Introduction:** Hepatic encephalopathy (HE) is a reversible neuropsychiatric syndrome associated with acute and chronic liver dysfunction. Lactulose is a non-absorbable disaccharide currently used as a first-line agent for treatment of HE. Nitazoxanide has a broad-spectrum activity against urease-producing bacteria, severe alcoholic hepatitis has very high short-term mortality. Compared to standard medical therapy (SMT), GCSF improves clinical and biochemical profiles, morbidity and mortality in these patients. We evaluated efficacy of G-CSF in modulating the disease course of severe alcoholic hepatitis over a period of 3 months in terms of mortality, morbidity by Discriminant function (mDF), Child–Turcotte–Pugh (CTP) and Model for End-Stage Liver Disease (MELD) scores and various complications viz. sepsis, GI bleed, encephalopathy, hepatorenal syndrome (HRS) in comparison to SMT. We also studied the mobilising effect of G-CSF on bone marrow stem cells measured by counting CD34+ cells from peripheral blood.

**Aims & Methods:** The present study was performed to evaluate the safety and efficacy of G-CSF on mortality and complications viz. sepsis, encephalopathy, hepatorenal syndrome (HRS) and quality of (GI Bleed) and also to investigate whether G-CSF therapy could improve the indices of severity of liver disease, such as Discriminant function (mDF), Child–Turcotte–Pugh (CTP), Model for End-Stage Liver Disease (MELD) score in patients with severe alcoholic hepatitis. 90 patients with severe alcoholic hepatitis were randomly assigned to groups A and B (25 in each). Both groups were given SMT, while in addition, patients in group A were given 5 ug/kg GCSF subcutaneous (10 doses for 5 days). We assessed survival, changes in CTP, MELD and mDF scores and the development of complications till 90 days.

**Results:** The baseline parameters in both groups were comparable. On day 6 group A had higher mean leucocyte and CD34 counts than group B (848–855). On day 90 days follow-up patients in group A (n = 25) vs group B (36%) survived (p = 0.04). Mean changes for different scores were greater in group A then group B i.e. CTP (–41.97% vs –8.84%), MELD (–50.89% vs 10.09%) and mDF (–7.4% vs 18%) (p < 0.001). The percentages of patients who developed HRS, HE, or sepsis were lower in group A than in group B (28% vs 64%, 32% vs 64% and 28% vs 68%, respectively) (p < 0.001). There was no significant difference in GI bleed in both groups.

**Conclusion:** In severe alcoholic hepatitis, GCSF therapy significantly improves the survival. It also significantly reduces CTP, MELD, and mDF scores and prevents the development of complications.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

References

**MONDAY, OCTOBER 30, 2017 10:30-12:00**

**BARIATRIC SURGERY, OBESITY AND WEIGHT LOSS – ROOM B5**

**OP039 INTRAGASTRIC BALLOON-INDUCED WEIGHT LOSS PRIOR TO SURGERY IN SUPER-OBESE PATIENTS – A SINGLE CENTER EXPERIENCE**

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**Introduction:** Bariatric surgery remains the most effective treatment for morbid obesity, and laparoscopic Roux-en-Y gastric bypass (LRYGB) continues to be the preferred operation. However, extreme obesity increases morbi-mortality in bariatric surgery. In super-obese patients (BMI ≥ 50 kg/m²), pre-operative weight loss can be achieved with minimally invasive endoscopic intragastric balloon (IGB) placement.

**Aims & Methods:** We aimed to explore the potential benefits of preparative IGB on the outcomes of LRYGB in super-obesity. Methods: We performed a
retrospective analysis of the patients with a BMI > 50kg/m² treated at our obesity center between 2008 and 2016 with LRYGB alone (controls) or with prior placement of an IGB (cases). Clinical success of IGB was considered a body weight loss (BWL) of ≥10% and surgical success – an excess body weight loss (EBWL) ≥50% by the second year of post-operative follow-up (FU). Mean age was 42 vs. 40 (p = 0.004), BMI 56.3 vs. 51.7 (p = 0.0001). The proportion of females was 53% (cases) vs. 45% (controls); 52% (cases) vs. 49% (controls) with comorbidities): 46 cases vs. 87 controls. Cases were significantly more overweight than controls (BMI 57.5 vs. 53Kg/m²; p = 0.05, excess body weight 83.7 vs. 70.2 Kg; p < 0.01). The median time of IGB therapy was 196.8 days with 100% technical success rate in placement and removal of the device. 16 patients (34, 8%) had any complaint during IGB treatment (nausea, vomiting, epigastric pain) and in (2%) of these, the IGB was removed before the scheduled date. Average weight effects of IGB were: weight loss: 27Kg, BWL: 11%, BMI loss 10.4Kg/m² and EBWL of 32.6%, with a clinical success rate for IGB of 87%. 71, 7% of cases had more than 25% EBWL at time of removal. 26.1% improved fitness for surgery as assessed by ASA score (drop from III to II) and 6.5% reported improvement in comorbidities during IGB treatment. The average weight loss for IGB to surgery was 139 days, with a mean increase of 4.9Kg. At time of surgery, average BMI was lower in cases than controls (48.6 vs. 53Kg/m²; p = 0.01). There were no records of major surgical complications. Average EBWL effect of LRYGB in cases vs. controls was: 46.6 vs. 53.5% (p = 0.05) at 6 months, 56.9 vs. 70.7% (p = 0.05) at 12 months and 51.2 vs. 73.8% (p < 0.02) at 2 years after surgery. When initial excess body weight was compared, EBWL in controls maintained superiority over the cases (73.8% vs. 64% (p = 0.05) at 24 months. 74.4% (n = 99) had a post-surgical FU of more than 2 years and of these, 81% had reached a clinical success (EBWL ≥ 50%). At most recent post-surgery FU (average 42.8 months), there was no difference between the two groups in total EBWL (63.7 vs. 66.5, p > 0.05). 57.8% (n = 77) reported improved in comorbidities after surgery. Dyslipidemia, type II diabetes and joint pain were the comorbidities that most frequently improved.

Conclusion: IGB is a safe and effective method to promote weight loss in super-obese patients undergoing bariatric surgery, with subsequent improvement in aneurotic risk in a quarter of patients. Prior to surgery, patients submitted to IGB had lower BMI, despite initially being more overweight and at last post-surgical follow-up, there was no statistical difference in EBWL between the two groups. Aims & Methods: We aimed to prospectively evaluate the prevalence of gastroesophageal reflux disease in obese individuals and following laparoscopic sleeve gastrectomy (LSG). Gastroesophageal reflux disease was measured after a standardized nutrient drink pre-and post-LSG. Tissue morphology was determined by morphometric analysis. Tissue expression levels of chromogranin A, gut hormones, a-defensin, mucus 2 and Na+/glucose co-transporter 1 (SGLT1) were assessed by combination of immunohistochemistry, western blotting and quantitative PCR. Protein expression of transcriptome (He1, HATH1, NeuroD1, and Ngn3) were determined by western blotting. Results: In the obese, the total number of enteroneuroendocrine cells (EEC) containing gastrointestinal peptides was significantly reduced (p < 0.001); they were restored post-LSG (p < 0.01). This profile matched the levels of circulating gastrointestinal peptides (p < 0.001, respectively). A significant increase in SGTL1 (p < 0.05) expression was detected in the obese duodenum. Expression levels of transcription factors required for differentiation of absorptive and secretory cell lineages were reduced (p < 0.05).

Conclusion: In conclusion, obesity, there is a deregulation of developmental programming of intestinal epithelial cell lineages. The programming is restored post-surgery leading to an increase in secretion of gut hormones and reduced blood glucose levels.

Disclose of Interest: All authors have declared no conflicts of interest.

OP040 EROSION EROSIVE ESOPHAGITIS IS PREVALENT AND PREDICTABLE BY PRE-OPERATIVE GERDQ QUESTIONNAIRE IN GASTRECTOMY: A PROSPECTIVE STUDY IN SUBJECTS WITH THE NEED FOR CONTINUED PPI USE AFTER LAPAROSCOPIC SLEEVE GASTRECTOMY


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Introduction: Gastroesophageal reflux disease (GERD) is common in obese individuals and following laparoscopic sleeve gastrectomy (LSG). There is limited information on the true prevalence, risk factors, and outcome of GERD before and after LSG.

Aims & Methods: We aimed to prospectively evaluate the prevalence of gastroesophageal reflux disease in obese patients considered for bariatric surgery and to identify risk and predictive factors for erosive esophagitis (EE) and continued PPI therapy post-LSG.

Methods: Consecutive patients undergoing routine esophagogastroduodenoscopy (EGD) for bariatric surgery were enrolled after informed consent. Patients completed the GERDQ and Nocturnal GERD Symptom Severity and Impact Questionnaires (N-GSIIQ). Demographic data included gender, age, BMI, waist circumference, and use of PPI or H2-antagonists. Endoscopic data included presence of erosive esophagitis (EE), hiatal hernia (HH), and gastroesophageal flap valve, endoscopic grade (HI). Patients were assessed 6 months post-LSG for BMI, GERDQ, and need for PPI. Results: Patients included were recruited to date (76 males and 99 females). The mean age was 38.4 ± 11.7 and mean BMI was 40.0 ± 6.6, nearly equally divided between BMI < or ≥ 40. Forty four patients (25.1%) were on PPIs at baseline. EE was documented in 48 of 131 patients on no PPI (36.6%). [EDP] patients with PPIs was 85.0%. On multivariate analysis, presence of HH and a high GERDQ score (38) were significantly associated with EE (p = 0.025 and <0.001 respectively). Patients with high probability GERDQ scores had a significantly higher prevalence of EE compared to those with 5% or less (5.8% vs. 21.6%, p < 0.001), 18.2% and 41.8%, respectively. DPP was measured in 100% of patients. In patients with HH vs. those without (48.4% vs. 27.8%, p = 0.025), BMI ≥40 vs. < 40 and WC were not associated with the presence of EE. Logistic regression analysis showed that GERDQ > 30 was the only independent risk factor for EE (OR: 7.6, 95% CI 1.5-5.96). Forty-seven patients had LSG and completed the follow-up assessment. At 6 months post-LSG, mean BMI declined to 29.8 ± 11.5 and 15 of 47 patients (31%) continued required PPI therapy to control their symptoms. EE on baseline EGD was the only factor associated with need for continued PPI use (58.8% in EE patients vs. 16.7% without EE; p = 0.003).

Conclusion: Gastroesophageal reflux disease is very prevalent in obese patients undergoing GERDQ score ≥38 with the presence of erosive disease in this population. The presence of erosive esophagitis, but not PPI use pre-operatively is highly predictive of the need for continued PPI requirement post-laparoscopic sleeve gastrectomy.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP042 A WEIGHT LOSS INTERVENTION REDUCES BOWEL SYMPTOMS: A PROSPECTIVE STUDY IN SUBJECTS WITH MORBID OBESITY

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Introduction: Low-grade inflammation and dietary habits are possible explanations for the high prevalence of irritable bowel syndrome (IBS) in subjects with morbid obesity.

Aims & Methods: We aimed to study changes in bowel symptoms, BMI, physical and mental health and a selection of blood tests during a weight loss intervention, and to study the associations between the changes in bowel symptoms and the other variables. Subjects referred to a hospital for treatment of morbid obesity were included. The intervention included personalized personalized (regular, healthy meals and physical activity) and frequent group-based follow-up for six months. IBS was diagnosed with the Rome III criteria. Bowel symptoms were assessed with the irritable bowel syndrome symptom severity scale (IBS-SSS) and gastrointestinal symptom rating scale for IBS (GIRS-IBS). Health was assessed with eight questionnaires including WHO-5 Well-Being Index for emotional well-being and the Sense of Humor Questionnaire. CRP, lactoferrin, neopterin, low-density lipoprotein, high-density lipoprotein, cholesterol, HbA1c, thyroid stimulating hormone, fasting blood glucose levels.

Results: Eighty-eight subjects (71% (81) females) with mean age 44 years (SD 8) were included. BMI was reduced from 42 (SD 4) to 39 (SD 4) kg/m² (p < 0.001). The prevalence of IBS was 24.8% (27%) before and 17.8% (19%) after the intervention (p = 0.19). The IBS-SSS was reduced from 116 (SD 104) to 81 (SD 84) (p = 0.001). The GIRS-IBS was reduced from 1.8 (SD 0.8) to 1.6 (SD 0.6) (p = 0.006). Scores on GRS-IBS subscales changed significantly: Bloating, diarrhea and satiety decreased while constipation increased. The markers of low-grade inflammation and most of the other health scores and blood tests improved significantly. The reduction in IBS-SSS was negatively associated with reduction in BMI (partial correlation (ρ) = −0.29, p = 0.012) and associated with improved sense of humor (ρ) = −0.30, p = 0.012). The reduction in GRS-IBS
was associated with improvement in emotional well-being (p = 0.23, r = 0.038) and increased satisfaction (p = 0.29, r = 0.010). Neither the changes in IBS-SSI nor GSRS-IBS were significantly associated with changes in inflammatory markers, the other health scores or blood tests.

Conclusion: The bowel symptoms were markedly reduced during the weight loss intervention. Gastrointestinal and abdominal symptoms were not associated with the changes in low-grade inflammation. These results weaken the hypothesis that low-grade inflammation from adipose tissue is the cause of the high prevalence of IBS in subjects with obesity. Dietary habits (size of meals, fat intake) or psychosocial factors are alternative explanations.

Disclosure of Interest: All authors have declared no conflicts of interest.

QF043 DYNAMICS OF DECREASE OF ABDOMINAL FAT AFTER BARIATIC SURGERY: A NONINVASIVE ASSESSMENT OVER 24 MONTHS BY MRI

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Introduction: Non-alcoholic fatty liver disease (NAFLD) is characterized by atherogenic dyslipidemia. NAFLD patients are at an increased risk for both cardiovascular and non-cardiac vascular diseases. The effect of bariatric surgery on fat distribution in the liver has so far been studied with liver biopsies and single voxel MR techniques. The objective of this study was to assess liver fat fraction (LFF), subcutaneous (SAT) and visceral adipose tissue (VAT) using MRI in combination with blood lipids to monitor the efficiency of bariatric surgery.

Aims & Methods: In 15 morbidly obese patients an iterative decomposition of water and fat with echo asymmetry and least-squares estimation (IDEAL) approach was used for whole liver fat quantification in combination with a 2-point Dixon technique for volumetric fat imaging of adipose tissue pre- and post 6, 12, and 24 months after surgery. SAT, VAT and adipo- se tissue volumes were assessed from fat images and separated by statistical shape models. Serum: total cholesterol, HDL, LDL and TG were measured.

Results: LFF, SAT and VAT volumes decreased postoperatively with a good positive correlation using an iterative decomposition and model of form. t is the time (in days) after intervention, $A = [A_1, A_2, \ldots, A_t]$ refers to the individual patient specific LFF, SAT or VAT volumes, in combination with a global time constant $T_{sat}$, SAT, SAT for each measure. The LFF reduced the fastest, (time constant $T_{sat}$ = 21 ± 0.21 d). LFF measures showed a clear correlation with total cholesterol, cholesterol/HDL ratio and LDL (each: p < 0.001) and a trend for HDL (p = 0.006). Decrease in VAT and SAT did not correlate with blood lipids.

Conclusion: In conclusion, the decrease of body fat after bariatric surgery follows a distinct time pattern: liver fat decreases fastest followed by subcutaneous and last visceral fat, and decrease in liver fat correlates with changes in blood lipids.

Disclosure of Interest: All authors have declared no conflicts of interest.

QF044 FINAL RESULTS OF MULTI-CENTER, PROSPECTIVE, CONTROLLED TRIAL OF THE DUODENO-JEJUNAL BYPASS LISS FOR PREVENTION OF TYPE 2 DIABETES MELLITUS IN OBSESE PATIENTS: EFEICACY AND FACTORS PREDICTING A SUBOPTIMAL EFFECT

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Introduction: The global increase in obesity incidence results in an increase of type 2 diabetes mellitus (T2DM). Surgical treatment has proven to be effective; however, it carries a high risk of complications. The duodenal-jejunal bypass line (EndoBarrier®, GI Dynamics, EB) is an endoscopic implant that mimics the intestinal bypass portion of the Roux-en-Gastric Bypass. It results in weight loss and improvements in glucose control in obese patients with T2 diabetes mellitus (T2DM).

Aims & Methods: This is a final report of a prospective, controlled, multicentre study aimed to determine the effectiveness of EB and to identify factors associated with a sub-optimal outcome of EB.

Results: Seventy subjects (45 with an implant, 25 controls) were included in the study. The groups were comparable with respect to age, gender, BMI (mean 41.7 vs. 39.5 kg/m2), T2DM duration (7.8 vs. 8.3 years), HbA1c level (88 vs 86 mmol/mol, respectively). In the EB group all devices were fully implanted. Only 6 devices had to be explanted prior to the end of the 10 months study period (bleeding, dislocation and need for ERCP because of cholelithocholitis). The mean procedure time was 17 minutes for an implantation and 16 minutes for an explantation. At 10 months there was significantly greater weight loss and %EWL (19% vs. 7% and 43 vs. 12) and significantly improved long-term compensation of T2DM marker HbA1c (decreased by 25 vs. 10 mmol/mol) in the EB group. T2DM medication could be reduced in more device subjects than controls. There was no serious adverse event. Mild abdominal pain and nausea after implantation was not associated with the changes in low-grade inflammation. These results weaken the hypothesis that low-grade inflammation from adipose tissue is the cause of the high prevalence of IBS in subjects with obesity. Dietary habits (size of meals, fat intake) or psychosocial factors are alternative explanations.

Disclosure of Interest: All authors have declared no conflicts of interest.

MONDAY, OCTOBER 30, 2017

10:30-12:00

ABSTRACTS ON FIRE: ADVANCES IN ENDOCOPIC RESECTION OF EARLY COLORECTAL NEOPLASIA - HOT-SPOT

QF045 UNDERWATER ENDOSCOPIC COLORECTAL POLYP RESECTION IS A SAFER AND MORE EFFECTIVE TECHNIQUE THAN GAS INSUFLATION POLYPECTOMY FOR EVERYDAY CLINICAL PRACTICE

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Introduction: Endoscopic mucosal resection (EMR) is a well-established technique for resecting flat or sessile benign colon polyps. Underwater endoscopic mucosal resection (UEMR) is a novel technique that eschews submucosal injec-

Disclosure of Interest: All authors have declared no conflicts of interest.

Table 1

<table>
<thead>
<tr>
<th>Variable</th>
<th>Underwater polypectomy (UWP)</th>
<th>Gas insufflation polypectomy (GIP)</th>
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<tbody>
<tr>
<td>n</td>
<td>195</td>
<td>186</td>
</tr>
<tr>
<td>Polypectomy (%)</td>
<td>51.2%</td>
<td>48.6%</td>
</tr>
<tr>
<td>Resection time in minutes</td>
<td>n = 119 1.5, median (IQR) = 0.8–3.8</td>
<td>n = 138 3.4, median (IQR) = 2.5–5.4</td>
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<tr>
<td>&lt;0.001 *</td>
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<tr>
<td>Resection time in minutes</td>
<td>n = 64 2.0, median (IQR) = 0.8–5.0</td>
<td>n = 75 3.3, median (IQR) = 2.5–6.0</td>
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<td>&gt;0.001 a</td>
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Conclusion: Compared with GIP, UWP including UEMR achieved comparable proportions of en bloc and R0 resections, and R1A; with a significantly shorter resection time (all polyps) and lower bleeding episodes (pedunculated polyps) than in the GIP group. These results suggest that UWP can be easily and safely used in routine clinical practice, also by not very expert colonoscopists. Its use should be encouraged.
Underwater polypectomy (n = 195)
Gas insufflation polypectomy (GIP) (n = 186)

| Variable | n | % | n | % | P value
<table>
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<tbody>
<tr>
<td>Resection time in minutes for pedunculated polyps, mm (IQR)</td>
<td>55.10</td>
<td>(51.2%)</td>
<td>63.35</td>
<td>(2.5–5.0)</td>
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<tr>
<td>Resection time in minutes for lesions ≥10 mm, median (IQR)</td>
<td>56.32</td>
<td>(1.0–6.8)</td>
<td>64.47</td>
<td>(3.3–8.3)</td>
<td>0.009 a</td>
</tr>
</tbody>
</table>

En bloc resection for flat and sessile polyps n/N (%) 85/108 (78.7) 86/112 (76.8) NS
En bloc resection for flat and sessile polyps ≥20 mm n/N (%) 5/10 (50) 1/7 (14.3) NS
R0 resection for flat and sessile polyps n/N (%) 83/95 (96.7) 86/96 (100) NS
R0 resection for flat and sessile polyps ≥20 mm n/N (%) 9/10 (90) 7/10 (70) NS

Adverse events, n (%) Immediate bleeding (IB) n (%) 14 (7.2) 22 (11.8) NS
Delayed bleeding n (%) 2 (1.0) 1 (0.5) NS
IB By polyph morphology Flat and sessile polyps n/N (%) 11/108 (10.2) 12/112 (10.7) NS
Pediculated polyps n/N (%) 3/87 (3.4) 10/74 (13.5) 0.031 b
Residual or recurrent adenoma (RRA) at follow up n/N (%) 0/16 (0) 3/20 (15) NS

QTR, interquartile range. NS, not significant. Polyph morphology assignment according to Paris classification: Endoscopy 2005;37:570–8. R0 defined as a complete en bloc resection with tumor-free lateral and vertical margins. a Chi Square test or Fisher’s exact test, as appropriate. b Mann-Whitney U test.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP047 WHAT ARE THE RESULTS OF RECTAL ESD IN FRANCE: A LARGE RETROSPECTIVE MULTICENTER STUDY IN EXPERTS CENTERS

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Introduction: Endoscopic Submucosal Dissection has become the standard of care for large superficial rectal precancerous and cancerous lesions. Despite increasing practice in the western world, few European studies have been reported. First French results were far from those reported by Japanese teams: En bloc resection: 64%; R0 resection: 53%. Since these first results, experts teams have trained with animal models or in Japanese centers. We report here the largest European retrospective multicenter study of four French leading teams in rectal ESD.

Aims & Methods: We performed a retrospective multicenter study of all cases of rectal resection performed for precancerous or superficial cancerous lesions in four French teams that performed more than 150 ESDs in the last 5 years. All these teams had individual databases of their cases of rectal ESDs that were merged. Primary Endpoint was to evaluate the En bloc, R0 and curative resection rate. Secondary endpoints were: -evaluation of risk factors for non R0 resection -evaluation of risk factors for non en bloc resection -evaluation of the effect of learning curve (before and after 40 ESDs) on the results.

Results: 349 rectal ESDs were performed between 01/06/2010 and 31/12/2016. Demographic results: male 49.7%; mean age of the specimen: 56.4 years; mean duration of procedure 118.9 min, mean speed of ESD: 23.9 mm2/min, perforation rate: 6%, post procedural bleeding rate: 6.3%, secondary surgery 6.6% (p = 0.009) for a complication; 95% for a pathology risk factor or lymph node metastasis; 5% for ulcerative lesions. Pathological analysis: low grade dysplasia in 22%, high grade dysplasia in 32, 4%, superficial submucosal carcinoma in 6, 3%, deep submucosal carcinoma in 4.6% and T2 adenocarcinoma in 23%. 5 patients (1.5%) had a recurrent disease during endoscopic follow up: 2 that had an ESD failure and a piece-meal resection, 2 that had low-grade dysplasia in lateral margin and one high-grade dysplasia lesion R0 resected. Primary Endpoint: En bloc resection rate: 95.3%, R0 resection rate: 73.5%, curative resection rate: 68.5%. Secondary endpoints: non-en bloc resection was associated with a longer procedure duration (221 vs 113 min, p = 0.002); a lower speed (12.9 vs 24.2 mm2/min, p = 0.0005); a higher perforation rate (21.05% vs 5.2%, p = 0.005); a higher rate of secondary surgery (21% vs 5.2%, p = 0.002) and a higher rate of recurrent disease (10.5% vs 0.9%, p = 0.02) -the beginning of the learning curve (<40 ESDs whatever the location) was associated with a higher procedure duration (165.2 vs 105 min, p = 0.002); a lower speed (17.4 vs 25.9 mm2/min, p = 0.0005); a higher rate of non exclusive ESD (17.2% vs 1.7%, p = . . .) and a higher rate of non exclusive ESD (4.3% vs 0.4%, p = 0.02) -the beginning of the learning curve (<40 ESDs whatever the location) was associated with a longer procedure duration (167 vs 107 min, p = 1.2 x 10−5); a lower speed (15.49 vs 25.83 mm2/min, p = 1.6 x 10−5); a higher rate of post procedural bleeding (13.3% vs 4.4%, p = 0.004) a lower rate of deep sm or T2 adenocarcinoma (0% vs 5% and 0% vs 2.6%, p = 0.05); a lower rate of secondary surgery (0% vs 8.4%, p = 0.009) and longer hospital stay (3.76 vs 2.82 days, p = 0.0011).

N = 349 results Standard deviation
Age (years) 67 ± 12.5
Duration (mn) 118.6 ± 91.4
Large diameter (mm) 56.4 ± 25.3
Surface (mm2) 2173 ± 2268
Speed (mm2/min) 23.9 ± 17

(continued)
Patients with superficial colorectal neoplasms (SCNs) were enrolled and randomly assigned to conventional-ESD group or TAC-ESD group to fully evaluate the efficacy of TAC-ESD.

Introduction:

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Introduction: Endoscopic submucosal dissection (ESD) is technically challenging because of poor visualization and instability in the operative field. Although mucosal flap formation improves visualization of the cutting area, it is difficult to achieve, especially in colorectal ESD. To facilitate mucosal flap creation, we developed the “clip-flap method” as a strategy for submucosal dissection. In a small number of cases, ESD in the rectum was performed using the clip-flap method, but we have not evaluated the efficacy of the clip-flap method in this organ. In this study, we report the results of the largest study of rectal ESD in the western world.

Disclosure of Interest: All authors have declared no conflicts of interest.

References


OPO49 EFFICACY OF ENDOSCOPIC SUBMUCOSAL DISSECTION USING THE “CLIP-FLAP METHOD” FOR COLORECTAL TUMORS

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References

OP050 EFFICACY AND SAFETY OF ENDOSCOPIC FULL-THICKNESS RESECTION IN THE COLORECTUM WITH THE FTRD SYSTEM – INTERIM RESULTS OF A GERMAN REGISTRY

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Introduction: The Full-Thickness Resection Device (FTRD) is an over-the-scope system approved for endoscopic full-thickness resection (EFTR) in the lower GI tract. Small retrospective studies and a recent prospective study have shown good efficacy and acceptable safety of the device. We present the interim analysis of the German multicenter registry.

Aims & Methods: The prospective multicenter German online registry was designed to generate “real-life” data on efficacy and safety of the device. Data of patients (n = 250) which was entered by 31 German centers between 09/2015 and 10/2016 was analysed.

Results: 250 FTRD procedures were registered. Major indications for EFTR were non-lifting adenomas (49%), early carcinomas (21%), adenomas at the antecolic orifice (7%) and subepithelial tumors (6%). 173/250 lesions (69%) were located in the colon and 77/250 (31%) were located in the rectum. Median lesion size was 20 x 15 mm. Median procedure time was 45 min (5–150 min). 80 resection rate was 79%. Adverse events were recorded in 20/250 (8%) of cases including 8 perforations (3.2%; 5/8 were due to wrong sequence of procedural steps) and 7 minor bleedings (2.8%). Follow-up was available from 200 cases, median follow-up time was 10 weeks (0.5–77). Residual or recurrent lesions were observed in 12% of cases.

Conclusion: The preliminary results of this registry show good efficacy and safety of EFTR with the FTRD system. These “real-life” results are consistent with previous studies.

Disclosure of Interest: A. Schmidt received lecture fees and a study grant from ovesco endoscopy K. Caca has received lecture fees and a study grant from ovesco endoscopy All other authors have declared no conflicts of interest.

References

OP051 MINIMISING THE RISK OF DELAYED BLEEDING IN COLONIC ENDOSCOPIC SUBMUCOSAL DISSECTION: IS THERE A ROLE FOR A NOVEL HAEMOSTATIC PEPTIDE?

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Introduction: Endoscopic submucosal dissection (ESD) for colorectal tumors has been widely accepted in the last decades as a minimally invasive treatment option with a higher en bloc resection rate and a lower recurrence rate. Although structure formation after ESD of large colorectal tumors has been reported, underlying mechanisms in developing structure is not fully understood. Mesenchemal stem cells (MSCs) are a valuable cell source in regenerative medicine, and MSC culture supernatant (MSC-CS) has reportedly inhibited inflammation and fibrosis.

Aims & Methods: The aims of this study were to investigate whether circumferential ESD in the colorectum causes structure formation, and to examine the effect of MSC-CS enema on post-ESD structure. We performed circumferential...
ESD with 5 cm long axis in the rectum or distal colon in 20 kg pigs. We prepared M5CS-CS with 5% collagen gel and administered into the rectum immediately after ESD from day 1 through day 4. We applied standard medium gel as a control group. We euthanized the pigs on day 22, measured the rectal size, and performed histological analysis. The experimental protocol was approved by the Animal Care and Use Committee of Hokkaido University.

Results: Severe stricture was observed in the rectum but not distal colon (Stricture rate: 60.7 ± 16.8% versus 16.1 ± 12.6%, P < 0.01, n = 4 in each group). Moreover, extensive fibrosis and hypertrrophy of the muscularis propria were observed in the rectum, but not distal colon. In addition, the numbers of infiltrated neutrophils and activated myofibroblasts were significantly higher in the rectum than in the distal colon. Rectal stricture rate was significantly lower in the M5CS-CS group compared with control group on day 22 (14.7 ± 0.0% versus 63.9 ± 27.4%, P < 0.05, n = 3 in each group). Furthermore, M5CS-CS significantly attenuated the numbers of infiltrated neutrophils and activated myofibroblasts as well as fiber accumulation on day 22.

Conclusions: Stricture after circumferential ESD was developed only in the rectum, and associated with the activation of myofibroblasts and fiber accumulation. In addition, M5CS-CS enema prevented the stricture formation after circumferential ESD in the rectum by suppressing the infiltration of neutrophils and following myofibroblast activation and fibrosis. MSC-CS enema was a promising treatment to prevent post-ESD stricture.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

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Introduction: Endoscopic submucosal dissection (ESD) can remove large size of early cancers in the stomach or colorectal cancer en bloc; however, this procedure has a risk of intraprocedure perforation. Although an appropriate endoscopic closure using endoclipping is required, this technique is sometimes technically difficult. Recently, we developed a biodegradable injectable collagen sol that forms liquid to gel formation in response to body temperature.

Aims & Methods: The aim of this study was to determine the feasibility of this novel injectable collagen sol for endoscopic closure of iatrogenic perforation. The ethics committee of our institution approved the use of four living 25–30 kg female pigs under the general anesthesia in this experiment. An ESD knife with an electric current made a 3–5 mm perforation hole in the colon at 30 to 40 cm from the anal verge resulting in the collapse of the colonic lumen. We performed two studies using 12 and 5 perforation holes on 4 and 3 pigs, respectively. Study 1: At the beginning of the collapse of the colon due to perforation, the 1.4–1.6% neutral collagen sol containing 4 mM of genipin was delivered to the perforation hole using an endoscopic catheter. When the colon was expanded by CO2 insufflation, one-minute pass of endoclips were applied to the perforation area. Study 2: We only included the use of the collagen sol for endoscopic closure. Collagen sol which was adjusted based on the result of Study 1 was delivered to perforation holes in the same manner to Study 1. After expanding an expanded colon by CO2 insufflation after one-minute pass, an endoscope was withdrawn. All pigs were euthanized immediately after clipping and an hour after endoscopic evaluation in Study 1 and 2, respectively. A leak test was performed for every colon and we also evaluated histology of all perforation sites.

Results: In both studies, collagen sol was smoothly delivered to the target area and fixed as a gel on perforation hole in response to body temperature. Study 1: Although collagen gel was not fixed on two perforation holes, ten of 12 perforation holes were completely closed and then endoclips were placed with com- porure. There was no leak from the perforation hole. Study 2: An endoscope confirmed complete closure of the perforation holes with collagen gel in all pigs. There was also no leak from the perforation hole. Histology revealed a fixation of collagen gel as a thrombus agent in the perforation hole.

Conclusion: A novel temperature-responsive, biodegradable and injectable collagen sol may be used for endoscopic closure of intra-procedure perforation.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

Mondays, October 30, 2017 14:30-15:30

Imaging and Endoscopy in IBD - Room A1

OP054 Eearly mMUCosal HEaling in PATiENTS witH MODERATE to SEvere UlCerative Colitis TrEatEd with Golimumab PrEdicts FAVorable OUTcomes: DATA FROM the REAL-LiFE BE-SMART COHORT


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Introduction: Golimumab (GOL) is registered for moderate to severe ulcerative colitis (UC). Data on the use of GOL in daily clinical practice are limited. Currently, it is unclear which factors are predictive for a favorable outcome.

Aims & Methods: The aim of the study is to evaluate the mid-term outcome of GOL in patients with moderate-to-severe UC and to determine predictors of favourable outcome. Patients included in the SMART study (NCT02155335) were evaluated for their mid-term outcome. Demographic data, disease charac- teristics and medical history were recorded retrospectively. Data on disease activity based on total Mayo score, previous and concomitant medication, GOL dosing, mucosal healing (Mayo 0 or 1), adverse events (colectomy, hospitaliza- tion) and biomarkers (C-reactive protein, fecal calprotectin, histamine and albumin) were collected at baseline, week 2, 6, 14, 26 and 52. The primary end- point was steroid-free GOL continuation at week 26.

Results: Eight out of 100 patients from the SMART study had to be excluded (low baseline disease activity, undiagnosed, loss of follow-up). From the 92 patients (42% female, median age 41 years, median disease duration 5 years) 4% were active smokers, 25% had extensive colitis, and 38% had an endoscopic Mayo score of 3 at baseline. The median (IQR) Mayo score was 9 (0-10). With 76% of patients having previously failed immunomodulators (IMM), the majority (87%) were anti-tumor necrosis factor (TNF) naïve. GOL was started in combination with IMM and steroids in 38% and 64%, respectively. The median (IQR) follow-up of GOL therapy was 36 (12–106) weeks. Twenty six weeks after GOL induction, 38 patients (41%) were steroid-free and still on GOL, of whom 6 required GOL dose optimization. Short-term mucosal healing (STMH) at week 14 could be evaluated in 52% of the patients and was achieved in half of them. In multivariate analysis, only concomitant systemic steroids (p = 0.044) were pre- dictive of STMH. Patients with STMH more frequently achieved the primary endpoint [67% vs. 29%, OR 4.86 (95%CI 1.43–16.50), p = 0.011]. During a median (IQR) follow-up of 26 (23–30) months, 78% needed a therapeutic inter- vention and 63% discontinued GOL. STMH was significantly associated with intervention free survival (p = 0.030) and prolonged treatment of GOL (p = 0.002).

Conclusion: Real-life data confirm the effectiveness of GOL on the mid-term in moderate to severe UC, although therapeutic interventions are needed fre- quently. Short-term mucosal healing predicts a favorable outcome.

Disclosure of Interest: P. Bossuyt: has received educational grants from AbbVie; speaker fees from AbbVie, Takeda, and Vifor Pharma; and advisory board fees from Hospira, Janssen, MSD, Mundipharma, Roche, Pfizer, and Dr Falk Benelux.

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All other authors have declared no conflicts of interest.

A23

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Association between baseline CLE assessment and clinical outcomes during follow-up

<table>
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<th>CLE-</th>
<th>P</th>
<th>RR</th>
<th>Sensitivity</th>
<th>Specificity</th>
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<td>Treatment escalation at 12 mo</td>
<td>27/31</td>
<td>6/18</td>
<td>&lt;.001</td>
<td>2.6</td>
<td>82%</td>
<td>75%</td>
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<tr>
<td>Transmural lesions at 12 mo</td>
<td>32</td>
<td>12</td>
<td>4/3</td>
<td>.052</td>
<td>2.1</td>
<td>79%</td>
</tr>
<tr>
<td>Hospitalisation/Surgery at 32 mo</td>
<td>20</td>
<td>2</td>
<td>1/1</td>
<td>.052</td>
<td>2.1</td>
<td>79%</td>
</tr>
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CLE, confocal laser endomicroscopy; RR, relative risk; LR, likelihood ratio.

Conclusion: This prospective multicenter study confirms that CLE can reveal CD-related features of mucosal inflammation during ongoing endoscopy, thereby predicting two highly reproducible histopathological hallmarks of active large-bowel mucosal inflammation. In addition, the CLE assessment allows for early prediction of relevant clinical outcomes related to CD such as the need for treatment escalation and the risk of transmural complications at one-year follow-up. Further studies should now address whether this promising prognostic tool could refine the timing of treatment strategies in patients suffering from CD.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference
explicit clinical and laboratory data, including fecal calprotectin (FC), at disease onset or thereafter. PCDAI items, laboratory tests and FC were associated with the Simple Endoscopic Score for CD (SES-CD) in a multivariate analysis and validated on an independent prospective cohort from Korea of children whose workup included ileocolonoscopy, clinical and lab assessment and FC. We employed a blinded clinimetric judgmental and psychometric mathematical approach.

Results: The derivation and validation cohorts included 134 and 86 children, respectively (n = 240; age 14.6 ± 2.6 years; SES-CD 7.8 ± 8.2), of whom 24 (16%) and 9 (10.5%) had a RS of 0–1 (i.e. SESCD < 3), respectively. In a multivariable regression analysis, the stool and weight items of the PCDAI, ESF and FC were associated with SESCD (all p < 0.05). Judgementally, we removed the weight item and included CRP, to form a weighted categorized MINI index (Table). In the validation cohort the sensitivity, specificity, PPV and NPV of the MINI to reflect MH using a cutoff of ≤ 8 was 91%, 67%, 84% and 80% (AUROC curve 0.90 (95%CI 0.84–0.96)). In the entire cohort (n = 216) the correlation between MINI and SESCD was r = 0.783 (p < 0.001).

**ITEM** | **POINTS**
---|---
1. Stool | 0–1 liquid stools, no blood ≤ 2 semi-formed with small blood, or 2–5 liquid Gross bleeding, or ≥ 6 liquid, or nocturnal diarrhea | 0 4 8
2. Fecal calprotectin | < 50 50–99 99–399 300–599 600–899 ≥ 900 | 3 0 4 7 9 12
3. ESR (mm/hr) and CRP (mg/L) | ESR < 30 and CRP < 10 50 > ESR > 30 Or 50 > CRP > 10 30 ESP ≥ 50 | 0 2 5
4. SUM OF MINI (0–25)

Conclusion: In children with ileocolonic CD, the MINI-index can reflect MH with a good accuracy. The likelihood of MH with a MINI-score ≤ 8 points is 84%.

OP059 TOFACITINIB FOR MAINTENANCE THERAPY IN PATIENTS WITH ACTIVE ULCERATIVE COLITIS IN THE PHASE 3 OCTAVE SUSTAIN TRIAL: RESULTS BY LOCAL AND CENTRAL ENDOSCOPIC ASSESSMENTS


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Introduction: Tofacitinib is an oral, small molecule Janus kinase inhibitor that is being investigated for ulcerative colitis (UC). A Phase 3, randomised, double-blind, placebo-controlled maintenance study (OCTAVE Sustain, NCT01458574) demonstrated the efficacy of tofacitinib 5 and 10 mg twice daily (BID) vs placebo in patients (pts) with moderate to severe UC. Aims & Methods: We describe the clinical endpoints assessed by local endoscopy readings and previously reported results assessed by central readings. Pts who completed one of two studies (OCTAVE Induction 1, NCT01465763; OCTAVE Induction 2, NCT01458951) and achieved clinical response were for time from index endoscopy to CR, ED and NSI and compared through Log rank test.

Results: The study population consisted of 296 patients [123 males, median age 40 years]. At index endoscopy, 61 patients (20.6%) had a RS of ≥ 2, 24 (8.1%) 1, 81 (27.4%) i2a, 69 (23.5%) i2b, 35 (11.5%) i3 and 26 (8.8%) i4. Medical treatment was optimized according to index colonoscopy in 4 (4.7%) patients with a RS of i0/i1 and 88 (41.7%) with > i2a [Odds ratio 11.0 (95%CI 5.6–24.4), p < 0.001]. During a median (IQR) follow-up of 76 (48–113) months, CR, ED and NSI were observed in 150 (50.7%), 51 (17.2%) and 36 (12.2%) patients, respectively. Patients with a i2a and i2b had a similar risk for CR, ED or NSI (Log Rank p = 0.19, p = 0.10 and p = 0.30, respectively). Also after exclusion of patients with immediate post-endoscopy treatment optimization, i2a and i2b scores were not predictive (Log Rank p = 0.22, p = 0.21 and p = 0.41, respectively). Probability of CR was higher in patients with an i3 or i4 compared to the others (Log Rank p < 0.001). A RS ≥ i2a [1.62 (1.06–2.50), p = 0.03], active smoking at endoscopy [1.61 (1.08–2.39), p = 0.02] and CRP > 5 mg/L at endoscopy [1.76 (1.17–2.63), p = 0.01] were associated with CR during the follow-up in patients without clinical relapse at endoscopy. In patients with a RS = i2, initiation of an immunosuppressant or biological therapy after endoscopy was not associated with a different outcome in terms of CR or NSI (p = 0.59 and p = 0.66, respectively). Only a modest benefit in terms of CR was observed for patients with a RS = i3 or i4 when an immunosuppressant or biological therapy was introduced after endoscopy (p = 0.03), but the risk of NSI was not influenced (p = 0.14).

Conclusion: No difference was observed in terms of clinical relapse and need for endoscopic/surgical intervention between patients with i2a or i2b endoscopic recurrence after ileo-colonic resection with ileo-colonic anastomosis. In patients with a RS = i2, no effect on probability of clinical relapse or need for a new intervention was observed when an immunosuppressant or a biological treatment were initiated after the index endoscopy. Despite intensification of therapy based on endoscopic findings, outcomes of i3 and i4 patients remain poor in our cohort.

References of Interest: S. Vermeire: AbbVie, MSD, Takeda, Ferring, Dr. Falk Pharma, Hospira, Pfizer Inc, Tillotts, Genentech/Roche, Shire, Galapagos, Mundipharma, Hospira, Celgene, Second Genome and Janssen G. Van Assche: AbbVie, MSD, Ferring, Janssen, Takeda P. Rutgeerts: Centocor, Merck, UCB, Abbvie, Millenium/Takeda, Genentech/ Hoffman LoRoche, Merck/Serono, Bristol Myers Squibb, Robarts, Tillotts, Pfizer, Falk Pharma M. Ferrante: Takeda, Abbvie, Boehringer-Ingelheim, Chiesi, Falk, Ferring, Janssen, Mitsubishi Tanabe, MSD, Tillotts, Zeria All other authors have declared no conflicts of interest.
eligible to participate in OCTAVE Sustain. Clinical response was defined by a decrease from induction study baseline in Mayo score of ≥5 points and ≥30%, with an accompanying decrease in rectal bleeding subscore ≥1 or an absolute rectal bleeding subscore ≤1. 593 pts were randomised (1:1:1) to receive placebo, tofacitinib 5 or 10 mg BID for 53 weeks (wks) in OCTAVE Sustain. Pts eligibility was assessed based on central endoscopic readings. Pts entering OCTAVE Sustain were permitted concomitant treatment with oral corticosteroids, although tapering was mandatory from study baseline. Concomitant treatment with immunosuppressants and biologics was prohibited. Efficacy endpoints assessed at Wk 52 included remission (primary endpoint: Mayo score ≤2, no individual subscore >1 and rectal bleeding subscore of 0), mucosal healing (Mayo endoscopic subscore ≤1) and clinical response.

Results: At Wk 52, remission was achieved by significantly more pts treated with tofacitinib 5 or 10 mg BID compared with placebo, as demonstrated by both central and local endoscopic readings (Table). Similar results were observed at Wk 52 with mucosal healing, clinical response and sustained, steroid-free remission among pts in remission at baseline. Efficacy assessed by local endoscopic readings was numerically greater than central readings, except for clinical response. There was good agreement between locally and centrally read endoscopic subscores (kappa = 0.6 [95% CI 0.5, 0.6]).

Conclusion: Efficacy assessed by local endoscopic readings was numerically greater than efficacy assessed by central readings for tofacitinib 5 and 10 mg BID compared to placebo. Overall, local endoscopic readings were consistent with central readings. Both methods demonstrated that tofacitinib 5 and 10 mg BID were both more effective than placebo for maintenance therapy in pts with moderately to severely active UC.

Disclosure of Interest: B.G. Feagan: Grant support/ Consultancy/ Advisory/ member boards: Pfizer Inc. S. Vermeire: Grant support/Speaker Fees/Consultancy; AbbVie, MSD, Takeda. Speaker fees: Ferring, Dr Falk Pharma, Hospira, Tillsot. Consultancy: Ferring, Genentech/Roche, Shire, Pfizer Inc, Galagapos, Mundipharma, Hospira, Celgene, Second Genome, Janssen.

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Introduction: The explanation for symptoms experienced by celiac disease (CeD) patients within hours of gluten ingestion has puzzled researchers because the early onset seems incompatible with a T-cell mediated (delayed hypersensitivity) effect. We hypothesized the role for gluten-specific CD4+ T cells in gluten-responsive symptoms could be tested by comparing acute immune effects of ingesting gluten with intradermal injection of Nexvax2®, an experimental adjuvant-free therapeutic vaccine that is a mixture of three short peptides including immunodominant epitopes for gluten-specific CD4+ T cells.

Aims & Methods: To assess changes in circulating cytokines in CeD volunteers on GFD after eating gluten or after intradermal administration of Nexvax2.

Methods: A time course assessment of 19 cytokines and chemokines in plasma and sera from adult HLA-DQ2.5+ CeD volunteers on a GFD were compared from two separate studies. The first was a double-blind, placebo-controlled food challenge (DBPCFC) with ~3g wheat gluten flour compared to a matched gluten-free drink over 10min. The second study was a double-blind, placebo-controlled phase 1 clinical trial of Nexvax2 (Goel et al. Lancet Gastro Hepatol 2017) with plasma assessed after the first dose of Nexvax2 150 mg or normal saline i.d. in 0.1 mL. Chemokines (eotaxin, MIP-1B, eotxin-3, TARC, IP-10, MIP-1α, MCP-1, MDC, MCP-4) and cytokines (IFN-γ, IL-1B, IL-2, IL-4, IL-6, IL-8, IFN-γ, IL-12/20, IL-13, TNF-α) were measured by the Meso Scale Discovery multiplex ELISA platform.

Results: Cytokine and chemokine assessments were performed in 19 subjects after DBPCFC (11 administered gluten, & 8 non-gluten), and in 14 subjects in the final “biopsy” cohort of the phase 1 study of Nexvax2 (7 administered Nexvax2, & 7 placebo). In the first 5 subjects after gluten ingestion, hourly profiling indicated IL-2 elevation from 2h (median 5-fold rise compared to predose, range 1.1–117) and plateauing between 3 to 5h (median maximal fold-change 21, range 2.6-94). Median fold increase in IL-8 was between 1.8 and 2.4 from 3 to 6h (median maximal fold-change 2.5, range 1.3–28). Median fold increases were less than 2 from placebo for other cytokines and chemokines for all time points. Overall, serum assessed from before, and at 4 and 6h showed median IL-2 fold change of 15 at 4h after...
gluten (range: 1.9–39, n = 11) compared to 1.0 for non-gluten (0.5–1.6, n = 8; p = 0.05). For IL-4, median fold change at 6 h post-dose in IL-4 was 2.4 (range: 1.0–8.4, n = 11) compared to 1.1 for placebo (0.7–1.3, n = 8; p = 0.012 Mann Whitney). Apart from IL-2 at 6 h, no other cytokines or chemokines showed median elevation above 2-fold at any time points after gluten ingestion. After Nexva2, median fold changes at 2, 4 and 6 h post-dose in IL-2 were 14 (range: 1.3–68), 127 (range: 2.1–915), and 70 (range: 1.6–396), and in IL-8 were 1.6 (range: 0.9–2.8), 11 (range: 2.1–28), and 5.3 (range: 2.0–12). Weaker median fold rises of at least 2 were observed after Nexva2 but not placebo in MCP-1, IL-1β, IL-10, IFN-γ, MIP-1β, IP-10, IL-4, IL-13, eotaxin, and TNFα.

Conclusion: IL-2, a T-cell specific cytokine, dominates the cytokine signature present between 2-6 h after gluten ingestion or intradermal administration of Nexva2. These findings suggest gluten ingestion or injection of peptides activating T cells rapidly and could account for symptoms triggered by gluten.

Disclosure of Interest: J.A. Tye-Din: JAT-D is coinventor of patents relating to treatment and diagnosis of coeliac disease, and shareholder in Nexeppt Pty Ltd. J.J. Druras: JJD is an employee of ImmusanT, Inc S. Wang: SW is an employee of ImmusanT, Inc. K.E. Goldstein: KEA is an employee of ImmusanT, Inc L.J. Williams: LJW is an employee and shareholder in ImmusanT, Inc. R.P. Anderson: RPA is employed by and shareholder of ImmusanT, a shareholder in Nexeppt Ltd, and is coinventor of patents relating to treatment and diagnosis of celiac disease.

All other authors have declared no conflicts of interest.

Reference

OP061 BACTERIAL MODULATION OF INTESTINAL INNATE IMMUNE ACTIVATION INDUCED BY WHEAT AMYLASE TRYSIN INHIBITORS (ATI) IN NOD-DQ8 MICE
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Introduction: Wheat-amylase/trypsin inhibitors (ATI) are nutritional activators of intestinal innate immunity via the toll-like receptor 4 (TLR4)-MD2/CD14 complex in myeloid cells. We have observed that wheat ATIs enhance innate immune responses towards gluten in a host at risk, such as SPF NOD-DQ8 mice.

Aims & Methods: The aim of the study was to screen, identify and test bacterial strains with a capacity to degrade ATIs and therefore reduce their immune stimulatory activity in-vitro and in-vivo. Supernatants of a large group of intestinally isolated bacteria were tested against pre-defined ATI subtypes (CM3 and 0.19). The in vivo effects of two groups of bacteria with low and high ATI degrading capacities were assessed in in-concomitant gavage with a single dose of ATIs in NOD-DQ8 mice on a gluten-free diet after 6 h.

Results: We identified commensal bacteria in vitro that have the capacity to degrade the major ATI subtypes. When the ATI-degrading bioactivity of those bacterial strains was tested in mice gavaged with ATIs, the bacteria combined or individually significantly reduced intestinal expression of TLR4-dependent proinflammatory cytokines and chemokines, and serum levels of IL-6 when compared to mice that received ATIs without the bacteria. Data were confirmed in myeloid cell cultures in vivo that were exposed to bacterial or control supernatants of ATIs with and without prior depletion of potential traits of LPS.

Conclusion: Some Lactobacillus strains have the capacity to modulate the innate inflammatory effects of ATIs in vitro and in vivo. Since wheat-ATIs are implicated in the pathogenesis of celiac disease as well as non-celiac wheat sensitivity, modulation with ATI degrading bacteria may be an attractive therapeutic target.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP062 HLADQ/GLUTEN TETRAMER TEST IN BLOOD GIVES BETTER DETECTION OF CELIAC PATIENTS THAN BIOPSY AFTER 14-DAY GLUTEN CHALLENGE
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Introduction: Initiation of a gluten-free diet without proper diagnostic work-up of coeliac disease is a frequent and demanding problem. Recent guidelines suggest a gluten challenge of at least 14 days followed by duodenal biopsy to establish a diagnosis. This approach is associated with a false negative outcome of this approach remains unclear. We aimed to study responses to 14-day gluten challenge in subjects with treated coeliac disease.

Aims & Methods: We challenged 20 subjects with biopsy-verified coeliac disease, 20 healthy volunteers and 8 confirmed mucosal remission, for 14 days with 5.7 g per oral gluten daily. Duodenal biopsies were collected. Blood was analyzed by flow cytometry using HLA-DQ/gluten tetramers, and by multiplex assay for cytokine detection.

Results: Nineteen participants completed the challenge. Villous blunting in blood appeared after 4 days of the gluten challenge but was confirmed mucosal remission, for 14 days with 5.7 g per oral gluten daily. Duodenal biopsies were collected. Blood was analyzed by flow cytometry using HLA-DQ/gluten tetramers, and by multiplex assay for cytokine detection.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP063 RAPID HOME TESTS THAT REVEAL GLUTEN-FREE DIET TRANSGRESSIONS
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Introduction: To date, the only effective management of celiac disease is the adherence to a strict, lifelong gluten-free diet (GFD). However, there has been no reliable method to confirm adherence to a GFD or to ascertain whether the origin of acute symptoms in a celiac or gluten-sensitive patient may be related to gluten exposure. There is poor or no correlation of celiac serology and dietary adherence. To address this need, we recently developed laboratory tests to detect gluten immunogenic peptides (GIP) in faeces and urine, excreted after gluten consumption. Our studies demonstrated that 31-60% of adult celiac patients following a GFD have GIP in either faecal or urine samples. Additionally, there was a high correlation between GIP detection and gut mucosal damage (references 1 and 2). To facilitate the self-monitoring of the GFD by consumers, we have adapted the method to be directly used at home.

Aims & Methods: Our goal was to develop and validate a novel, rapid, home test for the monitoring of GFD adherence, which will enable celiac patients and other subjects avoiding gluten to detect GIP in faeces and urine samples by means of a lateral flow immunosassay (LFIA). A total of 233 faecal samples (75 GIP positive (+) and 158 GIP negative (-)) according to the previous laboratory tests were analyzed by the LFIA method. In addition, 290 urine samples from volun- teers under different gluten exposure conditions were analyzed with the LFIA. Faecal and urine samples included positive samples from healthy volunteers who had ingested gluten 16 hours before urine collection (n = 110), and negative samples from celiac patients on a reportedly strict gluten-free diet (n = 180).

Results: For the faecal home test, 74 out of 73 GIP (+) samples were correctly detected as positives with the LFIA. Of the 158 GIP (-) samples, 151 were correctly classified as negative by the LFIA. These results thus indicated a diagnostic sensitivity of 99% and a specificity of 96% for the home test versus the reference laboratory method. The positive predictive value of the home test method for faecal samples was of 91% and the negative predictive value was 99%. In urine, GIP were detected by the LFIA in 100 out of 110 samples of volunteers on a gluten-containing diet. No GIP were detected in 179 out of 180 samples from celiac patients on a GFD. The diagnostic sensitivity and specificity for urine LFIA were therefore 99% and 98% respectively. The positive predictive value for the urine home test was 99% and the negative predictive value was 95%.

Conclusion: The point-of-care/home tests for GIP detection in faeces and urine are highly sensitive and specific to assess adherence to GFD and to detect dietary transgressions, with superior performance over other methods. These tests will enable monitoring of the GFD to subjects avoiding gluten, including celiac patients.

Disclosure of Interest: A. Rodríguez-Herrera: The urine method of this manuscript was included in a patent application and I am one of its inventors. R. Domínguez-Flores: Employee of Biomedal S.L. C. Sousa: The stool and urine methods of this manuscript have been included in patient applications and I am one of the inventors. A. Muñoz-Suano: Employee of Biomedal S.L. M. Arévalo-Rodríguez: Employee at Biomedal S.L. F. León: I am a Biomedal’s shareholder. A. Cebolla: I am a employee at Biomedal S.L and a company’s shareholder. The stool and urine methods of this manuscript have been included in patent applica- tions and I am one of the inventors.
References

OP064 ‘CELIAC-LITE SCORE’: A PREDICTIVE SCORE OF RESPONSE TO A GLUTEN-FREE DIET IN PATIENTS WITH LYMPHOCYTIC ENTERITIS AND SUSPICION OF COELIAC DISEASE
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Introduction: The criteria to diagnose patients with lymphocytic enteritis as coeliac disease (CD) are not well established. Increase in gamma delta+ intraepithelial lymphocytes (IEL) has been suggested as a permanent marker of CD (1, 2). The IEL normal cut-off level is not well known, and we have observed that 30% of patients with suspected CD, irrespective of the number of IEL, had increased gammadelta+ IEL.

Aims & Methods: Aim: 1) To assess predictive variables of response to a GFD in patients with lymphocytic enteritis and suspicion of CD; 2) To develop a score for diagnosing CD patients with low-grade enteropathy (coeliac-lite). Methods: From 2010 to 2016 all patients in whom duodenal biopsies were taken to rule out CD were prospectively registered. The inclusion criteria for the present study were: 1) Duodenal biopsies performed on a normal diet; 2) Absence of villous atrophy; 3) Starting with a GFD; 4) Having a follow-up biopsy. Patients were excluded if they were taking NSAI or ARFA drugs, if they had H. pylori or parasitic infection or in case of chronic and non bacterial histological response to GFD (since these patients could not be correctly classified). All included patients had clinical symptoms in the spectrum of CD and HLA-DQ2.5+ or at least one allele of the DQ2-5 haplotype. Standard histological studies and IEL flow cytometry of gamma delta+ and CD3- IEL on duodenal samples were routinely performed. In patients with sustained clinical response to a GFD, a follow-up biopsy was performed after one year. Response to a GFD was considered if there was a clinical and histological (or serological) response. The ‘gold standard’ in diagnosing a patient with CD was applied using the Catassi’s rule of ‘4 of 5’. A logistic regression analysis was performed to assess predictors of GFD response. The ORs were used to derive a new scoring system. ROC was used to define the better cut-off point.

Results: 135 patients fulfilled the inclusion criteria, 42 had normal histology and better cut-off point.

Conclusion: The ‘coeliac-lite score’ allowed to predict response to GFD and thus, to diagnose ‘coeliac-lite’ disease with an acceptable accuracy. In a quarter of patients this score provided a definitive diagnosis of CD at baseline.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

OP065 EFFECTIVE GLUTEN DEGRADATION IN NON-COELIAC GLUTEN-SENSITIVE SUBJECTS BY ASPERGILLUS NIGER DERIVED ENZYME: A PLACEBO-CONTROLLED RANDOMIZED CLINICAL TRIAL
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Introduction: Gluten may cause gastrointestinal complaints in individuals sensitive to gluten. Aspergillus niger derived prolly endoprotease (AN-PEP) has previously been shown to degrade gluten into non-immunogenic compounds in vivo in settings in healthy subjects in which AN-PEP was added to a liquid, intragastrically infused meal.

Aims & Methods: The aim of the current study was to investigate the efficacy of AN-PEP to degrade gluten in a physiological meal setting in gluten-sensitive subjects. This randomized controlled cross-over study included 18 self-reported gluten-sensitive subjects attended three test days. A multimilen nasoduodenal feeding catheter was placed to collect gastric and duodenal aspirates. Subjects consumed a porridge containing approximately 0.5 g gluten in the form of two crumbled wheat cookies as well as two tablets either containing 160 000 PPI of AN-PEP (high dose), or 80 000 PPI (low dose), or placebo in a double-blinded, randomised manner. Gastric and duodenal content was sampled at several time points over 180 minutes and analysed for gluten epitopes using the Gluten-Tec ELISA. 180-min areas under the curve (AUC) of epitope concentration were calculated using curve fitting. Additionally, participants were asked to fill in questionnaires (GSRS) after each test day. The non-parametric Wilcoxon signed-ranked paired test at a = 0.05 with a Bonferroni correction was used to detect significant differences.

Results: AN-PEP significantly lowered the gluten concentrations in the stomach and in the duodenum compared to the placebo in both the high dose and the low dose. In the stomach, gluten levels were reduced from 218 ± 155 μg/ml (mean ± STD) in the placebo to 31 ± 24 μg/ml in the high dose (p = 0.001) and to 31 ± 22 μg/ml in the low dose (p = 0.001). In the duodenum, gluten levels were reduced from 63 ± 88 μg/ml in the placebo to 12 ± 13 μg/ml in the high dose (p = 0.019) and to 8 ± 5 μg/ml in the low dose (p = 0.015).

Conclusion: Even in a physiological meal setting, AN-PEP significantly degraded most gluten before it entered the duodenum in self-reported gluten-sensitive subjects. In those subjects, the consumption of AN-PEP was well tolerated.

Disclosure of Interest: M.J. Bruns: DSM, the company that provided the enzymes. All other authors have declared no conflicts of interest.

Reference

MONDAY, OCTOBER 30, 2017
14:00-15:30
TSTM FREE PAPER: NEW CONCEPTS IN HOST-MICROBIOTA CROSSTALKS - ROOM E4

OP066 EXOSOMES RELEASED FROM INTESTINAL EPITHELIAL CELLS INFECTED WITH A PROKARYOTIC PATHOGEN ASSOCIATED ADHERENT-INVASIVE E. COLI TRANSFER MIRNAS INTO RECIPIENT CELLS TO INHIBIT AUTOBACTERIUM A. Larabi1, J. Carrier1, G. Dalmasso1, J. Delmas2, N. Barnich2, H. T.T. Nguyen2
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Introduction: Cronh’s disease (CD) is a chronic inflammatory disorder of the gastrointestinal tract characterized by an abnormal immune response against the intestinal microbiota in a genetically predisposed host. The intestinal mucosa of CD patients is abnormally colonized by the adherent-invasive E. coli (AIEC) strains, which are able to adhere to and to invade intestinal epithelial cells (IECs), to survive and replicate within macrophages and induce a strong pro-inflammatoryresponse (1). We recently reported that AIEC infection of IECs induces secretion of epithelial miRNAs which are extracellular vesicles of 30–100 nm having a role in cell-to-cell communication (2). Exosomes secreted by AIEC-infected IECs can activate innate immune response and increase AIEC replication in exosomes-receiving IECs and macrophages (2).

Aims & Methods: This study aimed at investigating the mechanism underlying the exosomes-mediated increased AIEC replication in recipient cells. Exosomes released by uninfected human intestinal epithelial T84 cells (Exo-uninfected) or by T84 cells infected with the AIEC LF82 reference strain (Exo-AIEC), the non pathogenic E. coli K12 MG1655 strain (Exo-K12) or the commensal E. coli HS strain (Exo-HS) were purified using the ExoQuick reagent and used to stimulate T84 cells or human THP-1 macrophages.

Results: We found that stimulation of T84 and THP-1 cells with Exo-AIEC induced an autophagy activation in response to AIEC infection compared to Exo-uninfected, Exo-K12 or Exo-HS. This was due to decreased expression of several autophagy genes. In silico analysis revealed a subset of miRNAs potentially targeting these autophagy genes. Several autophagy gene-targeting miRNAs were found in exosomes with increased levels in Exo-AIEC compared to Exo-uninfected, Exo-K12 or Exo-HS. These exosomal miRNAs were then transferred from exosomes to recipient cells, inhibiting autophagy genes and therefore autophagy response to AIEC infection. This consequently led to increased AIEC replication in cells stimulated with Exo-AIEC compared to that in cells stimulated with Exo-uninfected, Exo-K12 or Exo-HS. Exo-AIEC derived from T84 cells transfected with antisense of the autophagy gene-targeting miRNAs did not carry the corresponding miRNAs and failed to inhibit autophagy activation and to increase bacterial replication in recipient cells.

Conclusion: Our study shows that upon AIEC infection, IECs secrete exosomes that can target specific miRNAs to recipient IECs or macrophages, inhibiting autophagy gene expression and thus autophagy-mediated control of AIEC replication.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

**OP067** DIETARY EMULSIFIERS DIRECTLY IMPACT THE TRANSCRIPTOME OF A CROHN’S DISEASE-ASSOCIATED ENTEROBACTERIACEAE, INCREASING ITS ABILITY TO INDUCE INTESTINAL INFLAMMATION

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**Introduction:** In mice, consumption of dietary emulsifiers, which are detergent-like components of many processed foods, disturbs the intestinal microbiota in a manner that enhances its pro-inflammatory potential and promotes its encroachment into the mucosa [1]. Such disturbance of the microbiota promotes a range of chronic inflammatory diseases, including colitis. We recently demonstrated that such disturbance of the microbiota can be recapitulated, in part, in an in vitro microbiota model, arguing that at least a portion of the effects of emulsifiers in vivo result from direct action of these compounds on the microbiota [2]. Notably, carboxymethylcellulose (CMC), a commonly used synthetic emulsifier, was found to increase the pro-inflammatory potential of the microbiota by inducing expression of flagellar-related genes, without altering species composition. Aims & Methods: We hypothesize that dietary emulsifier may directly impact the pathogenicity of adherent and invasive Enterobacteriaceae (AIEC), which are associated with Crohn’s disease, by promoting their ability to induce intestinal inflammation. AIEC reference strain LF82 was treated with emulsifiers (Carboxymethylcellulose (CMC) or Polysorbate-80 (P80)) in vitro, and the impact on virulence gene expression, whole transcriptome, and adhesion/invasion properties were investigated. Germfree mice were mono-associated with LF82 strain, and the impact of dietary emulsifier consumption on LF82 virulence and intestinal inflammation was investigated.

**Results:** Transcriptomic analysis revealed that, in vitro, CMC altered gene expression of AIEC by favoring expression of genes related to virulence and induction of intestinal inflammation. Moreover, CMC dramatically increased the adhesion ability of AIEC LF82 bacteria to intestinal epithelial cells, while P80 only slightly impacted this process. Moreover, pre-treatment of AIEC LF82 bacteria with CMC significantly increased bacterial motility while using of an isogenic flagellate LF82 strain demonstrated that flagella is playing a central role in AIEC penetration of mucus layer in vivo. AIEC LF82 mono-associated mice are currently being treated with dietary emulsifier in order to investigate the emulsifiers + AIEC combination is sufficient to induce intestinal inflammation.

**Conclusion:** Some dietary emulsifiers have the ability to directly impact micro- biota members including AIEC in a manner that potentiates their ability to promote intestinal inflammation. Our demonstration that some dietary component may directly impact the virulence of Crohn’s disease associated bacteria may explain why only a subset of AIEC positive individual develop Crohn’s disease. Hence, this research may ultimately influence dietary recommendation for AIEC carriers as risk for IBD flares or disease development.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**References**


**OP068** GUT DYSBIOSIS CAN LEAD TO VISCERAL HYPERSENSITIVITY AND DEPRESSION IN GERM-FREE RATS

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**Introduction:** Gut dysbiosis is implicated in both irritable bowel syndrome (IBS) and depression, which are often comorbid with each other, but the causal relationship is not verified. Our previous study found similar structure but different function of gut microbiota between IBS-D and depression patients.

**Aims & Methods:** Aim: To verify whether shift of gut microbiota function can disturb brain-gut axis function by transplanting fecal microbiota obtained from IBS-D patients and depression patients to germ-free (GF) rats respectively.

**Methods:** Fecal samples from a health control, an IBS-D patient and a depression patient were recruited in our previous study were transplanted to 7 weeks old GF rats by gavage (once/rat, n = 5–6/group). Fourteen days after transplantation, fecal samples of rats were collected for 16S rRNA gene sequencing on Illumina MiSeq and short-chain fatty acids (SCFAs) measurement on UPLC-MS/MS. Open field test, sucrose preference test, forced swimming test (FST) and colorectal barostat were performed for anxiety, depression behavior and visceral sensitivity, respectively.

**Table:** Visceral sensitivity, anxiety, depression behavior and fecal SCFAs levels of recipient rats (Mean ± SE)

<table>
<thead>
<tr>
<th>SCFAs</th>
<th>Health control (n = 5)</th>
<th>IBS-D (n = 6)</th>
<th>Depression (n = 6)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Butyrate</td>
<td>228.3 ± 34.2</td>
<td>80 mmHg</td>
<td>164.4 ± 10.4</td>
<td>0.001</td>
</tr>
<tr>
<td>Acetate</td>
<td>752.2 ± 25.4</td>
<td>20 mmHg</td>
<td>13868.0 ± 537.1</td>
<td>0.006</td>
</tr>
<tr>
<td>Propionate</td>
<td>5153.4 ± 588.8</td>
<td>40 mmHg</td>
<td>1925.0 ± 246.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Valerate</td>
<td>189.9 ± 13.7</td>
<td>60 mmHg</td>
<td>17.1 ± 6.9</td>
<td>0.005</td>
</tr>
</tbody>
</table>

**Results:** The abdominal withdrawal reflex (AWR) is higher in IBS-D recipient (GI) rats than in health control (GH) and depression (GD) recipient rats at colorectal distension of 20 mmHg, 40 mmHg and 60 mmHg, and higher in GI and GD rats than in GH rats at 80 mmHg. The percentage of time in open field center area of GD rats was lower than that of GH and GI rats; the sucrose preference rate is lower in GD rats than in GH and GI rats; the immobile time after strong stress and GI rats in the FST was longer than that of GH rats. Principle component analysis revealed that the fecal microbiota structure of the three groups of rats was significantly different. Fecal formate level was higher in GI rats than in GH and GD rats; fecal acetate and propionate levels were higher in GI rats than in GD and GI rats; fecal valerate level was lower in GD rats than in GH rats (see Table).

**Conclusion:** Gut microbiota from IBS-D patients can lead to visceral hypersensitivity, from depression patients can lead to depression behavior in GI rats. Those suggest an important role of gut microbiota in the pathogenesis of IBS-D and depression; and provide clues for the influence of gut microbiota on brain-gut axis.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**OP069** INFLAMMATION MODULATION BY STOMACH MICROBIOTA VIA TLR2/NF-KB SIGNALING PATHWAY IN HP-INDUCED GASTRIC CANCER

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**Introduction:** The mechanisms of Helicobacter pylori (HP) initiated cancer have not been well studied. Our previous studies demonstrated that 1) stomach microbiota interacted dynamically within the development from gastritis to gastric cancer; 2) TLR2/NF-KB signaling pathway can be activated by HP infection; the overexpression of TLR2 played an important role in the interaction between HP and non-Hp bacteria; 3) significantly more butyrate was observed after Hp infection, it promoted the proliferation and migration of AGS cell, and up-regulated the expression of TLR2 and NF-KB.

**Aims & Methods:** This study investigated how the stomach microbiota transformed within the development from gastritis to gastric cancer; 2) how the TLR2/NF-KB signaling pathway is activated via the interaction between Hp and non-Hp bacteria. Tissue samples of chronic gastritis, atrophic and IM gastritis, and early gastric cancer were collected through endoscopy. WT and TLR/KO mice were used to build Hp infection animal models. Comprehensive Illumina Miseq microbiota was used to analyze microbiota constructions in clinical samples and animal models. HPLC was used to detect short chain fatty acid (SCFA) in gastric tissue. IHC, Western blot were used to observe TLR2 and NF-KB expression. Inflammatory cytokines such as IL-1β, IL-6, IL-8, TNF-α were tested by real-time PCR. Cell function tests including CCK8 and Transwell were performed in AGS and SGC7901 cells.

**Results:** Bacterial composition analysis in chronic gastritis, atrophic and IM gastritis, and early gastric cancer tissue by Illumina Miseq microbiota demonstrated that 1) Hp was detected in five samples, 2) the total amount of...
Neisseria in the atrophic and IM gastritis sample was nine times more than that in the atrophic and IM gastritis sample. The total amount of *Haemophilus parasuis* in the atrophic and IM gastritis sample was four times more than that in the chronic gastritis. 4) the worse the condition, the more the Pseudomonas, Sphingomonas, Chryseobacterium, Ruminococcus. In addition, it was also found that Hp infection can upregulate TLR2 expression, in turn TLR2-activated RelA/p65 can increase the levels of IL-1/IL-6/IL-8/TNF-α. The total amount of Hp, Clostridium leptum, Clostridium quinshall were increased and Lactobacillus, Enterobacteria, non-Helicobacter were decreased after Hp infection in WT mice. The amount of class Cladostia and class Bacilli showed no significant change after Hp infection in TLR2/KO mice. It was also observed that increased butyrate model can promote proliferation and migration of AGS cells after Hp infection.

Conclusion: Hp infection can induce the alteration of stomach microbiota via the up-regulation of TLR2, in turn leads to the imbalance of stomach microbiota characterized by the increase of butyrate-producing bacteria. Thereafter, TLR2/NF-κB signaling pathway can be activated by the overexpressed butyrate and then promote cytokines at the downstream can also be up-regulated by RelA/p65. All the newly found interactions between bacteria and signaling pathway may finally contribute to the epithelial transformation.

Disclosure of Interest: All authors have declared no conflicts of interest.

**OP070 CARD9 MEDIATES SUSCEPTIBILITY TO INTESTINAL PATHOGENS THROUGH MICROBIOTA MODULATION AND CONTROL OF BACTERIAL VIRULENCE**

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Introduction: In association with innate and adaptive immunity, the microbiota controls the colonization resistance against intestinal pathogens. Caspase recruitment domain 9 (CARD9), an inflammatory bowel disease susceptibility gene, is required to shape a normal gut microbiota. CARD9 mice are more susceptible to the enteric mouse pathogen *Clostridium rodentium* that mimics human infections with enteropathogenic and enterohemorrhagic *Escherichia coli*. Here, we examined how CARD9 controls *C. rodentium* infection susceptibility through microbiota-independent mechanisms.

Aims & Methods: *C. rodentium* infection was assessed in conventional and germ-free (GF) wild-type (WT) and Card9−/− mice. To explore the impact of Card9−/− microbiota in infection susceptibility, GF WT mice were colonized with WT (WT→GF) or Card9−/− (Card9−/−→GF) microbiota before *C. rodentium* infection. Mice were fed a standard diet or a customized version of standard diet in which polysaccharides (PS) or monosaccharides (MS) were used as hydrocarbon source. Microbiota composition was determined by 16S DNA gene sequencing. Inflammation severity was determined by histology score and lipocalin level. Microbiota – host immune system interactions were assessed by qPCR analysis.

Results: The specific intestinal immunoglobulin (Ig) G response against *C. rodentium* was impaired in GF Card9−/− mice compared to GF WT mice. Moreover, heightened *C. rodentium*-induced colitis was observed in Card9−/−→GF mice. Gut microbiota composition of Card9−/−→GF mice was altered and inferred metagenomics revealed that Card9−/−→GF gut bacteria used monosaccharides. MS diet increased *C. rodentium* susceptibility in Card9−/−→GF mice whereas PS diet rescued the phenotype. The specific intestinal IgG response against *C. rodentium* was increased in Card9−/− mice fed the PS diet compared to Card9−/− mice fed the MS diet. Interestingly, the specific intestinal humoral response was also defective in WT mice fed the MS diet compared to WT mice fed the PS diet.

Conclusion: CARD9 controls pathogen virulence in a microbiota-independent manner by supporting a specific humoral response. The microbiota of Card9−/− mice failed to outcompete the monosaccharide-consuming *C. rodentium*, worsening the infection severity. A polysaccharide-enriched diet counteracted the ecological advantage of *C. rodentium* and the defective pathogen-specific antibody response in Card9−/− mice. Thus, CARD9 modulates the susceptibility to intestinopathogenic pathogens virulence independently of the microbiota and by shaping a microbiota competing with pathogens. Genetic susceptibility to intestinal pathogens can be overridden by diet intervention that restores humoral immunity and a competing microbiota.

Disclosure of Interest: All authors have declared no conflicts of interest.

**OP071 A C-TYPELECTIN TRIGGERS IMMUNE SURVEILLANCE BY INNATE LYMPHOCYTE CELLS FOR ERADICATION OF ATTACHING AND EFFACING BACTERIA**


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Introduction: Although gut protection to infections is ensured by innate lymphoid cells (ILCs), how ILCs are regulated remains poorly understood. Here, we show that secretion of the c-type lectin Reg3b downstream of Ripk2 signaling pathway was crucial for immune surveillance by ILCs against *Citrobacter rodentium* that mimics human infection with enteropathogenic and enterohemorrhagic *Escherichia coli*. We aimed to identify crucial factors that impact clearance of *C. rodentium* in mice. Ripk2 KO, Reg3b KO, and wild-type mice were orally inoculated with *C. rodentium* and infection course was monitored for three weeks. Sampling was performed on days 0 (pre-infection), 7, and 14. Microarray analysis was performed on total tissues from cecum. Total tissue was further analyzed by histology, qPCR, Western blot, and flow cytometry. Lamina propria mononuclear cells (LPMCs) from *C. rodentium*-infected Ripk2 KO, Reg3b KO, and wild-type mice were isolated through cell sorting and co-culture experiments were performed with intestine-derived ILCs to assess cytokine secretion.

Results: We found that Ripk2 signaling significantly controls epithelial Reg3b expression, which is required for efficient control of *C. rodentium* infection. Both, Ripk2 KO and Reg3b KO mice displayed an enhanced susceptibility to *C. rodentium*-induced colitis associated with an impaired clearance of the pathogen. Phosphorylation of signal transducer and activator of transcription 3 (STAT3) was decreased in both tumoral and colonic macrophages of *C. rodentium* infected mice. STAT3 phosphorylation downstream of Reg3b secretion was not observed. Cytokine secretion by intestinal phagocytes lowering their propensity to promote IL17A secretion by ILCs early in infection.

Conclusion: These results provide a previously unrecognized mechanism by which intestinal epithelial cells reciprocally regulate production of IL-17A by ILCs promoting immunophagocytic and enterohemorrhagic bacterium.

Disclosure of Interest: All authors have declared no conflicts of interest.

**OP072 STUDY ON THE ANTI-INFLAMMATORY MECHANISMS OF ROSEBURIA INTESTINALIS MEDIATED BY INDUCING THE DIFFERENTIATION OF THE TREG CELLS VIA TLR5 OF THE INTESTINAL EPITHELIAL CELLS IN INFLAMMATORY BOWEL DISEASE**


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Introduction: IBD, a chronic recurrent autoimmune disease, is currently associated with poor prognosis. We need explore new therapeutic strategies for IBD. Intestinal flora is closely related to the pathogenesis of IBD. In order to explore the role of probiotics in the treatment of IBD, we use the family of *Clostridium* enteritidis XVa, which has a strong regulatory effect on the development and differentiation of Treg cells, and its community stability in the intestine determines the homeostasis of intestinal mucosal tolerance [1]. Does *R. intestinalis* have an anti-inflammatory effect in IBD? Receptors which are associated with bacterial identification contain TLR2, TLR4 and TLR5 in the TLRs family [2]. Our early study has found that *R. intestinalis* was able to up-regulate expression of TLR5, whereas it had little effect on TLR2 and TLR4. Does the regulation of intestinal microbial immunity by *R. intestinalis* achieve via TLR5 signaling? *R. intestinalis* in IBD No reports have been reported at home and abroad.

Aims & Methods: To elucidate the anti-inflammatory effect and mechanism of *R. intestinalis* in IBD, we propose to investigate the effects of *R. intestinalis* on Disease Activity Index (DAI) score, intestinal pathologies, the expressions of TLR5, TSLP, TGF-β, and the differentiation of Treg cells by using TNBS colitis models. At the cellular level, we use the human colon epithelial cell line Caco-2, overexpressing and silencing of TLR5 in HEK293 and Caco-2.
cells respectively to conduct inflammatory cell model with LPS and then co-culture with different concentrations of R. intestinalis (Ratio of bacteria and cells were 10:1, 5:1 and 1:1; namely R:I, R:12 and R:13) and detect changes of TSLP and TGF-β.

Results: R. intestinalis significantly decreased DAI scores (the day before mice were killed) in the Control group, TNBS group and TNBS+ R. intestinalis groups were 0.4±0.26, 2.33±0.14 and 1.25±0.3 respectively. Compared with the TNBS group, the DAI score of TNBS+ R. intestinalis group decreased, P < 0.05.

R. intestinalis reduced the degree of shortening of the colon (P < 0.05), and played the anti-inflammatory role by up-regulating the levels of TLR5, TSLP and Caco-2 significantly increased secretion of TSLP and TGF-β levels of the cells (P < 0.05). The co-culture supernatant TSLP of the control group, LPS group, LPS + R:11, LPS + R:12 and LPS + R:13 were (5.88±0.45pg/ml, (3.38±0.19pg/ml, (5.88±0.85pg/ml, (53.1±0.12) pg/ml and (4.97±0.62)pg/ml respectively. The co-culture supernatant TGF-β of the control group, LPS group, LPS + R:11, LPS + R:12 and LPS + R:13 were (394.23+75.935)pg/ml, (249.66±18.50)pg/ml, (415.1±12.58)pg/ml, (385.5±0.70)pg/ml and (412.6±30.54)pg/ml respectively. So it is with the results of Western blot and Real-time PCR. While the silencing of TLR5 cells did not change these cytokines.

Conclusion: R. intestinalis might promote the secretion of TSLP and TGF-β from intestinal epithelial cells via TLR5, thus inducing the differentiation of the Treg cells.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

Disclosure of Interest: All authors have declared no conflicts of interest.

Aims & Methods: We aim to identify sex-related molecular changes in the intestinal barrier in response to acute stress in healthy individuals as an initial step to understand the gender bias in inflammatory disease development. Methods Thirty-six healthy individuals (17 M and 19 F) were recruited. In each participant, two consecutive jejunal biopsies were obtained by Watson's capsule: the first at baseline and the second 90 min after 15 min of intermittent cold pain stress (CPS). Autonomic (blood pressure and heart rate), hormonal (plasma cortisol) and cytokine responses were measured. Stress Ratering Scale (SRS) was completed and measured throughout the study. Total mucosal RNA was isolated and expression levels of epithelial barrier (CLDN2, SLC26A3, TJP1 and TJP3) and mast cell activation-related genes (tryptase: TPASB1, SERPIN1) were analyzed by RT-PCR. Results: CPS induced a significant autonomic response characterized by increased heart rate, blood pressure, and plasma cortisol in association with enhanced stress perception in all participants. CPS increased CLDN2 and SLC26A3 expression (Fold vs. basal: 1.3, p = 0.002), and decreased SLC26A3 gene expression (Fold vs. basal: 0.7, p < 0.001). Interestingly, gene expression studies also uncovered differential responses to acute stress between M and F. Particularly, in the F group CPS induced an increased expression of TPSAB1 (expression Fold vs. basal: [F]: 1.1; [M]: 0.9; p = 0.012) along with a decrease in TJP1 (Fold vs. basal: [F]: 0.9; [M]: 1.1, p = 0.042) and a trend for TJP3 (Fold vs. basal: [F]: 1.0; [M]: 1.1; p = 0.08). Significant positive correlations between CPS-induced changes in TPASB1 and CLDN2 (r = 0.706, p = 0.002), and between TJP1 and TJP3 (r = 0.838, p < 0.001) were found.

Conclusion: Specific and independent gender-related molecular responses in epithelial barrier regulation are unraveled by acute stress exposure in the jejunum of healthy subjects. These molecular differences may explain, in part, female predominance in IBS.

Disclosure of Interest: All authors have declared no conflicts of interest.

Aims: To identify stress-mediated circadian rhythm changes in the intestinal mucosa, being circadian rhythm regulation the most relevant biological variables were recorded throughout the study. Mucosal RNA was isolated and analyzed by microarray analysis followed by differential gene expression and pathway identification and qPCR validation.

Results: CPS significantly increased heart rate, blood pressure and plasma cortisol, as well as stress perception in all participants. Stress significantly modified the mucosal transcriptome, being circadian rhythm regulation the most relevant biological function (P = 0.00001), with a significant decrease in specific clock genes (NFE2L2, NFIL3, NR1D1, NR2D2, PER1, PER3; P < 0.05).
Moreover, CPS altered epithelial barrier integrity gene expression (increasing CLDN2 and decreasing SLC26A3; P < 0.05). Notably, significant association was found between representative genes of the most significant biological functions altered by stress (Table 1).

Results: We received samples from 119 individuals with IBS, 186 asymptomatic controls and 114 individuals with unspecific GI symptoms. There was no difference in richness between the IBS (117.6 (standard deviation (SD): 16.6)) and control group (115.8 (SD: 16.6), p = 0.36), but richness was higher in samples from individuals with unspecific GI symptoms (126.0 (SD: 21.0), p < 0.01). Diversity was also higher in the IBS group compared with unspecific GI symptoms (0.307 (SD: 0.31), p = 0.06) and did not differ between the IBS (3.00 (SD: 0.29)) and the control group (2.98 (SD: 0.32), p = 0.59). Richness and diversity were significantly higher in parasite-positive samples across all four categories (Tables 1). For asymptomatic controls and those with unspecific GI symptoms, richness was higher for parasite-positive samples in all categories (Table 1). However, this did not apply to those with IBS symptoms. Diversity was higher for all categories of parasite-positive samples from individuals with unspecific GI symptoms and asymptomatic controls (with exception of multiple parasites) (Table 1). For those with IBS, diversity was only higher in relation to presence of Blastocystis or multiple parasites (Table 1). Number of observed operational taxonomic units and Shannons diversity index according to parasite colonization status, specified for symptom group. Difference in mean between positive and negative samples tested by two sided t-test.

Conclusion: Colonization with parasites, including D. fragilis and Blastocystis, was linked to increased microbiome diversity and richness. However, for individuals with IBS, the association to increased richness could not be confirmed and no association to increased diversity was observed for samples positive for any parasite or D. fragilis. This could reflect an altered relationship between bacteria and parasites in IBS. The clinical and public health significance of these findings should be explored in greater detail.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
2. Krogsgaard et al. Neurogastroenterol Motil; 2017; 29:e12986

MONDAY OCTOBER 30, 2017 14:00-15:30
ADVANCES IN ENDOSCOPIC IMAGING: WHAT DOES THE FUTURE HOLD? - ROOM E2

OP077 ENDOSCOPIC MACROSCOPIC TYPE IS A SIGNIFICANT PREDICTOR FOR HISTOLOGICAL TYPES OF EARLY GASTRIC CANCER
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2Endoscopy, Fukuoka University Chikusho Hospital, Chikusino/Japan
3Dept Of Gastroenterology, Ishikawa Prefectural Central Hosp., Kanazawa/Japan
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Introduction: Gastric cancer is classified into the differentiated and undifferentiated types according to the degree of histological differentiation. The risk of lymph node metastasis of undifferentiated-type early gastric cancer is higher than the differentiated type. 1, 2, 3 therefore these indication criteria for endoscopic resection are different.4

Aims & Methods: This study aimed to clarify the diagnostic abilities of clinical predictors for distinguishing between differentiated-type early gastric cancer and undifferentiated-type early gastric cancer. This was a post hoc study of a multicenter prospective trial in five Japanese hospitals (clinical trial registration number: UMIN000014628). In the trial, 384 patients with eT1 gastric cancer were enrolled and 343 patients were analyzed. According to the protocol, age, gender, and the endoscopic findings of cancer (location, macroscopic type,
diameter, and invasion depth) were evaluated and the final diagnosis using the result was confirmed. All data of the present study were evaluated before the final diagnosis using the resected specimens. In this study, associations between those clinical factors and histological types of cancers were evaluated. Then, those diagnostic abilities for differentiated-type early gastric cancer were calculated. Diagnostic abilities of foresips biopsy were also calculated as a reference.

Results: Multivariate analysis identified older age ($\geq 72$), male, elevated type, and shallower invasion depth ($\leq 10$ mm) as independent significant predictors for differentiating early gastric cancer. Elevated type cancer had the highest sensitivity, specificity, accuracy, positive likelihood ratio, and negative likelihood ratio of it for differentiated-type early gastric cancer were 25.1%, 94.8%, 90.5%, 9.7, and 0.09. Those of the foresips biopsy were 95.6%, 94.8%, 21.1%, 1.0, and 0.09. Conclusion: Elevated type cancer is significant predictors for differentiated-type early gastric cancer and may exclude undifferentiated-type early gastric cancer without a foresips biopsy.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

OP079 THE MOLECULAR BASIS OF 5-AMINOLEVULINIC ACID (ALA)-MEDIATED LASER-BASED PHOTODYNAMIC ENDOSCOPIC DIAGNOSIS (LPDED) FOR DIVERSE EARLY GASTRIC CANCER

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Introduction: Laser-based photodynamic endoscopic diagnosis (LPDED) is an emerging technology for the detection and differentiation of early gastric cancer in the excised samples. Its accuracy has already been established in the histopathological diagnosis of early gastric cancer. In this study, we report the accuracy of LPDED in the detection of differentiated-type early gastric cancer.

Methods: The present report is the results of a prospective study conducted in the Division of Medicine and Clinical Science, Tottori University Faculty of Medicine. During the period from January 2015 to December 2017, 120 patients with early gastric cancer were included in this study. The patients were subjected to LPDED and histopathological examination. The results of LPDED and histopathological examination were compared.

Results: The results of LPDED and histopathological examination were compared. The accuracy of LPDED in the detection of differentiated-type early gastric cancer was 94.2%.

Conclusion: LPDED is a reliable tool for the detection of differentiated-type early gastric cancer.

References
Aims & Methods: In this work we explored different application scenarios of VR in endoscopy to overcome common problems in daily work and improve training experience. The head-mounted display (HMD) HTC VIVE was used to visualize the datasets generated during gastroenterological work-up. Training videos of different endoscopic procedures like advanced polypectomy, closure of a perforating duodenal ulcer, and gastrointestinal bleeding were recorded in high-definition real-time endoscopy and helped during interventions. Still interface problems like acquiring 3D images using standard endoscopes need to be investigated in future work. This work was supported by the German Science Foundation (DFG) under Grant FOR 1321.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

Disclosure of Interest: All authors have declared no conflicts of interest.

Aims & Methods: The electronic patient records were studied of all patients diagnosed in 2016 with UGI cancer within our institution, with a serves a population of 350,000. For those patients who had undergone an UGI endoscopy, in the preceding 3 years, demographics, site and stage of lesion and outcomes were recorded. Endoscopy KPIs were reviewed for the prior examination.

Results: 9187 UGI endoscopies were performed in 2016. UGI cancer identified 95 patients, of which 7 (7.38%) had an endoscopy in the preceding 3 years; however 1 within national guidance for gastric ulcer follow-up (initial histology negative for dysplasia), 85.7% were male. Mean age 68 years. All presented with UGI alarm symptoms: 4 oesophageal and 3 non-junctional gastric cancers. 42.3% have been offered treatment with curative intent, but unfortunately the remainder were offered palliation due to co-morbidity and/or advanced stage at diagnosis. The prior endoscopies were undertaken for investigation of persistent dyspepsia (47%), anemia (27%) and variceal assessment. Mean interval between diagnostic and earlier endoscopy was 20 months (range 1–31 months). All past endoscopies were undertaken by different operators; 3 consultants, 3 nurse endoscopists and a specialist doctor. All but 1 endoscopist had an individual ‘miss’ rate of <1% of their mean annual UGI procedural numbers. 57.1% were done without sedation, all provided evidence of duodenal intubation but the ‘3’ manoeuvre was not recorded.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
4. JAG Summary guide to quality and safety indicators, April 2016.

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Disclosure of Interest: All authors have declared no conflicts of interest.

References
4. JAG Summary guide to quality and safety indicators, April 2016.

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Disclosure of Interest: All authors have declared no conflicts of interest.

References
4. JAG Summary guide to quality and safety indicators, April 2016.
tumor characteristics, surgical and pathological outcomes are summarized in Table 1. MDPC successfully predicted resection in 64 out of 70 patients (91.4%). Six patients were found to have metastatic disease on surgical exploration. 78.6% (55/70) patients had R0 resections and 12.8 % (9/70) patients had R1 margins. There were no grossly positive margins (R2 resection). Patients went to surgery at a median of 22 days from diagnosis and 15 days from the MDPC decision to resect.

Table 1: The demographic, clinical characteristics, surgical and pathologic outcomes of 70 patients explored for ‘resectable’ pancreatic cancer. Outcomes were analyzed on an intention-to-treat basis as all patients underwent surgery with curative intent.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No of patients = 70</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years), mean (S.D)</td>
<td>69.2 (9.9)</td>
</tr>
<tr>
<td>Male %</td>
<td>40 (57.1%)</td>
</tr>
<tr>
<td>Race Caucasian %</td>
<td>65 (92.9%)</td>
</tr>
<tr>
<td>CA 19–9 (U/mL), mean (SD)</td>
<td>567.2 (1163.1)</td>
</tr>
<tr>
<td>Interval to surgery after EUS tissue diagnosis (days), mean (SD)</td>
<td>28.2 (16.1)</td>
</tr>
<tr>
<td>Interval to surgery after MDPC decision to resect (days), mean (SD)</td>
<td>17.8 (14.7)</td>
</tr>
<tr>
<td>Mass Location Head/Body/Tail</td>
<td>65 (92.9%), 5 (7.1%)</td>
</tr>
<tr>
<td>EUS Tumor size (mm), mean (S.D)</td>
<td>23.3 (9.1)</td>
</tr>
<tr>
<td>Type of Surgery (% of Whipple/pancreaticoduodenectomy Pancreatectomy Exploratory Laparotomy</td>
<td>61 (87.1%), 3 (4.3%)</td>
</tr>
<tr>
<td>Surgical Tumor size (mm), mean (S.D)</td>
<td>32.6 (12.6)</td>
</tr>
<tr>
<td>Tumor Histology Well differentiated</td>
<td>2 (2.9%)</td>
</tr>
<tr>
<td>Moderately differentiated Poorly</td>
<td>34 (49.3%), 3 (47.8%)</td>
</tr>
<tr>
<td>Differentiated</td>
<td></td>
</tr>
<tr>
<td>Pathological T stage T1 T2 T3 T4</td>
<td>3 (4.7%), 7 (10.9%), 53 (78.2%), 1 (1.6%)</td>
</tr>
<tr>
<td>N stage N0 N1</td>
<td>24 (35.7%), 40 (62.5%)</td>
</tr>
<tr>
<td>Metastasis No Yes</td>
<td>6 (8.6%), 64 (91.4%)</td>
</tr>
<tr>
<td>AJCC stage, 7th edn. IB II B III IV</td>
<td>4 (5.7%), 20 (28.5%), 38 (54.3%), 2 (2.9%)</td>
</tr>
<tr>
<td>Resection R0 R1 R2</td>
<td>64 (91.4%), 5 (78.6%), 9 (12.8%)</td>
</tr>
</tbody>
</table>

Conclusion: A MDPC demonstrated a high rate of predicting resectability along with achieving a high percentage of R0 resections at an experienced center. Data from other large centers may help validate the importance of utilizing a MDPC to predict resectability. Moreover, benchmark R0 resection rates are needed and can provide a quality metric for the treatment of resectable pancreatic cancer.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

cultured from PLD patients with PRKCSH mutation, patients without mutation and patients with other PBD mutations were grouped in a separate group without a clear expression pattern within their group. PRKCSH mutants shared expression of a subset of genes. The changes indicate endoplasmic reticulum related processes, such as 'protein folding in endoplasmic reticulum' and 'response to endoplasmic reticulum stress'. Mass-spectrometry analysis distinguishes glycopeptide profiles from cyst fluid of PLD patients with (n = 4) and without (n = 8) PRKCSH mutation.

Conclusion: These data strongly suggest a specific defect in protein maturation and localization in the endoplasmic reticulum, and protein glycosylation play a role in the development of hepatic cysts in PLD patients.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
OP088 A SYSTEMATIC REVIEW ON THE DEVELOPMENT OF MALIGNANCY AFTER CHOLEDOHAL MALFORMATION
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Introduction: Choledohal malformation (CM) comprises a variety of rare congenital cystic dilatations of the extrahepatic and/or intrahepatic biliary tree, classified according to Todani. Its etiology remains unclear. Although CM is generally considered a premalignant condition, the literature with respect to the risk of malignancy and optimal surgical treatment has not been reviewed systematically. Partly due to its rarity, guidelines for treatment and follow-up are difficult to establish.

Aims & Methods: The aim of this systematic review was to assess the prevalence of malignancy in CM and the differences between its subtypes. Secondary goal was to investigate the risk of malignancy following a cystic drainage procedure versus complete cyst excision.

Methods: This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statement and was registered in PROSPERO, the international prospective register of systematic reviews (ERP2016048392). A systematic search of PubMed and Embase was performed for articles published between January 1995 and June 2016 (cut-off date June 1st, 2016) relevant to malignancy prevalence and/or malignancy in patients with CM. A meta-analysis on the risk of malignancy following cystic drainage procedure versus complete cyst excision was carried out in accordance with the Meta-analysis Of Observational Studies in Epidemiology (MOOSE) guidelines.

Results: We included 18 observational studies with a total of 2904 patients, median age 36 years (range 0-87), 76% female. Overall, 312 (2904 patients developed a malignancy (10.7%). In 212 patients (7.3%) tumors were present during initial surgery, in 100 patients (3.4%) tumors developed during follow-up. The median age at detection of malignancy was 49.5 years (range 12–82 years). Malignancy occurred mainly in CM type IV cysts (in 14%). In CM type I, II, III, and V the malignancy rate was 9%, 3%, 8%, and 6%, respectively (Pearson χ², 17, 986, 4 df, P = 0.001). Of 18 observational studies identified, 9 studies included all CM patients; 9 studies included only CM patients that were subjected to meta-analysis of the different surgical techniques. Compared with patients who underwent complete cyst excision followed by bilo-digestive reconstruction, those who underwent a cystic drainage procedure had a significantly increased risk to develop a biliary malignancy (odds ratio 3.39, 95% confidence interval 2.3% to 10.3% (P = 0.001).

Conclusion: Overall, some 11% of patients with CM may develop a malignancy, especially those with type IV and type I cysts. Patients treated with a cystic drainage procedure had an up to fourfold increased risk to subsequently develop a malignancy following surgery, compared to those who underwent complete cyst excision. Reoperation with complete cyst excision in these patients should be considered. Malignant transformation may occur up to 30 years after initial surgery, therefore careful monitoring of these patients is mandatory, especially those patients who underwent cystic drainage procedures and those with CM types I and IV.

Disclosure of Interest: All authors have declared no conflicts of interest.

MONDAY, OCTOBER 30, 2017
14:00-15:30

DRUGS, LIVER AND PANCREAS - ROOM B5

OP089 A NOVEL IN VITRO TEST FOR CAUSALITY ASSESSMENT IN POLYMEDICATED PATIENTS WITH DRUG-INDUCED LIVER INJURY: CASES WITH DRUG RECHALLENGE
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Introduction: Idiosyncratic drug-induced liver injury (iDILI) is one of the most challenging diagnoses in hepatology [1]. Drug metabolism, iDILI aetiologies of liver damage in combination with typical drug signatures. Correct causality assessment may be impossible in polymedicated patients. We have investigated a novel in vitro test employing monocyte-derived hepatocyte-like (MH) cells and its possible use to support causality assessment in polymedicated iDILI.

Aims & Methods: This study prospectively included patients with suspected iDILI referred to the University Hospital Munich. Patient data for causality assessment and all drugs and cell generation were collected. Diagnosis by expert review was used as reference standard. Additionally the RUCAM score was calculated. MH cells were generated by a proprietary protocol[2], and were treated with the respective drugs and toxicity response was determined by release of lactate dehydrogenase, Tel-PCR and panel analysis was performed as described in [3]. Performance of MH testing in drug causality was assessed in a subset of patients with data on positive or negative drug rechallenge.

Results: A total of 146 patients were included, 93 adjudicated as iDILI and 53 patients with liver injury unrelated to medication. A majority of the iDILI patients was exposed to at least two drugs (n = 79, 85%). In the subset of 120 polymedicated patients (n = 79 iDILI; 41 non-DILI) the RUCAM test sensitivity was 86% and specificity was 98% for iDILI diagnosis, respectively. In polymedicated cases RUCAM showed a sensitivity of 73% and a specificity of 81%, respectively. In 32 polymedicated iDILI patients re-exposures occurred: of 11 drugs with invalid negative rechallenge results were correctly identified by the MH cell test. All of the 69 drugs that showed negative re-exposure were negative in the MH cell test.

Conclusion: Polymedication is a very frequent issue in iDILI causality assessment. RUCAM has a low sensitivity in polymedicated cases, and as such it lacks sensitivity for iDILI diagnosis and drug causality in polymedicated iDILI patients with rechallenge. Thus, the MH cell test seems to be a valuable tool for causality assessment in complex iDILI cases.

Disclosure of Interest: A. Benesic, W. Krug, and A. L. Gerbes, MetaHeps GmbH, Germany

References

OP090 SCREENING RATE FOR HEPATITIS B VIRUS AMONG CANCER PATIENTS RECEIVING CHEMOTHERAPY IN TAIWAN: A NATIONWIDE POPULATION-BASED STUDY
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Aims & Methods: The aim of this study was to evaluate the screening rate for HBV among cancer patients receiving chemotherapy in Taiwan. We collected data from National Health Insurance Research Database in Taiwan on cancer patients receiving chemotherapy from January 1, 2000 to December 31, 2012. The data were collected regarding age, gender, case-loading, department, and specialist of doctor administering chemotherapy, age, gender, and department of patient, type of cancer, and HBV testing (HBsAg, anti-HBc, and anti-HBs) within 2 years prior to chemotherapy. HBV screening was identified based on testing code A108. Overall screening rates were compared between different types of cancer, departments of patient, and time periods before and after the announcement of Taiwanese guideline and the implementation of NIH regulation. Annual percentage change of screening rate and factors associated with screening were also investigated.

Introduction: Many clinical practice guidelines recommend that all cancer patients should be screened for HBV infection before chemotherapy, but the screening rate of 14% - 34% reported from previous studies remains unsatisfactory. In Taiwan, an endemic area of HBV infection, HBV testing (HBsAg, anti-HBc, and anti-HBs) among cancer patients receiving chemotherapy in Taiwan. We collected data from National Health Insurance Research Database in Taiwan on cancer patients receiving chemotherapy from January 1, 2000 to December 31, 2012. The data were collected regarding age, gender, case-loading, department, and specialist of doctor administering chemotherapy, age, gender, and department of patient, type of cancer, and HBV testing (HBsAg, anti-HBc, and anti-HBs) within 2 years prior to chemotherapy. HBV screening was identified based on testing code A108. Overall screening rates were compared between different types of cancer, departments of patient, and time periods before and after the announcement of Taiwanese guideline and the implementation of NIH regulation. Annual percentage change of screening rate and factors associated with screening were also investigated.

Results: Of 379,639 cancer patients, 174,141 (45.9%) received pre-chemotherapy HBV screening. Of patients with screening, 73.2% were tested for HBsAg, 22.1% for HBsAg/anti-HBc, and 4.7% for HBsAg/anti-HBc/anti-HBs. The overall screening rate was 79.5% for hematological cancer and 43.6% for solid cancer; 55.3% for patients from medical departments and 30.9% for those from surgical departments; 38.1% during 2000–2008 and 57.5% during 2009–2012 (p < 0.0001). The annual screening rate for all patients increased from 31.5% in 2000 to 66.3% in 2012, from 64.5% to 90.7% for those with hematological cancer, and from 28.7% to 64.6% for those with solid cancer (p < 0.0001). There was a higher rate of screening rate by 35.9% for solid cancer than by 26.2% for hematological cancer (p < 0.0001). Factors significantly associated with HBV screening were treatment by younger doctor, female doctor, specialist, medical doctor, and doctor with higher-volume case-loading, younger patient, male patient, hematological cancer, and the time period during 2009–2012 (p < 0.0001).

Conclusion: The screening rate for HBV in cancer patients before chemotherapy is still suboptimal. Although the public policy can increase the screening rate, there are some barriers needed to be overcome to improve the awareness about HBV reactivation during chemotherapy.

Disclosure of Interest: All authors have declared no conflicts of interest.
Aims & Methods: In this nationwide study, we aimed to assess the clinical, biochemical, radiological and histological characteristics of NRH in order to identify risk factors and the clinical course of this disease. We requested the departments of gastroenterology and hepatology from all Dutch hospitals (n = 28) to participate in the study. Questionsnaires were sent in order to collect data on demographics, clinical presentation, blood counts, liver chemistry and abdominal imaging.

Results: In total, 72 hospitals (89%) responded to our primary questionnaire. Based on the completed questionnaires, approximately 22,500 IBD-patients are treated with thiopurines, annually. Out of a total of 85 identified cases of NRH, 54 were thiopurine using IBD-patients (64%); 38 men, mean age at NRH diagnosis 49 years (range: 17–74), mean disease duration 17 years (range: 3–44). Of these, 35 patients were (historically) treated with azathioprine (65%), 18 with mercaptopurine (33%) and 25 with thioguanine (46%). Of the NRH patients exposed to thioguanine, 80% received azathioprine and/or mercaptopurine before. At the time of diagnosis, 58% of the patients had thrombocytopenia, 45% had elevated liver enzymes and 63% had liver-related abdominal pain at abdominal imaging. Furthermore, 20 out of 54 patients (37%) presented with signs of portal hypertension (i.e. esophageal varical bleeding in 45%, thrombocytopenia in 95%, splenomegaly in 55% and ascites in 10%).

Conclusion: In this largest NRH case series to date, the majority of the patients were men (70%) and had an asymptomatic clinical presentation (63%) at time of diagnosis, consistent with earlier literature reports.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
1. Vernier-Massouille G, Cosnes J, Lemann M, et al. Nodular regenerative hyperplasia (NRH) of the liver is a poorly understood condition which has previously been related to, amongst others, the use of thiopurines in patients with inflammatory bowel disease (IBD). The diagnosis and management of NRH are challenging since the natural history of this disease is unknown, and the clinical presentation varies from asymptomatic to severe complications of portal hypertension, such as variceal bleeding or ascites.

Aims & Methods: The aim of this systematic review and meta-analysis was to evaluate the association between the use of statins and the risk of developing AP. The inclusion and exclusion criteria were defined according to the PRISMA statement. Pooled adjusted ORs with corresponding 95% CIs were estimated. Analyses were performed using RevMan 5.3. Studies were sorted by decision of a third author. Eligible studies were selected according to the PRISMA statement. Pooled adjusted ORs with corresponding 95% CIs were calculated using random effects model. Publication bias was assessed through Begg and Mazumdar test. Heterogeneity was assessed by means of the I² value. The latest meta-analysis on this topic evaluated only clinical trials, excluding observational studies and found a reduced risk of AP in statin users.

Aims & Methods: The aim of this systematic review and meta-analysis was to evaluate the association between the use of statins and the risk of developing AP. The inclusion and exclusion criteria were defined according to the PRISMA statement. Pooled adjusted ORs with corresponding 95% CIs were calculated using random effects model. Publication bias was assessed through Begg and Mazumdar test. Heterogeneity was assessed by means of the I² value.

Disclosure of Interest: All authors have declared no conflicts of interest.

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Disclosure of Interest: All authors have declared no conflicts of interest.

References
Conclusion: The results of the first meta-analysis of observational studies for the association between statin use and AP suggest the absence of an increased risk in statin users. Evidence for an increased risk is limited to case-control studies, while cohort studies showed no global effect, similarly to previous data from controlled trials. Further research on the topic is needed to clarify whether statin type, dosage, length of use, or ethnicity of AP might account for this difference.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP099 TOFACITINIB, AN ORAL JANUS KINASE INHIBITOR, IN THE TREATMENT OF ULCERATIVE COLITIS: OPEN-LABEL, LONG-TERM EXTENSION STUDY


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Table Summary of safety and efficacy in OLE study

<table>
<thead>
<tr>
<th></th>
<th>Tofacitinib 5 mg BID (N = 156)</th>
<th>Tofacitinib 10 mg BID (N = 758)</th>
<th>Total (N = 914)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Discontinuations, n (%)</td>
<td>28 (17.6)</td>
<td>153 (20.0)</td>
<td>181 (20.0)</td>
</tr>
<tr>
<td>AEs due to study drug</td>
<td>19 (2.5)</td>
<td>23 (2.5)</td>
<td>42 (4.6)</td>
</tr>
<tr>
<td>Due to insufficient clinical response</td>
<td>7 (4.5)</td>
<td>276 (36.4)</td>
<td>283 (31.0)</td>
</tr>
<tr>
<td>TEAEs, n (%)</td>
<td>101 (64.7)</td>
<td>562 (74.1)</td>
<td>663 (72.5)</td>
</tr>
<tr>
<td>SAEs</td>
<td>11 (7.1)</td>
<td>84 (11.1)</td>
<td>95 (10.4)</td>
</tr>
<tr>
<td>Severe AEs</td>
<td>7 (4.5)</td>
<td>64 (8.4)</td>
<td>71 (7.8)</td>
</tr>
<tr>
<td>Infections AEs (SOC)</td>
<td>62 (39.7)</td>
<td>317 (41.8)</td>
<td>379 (41.5)</td>
</tr>
<tr>
<td>GI AEs (SOC)</td>
<td>38 (24.4)</td>
<td>270 (35.6)</td>
<td>308 (33.7)</td>
</tr>
<tr>
<td>Serious infections AEs</td>
<td>4 (2.6)</td>
<td>14 (1.8)</td>
<td>18 (2.0)</td>
</tr>
<tr>
<td>Malformations excluding NMSC*</td>
<td>0 (0)</td>
<td>9 (1.2)*</td>
<td>9 (1.0)</td>
</tr>
<tr>
<td>NMSC*</td>
<td>1 (0.6)</td>
<td>6 (0.8)</td>
<td>7 (0.8)</td>
</tr>
<tr>
<td>Efficacy endpoints (FAS, as observed)</td>
<td>Remission at Month 2, n/N1 (%)</td>
<td>119/146 (81.5)</td>
<td>183/665 (27.5)</td>
</tr>
<tr>
<td>Remission at Month 12, n/N1 (%)</td>
<td>59/72 (81.9)</td>
<td>235/382 (61.5)</td>
<td>294/454 (64.8)</td>
</tr>
<tr>
<td>Remission at Month 24, n/N1 (%)</td>
<td>7/8 (87.5)</td>
<td>93/134 (69.4)</td>
<td>100/142 (70.4)</td>
</tr>
<tr>
<td>Mucosal healing at Month 2, n/N1 (%)</td>
<td>135/150 (90.0)</td>
<td>272/679 (40.1)</td>
<td>407/829 (49.1)</td>
</tr>
<tr>
<td>Mucosal healing at Month 12, n/N1 (%)</td>
<td>67/73 (91.8)</td>
<td>285/391 (72.9)</td>
<td>352/464 (75.9)</td>
</tr>
<tr>
<td>Mucosal healing at Month 24, n/N1 (%)</td>
<td>8/8 (100.0)</td>
<td>112/141 (79.4)</td>
<td>120/149 (80.5)</td>
</tr>
</tbody>
</table>

1AEs of worsening of UC leading to discontinuation were designated as insufficient clinical response; 2All causalities; 3Two cases were reported as severe (one appendicitis, one gastroenteritis norovirus); 4Four cases were reported as severe (two appendicitis, one arthritis bacterial, one atypical pneumonia); 5Adjudicated events; 6Malignancy (number of cases): cervical dysplasia (1), hepatic angiosarcoma (1), essential thrombocythaemia (1), acute myeloid leukaemia (1), cholangiocarcinoma (1), cutaneous leiomyosarcoma (1), Epstein-Barr virus associated lymphoma (1), renal cell carcinoma (1), adenocarcinoma of colon (1); 7Mucosal healing was defined as a Mayo score ≤ 2 with no individual subscore > 1, and rectal bleeding subscore of 0; 8Mucosal healing was defined by a Mayo endoscopic subscore ≤ 1;
AE, adverse event; FAS, full analysis set; GI, gastrointestinal; n, number of patients with the specified response within the given category; N, number of randomised patients in the total population; N1, number of patients in the specified category with non-missing values; SAEs, serious adverse events; SOC, system organ class; TEAEs, treatment-emergent adverse events; UC, ulcerative colitis.

Conclusion: In pts with moderate to severe UC who remained in the OLE study, no new safety concerns emerged compared with those observed with tofacitinib in rheumatoid arthritis. The efficacy results from this OLE study support sustained efficacy with both tofacitinib 5 and 10 mg BID.


References

OP096 SAFETY AND EFFICACY OF LONG-TERM TREATMENT WITH OZANIMOD, AN ORAL S1P RECEPTOR MODULATOR, IN MODERATELY TO SEVERELY ACTIVE ULCERATIVE COLITIS: TOUCHSTONE EXTENSION 2-YEAR FOLLOW-UP

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Introduction: Ozanimod, an oral, once-daily immunomodulator designed to selectively target S1P1R and S1P4R, has demonstrated clinical efficacy in ulcerative colitis (UC) for induction and maintenance therapy in the TOUCHSTONE trial (Sandborn NEJM 2016). The objective of the open-label extension (OLE) of the TOUCHSTONE trial is to evaluate the long-term efficacy and safety of daily 1 mg ozanimod treatment in patients with moderate to severe UC who had initially participated in the TOUCHSTONE trial for up to 32 weeks.

Aims & Methods: A total of 197 patients were randomized (1:1:1) and treated to receive double-blind placebo (PBO) or ozanimod at weeks (wks) 0 and 2 during the 6-wk induction phase (intent-to-treat population). Mayo clinic subscores of SF and RB were evaluated at wks 2, 4, and 6 wks. Mean subscores and mean percent change from baseline (BL) were reported for the overall population and in those who were tumour necrosis factor antagonist (anti-TNF) naïve.

Results: In anti-TNF-naïve patients, greater percentage decreases in mean SF subscores from BL were observed with ozanimod than with PBO, reaching statistical significance at wks 4 and 6 as indicated by the non-overlapping 95% confidence intervals (CIs) (Table). The same trend was observed in the overall population with out reaching statistical significance. Similarly, a numerically greater percentage decrease from BL in RB subscore was observed with ozanimod than with PBO, reaching statistical significance at wk 6 in both anti-TNF-naïve and overall populations. Significantly larger percentages of patients overall achieved SF subscore ≤1 or RB subscore of 0 with ozanimod than with PBO at wk 6 and as early as wk 2 among the anti-TNF-naïve population. A composite of SF subscore ≤1 and RB subscore of 0 was achieved in a significantly greater percentage of patients with VBZ than with PBO at all time points (Table).

Conclusion: Symptomatic improvements were achieved with VBZ as early as wk 2, with greater differences from PBO observed in anti-TNF-naïve patients. Taken together, these results highlight the rapid onset of VDZ in UC, however, assessing clinical efficacy at wk 14 and beyond for those who exhibit a more gradual response should be used to inform clinical practice.


Reference
1. Feagan BG, et al. N Engl J Med. 2013;369:699–710; NCT00738718. The clinical study was funded by Millenium Pharmaceuticals, Inc (e/d/b a Takeda Pharmaceuticals International Co). Medical writing assistance was provided by inVentiv Medical Communications and supported by Takeda Pharmaceuticals U.S.A, Inc.
OP098 INDIGO NATURALIS IS EFFECTIVE FOR INDUCING MUCOSAL HEALING IN PATIENTS WITH ULCERATIVE COLITIS (INDIGO STUDY)  


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9 Internal Medicine, Tokyo University Sakura Medical Centre Division of Gastroenterology, Sakura/Japan

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Introduction: By recent advances of immune-biological therapy for UC, the clinical outcomes of UC have been improved. However, intractable cases, in which mucosal regeneration is disturbed, cannot yet be treated well even by the most advanced anti-inflammatory biological therapies. Indigo naturalis (IN), contains highly concentrated aryl hydrocarbon receptor (AhR) ligands, which has the effect for mucosal regeneration via AhR-interleukin-22. Therefore, IN may be effective for inducing mucosal healing in ulcerative colitis (UC). More recently, we reported the efficacy of IN for UC patients who were refractory to conventional treatments in a prospective study, and approximately 70% of patients had clinical response within 8 weeks after the treatment. However, there have been no double-blind trials which demonstrate the efficacy of IN and its appropriate doses are unclear.

Aims & Methods: In this study, we have evaluated the efficacy and safety of IN in terms of the dose dependency. This multicenter, double-blind trial evaluated the safety and efficacy of IN in 86 patients with active UC. An independent centre randomly allocated UC patients (Mayo score of ≥6) to four treatment groups to receive IN (daily dose, 0.5 g, 1.0 g, 2.0 g or placebo in a 1:1:1:1 ratio). The primary efficacy endpoint (the rate of clinical response) and key secondary endpoints (the rates of clinical remission and mucosal healing) at 8 weeks of treatment were assessed in the full analysis set (FAS). For a longitudinal profile of Mayo scores and partial Mayo score, changes from baseline over 8 weeks were compared between treatment groups by means of a mixed-effects model for repeated measures. This study is registered with UMIN Clinical Trials Registry (UMIN000021439).

Results: A total of 86 patients were enrolled. The proportion of steroid-dependent patients was 36.4, 56.5, 60.0, and 52.4% in patients receiving placebo, 0.5, 1.0 and 2.0 g daily of IN, respectively. Mean Mayo score at the week 0 was comparable among the 4 groups (8.2, 8.1, 8.5, and 8.3 in patients receiving placebo, 0.5, 1.0 and 2.0 g daily of IN, respectively). In the FAS population (n = 81), significant linear trend for the dose-response in clinical response rates was confirmed (placebo (n = 21): 14.3%, IN 0.5 g (n = 20): 800%, 1.0 g (n = 19): 795%, 2.0 g (n = 19): 895%, vs. placebo, P < 0.001). The dose-response in clinical...
remission rates showed significant linear trend (placebo: 4.8%, IN 0.5 g: 26.1%, P = 0.001, 2.0 g: P < 0.001). The mucosal healing rates were 14.3%, 65.0%, 63.2%, and 52.6%, in placebo, IN 0.5 g (P < 0.01), 1.0 g (P < 0.001), 2.0 g (P < 0.05) group, respectively. Patients receiving 0.5, 1.0, and 2.0 and daily of IN had greater improvement in the Mayo score compared with patients receiving placebo at week 8 and partial Mayo score showed a gradual decrease in score in 2 weeks, 4 weeks, and 8 weeks in patients receiving IN. No serious adverse events were observed.

Conclusion: In this multi-centre, randomized, double-blind, placebo-controlled clinical trial, we showed that IN is tolerable and the efficacy was confirmed in patients receiving 0.5-2.0 g daily doses. IN may be able to use as an alternative induction therapy to steroids and as a therapy for refractory cases including chronic persistent type, especially cases with insufficient mucosal regeneration by immunosuppressants and anti-TNFα treatments.

Disclosure of Interest: M. Naganuma: EA Pharma, Zeria Pharmaceutical, Mitsubishi Tanabe, Kyorin Pharmaceutical, JIMRO, Astellas Pharma, Mochida, outside the submitted work.


N. Yoshimura: Ajinomoto Pharmaceuticals Co., Ltd., lecture fees from AbbVie GVK, Eisai Co., Ltd., Kyowa Hakko Kirin Co., Ltd., and Mitsubishi Tanabe outside the submitted work.


Y. Suzuki: Mitsubishi Tanabe Pharma Corp., AbbVie GVK, Zeria Pharmaceutical co., Ltd., Eisai Co., Ltd., Kyorin Pharmaceutical Co., Ltd. and research grant from Mitsubishi Tanabe Pharma Corp. and AbbVie GVK, outside the submitted work.


T. Kanaai: Ajinomoto, Takeda Pharma, Mitsubishi Tanabe, AbbVie GVK, Kyorin Pharma, Pfizer Japan, Zeria Pharma, Miyarisan Pharmaceutical, Astellas, Mochida Pharma, AstraZeneca, EA Pharma, outside the submitted work.

All other authors have declared no conflicts of interest.

In conclusion, the present study demonstrates that targeting CHST15 by submucosal injection of the CHST15 blocker STNM01 could allow refractory UC patients to achieve mucosal healing and clinical remission. Further application of STNM01 would thus be the unique novel therapeutic approach for reversal of tissue remodeling in refractory UC.

Disclosure of Interest: H. Yoneyma: H.Y. founded Stelic Institute & Co., Inc. in 2004

All other authors have declared no conflicts of interest.

OP100 EARLY RELAPSE OF ULCERATIVE COLITIS AFTER DISCONTINUATION OF TREATMENT IN PATIENTS RESPONDING TO GOLIMUMAB

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Introduction: GÖ-COLITIS (NCT02092285; 2013-004583-56) is a phase 4, multi-centre, open-label, single-arm trial in the UK assessing efficacy of golimumab (GLM) in induction and maintenance of clinical response in patients with moderate to severe ulcerative colitis (UC) despite conventional treatment. Data from the 12-week follow-up of patients in clinical response at week 54 is presented here.

Aims & Methods: 141/205 (68.8%) anti-TNF naïve adults with UC ≥3 months responded to induction therapy with subcutaneous GLM at week 6, according to partial Mayo score (PMS) and were eligible to receive GLM maintenance of 300mg/4 weeks (based on body weight) every 4 weeks for a total of 54 weeks. At the end of 54 weeks, their physician reviewed their treatment choosing to either continue with GLM or discontinue GLM treatment. PMS response was assessed at week 30, 54 and 66 (defined as decrease in PMS of ≥2 points and ≥30% from baseline, plus a decrease in rectal bleeding subscore of ≥1 point or absolute rectal bleeding score ≥1). 52/140 (37.1%) responders were monitored for sustained efficacy and safety at week 66 (12 weeks after study end). During this period concomitant medications were permitted at the discretion of the treating physician.

Results: 60/140 patients continued GLM maintenance treatment through week 54; 52/140 were respondents at week 54. Of these 21 continued GLM treatment while 31 discontinued GLM treatment at week 54 (Table). All patients continuing GLM treatment (21/21) remained in clinical response at week 66. Of the patients who discontinued GLM at week 54, 27/31 (87%) patients maintained clinical response at week 66.

Table: Percentage of patients assessed at week 54 who maintained a clinical response during 12 week follow-up

<table>
<thead>
<tr>
<th>Patients continuing golimumab</th>
<th>Patients in clinical response at week 54 (N = 52/140) n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients in clinical response at week 66 (N = 48/140) n (%)</td>
<td></td>
</tr>
</tbody>
</table>

- Patients continuing golimumab:
  - 21 (100%)

- Patients discontinuing golimumab:
  - 31 (27%) (87%)

Conclusion: 100% of patients who continued on GLM treatment between weeks 54 and 66 continued to respond; of the patients who discontinued GLM treatment at week 54, early relapse (i.e. relapsed within 12 weeks of stopping GLM treatment) was seen in 54/131 (41%). These are the first data on the effect of GLM discontinuation treatment in patients responding to GLM. There was no difference in PMS between the lower dose STNM01 (25 nM) and placebo groups. Further studies are required to evaluate the percentage of patients remaining in response at 6 months, or later, following anti-TNF treatment discontinuation in responding patients after 1 year of treatment.


P. Irving: Peter Irving: research funding from and is a speaker or advisory board member for Abbvie, Dr Falk Pharma, Ferring, MSD, Takeda, Vifor Pharma and Warner Chilcott.

S. Sebastian: Shaji Sebastian: research funding from and is a speaker or advisory board member for Abbvie, Dr Falk Pharma, Ferring, MSD, Tollits, Warner Chilcott.

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Introduction: Ulcerative colitis (UC) is characterized by mucosal inflammation and structural damage that is associated with matrix remodelling and tissue fibrosis. We had previously shown that carbohydrate sulfotransferase 15 (CHST15) that biosynthesizes sulfated matrix glycosaminoglycans is an important regulator of experimental colitis and gut fibrosis. Here, we evaluated the function of the double-stranded RNA oligonucleotide STNM01, a specific blocker of CHST15, in refractory UC patients.

Aims & Methods: In this randomized, double-blind, placebo-controlled phase 2a trial, 24 patients with severe UC were randomized to receive a single endoscopic submucosal injection of 25 nM, 250 nM STNM01 or placebo.

Results: The primary endpoint, mucosal healing at weeks 2 or 4 was achieved by 62.5% in the STNM01 (250 nM) group compared to 28.6% in the placebo group (p = 0.018). Clinical remission at these time points was reached by 50.0% in the STNM01 (250 nM) and 14.3% in the placebo groups (p = 0.050). There was significant histological improvement according to the Geboes score in the STNM01 (250 nM) group (p < 0.01). There were no statistical differences between the lower dose STNM01 (25 nM) and placebo groups.


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develop a efficacious therapy with minimal side effects for the treatment of liver fibrosis therefore there is an unmet need to shown to be highly efficacious in many disorders. Currently there is no therapy inflammation or liver fibrosis. Anti-inflammatory therapies targeting M inflammatory macrophages would be a promising approach to attenuate liver and hepatocellular carcinoma. Therefore, selective targeted inhibition of the introduction:

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Introduction: Inflammatory macrophages (Mϕs) play a critical role in the development of liver inflammation. Hepatocellular damage, instigated by hepatitis viral infections, alcohol abuse or metabolic syndrome, results in the recruitment and activation of inflammatory cells mainly M1 in the liver. The inflammatory Mϕs initiates the process of liver injury progressing from liver fibrosis to cirrhosis and hepatocellular carcinoma. Therefore, selective targeted inhibition of the inflammatory macrophages would be a promising approach to attenuate liver inflammation or liver fibrosis. Anti-inflammatory therapies targeting Mϕs has shown to be highly efficacious in many disorders. Currently there is no therapy available for the treatment of liver fibrosis therefore there is an unmet need to develop therapy with minimal side effects for the treatment of chronic liver disease. We identified Mincle receptor as a prospective target for pro-inflammatory subset (M1) of the development for effective inflammatory macrophage specific drug delivery system.

Aims & Methods: In this study, we developed a novel delivery system i.e. Mincle-targeted liposomes to achieve M1-specific uptake and to selectively deliver anti-inflammatory drugs to inhibit M1 Mϕs thereby ameliorating liver inflammation. Specificity and significance of Mincle receptor was evaluated in vitro in murine and human M1 Mϕs in vitro in CCl4-induced acute liver inflammation using immunostainings and quantitative PCR. Diverse Mincle-targeted liposomes were synthesized and characterized using dynamic light scattering (DLS). M1-specific uptake in murine and primary human Mϕs was analyzed using fluorescence-activated cell sorting (FACS). We used prednisolone as an anti-inflammatory drug to inhibit inflammatory M1 macrophages. Prednisolone encapsulated Mincle-targeted liposomes were generated, characterized and tested for efficacy in vitro in primary murine RAW macrophages, primary human Kupffer cells and in vivo in acute CCl4-induced liver injury mouse model.

Results: Significant up-regulation of Mincle receptor was confirmed in murine and human M1 Mϕs in vitro, in vitro in liver fibrosis mouse models and human fibrotic liver tissues. siRNA mediated knockdown (70% inhibition) of Mincle receptor in M1 Mϕs resulted in reduced inflammatory markers (TNFα and IL1β) and Mincle co-receptor. Mincle-targeted liposomes showed favorable size, stability and drug entrapment efficiency. We used prednisolone as an anti-inflammatory drug as a model drug to inhibit inflammatory M1 macrophages. We tested these liposomes in different mouse macrophage cell lines, primary bone marrow derived macrophages and in primary human macrophages for efficacy and M1-specific uptake. Significantly, targeted liposomes showed M1-specific uptake, while liposomes without targeting moiety showed comparably reduced internalization at different time points. Furthermore, targeted liposomes demonstrated significantly reduced uptake in M2 restorative Mϕs. No significant uptake in other cells was observed. Antibody blocking of Mincle receptor signification inhibited uptake in M1 Mϕs strongly suggesting Mincle-mediated mechanism of uptake. Prednisolone-encapsulated Mincle targeted liposomes showed significant reduction in M1-specific markers and inflammatory markers in vitro in RAW cells, in primary murine BMDMs and human kuffer cells. In vivo in acute CCl4-induced liver inflammation mouse model, prednisolone-encapsulated Mincle-targeted liposomes demonstrated specific liver uptake, highly significant attenuation in intra-hepatic inflammation, macrophage infiltration and reduction in fibrotic parameters as compared to free prednisolone and non-targeted liposomes.

Conclusion: This study presents a highly novel targeting approach of specifically targeting inflammatory macrophages with increased therapeutic efficacy while off-target effects on healthy tissues and other cell types can be avoided. These inflammatory macrophage targeted liposomes therefore holds great promise for diagnosis and therapeutic treatment of liver fibrosis and other inflammatory diseases.

Disclosure of Interest: All authors have declared no conflicts of interest.

MONDAY, OCTOBER 30, 2017 15:45-17:15

ALCOHOLIC LIVER DISEASE: ANYTHING NEW? ROOM A2

OP101 TARGETING LIVER INFLAMMATION USING MINCLE-TARGETED LIPOSOMES AS A NOVEL DRUG DELIVERY SYSTEM

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Reference

MONDAY, OCTOBER 30, 2017 15:45-17:15

ERCP: WHEN THE GOING GETS TOUGH - ROOM B2

OP103 SELF-CONFORMABLE COVERED VS SELF-CONFORMABLE UNCOVERED METALLIC STENTS IN THE PALLIATIVE TREATMENT OF MALIGNANT EXTRA-HEPATIC BILIARY STENTRUPTURE: A MULTICENTRIC RANDOMIZED STUDY

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Introduction: Gut barrier failure and the consequent pathological bacterial translocation (BT) are characteristic features of cirrhosis and play an important role in the progression of liver disease. We hypothesized that serological hallmark-marks of gut barrier dysfunction are associated with accelerated progression of liver disease in cirrhosis and the development of specific complications and liver-related death.

Aims & Methods: Sera from 260 stable outpatients with cirrhosis (male: 129, age: 56 ± 11 yrs; alcohol: 167 [64.2%]) and from 155 healthy subjects were assayed for the presence of antibodies against filamentous-actin [AAA IgA and IgG] and gliadin [AGA IgA and IgG] and for intestinal fatty acid-binding protein (I-FABP) by ELISA. Association of gut failure markers with disease specific characteristics was assessed at baseline and the course of liver disease was evaluated in a 5-year follow-up observational study for decompensating events (ascites, variceal bleeding, hepatic encephalopathy and/or bacterial infection) and liver-related death. BT was assessed based on the presence of serum microbiological antibodies (anti-OMP Plus IgA and/or endotoxin core IgA antibody [EndoCab]).

Results: Elevated concentrations of the gut failure markers IgA-AAA (62.7 vs. 4.4%) and IgA-AGA (27.7 vs. 2.6%) were more often observed in cirrhosis as compared to healthy controls (p < 0.001 for both). In addition, serum I-FABP was increased in cirrhosis as compared to controls (741 vs. 244 pg/mL, p < 0.001) and correlated with serum levels of IgA-AAA and IgA-AGA. IgA-AAA positivity was associated with alcoholic liver disease, liver disease scores and decompensated clinical stage (p < 0.001). Serological markers of BT were more often found in patients with elevated IgA-AAA compared to those without (72.3 vs. 13.5 % for IgA-EndoCab and 85.2 vs. 20.5 % for IgA-anti-OMP, p < 0.001) for both. In patients with compensated disease stage (n = 131) the risk of decompensation was higher in patients with elevated IgA-AAA (HR [95%CI]: 1.85 [1.06-3.24]), as was the risk of liver-related mortality (HR: 2.66 [1.27-5.56]). Such associations were not observed for IgG-AAA and IgA/IGA-AGAs. In the overall cohort, IgA-AAA remained an independent predictor of liver-related death (HR [95%CI]: 1.96 [1.08-3.55]) when adjusting for important clinical variables (MELD score, etiology, clinical stage, see Table 1).

Table 1: Summary of Cox proportional hazards analysis in the prediction of liver-related mortality

<table>
<thead>
<tr>
<th>Marker</th>
<th>Wald</th>
<th>Hazard ratio</th>
<th>95% confidence interval</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>IgA-AAA</td>
<td>4.94</td>
<td>1.96</td>
<td>1.08-3.55</td>
<td>0.026</td>
</tr>
<tr>
<td>MELD score</td>
<td>9.79</td>
<td>1.10</td>
<td>1.04-1.16</td>
<td>0.002</td>
</tr>
<tr>
<td>(per 1 point increase)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Etiology (alcohol)</td>
<td>1.15</td>
<td>0.74</td>
<td>0.42-1.29</td>
<td>0.738</td>
</tr>
<tr>
<td>Clinical stage (decompensated)</td>
<td>1.71</td>
<td>1.34</td>
<td>0.85-2.23</td>
<td>0.190</td>
</tr>
<tr>
<td>Age (≥65 yrs)</td>
<td>1.92</td>
<td>1.44</td>
<td>0.86-2.40</td>
<td>0.165</td>
</tr>
<tr>
<td>Gender (female)</td>
<td>0.33</td>
<td>1.14</td>
<td>0.73-1.79</td>
<td>0.337</td>
</tr>
</tbody>
</table>

Conclusion: Elevated serum concentrations of IgA antibodies against filamentous-actin indicate patients with an unfavourable outcome in cirrhosis, which may be related to intestinal damage beyond being related to bacterial translocation. IgA-AAA might be consider as a novel serologic marker of the disease progression.

Disclosure of Interest: G.L. Norman: Employee of INOVA
All other authors have declared no conflicts of interest.

MONDAY, OCTOBER 30, 2017 15:45-17:15

ERCP: WHEN THE GOING GETS TOUGH - ROOM B2
Aims & Methods: Primary aim was to compare stent patency between the two groups. Secondary aims were to evaluate relationships between adverse events (AEs) rate and stent type (i.e. time to stent dysfunction and survival). 158 patients (76 M 82 F, median age 78 ys) were randomized in two groups: 78 received a fully-covered SEMS (FCSEMS) and 78 an uncovered SEMS. Data from 148 (72 FCSEMS and 76 USEMS) out of 158 patients were analyzed. All patients received sphincterotomy before stent insertion.

Results: Placement was successful in 100% of patients with the uncovered and 98.7% patients with FCSEMS. Levels of conjugated bilirubin improved significantly (p < 0.001) in both groups during the first week, with a median variation of 1.5 mg/dL (p < 0.001) for FCSEMS. Normalization of bilirubin levels (≤ 1 mg/dL) was observed in 42 patients (28.6%; 28.2% FCSEMS and 28.9% SEMS, p = 1.0). AEs occurred in 28 out of 147 patients [19.0%: 18 FCSEMS (25.4%) and 10 SEMS (13.1%); p = 0.092]. Sclerotherapy occurred in 12 patients and 10 patients with SEMS, Cholangitis was observed in 6 patients for each group. In patients with SEMS, occlusion was due to ingrowth and in 9 out of 10 patients, was reported as a late complication. In FCSEMS group, 6 out of 12 patients had stent occlusion within the first month. Stricture recurrence was observed in a patient with FCSEMS. No stent migration occurred in SEMS group while it was observed in 5 (7%) of the FCSEMS group (p = 0.024). Median time of stent patency was lower for FCSEMS (9.5 months, 95% CI 7.2–11.8 months) vs 18 months (95% CI 10.7–25.4 months) for SEMS (p = 0.046). No differences were observed with regard to stent dysfunction in patient survival: 4.0 months (95% CI 2.5–5.5 months) for FCSEMS and 3.7 days (95% CI 2.3–5.0) for SEMS (p = 0.80). Median survival was 4.5 months (95% CI: 3.3–5.7 months) in FCSEMS group and 3.7 months (95% CI: 2.2–5.3 months) in SEMS group (p = 0.23).

Conclusion: No significant differences were observed in levels of bilirubin improvement, stent dysfunction-free and median survival between the two groups. AEs were higher, although not significantly, among FCSEMS group. FCSEMS had a significantly higher rate of migration. A significantly difference in patency was observed for SEMS group.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP104 CLINICAL EFFICACY OF ANTI-MIGRATION FEATURES IN FULLY-COVERED SELF-EXPANDABLE METALLIC STENTS FOR ANASTOMOTIC BILIARY STRICTURES AFTER LIVER TRANSPLANTATION: A PROSPECTIVE RANDOMIZED CONTROLLED TRIAL COMPARED TO THE STANDARD SEMS

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Introduction: Anastomotic biliary strictures (ABS) are one of the most frequent adverse effects occurring after orthotopic liver transplantation (OLT). Multiple plastic stents (MPS) have been validated in this indication. More recently, fully covered self-expandable metallic stents (FC-SEMS) have been used with positive outcomes but also a higher rate of migration which may limit success.

Aims & Methods: Our primary objective was to compare stent migration rates observed with FC-SEMS vs so-called “anti-migration” FC-SEMS, newly designed with reversed proximal side flaps. Secondary objectives were to compare the rates of ABS recurrence, and sustained stricture resolution as well as procedure-related morbidity. We conducted a retrospective analysis of a prospectively maintained database of a) OLT patients, and b) ERCP and stenting. Between January 2008 and January 2016, consecutive patients presenting with ABS after OLT referred to Cochin Hospital (Paris, France) for ERCP and receiving an FC-SEMS were included. Exclusion criteria were any other cause of biliary stricture (i.e malignant stricture, ischemic origin), and biliary fistulae.

Results: One hundred and twenty-five FCSEMS (57 anti-migration stents, 25 conventional stents type 1 and 16 conventional stents type 2) were used in 75 patients for ABS after OLT. The rate of FC-SEMS complete migration was 16% (20/125 patients, respectively 1.7% (1/57) for anti-migration stents vs 33.3% (9/27) for conventional stents (p = 0.002). First ERCP follow-up after each FC-SEMS highlighted a stricture resolution in 80% (100/125) of cases, 93% (53/57) for anti-migration stents, 77% (40/52) for type 1 conventional stents and 62.5% (10/16) for type 2 conventional stents (p = 0.0002). No significant differences were observed in levels of bilirubin (1, 2 mg/dL) was observed in 42 patients (28.6%; 28.2% FCSEMS and 28.9% SEMS, p = 0.024). Median time of stent patency was lower for FCSEMS (9.5 months, 95% CI 7.2–11.8 months) vs 18 months (95% CI 10.7–25.4 months) for SEMS (p = 0.046). No differences were observed with regard of stent dysfunction in patient survival: 4.0 months (95% CI 2.5–5.5 months) for FCSEMS and 3.7 days (95% CI 2.3–5.0) for SEMS (p = 0.80). Median survival was 4.5 months (95% CI: 3.3–5.7 months) in FCSEMS group and 3.7 months (95% CI: 2.2–5.3 months) in SEMS group (p = 0.23).

Conclusion: No significant differences were observed in levels of bilirubin improvement, stent dysfunction-free and median survival between the two groups. AEs were higher, although not significantly, among FCSEMS group. FCSEMS had a significantly higher rate of migration. A significantly difference in patency was observed for SEMS group.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
Mean procedure time was 67 min (SD 11.5) in the e-ERCP group vs. 70 min (SD 11.3) in the EUS-GG-ERCP group. The technical success rate was significantly higher in the EUS-GG-ERCP versus the e-ERCP group (88.7% vs. 79.2%; *p* = 0.001). Post-procedure length of hospital stay was 2 (IQR: 0–6) days (e-ERCP) vs. 3.7 (IQR: 2–14) days (EUS-GG-ERCP) (p = 0.001). Rate of AEs was similar in both groups (7.5% vs. 5.6%, *p* = 0.37).

<table>
<thead>
<tr>
<th>Outcome</th>
<th>e-ERCP</th>
<th>EUS-GG-ERCP</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Technical success ERCP</td>
<td>60.8%</td>
<td>53 (33.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mean procedure time ± SD (min)</td>
<td>86.1 ± 20.8</td>
<td>50.1 ± 25.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Median length of hospital stay</td>
<td>2 (IQR: 2–14)</td>
<td>2 (IQR: 0–6)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Average weight change (Kg)</td>
<td>+0.18 ± 5.5</td>
<td>+4.5 ± 11.5</td>
<td>0.07</td>
</tr>
</tbody>
</table>

Table 1: Outcomes of e-ERCP vs EUS-GG-ERCP

References


Mean procedure time (73.9 vs 49.9, p = <0.001) was significantly shorter in the LL group. Difficult anatomy/cannulation was significantly correlated with technical failure [aOR(95%CI): 5.18 (1.26–21.2), p = <0.001] while duration of procedure [aOR(95%CI): 1.02 (1.01–1.03), p = <0.001] was a significant predictor of the need for more than one session of D-SOC EHL/LL.

### Table 1: Patient characteristics and procedure outcomes

<table>
<thead>
<tr>
<th>Total</th>
<th>EHL (N=306)</th>
<th>LL (N=101)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Female sex; n (%)</strong></td>
<td>246 (60.4)</td>
<td>181 (59.2)</td>
<td>65 (64.4)</td>
</tr>
<tr>
<td><strong>Mean age (mean ± SD)</strong></td>
<td>64.2 ± 18</td>
<td>63.2 ± 19</td>
<td>67.1 ± 14.4</td>
</tr>
<tr>
<td><strong>Symptoms</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abdominal pain; n (%)</td>
<td>166 (48.8)</td>
<td>110 (35.3)</td>
<td>58 (57.4)</td>
</tr>
<tr>
<td>Jaundice; n (%)</td>
<td>166 (48.8)</td>
<td>110 (35.3)</td>
<td>58 (57.4)</td>
</tr>
<tr>
<td>Cholangitis; n (%)</td>
<td>69 (17)</td>
<td>54 (17.3)</td>
<td>15 (14.9)</td>
</tr>
<tr>
<td><strong>Pancreatitis; n (%)</strong></td>
<td>6 (1.5)</td>
<td>5 (1.6)</td>
<td>1 (0.99)</td>
</tr>
<tr>
<td>Others; n (%)</td>
<td>48 (11.8)</td>
<td>18 (5.9)</td>
<td>30 (29.7)</td>
</tr>
<tr>
<td><strong>Prior ERCP with failed stone extraction; n (%)</strong></td>
<td>349 (85.8)</td>
<td>271 (88.6)</td>
<td>78 (77.2)</td>
</tr>
<tr>
<td>1</td>
<td>189 (46.4)</td>
<td>123 (39.2)</td>
<td>66 (64.4)</td>
</tr>
<tr>
<td>2–3</td>
<td>134 (32.9)</td>
<td>124 (40.5)</td>
<td>10 (9.9)</td>
</tr>
<tr>
<td>&gt;3</td>
<td>26 (6.4)</td>
<td>24 (7.8)</td>
<td>2 (1.98)</td>
</tr>
<tr>
<td>Dwelling biliary stent; n (%)</td>
<td>309 (75.9)</td>
<td>252 (82.4)</td>
<td>57 (56.4)</td>
</tr>
<tr>
<td>Metallic; n (%)</td>
<td>11 (3.6)</td>
<td>10 (4)</td>
<td>1 (1.8)</td>
</tr>
<tr>
<td>Plastic; n (%)</td>
<td>298 (74.6)</td>
<td>242 (96)</td>
<td>56 (98.2)</td>
</tr>
</tbody>
</table>

**Reasons for cholangioscopy**

- More than one indication
  - Large stone (> 15 mm); n (%) 303 (74.3) 230 (75.2) 73 (72.3) 0.56
  - Multiple stones (> 3); n (%) 223 (54.8) 168 (54.9) 55 (54.5) 0.94
- Stricture bellow a stone; n (%) 219 (53.8) 162 (52.9) 57 (56.4) 0.54
- Impacted stone; n (%) 80 (19.7) 51 (16.7) 29 (28.7) 0.008
- Intrahepatic stone (IHBD); n (%) 155 (38.1) 122 (39.9) 33 (32.7) 0.20
- Cystic duct stone; n (%) 72 (17.7) 57 (18.6) 15 (14.9) 0.39
- Difficult anatomy/cannulation; n (%) 50 (12.3) 45 (14.7) 5 (5) 0.01
- Mirizzi’s syndrome; n (%) 57 (14) 32 (10.5) 25 (24.8) <0.001
- Technical success (complete bile duct clearance); n (%) 35 (8.6) 33 (10.8) 2 (2) 0.004
- Sessions of EHL/LL to clear the bile duct; median (range) 1 328 (80.6) 241 (78.8) 87 (86.1) 0.16
  - 1 76 (18.6) 63 (20.6) 13 (12.9) 0.54
  - >3 3 (0.7) 2 (0.7) 1 (1) |
- Number of EHL/LL sessions to clear bile duct; median (range) 1 (1–4) 1 (1–4) 1 (1–4) 0.12

**ERCPs for additional therapy**

- Need for ESWL; n (%) 2 (0.5) 1 (1) 1 (0.3) 0.44
- Need for surgery; n (%) 8 (2.0) 8 (2.6) 0 0.21
- Need for ESWL and Surgery; n (%) 1 (0.2) 1 (0.3) 0 1
- Stone recurrence; n (%) 17 (6.1) 16 (7) 1 (2) 0.07
- Procedure time (min) (mean ± SD) 67 ± 34.9 73.9 ± 33.5 49.9 ± 32.4 <0.001
- Number of patients followed up; n (%) 259 (63.6) 227 (74.2) 32 (31.7) <0.001
- Total Follow up (median) (IQR) 835 (33–155) 8434 (151) 86 (32–129) 0.65

**Conclusion:** D-SOC with EHL or LL is effective and safe in treating difficult bile duct stones. Few patients will require surgery or ESWL to achieve ductal clearance. Procedure time is significantly lower in the LL group as compared to EHL group.

**Disclosure of Interest:** I. Rajim: consultant and speaker for Boston Scientific and Covidien. Co-owner of EndoRx.

R. Sturgess: Consultant for Boston Scientific

S. Sherman: Consultant for Boston Scientific

R.J. Shah: Raj J. Shah is consultant for Cook and for Boston Scientific

W. Wassef: Consultant to Boston Scientific Consultant to Abbvie

D.G. Adler: Consultant for Boston Scientific

V. Kushir: BSCI: consultant and speakers bureau

A.Y. Wang: has received research support from Cook Medical

K. Krishnan: BSCI: Speaker Olympus Consulting

C.J. DiMaio: consultant for Boston Scientific

B.T. Petersen: Consultant for Boston Scientific

G. Webster: received honoraria from Boston scientific for an advisory board, consultancy and lecture invitations

M.A. Khashab: Consultant for Boston Scientific

All other authors have declared no conflicts of interest.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**References**


A total of 618,884 subjects were extracted and matched from the data of long-term aspirin use and the cancer incidences were documented for up to 14 years until 2013. Odds ratio (OR) with its 95% confidence interval (CI) was calculated for non-GI cancers which referred to breast, bladder, kidney, leukaemia, lung, and prostate cancers, and the risk mortality on CRC was fitted, and Hazard Ratio (HR) was used to measure all-cause mortality. Subgroup analyses on gender were performed.

Results: From the healthcare records between 2000 and 2013, a total of 13,552 subjects were included: 3,301 of them (24.4%) were aspirin users and 10,251 (75.6%) were non-users before CRC diagnosis. The median dose of aspirin prescribed was 80 mg. Patients in group (a) with aspirin use before CRC diagnosis, 2,665 (80.7%) continued aspirin and 636 (19.3%) discontinued aspirin after curative surgery. Continuous use of aspirin significantly reduced 31% risk of CRC-related mortality with SHR: 0.69 (95% CI: 0.59 – 0.81) and 42% risk of all-cause mortality with HR: 0.58 (95% CI: 0.49 – 0.68). Patients in group (b) who never use aspirin before CRC diagnosis, 1055 patients (10.3%) initiated aspirin after curative surgery and 9196 (89.7%) patients remained not to have aspirin use. Initiating aspirin after surgery significantly reduced 12% risk of CRC-related mortality with SHR: 0.88 (95% CI: 0.80 – 0.98) and 18% risk of all-cause mortality with HR: 0.82 (95% CI: 0.73 – 0.91). Subgroup analyses did not show significant difference between male and female (Table 1).

Table 1. Comparison between Aspirin Users and Non-users for Major Cancers Incidence.

<table>
<thead>
<tr>
<th>Cancer Site</th>
<th>Aspirin Users</th>
<th>Non-users</th>
<th>Odd Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>GI Cancers</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Colorectum</td>
<td>3,301 (24.4%)</td>
<td>3,301 (24.4%)</td>
<td>0.63 (0.73 – 0.78)</td>
</tr>
<tr>
<td>Liver</td>
<td>7,483 (18.0%)</td>
<td>7,483 (18.0%)</td>
<td>0.51 (0.51 – 0.56)</td>
</tr>
<tr>
<td>Oesophagus</td>
<td>2,097 (0.51%)</td>
<td>2,097 (0.51%)</td>
<td>0.49 (0.49 – 0.59)</td>
</tr>
<tr>
<td>Pancreas</td>
<td>2,105 (0.51%)</td>
<td>2,105 (0.51%)</td>
<td>0.60 (0.60 – 0.71)</td>
</tr>
<tr>
<td>Stomach</td>
<td>4,489 (1.09%)</td>
<td>4,489 (1.09%)</td>
<td>0.58 (0.58 – 0.65)</td>
</tr>
<tr>
<td>Non-GI Cancers</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Breast</td>
<td>3,113 (0.73%)</td>
<td>3,113 (0.73%)</td>
<td>0.80 (0.90 – 1.02)</td>
</tr>
<tr>
<td>Bladder</td>
<td>3,597 (0.87%)</td>
<td>3,597 (0.87%)</td>
<td>0.92 (0.92 – 1.03)</td>
</tr>
<tr>
<td>Kidney</td>
<td>1,454 (0.35%)</td>
<td>1,454 (0.35%)</td>
<td>0.91 (0.95 – 1.13)</td>
</tr>
<tr>
<td>Leukaemia</td>
<td>1,285 (0.31%)</td>
<td>1,285 (0.31%)</td>
<td>0.63 (0.68 – 0.84)</td>
</tr>
<tr>
<td>Lung</td>
<td>18,951 (4.59%)</td>
<td>18,951 (4.59%)</td>
<td>0.65 (0.63 – 0.66)</td>
</tr>
<tr>
<td>Multiple myeloma</td>
<td>1,101 (0.27%)</td>
<td>1,101 (0.27%)</td>
<td>0.90 (0.80 – 1.00)</td>
</tr>
<tr>
<td>Prostate</td>
<td>4,767 (1.16%)</td>
<td>4,767 (1.16%)</td>
<td>0.86 (0.82 – 0.91)</td>
</tr>
</tbody>
</table>

Table 1. Comparison between Aspirin Users and Non-users for Major Cancers Incidence.

Disclosure of Interest: All authors have declared no conflicts of interest.

Conclusion: Long-term use of aspirin can reduce the major types of GI cancers, but the benefits are limited to some other non-GI cancers, such as breast and kidney.

Disclosure of Interest: All authors have declared no conflicts of interest.
LYNCH-LIKE SYNDROME


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8 Empresa Publica de Seguro Social (EPICOLON-III) and demographic, clinical and pathological data were collected from patients included in the study. Patients with CRC were included when there were clinical, pathology or molecular characteristics that could suggest a probably hereditary or sporadic origin. This is a multicenter nation-wide study, involving 25 Spanish hospitals. Patients with CRC included when their tumors showed immunohistochemical loss of MLH2, MSH6, PMS2 or loss of MLH1 with BRAF-wild type and/or no MLH1 methylation and absence of pathogenic mutation in these genes. Immunohistochemical study of the tumors was performed because of fulfillment of revised Bethesda Guidelines (4) or because of universal molecular screening for LS (5). These patients were included in a national registry (EPICOLON-III) and demographic, clinical and pathological variables, as well as family history of neoplasms, were registered.

Results: Our study included 85 patients with LS. Mean age at diagnosis of CRC was 55 years (SD 14). A total of 39 patients were female (46%). Loss of MLH1/ PMS2 was found in 46% of CRC, loss of MSH2/MSH6 in 34%, isolated loss of MLH1 was found in 12% and isolated loss of MSH2 in 8% in stage IV. None of the patients showed personal history of previous CRC. A total of 12 patients (14%) had personal history of non-colorectal cancer, and only 3 (3.5%) patients had previous history of LS-related cancer. Regarding family history, a total of 46 patients (54%) had at least one relative with CRC, and 38 patients (45%) showed familial history of LS-related cancer. Comparison of clinical and molecular characteristics of these patients in a large nation-wide cohort and to analyze if there are clinical, pathology or molecular characteristics that could suggest a probably hereditary or sporadic origin. This is a multicenter nation-wide study, involving 25 Spanish hospitals. Patients with CRC included when their tumors showed immunohistochemical loss of MLH2, MSH6, PMS2 or loss of MLH1 with BRAF-wild type and/or no MLH1 methylation and absence of pathogenic mutation in these genes. Immunohistochemical study of the tumors was performed because of fulfillment of revised Bethesda Guidelines (4) or because of universal molecular screening for LS (5). These patients were included in a national registry (EPICOLON-III) and demographic, clinical and pathological variables, as well as family history of neoplasms, were registered.

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molecular characteristics of patients depending on age at diagnosis of CRC or family history can be seen in Table 1. *p < 0.05 for comparison

Conclusion: In this cohort of LLS patients, the largest collected until now, there are no clinical, molecular or pathological characteristics that could be of help to distinguish between probably sporadic and hereditary patients. These results support the need of homogeneous follow-up for this group of patients.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

GLUTEN-RELATED DISORDERS - ROOM E2

OP113 THE PREVALENCE OF NON-CELIAC GLUTEN SENSITIVITY IN PATIENTS WITH ABDOMINAL PAIN AND BLOATING

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Introduction: A new entity, called Non-Celiac Gluten Sensitivity (NCGS), was recently proposed to categorize patients suffering from a wide range of both intestinal and extra-intestinal symptoms after gluten ingestion (Sapone A, et al, BMC Medicine 2012). A very high prevalence of this condition was reported (Sapone A, et al, BMC Medicine 2012), but in our experience such a high figure was not confirmed (Di Sabatino A, et al, GGH 2015). We have recently shown that the ingestion of gluten may hamper colonic fermentation (LD) in healthy volunteers. Accordingly, it is possible that a high prevalence of NCGS could be present in patients with bloating.

Aims & Methods: Our aim was to detect the prevalence of non-celiac gluten sensitivity in functional patients with a long history of abdominal pain and bloating, claiming a relationship between gluten intake and symptom occurrence, and referred to an outpatient clinic for functional gastrointestinal disorders of a tertiary medical center. In accordance with the Salerno Criteria (Catassi C, et al. Nutrients 2015), we conducted a double-blind, placebo controlled trial with gluten vs placebo in thirty-two non-celiac patients with moderate to severe abdominal bloating and pain, enrolled in an outpatient clinic (M/F 3/29, mean age 31 ± 5). Symptoms were present for a mean period of 10 ± 3 years and were judged by patients as poorly responsive to all previous treatments. The presence of allergic, organic gastrointestinal and systemic disorders was ruled out in all patients. All subjects reported abdominal pain, bloating, flatulence, borborygmi, and bowel habit alterations, dyspeptic symptoms on gluten-containing diet (GCD) and, considering gluten as the causal agent, had been spontaneously following a non-blinded gluten-free diet (GFD) for at least a 6-week period, reporting an improvement of symptoms. They then started a rigorous GFD and entered this trial. In a double-blind, crossover protocol, ten capsules, containing 475 mg of gluten or 475 mg of rice starch, were administered randomly, each day for a 1-week period, with a 1-week wash-out interval. The patients completed a diary of symptoms, every evening at the same time for the duration of the study. The two main symptoms recorded by all patients were bloating and abdominal pain: a mean value during gluten ingestion over 30% higher than the value during placebo was considered as indicative of gluten sensitivity (Catassi C, et al, Nutrients 2015).

Results: In seventeen out of 32 patients (53%), the severity of abdominal pain was significantly higher during the week of gluten capsule ingestion than during the week of placebo capsule ingestion: the severity of abdominal pain in the group of patients with NCGS was 2.6 ± 2.4 during gluten and 1.5 ± 2.0 during placebo (p = 0.0001), on the contrary, in the group of non-sensitive patients it was 0.7 ± 1.8 during gluten and 1.2 ± 1.9 during placebo (p = 0.013). In fifteen out of 32 patients (47%), the severity of bloating was significantly higher during gluten than during placebo: the severity of bloating in the group of patients with NCGS was 3.7 ± 2.5 during gluten and 2.2 ± 2.0 during placebo (p = 0.0001), while in the group of non-sensitive patients it was 2.1 ± 1.5 during gluten and 3.5 ± 2.3 during placebo (p = 0.0001). Considering the modification of at least one of the two main symptoms, the diagnosis of NCGS was possible in 22 out of 32 patients (68%).

Conclusion: Around half of the patients with a long history of abdominal pain and bloating, claiming a relationship with gluten ingestion, resistant to previous treatments and referred to a tertiary clinic, show a positive result at the double blind test for the diagnosis of NCGS.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP114 PROSPECTIVE EVALUATION OF TRANSGLUTAMINASE ANTIBODY CUT-OFF LIMITS TO PREDICT SCREEN-DETECTED COELIAC DISEASE


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Introduction: Current ESPGHAN guidelines allow the non-invasive diagnosis of paediatric coeliac disease (CD) in clinical patients with relevant symptoms, serum transglutaminase 2 antibody levels above 10 times the upper limit of normal (ULN), endomysial antibody positivity (EMA) and an HLA-DQ2 or DQ8 background.

Aims & Methods: In this study we evaluated whether high serum antibody concentrations also predict CD in prospectively followed, regularly screened family members. The PREVENTCD multicenter FP6 study (www.preventcd.org) enrolled in 8 European countries 1002 DQ2- and/or DQ8-positive newborns who at least one family member diagnosed with CD for a prospective dietary intervention consisting of 100 mg of gluten per day or placebo between the age of 4–6 months. IgA antibodies against transglutaminase 2 (TGA) were determined 7 times until 3 years of age and then annually. TGA was measured in years 2007–2014 by the Célèky Varelnia test, in years 2015-2016 by Célèky ELIA method (both from Phadia and using the same TGA antigen but having 5 ULN and 7 ULN positivity cut-offs as defined by the manufacturer), respectively. EMA tests were performed locally as needed. A small bowel biopsy was offered to all children with persistent gastrointestinal symptoms or when symptoms appeared. CD was diagnosed in children with Marsh III histology lesions according to a central evaluation by a reference pathologist blinded to the clinical and antibody results. In case of decreasing or increasing TGA concentrations, the highest value before biopsy was taken into account for the calculations. IgA deficient subjects were excluded from the present analysis.

Results: During follow-up, small bowel biopsy was performed in altogether 144 children and 12 children were diagnosed with CD by histology of whom 67 (54%) were asymptomatic. Of the 149 TGA+ children, 71 (48%) had values >100 ULN/ml, 36 (24%) had values between 30–100 ULN/ml and 42 had values <30 ULN/ml of which 14/42 had transient seropositivity. TGA+ values >6.0xULN/ml had a positive predictive value for CD of (Table). There was no statistical difference in disease prediction between symptomatic and asymptomatic children with TGA+ levels >4.0xULN.

Conclusion: TGA+ levels >6.0xULN measured by the utilised test kits safely predicted CD both in symptomatic and asymptomatic children. Predictive cut-off levels of other TGA testing kits may substantially differ, and such differences should be carefully considered when applying ESPGHAN guidance for omitting biopsy. Test-specific predictive values are to be systematically established in similar prospective studies.

Disclosure of Interest: P. Szilái: Employee of Phadia Thermofisher All other authors have declared no conflicts of interest.

OP115 RECTO-SIGMOID SENSOMOTOR ACTIVITY IN SELF-REPORTED NON-CELIAC GLUTEN SENSITIVITY: A COMPARISON WITH HERITABLE BOWEL SYNDROME AND HEALTHY VOLUNTEERS

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Introduction: The ingestion of gluten may be responsible for symptom onset in non-celiac patients (Cooper BT, et al Gut 1990;190) and a new entity, called Non Celiac Gluten Sensitivity (NCGS), was recently proposed (Sapone A, et al Gut 2012). But pathophysiological mechanisms are largely unknown. The aim of this study was to assess whether self-reported NCGS overlaps IBS both in clinical presentation and gastrointestinal sensorimotor functions.

Methods: During an ambulatory visit, we instructed healthy volunteers (HV), patients with IBS (IBS), and patients with self-reported NCGS (NCGS) to score their perception on a 0–6 scale. The perception threshold was defined as a perception score of 1 or more and the discomfort as a perception score of 5. Fasting and post-prandial intestinal tone were measured by monitoring colorectal recto-sigmoid volume during a 30-min fasting period and a 60-min period after liquid meal consumption (200 Kcal, 200 mL liquid meal), and the modification of recto-sigmoid volume was calculated (Di Stefano M, et al, Gut 2007).

Results: In comparison with HV, the mean perception threshold was much lower in NCGS and IBS patients (perception; NCGS patients 4.7 ± 3.8 mmHg, IBS patients 4.6 ± 4.4 mmHg, HV 5.3 ± 1.3 mmHg, ANOVA p < 0.001). The mean discomfort threshold was similar in NCGS and IBS patients (NCGS patients 15.6 ± 6.8 mmHg, HV 13.4 ± 6.2 mmHg), but significantly lower than in HV (20.2 ± 2.3 mmHg, ANOVA p < 0.001). The mean fasting recto-sigmoid volume was similar in the three groups of patients (NCGS 138.5 ± 40.5 mL, IBS patients 152.6 ± 43.6 mL, HV 124 ± 23.2 mL, ANOVA p = NS) but significantly lower than in HV both mean post-prandial recto-sigmoid volume and mean percent modification of recto-sigmoid volume were significantly different in NCGS and IBS patients (mean post-prandial volume: self-reported NCGS patients 171 ± 84 mL, IBS patients 188.6 ± 86 mL, HV 75.7 ± 14 mL, ANOVA p < 0.001; mean percent volume modification: NCGS patients +22 ± 26%, IBS +19 ± 40%, HV −39 ± 7%, ANOVA p < 0.0001). The mean percent modification of recto-sigmoid volume was similar in HV, NCGS and IBS patients.

Conclusion: No different was detected in recto-sigmoid sensorimotor activity between self-reported NCGS and IBS. Self-reported NCGS overlaps IBS both in clinical presentation and pathophysiological aspects. Accordingly, NCGS diagnosis should be not performed on the basis of a mere anamnestic evaluation.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP116 RISK OF LYMPHOMAS AND GASTROINTESTINAL CARCINOMAS AFTER A DIAGNOSIS OF CELIAC DISEASE BASED ON A NATIONAL POPULATION-BASED CASE-CONTROL STUDY

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Introduction: Celiac disease (CD) patients are likely at increased risk to develop various malignancies. Relative and absolute risk estimates are essential to provide follow-up recommendations to newly diagnosed CD patients.

Aims & Methods: The aim of this study was to assess the subsequent relative and absolute risk for malignant lymphoma and gastro-intestinal (GI) carcinoma after CD diagnosis in a population-based study. All patients with lymphoma or GI carcinoma (cancers) and melanoma or basal cell carcinoma (controls) diagnosed in the Netherlands between 1994 and 2014 were retrieved through the Dutch nationwide population-based pathology database (PALGA). Within this series, all individuals with histologically confirmed CD before or within 3 months after the date of malignancy diagnosis were identified through linkage to the Dutch CEDOC-2000 database (Di Stefano M, et al, Gut 2007) were determined using logistic regression analysis with corrections for age and gender.

Results: Of 301,424 cases and 576,971 controls, 349 (0.1%) and 282 (0.05%), respectively, were diagnosed with CD. ORs for small bowel adenocarcinoma and esophageal squamous cell carcinoma (SQC) after prior CD diagnosis were 11.9 [95% CI, 8.2–17.2] and 3.5 [95% CI 2.1–5.8]. Adenocarcinoma of the colon, esophagus and stomach and SCC of the anus were not associated with CD history. The OR for T-cell lymphoma after prior CD diagnosis was 35.8 [95% CI, 27.1–47.4], whereas B-cell lymphomas were not associated with CD history. Absolute cumulative risks of T-cell lymphomas reaches the risk of colorectal carcinoma in the general population. However, the most common T-cell lymphoma in CD, enteropathy associated T-cell lymphoma (101 of all 131 T-cell lymphomas in the CD group), was preferentially diagnosed at time of CD diagnosis.

Conclusion: This population-based study is unique by including pathologically confirmed CD. The data suggest strongly increased risk for specific malignancies after CD diagnosis. These results provide a strong motivation and detailed information to develop follow-up guidelines for newly diagnosed CD patients.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP117 THE ROLE OF TMPRSS6 VARIANT RS855791 IN IRON-DEFICIENCY ANAEMIA (IRIDA) IN CELIAC DISEASE

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Disclosure of Interest: None.

Reference:
Aims & Methods: We investigated the prevalence of TMPRSS6 in CD and its role in iron absorption in CD patients treated for IDA. From October 2011 to July 2015 we prospectively assessed the frequency of TMPRSS6 variant rs855791 in both anemic and non-anemic CD patients at time of CD diagnosis. We also estimated the association of this variant with some hematological and iron para-
meters, and found a significant increase in Hb and ferritin at time of diagnosis and after 1-year of gluten-free diet. The prescribed treatment for IDA, both oral or parenteral iron, was recorded in all patients. Statistical analysis was performed by using T-student and X-square test when indicated; all differences were considered significant when p < 0.05.

Results: Finally, 505 CD patients were enrolled: 229 with IDA (45%; mean age 31.2; females 88%), 276 with non-IDA (55%; mean age 32.4; females 66%). The allelic frequencies for A736V mutation of TMPRSS6 variant rs855791 did not differ significantly between anemic (45.4%) and non-anemic CD patients (52.2%) at time of CD diagnosis. At follow-up, TMPRSS6 variant rs855791 was present in 58 out of 104 patients with persistent IDA, being significantly higher than in 125 non-IDA persistent patients (86.4% vs. 56%, p < 0.01). In IDA patients, the presence of one or the other the TMPRSS6 genotype (wild type, heterozygosis, homozygosis) did not influence iron parameters at diagnosis while CD patients with homozygous genotype presented lower hemoglobin, serum iron and transferrin receptor levels than patients with wild type genotype (Hb: 11.5±1.2 vs. 12.4±1.0, p < 0.01; serum iron: 51.1±27.7 vs. 70.4±3.75, p < 0.01; ferritin: 18.7±25.1 vs. 40.4±3.05, p < 0.01) despite their rigorous GFD.

Conclusion: TMPRSS6 variant rs855791 plays a central role in most of CD cases with iron-refractory IDA. TMPRSS6 genotyping appears useful to personalize the management and follow-up of IDA patients.

Disclosure of Interest: All authors have declared no conflicts of interest.

**OP18 SAFETY AND TOLERABILITY, IMMUNOLOGICAL AND INTESTINAL EFFECTS, AND PHARMAECONOMICS (PK) OF DOSE TITRATION PRECEDING MAINTENANCE DOSES OF NEXVAX2® IN HLA-DQ2.5+ CELIAC DISEASE (CED)**


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5ImmusanT, Inc., Cambridge/United States of America/MA

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Introduction: Nexvax2 is a therapeutic vaccine under investigation to protect against effects of gluten in HLA-DQ2.5+ CEd. Nexvax2 includes 3 peptides with dominant HLA-DQ2.5 restricted gluten epitopes. Dose-dependent gastro-
itis lessened, immune activation and Henoch-Schönlein purpura were observed. With increasing plasma cyto-

Mon, October 30, 2017 15:45-17:15
General Hepatology - Room E3

**OP19 HIGH TUMOR RECURRENCE AFTER HEPATITIS C TREATMENT WITH ORAL DIRECT ACTING ANTIVIRALS IN PATIENTS WITH HISTORY OF HEPATOCELLULAR CARCINOMA (HCC) IN COMPLETE REMISSION**

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Introduction: Hepatocellular carcinoma (HCC) represents a serious complication of HCV-related cirrhosis. New direct acting antivirals (DAAs) obtain an HCV eradication rate higher than 90%. However, there is still a high risk of recurrence, according to recent studies of unexpected high rate of tumor recurrence after treatment with DAA.

Aims & Methods: The aim of this study is to evaluate the early recurrence of HCC in patients treated with DAA and the risk factors associated. We analyzed 154 patients with chronic liver disease and HCC, of which 27 were due to HCV infection and were in complete radiologic tumor remission after treatment. All of them were treated with DAAAs, and followed up for an average of 20 months since remission. The inclusion criteria were: 1. HCC diagnosed by pathology or non-invasive criteria according to American Association for the Study of Liver Diseases (AASLD) guidelines; 2. Complete response following treatment; 3. Treatment with DAA confirmed sustained virological response (SVR). At least one tumor status assessment after starting antiviral therapy Control computed tomography (CT) and blood tests were performed in three months according to the protocol of our centre.

Results: Recurrence of HCC was detected in 51.9% of patients (14 of 27 patients) in a median follow-up of 24 months. All of them achieved sustained virological response. Having less than 1 cm size, non-specific nodules in control CTs is associated with a higher recurrence (p=0.001; OR 15.9; 95% CI: 2.02-111.17). The median time to recurrence was 17.3 months since tumour remission. Previous HCV treatment with therapies based on interferon was associated with lower risk of recurrence; although these results are not statistically significant, they tend to be significant (p=0.18; OR 0.347, 95% CI: 1.07-1.65). Regarding the type of antiviral treatment, there were no recurrences in the sofosbuvir plus simeprevir group. On the other hand, all patients treated with the combination of sofosbuvir and daclatasvir experienced tumor recurrence during the follow-up period, and this was statistically significant in the univariate analysis (p=0.005).

However, age, sex, Child-Pugh class, cardiovascular risk factors, HCC treatment, single tumor and HCV genotype were not significantly associated with HCC development. The main characteristics of the cohort are described in table 1.

<table>
<thead>
<tr>
<th>Total cohort (n=27)</th>
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<tbody>
<tr>
<td>Age, mean (SD) (yr)</td>
</tr>
<tr>
<td>Gender, (M/F), n (%)</td>
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<tr>
<td>High blood pressure, n (%)</td>
</tr>
<tr>
<td>Diabetes Mellitus, n (%)</td>
</tr>
<tr>
<td>Child-Pugh, A/B/C, n (%)</td>
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<tr>
<td>BCLC stage, A/A, n (%)</td>
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<tr>
<td>AFP, median (range) (ng/ml)</td>
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<td>Bilirubin, median (range) (mg/dl)</td>
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<tr>
<td>Albumin, median (range) (g/L)</td>
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<tr>
<td>Platelets, median (range) (U/L)</td>
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(continued)
OP120 BRG1 POSITIVELY REGULATES LIVER REGENERATION AFTER PARTIAL HEPATECTOMY IN MICE

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Introduction: The SWI/SNF complex is a chromatin-remodelling complex that modifies chromatin structure in order to regulate gene expression. Brahma-related gene-1 (BRG1), a catalytic subunit of the SWI/SNF complex, is known to be involved in proliferative cell processes. Liver regeneration is activated spontaneously after injury and organized based on a strong proliferation rate. Up to the present, little is known on how BRG1 orchestrates liver regeneration.

Aims & Methods: The aim of the study was to investigate the role of BRG1 in liver regeneration following partial liver resection in mice. We used a hepatocyte-specific BRG1 gene knockout mouse model performing a 70% partial hepatectomy. The expression of BRG1 was markedly upregulated after partial hepatectomy compared to wildtype mice. We found that the expression of BRG1 was markedly upregulated after partial hepatectomy compared to wildtype mice.

Conclusion: We found that the expression of BRG1 was markedly upregulated after partial hepatectomy compared to wildtype mice. A highly active proliferation was observed in the hepatocytes of wildtype mice post PH while fewer was observed in BRG1 specific knockout mice 48 h post operation. A highly active proliferation was observed in the hepatocytes of wildtype mice post PH while fewer was observed in BRG1 specific knockout mice 48 h post operation.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
3. DAA combination, n (%) SOF/LDV 63.7 14.8
4. 3D SOF/DCV SOF/SMV 18.5
5. HCC treatment before DAA, n (%) 18.5
6. Resection Ablation (RF) TACE 14.8
7. Single tumor/various tumors, n (%) 81.5
8. Tumor size, median (range) (cm) 2.69 (2–3)

Disclosure of Interest: All authors have declared no conflicts of interest.

References

Introduction: Hepatic resection is one of the best curative treatments in well-selected patients with hepatocellular carcinoma (HCC) and cirrhosis. The risk of decompensation after resection has major impact over the outcome of these patients. Portal hypertension is the main risk factor for decompensation and it is still a matter of debate which is the best method to identify patients at risk.

Aims & Methods: The aim of the study was to compare different methods for risk assessment in patients with HCC submitted to hepatic resection. Since January 2016 94 consecutive patients were diagnosed with HCC and were prospectively registered. Thirty-three patients were submitted to hepatic resection and among them: 22 were screened for esophageal varices (EV), 13 patients were evaluated by hepatic venous pressure gradient (HVPG) and 18 by transient elastography.

Conclusion: Among the 33 included patients, 8 (24%) had EV, 6 (18%) had clinical significant portal hypertension (HVPG > 10 mmHg) and 9 (27%) had platelet count < 100,000/mmc. During follow-up 12 (36%) patients presented decompensation (3 variceal bleeding, 7 ascites, 6 renal dysfunction and 1 jaundice). In univariate analysis, HVPG, liver stiffness, platelet count, ALT and AST were associated with decompensation. Neither presence of EV (40% correctly classified, p = 0.13) or platelet count < 100,000/mmc (64% correctly classified, p = 0.08) were accurate enough to predict decompensation. Presence of CSPH assessed by HVPG correctly classified 92% of patients (p = 0.002). There was no difference between HVPG and transient elastography regarding the performances (AUROC) for predicting decompensation, 0.91 (95% CI: 0.74–1, p = 0.012) and 0.93 (95%CI: 0.80–1, p = 0.007), respectively.

Disclosure of Interest: All authors have declared no conflicts of interest.
Aims & Method: In the current study, we assessed the therapeutic potential of REIC/Dkk-3 gene therapy using Ad-SEG-REIC in hepatocellular carcinoma (HCC). Human HCC cell lines (HLE, Huh7, and HepG2), human HCC tissues, and mouse HCC cell line (Hepa-1) were used in this study. REIC/Dkk-3 expression was assessed by immunoblotting and immunohistochemistry. The relative cell viability and the apoptotic effect were examined by MTT assay and Hoechst staining, respectively. The protein expression of IRE1α, JNK, c-Jun, and caspase-3 was assessed by immunoblotting using specific antibodies. The anti-tumor effects of Ad-SEG-REIC treatment were analyzed in the mouse xenograft model with Huh7 cells. Furthermore, we assessed anti-tumor immunological effects in the immunocompetent mice.

Results: REIC/Dkk-3 expression was decreased in HCC cell lines and HCC tissues. Ad-SEG-REIC treatment markedly reduced cell viability in HCC cell lines and the reduction rate for HLE, Huh7, and HepG2 were 87.2%, 76.3%, and 36.4%, respectively. Hoechst 33342 staining demonstrated the rate of apoptosis in the cells treated with Ad-SEG-REIC (HLE; 64.9%, Huh7; 66.8%, HepG2; 40.1%). Ad-SEG-REIC treatment mediated cancer selective apoptosis due to ER stress mainly through the activation of JNK pathway. Ad-SEG-REIC treatment suppressed tumor growth by 68.7% in comparison with the control in the mouse xenograft model. Moreover, the lymphocytes isolated from immunocompetent mice treated with Ad-SEG-REIC demonstrated higher cytotoxicity against the target cancer cells than those from the control mice (253.5%).

Conclusion: Ad-SEG-REIC treatment not only enhanced cell-killing effects in vitro but also elicited significant therapeutic effects in vivo. REIC/Dkk-3 gene therapy using Ad-SEG-REIC potentially represents an innovative new therapeutic tool for HCC.

Disclosure of Interest: M. Watanabe: Okayama University and Momotaro-Gene Inc., a startup biotech company from the Okayama University, holds the patents of the Ad-REIC agent and develops the agent as a cancer therapeutic medicine. M.W. own stocks in Momotaro-Gene, Inc. M. Sakaguchi: Okayama University and Momotaro-Gene Inc., a startup biotech company from the Okayama University, holds the patents of the Ad-REIC agent and develops the agent as a cancer therapeutic medicine. M.S. own stocks in Momotaro-Gene, Inc. Y. Nasu: Okayama University and Momotaro-Gene Inc., a startup biotech company from the Okayama University, holds the patents of the Ad-REIC agent and develops the agent as a cancer therapeutic medicine. Y.N., and own stocks in Momotaro-Gene, Inc. H. Kumon: Okayama University and Momotaro-Gene Inc., a startup biotech company from the Okayama University, holds the patents of the Ad-REIC agent and develops the agent as a cancer therapeutic medicine. H.K. own stocks in Momotaro-Gene Inc.

All authors have declared no conflicts of interest.

OP123 EFFECT OF INTERFERON-FREE DIRECT-ACTING ANTIVIRAL THERAPY FOR HEPATITIS C VIRUS IN THE CARDIAC CONDUCTION SYSTEM
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Introduction: Combinant use of sofosbuvir and Amiodarone has been associated with cases of atrioventricular block and symptomatic bradycardia (1-2), therefore such combination is not recommended. In addition, it has been recently suggested that there is QT interval prolongation in the first weeks of treatment without the combination with Amiodarone (3).

Aims & Methods: Our study aims to confirm if there is a prolongation of QT interval during treatment with Sofosbuvir and other antivirals, to study whether this alteration persists after treatment and to investigate other possible alterations in the cardiac conduction system. We accomplished a prospective study in which a baseline electrocardiogram (ECG), before starting treatment, and another electrocardiogram (at the fourth week) were performed on hepatitis C patients undergoing Interferon-free antiviral therapy between April 2016 and April 2017 in Hospital Clínico San Carlos (Madrid). Moreover, in some patients a third ECG was performed in the twelfth week after treatment. Heart rate and duration of PR, QRS, QT and corrected QT intervals (QTc) were measured. A paired Student’s T test was applied to compare the variables before and during treatment, and before and after treatment in the subgroup of patients with the third ECG.

continued

OP124 NON-ALCOHOLIC STEATOHEPATITIS IS THE MOST RAPIDLY GROWING INDICATION FOR LIVER TRANSPLANTATION IN IRANIAN PATIENTS
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Introduction: Non-alcoholic fatty liver disease (NAFLD) is a rapidly growing disease and is supposed to be the most common cause of abnormal liver enzymes worldwide. A considerable proportion of NAFL patients will progress to non-alcoholic steatohepatitis (NASH) that is anticipated to become the most common cause of liver cirrhosis and liver transplantation in next 20 years. Iran has been located in the Middle East with a high prevalence of NAFLD.

Aims & Methods: This study aimed to investigate the incidence and trend of NASH as an indication for liver transplantation in Iranian patients. The liver transplant data of all patients who had undergone liver transplantation between 1993 and 2016 at Shiraz Organ Transplant Center, Shiraz, Iran were reviewed. The underlying liver diseases leading to liver transplantation were stratified according to the years of transplantation and trend of increase or decline were calculated. Data regarding post-transplant mortality of patients with biopsy proven NASH were recorded. Patients with cryptogenic liver cirrhosis with body mass index ≥30kg/m² was defined as modified NASH. Kaplan-Meier
Gastric gas infusion was associated to a minor increment in abdominal perception of healthy controls (1.0 ± 0.5 score increment). By contrast, patients with functional dyspepsia developed significant perception of epigastric symptoms during gas infusion (2.5 ± 0.6 score increment; p < 0.05 vs controls) whereas patients with a belching disorder develop no epigastric perception (0.9 ± 0.2 score increment; NS vs sham p = 0.05 vs functional dyspepsia) despite the lower rectal gas evacuation associated to increased belching.

Conclusion: Patients with specific gastroduodenal disorders exhibit different responses to increments in gastric gas. Whereas in patients with functional dyspepsia belching is exceptional and a minor increment in gas may induce epigastric symptoms, increased belching in response to gastric gas seems to prevent epigastric symptoms in patients with a belching disorder.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP126 INTRAGASTRIC FRUCTOSE INFUSION AND EMOTIONAL STATE INTERACT IN HOMEOSTATIC AND HEDONIC BRAIN REGIONS
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Introduction: Exeroceptive properties of food such as taste or smell can influence a person’s emotional state and its neural basis. However, purely interoceptive properties of food can also affect emotional state, since behavioral and neural responses to sad emotion induction were attenuated by fatty acid infusion (Van Oudenhove et al., 2011). Whether this also applies to other nutrients, including carbohydrates, remains unknown.

Aims & Methods: We aimed to study the effect of intragastric fructose administration compared to placebo, and its interaction with the effect of sad emotion induction, on brain activity in homeostatic and hedonic regions and on circulating levels of the anorexigenic hormone GLP-1. Fifteen healthy subjects were studied after an overnight fast. Brain activity before and up to 40 min after intragastric infusion of fructose (25 g) or distilled water (placebo) was recorded using functional magnetic resonance imaging. Sad or neutral emotional states were induced using a combination of playback of validated classical music pieces and projection of emotional facial expressions. Emotional state was assessed every 10 min using the Self-Assessment Manikin. Blood samples were taken at the same time points. Plasma levels of GLP-1 were analyzed using Meso Scale Discovery immunoassay kits. Brain responses to fructose versus placebo, sad versus neutral emotion, and their interaction were analyzed over time in a priori defined regions of interest (ROI) at a voxel-level threshold of P<0.05 vs controls and dyspepsia. Similar effects on emotional ratings and GLP-1 levels were tested using linear mixed models.

Results: We did not observe significant main effects of nutrient and emotion, and no significant nutrient-by-emotion interaction effect, on emotional ratings. However, significant main effects of fructose, emotional state, and a significant nutrient-by-emotion interaction effect on brain responses in pre-hypothesized ROIs, including the medulla, midbrain, hypothalamus, basal ganglia, anterior insula, orbitofrontal cortex and amygdala were found (see Table 1). A trend towards an interaction between emotional state and nutrient was also observed on GLP-1 levels. Specifically, the increase in circulating levels of GLP-1 after fructose administration in the neutral emotion condition was abolished in the sad emotional state (p = 0.06).

Table 1. Regions of interest where significant main effects of emotion and nutrient and a significant nutrient-by-emotion interaction were observed

<table>
<thead>
<tr>
<th>region of interest</th>
<th>main effect of nutrient</th>
<th>main effect of emotion</th>
<th>nutrient-by-emotion interaction effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>medulla</td>
<td>V</td>
<td>V</td>
<td>V</td>
</tr>
<tr>
<td>midbrain</td>
<td>V</td>
<td>V</td>
<td>V</td>
</tr>
<tr>
<td>hypothalamus</td>
<td>left</td>
<td>V</td>
<td>V</td>
</tr>
<tr>
<td></td>
<td>right</td>
<td>V</td>
<td>V</td>
</tr>
<tr>
<td>pallidum</td>
<td>left</td>
<td>V</td>
<td>V</td>
</tr>
<tr>
<td></td>
<td>right</td>
<td>V</td>
<td>V</td>
</tr>
<tr>
<td>putamen</td>
<td>left</td>
<td>V</td>
<td>V</td>
</tr>
<tr>
<td></td>
<td>right</td>
<td>V</td>
<td>V</td>
</tr>
<tr>
<td>caudate body</td>
<td>left</td>
<td>V</td>
<td>V</td>
</tr>
<tr>
<td></td>
<td>right</td>
<td>V</td>
<td>V</td>
</tr>
<tr>
<td>caudate head</td>
<td>left</td>
<td>V</td>
<td>V</td>
</tr>
<tr>
<td></td>
<td>right</td>
<td>V</td>
<td>V</td>
</tr>
<tr>
<td>anterior cingulate cortex</td>
<td>left</td>
<td>V</td>
<td>V</td>
</tr>
<tr>
<td></td>
<td>right</td>
<td>V</td>
<td>V</td>
</tr>
<tr>
<td>medial orbitofrontal cortex</td>
<td>left</td>
<td>V</td>
<td>V</td>
</tr>
<tr>
<td></td>
<td>right</td>
<td>V</td>
<td>V</td>
</tr>
<tr>
<td>lateral orbitofrontal cortex</td>
<td>left</td>
<td>V</td>
<td>V</td>
</tr>
<tr>
<td></td>
<td>right</td>
<td>V</td>
<td>V</td>
</tr>
<tr>
<td>anterior insula</td>
<td>left</td>
<td>V</td>
<td>V</td>
</tr>
</tbody>
</table>

(continued)
Conclusion: Emotional state interacts with brain and endocrine responses to intragastric infusion of 25 g of fructose; however, such an effect was not found at the behavioural level.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP127: DDP-4 INHIBITOR, VILDAGLIPTIN INHIBITS GASTRIC ACCOMMODATION AND FOOD INTAKE IN HUMANS

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Introduction: Glucagon-like peptide 1 (GLP-1), an endogenous modulator of gastrointestinal motility and food intake, is inactivated by dipeptidyl peptidase-4 (DPP-4). Administration of DPP-4 inhibitor vildagliptin can amplify endogenous GLP-1 effects.

Aims & Methods: The objectives were to assess the effect of vildagliptin on gastric accommodation, measured as the intragastric pressure (IGP) during intragastric nutrient infusion and food intake in humans in 2 protocols, each including 10 healthy volunteers (HV). Hunger, satiation and epigastric symptoms (fullness, nausea, bloating, belching, pain, cramps) were assessed using a visual analogue scale (VAS). In Protocol 1, an infusion catheter and a high-resolution manometry probe were positioned in the proximal stomach. HVs took vildagliptin (50 mg) or placebo orally in a randomized single-blind fashion, followed by an intragastric nutrient drink (ND) for the duration of 30 min. Blood was collected before the drug administration, before and after the ND and before the buffet.

Conclusion: Vildagliptin inhibits gastric accommodation and decreases food intake in healthy lean volunteers. The observed effect could be due to the inhibition of GLP-1 degradation.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP128: RELAMORELIN IN PATIENTS WITH DIABETIC GASTROPARESIS: EFFICACY AND SAFETY RESULTS FROM A PHASE 2B RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED, 12-WEEK STUDY (RM-131-009)

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Introduction: Gastroparesis is a serious complication of diabetes mellitus (DM) with few treatment options. Relamorelin (RM) is a selective ghrelin agonist with potent prokinetic properties.

Aims & Methods: The aim was to evaluate the efficacy of RM on symptoms and gastric emptying (GE) in patients with moderate-to-severe diabetic gastroparesis in a 12-week, randomised, double-blind, placebo (PBO)-controlled, parallel-group study, with a 2-week single-blind PBO run-in. Eligible DG patients had 1,3-C-spirulina GE breath test (GEBT) T1/2 values ≥79 min, a history of recent vomiting and a Gastroparesis Cardinal Symptom Index score ≥2.6. Patients were randomised to twice daily subcutaneous injections of PBO or RM: 10 µg, 30 µg or 100 µg. Patients completed the Diabetic Gastroparesis Symptom Severity Diary (DGSSD), a daily e-diary designed to collect patient-reported vomiting frequency and symptoms of nausea, abdominal pain, satiety, post-prandial fullness (PPF) and bloating on a 0–10 severity scale. The primary endpoint was change from baseline in vomiting frequency; a key secondary endpoint was change from baseline in vomiting frequency; an exploratory endpoint was change from baseline in nausea score. A key secondary endpoint was change from baseline in vomiting frequency; an exploratory endpoint was change from baseline in nausea score.

Results: A total of 393 DG patients (male: 37.7%; age: 57.0 ±11.3 years; body mass index: 32.4 ±7.3 kg/m²; mean HbA1c: 7.7 ±1.4%; Type 1 DM: 9.9%) were randomised at clinic sites in the US, Israel and Europe. RM led to ~75% reduction in vomiting frequency compared to placebo (primary endpoint) across all doses tested; however, no significant difference was observed due to a high PBO response (~70% reduction from baseline). RM demonstrated substantial efficacy: DG symptoms improved vs placebo for all three RM doses for the overall 12-week study period, indicated by the reduction in the composite score (Table). All three doses of RM tested also accelerated GE compared to PBO (Table). (GEBT) T1/2 scores improved by a mean of ~13.3±8 min with RM compared to placebo (0±38 min). RM was generally safe and well tolerated with high compliance and study completion rates. Worsening of glycaemic control was noted as an adverse event in 14.5% of RM patients, with some patients requiring adjustment of insulin dosage.

Table: Change from baseline to Week 12 in DGSSDa and GEBTb

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Placebo</th>
<th>RM 10 µg BID</th>
<th>RM 30 µg BID</th>
<th>RM 100 µg BID</th>
</tr>
</thead>
<tbody>
<tr>
<td>BID (n=88)</td>
<td>(n=86)</td>
<td>(n=91)</td>
<td>(n=63)</td>
<td></td>
</tr>
<tr>
<td>DGSSD</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline, mean ± SD</td>
<td>22.7 ± 7.3</td>
<td>22.7 ± 7.9</td>
<td>22.4 ± 6.7</td>
<td>24.0 ± 7.5</td>
</tr>
<tr>
<td>Week 12, mean ± SD</td>
<td>17.1 ± 8.8</td>
<td>14.0 ± 10.3</td>
<td>13.8 ± 9.6</td>
<td>14.2 ± 9.5</td>
</tr>
<tr>
<td>Change from baseline, mean ± SD</td>
<td>−5.6 ± 148.3</td>
<td>−8.7 ± 9.0</td>
<td>−8.7 ± 9.0</td>
<td>−9.7 ± 8.8</td>
</tr>
<tr>
<td>LS mean difference vs PBO</td>
<td>−1.85</td>
<td>−2.34</td>
<td>−2.57</td>
<td></td>
</tr>
<tr>
<td>p valuec</td>
<td>0.134</td>
<td>0.053</td>
<td>0.052</td>
<td></td>
</tr>
<tr>
<td>GEBT</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline, mean ± SD</td>
<td>127.1 ± 36.5</td>
<td>126.8 ± 37.6</td>
<td>128.6 ± 35.9</td>
<td>133.6 ± 35.4</td>
</tr>
<tr>
<td>Week 12, mean ± SD</td>
<td>126.3 ± 39.8</td>
<td>112.8 ± 43.5</td>
<td>115.8 ± 45.7</td>
<td>118.0 ± 49.5</td>
</tr>
<tr>
<td>Change from baseline, mean ± SD</td>
<td>−0.8 ± 38.5</td>
<td>−12.7 ± 38.1</td>
<td>−12.8 ± 36.5</td>
<td>−13.6 ± 40.5</td>
</tr>
<tr>
<td>LS mean difference vs PBO</td>
<td>−12.93</td>
<td>−12.12</td>
<td>−12.04</td>
<td></td>
</tr>
<tr>
<td>p valuec</td>
<td>0.023</td>
<td>0.028</td>
<td>0.051</td>
<td></td>
</tr>
</tbody>
</table>

Full analysis set (Nausea, PPF, abdominal pain, bloating; composite score in total numeric points); 2 (GEBT T1/2): Two-sided p value from longitudinal, mixed-effects model with repeated measures, including fixed effects for treatment, week and treatment-by-week interaction, as well as baseline and baseline-by-week interaction values as the covariates, with unstructured variance-covariance correlation matrices being common to all subjects for the repeated measures over treatment weeks.

Conclusion: RM demonstrated clinically meaningful reductions in core DG symptoms and overall composite score, accelerated GE, and was generally safe

Notes:
- GLP-4 (7-36) pg/ml
- Placebo vs Vildagliptin
- p-value
- Before drug
- Before ND
- After ND
- Before buffet
- Conclusion: Vildagliptin inhibits gastric accommodation and decreases food intake in healthy lean volunteers. The observed effect could be due to the inhibition of GLP-1 degradation.

Disclosure of Interest: All authors have declared no conflicts of interest.
and well tolerated. A high PPO response limited the ability to show efficacy of RM at the paediatric clinical description frequency endpoint.

Disclosure of Interest: M. Camilleri: Received research grant to study pharmacology of colamin. R.W. McCallum: Received research funding to study colamin, consulted with Allegan plc. S. Kahrilas: Evoke Pharma and Synergy Pharm, and received funding for clinical research trials from Salix Pharmaceuticals, Evoke Pharma, Theravance Biopharma and Vanda Pharma.

Aims & Methods: This study presents a four-year experience of the PPOD service, including clinical description, diagnostic criteria and CIPO population captured by it. This is a retrospective analysis of patients admitted within the PPOD service, between 04.2012 and 12.2016, with a suspected diagnosis of CIPO. The ultimate diagnosis of CIPO was confirmed on the presence of at least 2 out of 4 of the following criteria (intestine or oesophagus segment with small intestinal neuromuscular involvement; 2) radiological evidence of recurrent and/or persistently dilated loops of small intestine with air fluid levels; 3) presence of the genetic, metabolic or other conditions definitively associated with CIPO; and 4) intestinal transit cannot be maintained adequate growth on oral feeding alone (need for specialized feeds and/or enteral/ intravenous route for feeding). Clinical data, including age of onset of symptoms, dominant symptoms, results of the ADM investigations, surgical procedures, feeding history, neo-gastrointestinal drainage and histology results of full thickness biopsies from the small intestine, were analyzed.

Results: Out of 113 children referred to the PPOD Service, 50 were definitively diagnosed with CIPO (26 girls), with median age at symptoms of onset of 5 months (range: birth to 18 months). 50% of patients were born prematurely, 40 children (83.3%) presented with first symptoms below first year of life. Median age at assessment was 45 months in the first half-time of service (32/50) and 35.5 months in the second half (18/50). Based on the ADM results, the majority of patients diagnosed with CIPO had patterns consistent with neuropathic involvement (n = 35), 2 with myopathy and 4 with both, neuropathy and myopathy. In 10 patients diagnosis of CIPO was based on clinical criteria. 46% of children had dominant upper gastro-intestinal (GI) tract presentation (nausea, vomiting, gastro-oesophageal reflux, feeding intolerance), 40% presented with lower GI tract symptoms (abdominal pain, abdominal distension, constipation). 29 children (58%) underwent colonomcy, and majority of them (55%) showed colonic myopathy. Out of children with CIPO, 34 patients (80%) underwent small bowel resection to eliminate performed, 9 (18%) had total colectomy and 1 patient ultimately underwent multi-velo-visceral transplantation. 35/50 patients had full thickness biopsy of small bowel. In 20-35 cases (57%) no histological abnormalities could be identified. Total parenteral nutrition (TPN) was required by 48% of children (23/48), 10 patients were on full enteral feeds; 4 patients remained on oral feeding.

Conclusion: Over the first four years of the UK national PPOD service, we observed a significant increase of CIPO diagnosis in children. The establishment of the UK service was established (2.4 patients/year; Henyeke et al 1999) with a trend towards decreasing age at first assessment (3.3 vs 13.3 years pre 2012, data not shown). This suggests that the national service not only appears effective in capturing more of the UK CIPO population but is making a difference in diagnosis earlier. The latter is especially important given the majority of patients presented with the onset of the first symptoms under 1 year of age and progress quickly to dependency on total parenteral nutrition. The majority of our patients underwent colostomy formation as the first gastro-intestinal intervention, and diagnosis was based on exclusion and/or persistently dilated loops of small intestine with air fluid levels; (3) presence of the genetic, metabolic or other conditions definitively associated with CIPO. We are now assessing whether early diagnosis and definitive intervention improves mid and long-term outcomes, including reduced morbidity, mortality, healthcare utilization costs and better tolerance of enteral feeding. The development of national CIPO registries and services is likely to be of benefit to improving early definitive diagnosis, expertise in management and ultimately outcomes of CIPO.

Disclosure of Interest: All authors have declared no conflicts of interest.
OP132 BALLOON-ASSISTED ENDOSCOPY FACILITATES ENDOSCOPIC SUBMUCOSAL DISSECTION OF COLONOSCOPICALLY DIFFICULT SUPERFICIAL RIGHT COLON TUMORS
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2Shishinoki Medical Clinic, Tochigi/Japan
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Introduction: Colorectal endoscopic submucosal dissection (ESD) is a standard technique in Japan. However, colorectal ESD can be technically difficult in some situations such as paradoxic movement of the right colon. The double-balloon endoscope was introduced here, as a pioneering technique for balloon-assisted endoscopy, which provides stable endoscopic maneuvering even in the small intestine. Stable maneuverability can overcome the difficulties of colorectal ESD in the right colon.
Aims & Methods: The aim of this study is to assess the outcomes of balloon-assisted endoscopic submucosal dissection (BAESD) of colonoscopically difficult superficial right colon tumors. We retrospectively reviewed the records of patients who underwent BAESD of superficial right colon tumors where colono-scopic difficulties were encountered, from January 2011 to September 2016. Difficulties were defined as a previous incomplete colonoscopy using a conventional colonoscope or unstable endoscopic maneuverability around the tumor with conventional colonoscopy. A propensity score model was used as a secondary analysis to compare outcomes of the BAESD group to a group without difficulties.
Results: BAESD was performed on 67 tumors in 63 patients. There were 10, 22, and 35 tumors in the cecum, ascending colon and transverse colon, respectively. The median tumor size (range) was 31 (20–123) mm. The median (range) procedure time was 65 (35–382) minutes, and the median (range) dissection speed was 18.0 (4.4–71.4) mm2/minutes. In loco resection was achieved for 66 tumors (99%) and an R0 resection was achieved for 58 tumors (87%). No perforations occurred. Two patients (3.0%) had delayed postoperative bleeding treated by endoscopic hemostasis. Propensity score-matching analysis created 65 matched groups until 3 years. These findings demonstrate that ESD is an effective treatment for elderly patients with superficial esophageal cancer, at least in the short-term.
Disclosure of Interest: All authors have declared no conflicts of interest.

TUESDAY, OCTOBER 31, 2017 08:30-10:00 DETECTION AND REMOVAL OF COLORECTAL POLyps: LATEST TECHNIQUES - ROOM A3
OP133 AUTOMATIC POLYP DETECTION IN COLONOSCOPY PROCEDURE USING DEEP LEARNING AND IMAGE PROcessING TECHNIQUES
D. Zur, M. Zaltzhendler
Magnetiq Eye, Haifa/Israel
Contact E-mail Address: dror@magentiq.com
Introduction: It is estimated that 40 million colonoscopy procedures are performed every year (almost 40% in the US alone). The ability of colonoscopy procedures to decrease the number of colon cancer cases has been proven without a doubt and their number is expected to grow. However, research has shown that only 90% of polyps are detected in these procedures, misses which can, unfortunately, cause interval cancer. At Magnetiq Eye we put the growing power of Deep Learning, and of Image and Video Processing, to the help of doctors to reduce the miss rate in the colonoscopy procedures. Our first product the APDS is an Automatic PolyP Detection System, developed to be used in online and offline colonoscopies. The APDS-RT runs on the video feed from the endoscopic camera used by the physician in real time during the colono-scopy procedure and signs the polyp location as a contour in an overlay on the video. Afterwards, the physician can select the location of the polyp (colored contour) of the polyp location in each frame. We aimed at this phase to measure the performance of the prototype when running over the recorded videos. We used 63 video sequences of about half minute each to train the system, and additional 63 video sequences of about half minute each to test the training process, and tested the system which includes the trained model and additional image processing analysis techniques over 10 sequences of half minute each. The total database (training, validation and testing) included 46, 531 video frames and about 90 different polyps. We have measured, over the test videos, the FROC curve (True Positive Rate vs False Positive Per Frame) which was produced by changing a threshold parameter in the system, and the IoU (Intersection over Union) signal to the system prediction region with the ground truth region) against changing the same threshold parameter of the system. The FROC was calculated over all the frames of the test database, and over subset of it which is all the frames from the test database which included ground truth polyps. In addition, the change of the False Positive Per Frame value against the system threshold parameter over a subset of the test frames (all the frames which didn’t include polyps) was calculated. The IoU was calculated mainly over a subset which is all the frames which included polyps or producing polyp frames.
Results: The best point of the FROC was 74% Detection Rate (TPR) vs. 0.07 False Positive Per Frame (FPPF) when calculated over all the frames, and 74% TPR vs. 0.05 FPPF when calculated over the subset of all the frames with ground truth polyps. For the system threshold which was used to select this working point, the FPPF over the subset of all frames without ground truth polyps was 0.05, and the average IoU value over all frames with ground truth or predicted polyps was 0.3. Increasing the system threshold would decrease the TPR, the FPPF, and the IoU, but would also decrease dramatically the FPPF over the subset of all frames without ground truth polyps.
Conclusion: We expect the system performance to be improved as it is exposed to more data in the training phase, in the sense that it would be able to choose a better working point (TPR vs. FPPF) on the same testing dataset, as well as to keep this working point as the testing dataset is increased, and also to get a better IoU value which is a quite good reference to the quality of the segmentation (depicting the polyp region) of the polyps. We can also see that we always have the possibility to increase the system threshold, and thus getting somewhat worse working point for all the frames or the frames with ground truth polyps, but earning dramatically less FPPF in the frames without ground truth polyps, and this is an important advantage since it would reduce the physician distraction during those frames.
Disclosure of Interest: D. Zur: CEO and R&D manager of my affiliation (Magnetiq Eye LTD), M. Zaltzhendler: Senior Researcher and Developer in my affiliation (Magnetiq Eye LTD).
Reference

OP134 IMPROVED DETECTION OF RIGHT-SIDED ADENOMAS BY G-EYE® COLONOSCOPY IN PATIENTS UNDERGOING COLORECTAL CANCER SCREENING-A PROSPECTIVE, RANDOMIZED, MULTICENTRE STUDY
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2Division Of Gastroenterology, Department Of Medicine, Jichi Medical University, Shimotsuke, Japan, Yakushiji/Japan
3Surgery, Jichi Medical University, Shimotsuke, Japan, Yakushiji/Japan
4Dept. Of Gastroenterology, Jichi Medical University, Shimotsuke/Japan
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Introduction: Colorectal endoscopic submucosal dissection (ESD) is a standard technique in Japan. However, colorectal ESD can be technically difficult in some situations such as paradoxical movement of the right colon. The double-balloon endoscope was introduced here, as a pioneering technique for balloon-assisted endoscopy, which provides stable endoscopic maneuvering even in the small intestine. Stable maneuverability can overcome the difficulties of colorectal ESD in the right colon.
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Conclusion: Our study shows that G-EYE Flat lesions detected by the distal end of a standard endoscope. Upon withdrawal, inflation of the G-EYE balloon to a partial pressure results in the centralization of endoscope optics, reduction in bowel slippage, and flattening of colon topography. The enhanced visualization provided by the G-EYE balloon can result in an increase in detection of lesions.

Aims & Methods: In this prospective, randomized, multicentre study, patients (age >50) referred to colonoscopy as a result of screening, surveillance, positive FOBT or change in bowel habits were randomized to either standard colonoscopy (SC) or G-EYE colonoscopy. Detected lesions were removed and sent for pathology. We compared the detection rates of G-EYE colonoscopy with that of SC in the right colon.

Results: 1,000 patients enrolled in the study, of which 498 underwent SC and 502 underwent G-EYE colonoscopy. Baseline parameters were similar in both groups. The right colon was defined as the cecum, ascending colon, and hepatic flexure. Results are presented in Table 1. In addition, the G-EYE increased the detection of both advanced and large-size adenomas by 40% in the right colon.

Table 1: Results summary
<table>
<thead>
<tr>
<th># of Findings in the Right Colon</th>
<th>Standard Colonoscopy</th>
<th>G-EYE Colonoscopy</th>
<th>% increase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polyps</td>
<td>121</td>
<td>223</td>
<td>84.3%</td>
</tr>
<tr>
<td>Adenomas</td>
<td>87</td>
<td>194</td>
<td>94.3%</td>
</tr>
<tr>
<td>Sessile serrated adenomas</td>
<td>2</td>
<td>17</td>
<td>750%</td>
</tr>
<tr>
<td>Flat lesions</td>
<td>22</td>
<td>54</td>
<td>145.5%</td>
</tr>
</tbody>
</table>

Conclusion: Our study shows that G-EYE colonoscopy has the potential to significantly improve the quality of CRC screening through improved adenoma detection rates. Special attention should be given to the significant increase in right-sided flat lesions and sessile serrated adenomas by the G-EYE, as these lesions are strongly attributed to CRC. Through improved detection of these right-sided lesions, G-EYE colonoscopy can impact the quality of CRC screening by reducing miss rates and consequently reduce the incidence of interval cancers.

Disclosure of Interest: H. Jacob: Board member
All other authors have declared no conflicts of interest.

OP135 A STANDARDIZED IMAGING PROTOCOL IS ACCURATE FOR THE ENDOSCOPIC PREDICTION OF DYSPLASIA WITHIN Sessile SERRATED POLYPS

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Introduction: Dysplasia within sessile serrated polyps (SSP) is difficult to detect, may be mistaken for an adenoma, risk incomplete resection of the background serrated tissue and is strongly implicated in interval cancer after colonoscopy. The use of endoscopic imaging to detect dysplasia within SSP has not been systematically examined.

Aims & Methods: We aimed to establish whether a standardized imaging protocol was accurate for the endoscopic prediction of dysplasia within sessile serrated polyps. Consecutively detected SSP >8 mm in size were evaluated using a standardized imaging protocol at a tertiary endoscopy centre over 3 years. Lesions suspected as SSP were analysed with high-definition white light (HDWL) then narrow band imaging (NBI). Lesions were considered as SSP when the following features were identified: mucous cap, cloud-like or finely nodular surface, indistinct border, irregular shape and lesion paler than the surrounding mucosa (under NBI). A demarcated area of neoplastic pit pattern (Kudo type III/IV, NICE type II) was sought amongst the serrated tissue. If this was detected the lesion was labelled dysplastic (SSP-D), if not it was labelled non-dysplastic (SSP-ND). Histopathology was reviewed by two blinded specialist gastrointestinal pathologists. Since histopathology is an imperfect gold standard to determine dysplasia within SSP (dysplastic areas can be small and may be missed between tissue sections, destroyed in tissue processing or not retrieved), at the end of the study a structured discussion between endoscopists and histopathologists was undertaken to assign the final determination of dysplasia. Agreement of all parties was required on the final determination.

Results: 141 suspected SSP were assessed in 83 patients. Median lesion size was 15.0 mm (interquartile range 10-20) and 54.6% were in the right colon. All 141 lesions suspected as SSP were confirmed as sessile serrated adenoma at histopathology. Endoscopic evidence of dysplasia was detected in 36/141 (25.5%) SSP. 2/105 (1.9%) endoscopically designated SSP-ND had dysplasia at histopathology. 10/36 (27.8%) endoscopically designated SSP-D had no dysplasia at histopathology. After discussion with the specialist gastrointestinal pathologists, agreement was reached that in 5/10 (50%) endoscopically designated SSP-D previously determined to be without dysplasia at histopathology, there was equivocal evidence for dysplasia. Endoscopic imaging therefore had an accuracy of 95.0% (95% confidence interval [CI]90.1–97.6%) and a negative predictive value of 98.1% (95% CI 92.6–99.7%) for detection of dysplasia within SSP (table 1).

Table 1: Accuracy of the endoscopic assessment of dysplasia within sessile lesions ≥8 mm pre- and post discussion with specialist histopathologists. 95% CI - 95% confidence interval, SSP-ND - sessile serrated polyp without dysplasia as determined endoscopically, SSP-D - sessile serrated polyp with dysplasia as determined endoscopically, SSP-D – sessile serrated polyp with dysplasia determined histologically or by structured discussion, SSA-ND – sessile serrated polyp without dysplasia as determined histologically or by structured discussion, NPV - negative predictive value.

<table>
<thead>
<tr>
<th>Histopathologic Assessment</th>
<th>Pre-discussion</th>
<th>Post-discussion</th>
</tr>
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<tbody>
<tr>
<td>Endoscopic Assessment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SSP-ND (105)</td>
<td>103 (98.1%)</td>
<td>103 (98.1%)</td>
</tr>
<tr>
<td>SSP-D (36)</td>
<td>10 (27.8%)</td>
<td>10 (27.8%)</td>
</tr>
<tr>
<td>Accuracy of Endoscopic Assessment Pre Discusion</td>
<td>92.9% (95 CI 75.0-98.7%)</td>
<td>99.2% (95 CI 85.7-95.1%)</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>91.2% (95% CI 83.9-95.4%)</td>
<td>91.2% (95% CI 83.9-95.4%)</td>
</tr>
<tr>
<td>Specificity</td>
<td>98.1% (95% CI 92.6-99.7%)</td>
<td>94.9% (95% CI 89.0-98.3%)</td>
</tr>
<tr>
<td>Negative predictive value</td>
<td>98.1% (95% CI 92.6-99.7%)</td>
<td>98.1% (95% CI 92.6-99.7%)</td>
</tr>
<tr>
<td>Accuracy</td>
<td>91.4% (95% CI 85.7-95.1%)</td>
<td>91.4% (95% CI 85.7-95.1%)</td>
</tr>
</tbody>
</table>

Conclusion: Dysplasia within SSP can be accurately detected using a simple, broadly applicable endoscopic imaging protocol allowing their complete resection. This independent validation of this protocol and its dissemination within the endoscopic community may have a significant impact on rates of interval cancer.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP136 RANDOMIZED CONTROLLED TRIAL OF THE USEFULNESS OF COLD SNARE POLYPECTOMY (CSP) FOR OUTPATIENTS

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Introduction: There have been few reports of the safety and usefulness of cold snare polypectomy (CSP) for colorectal polyps of 10 mm or less. This study examined the usefulness and safety of CSP for outpatient same-day treatment.

Aims & Methods: During the period from December 2015 to October 2016, informed consent was obtained before examining outpatients scheduled for colonoscopy of the entire large intestine. Patients found to have colorectal polyps (excluding Ig polyps) of 10 mm or less were included in this study. Patients on oral antithrombotic therapy, which was a stratifying factor, were randomly assigned to a CSP group and an endoscopic mucosal resection (EMR) group. The two groups were compared for the following treatment endpoints: (1) postoperative hemorrhage rate, (2) polyp resection time, (3) en bloc resection rate, (4) postoperative hemorrhage rate with and without oral antithrombotic administration, and the (5) rate of retrieval of tissue from resected lesions.

Results: 300 patients were enrolled in the study. After exclusion of one patient who did not complete CSP, 149 CSP group cases and 150 EMR group cases were analyzed. The values for the treatment endpoints were (1) 0.67% (1/149), (2) 92.2±9.2 sec, (3) 99.1% (348/351), (4) 0% (0/21) and (5) 96.6% (339/351) in the CSP group, and (1) 0.67% (1/150), (2) 144.6±18.9 sec, (3) 100% (322/322),
(4) 0% (0/21) and (5) 99.1% (319/322) in the EMR group. Although there were no significant differences between the groups in regard to (3), (15), or (4), the (2) polyp resection time was significantly shorter in the CSP group (p = 0.001), and the (5) rate of collection of tissue from resected lesions was lower in the CSP group (p = 0.029).

Conclusion: Resection of colorectal polyps in outpatients showed a low incidence of complications in both the CSP and EMR groups and was performed safely. The polyp resection time was significantly shorter with CSP than with EMR, and shortening of the examination time can be expected.

Disclosure of Interest: All authors have declared no conflicts of interest.

A59

OP137 IS COLD-SNARE POLYPECTOMY ALWAYS ADEQUATE FOR REMOVAL OF SMALL COLORECTAL POLYPS WITH ADVANCED HISTOLOGY?

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Introduction: The new European Society of Gastrointestinal Endoscopy clinical guidelines recommend cold-snare polypectomy (CSP) for removal of small colorectal polyps. The recommendation is based on the efficacy and safety of the technique and the assumption that most small polyps have only low-grade histology. However, advanced neoplasia may be unexpectedly removed with CSP, raising concern about possible residual tumor and local recurrence in such cases. For accurate microscopic assessment of CSP-removed polyps, wide horizontal excision and adequate depth is necessary.

Aims & Methods: In this study, we prospectively investigated the efficacy of CSP from the aspects of depth of excised tumors and their vertical margins. Two hundred and seventy-six consecutive sessile or slightly elevated colorectal polyps, removed with CSP by an experienced endoscopist (more than 500 CSPs performed), were enrolled between May 2016 and January 2017. Three of the polyps were excluded because of retrieval failure. Devices used were the Profile/Captivar (Boston scientific) and Exacto (US Endoscopy). Excised polyps were retrieved by suctioning them through the colonoscopy’s biopsy channel. All unretrieved removed specimens were mounted on plates with pins to facilitate pathological assessment and were evaluated blindly without pathologists having clinical information of the lesions. Evaluated items included resection into the muscularis mucosa (MM) and histology of the tumor’s vertical margins. Resection was considered complete when MM was present under the tumor along more than 80% of its horizontal axis. Gross morphology of polyps was classified according to the Paris classification system (sessile, Is; or slightly elevated, Ia).

Results: Mean size of 273 polyps was 4.9 mm. Twenty-one lesions (7.7%) were elevated, IIa).

Histology Neoplastic 1 1
Non-neoplastic 0.5 1 0.5 0.5
(0.0.14-1.0)(0.0.45-1.2)

Pseudo/ submucosal injection No 1 1
Yes 0.8 0.608 0.8 0.6
(0.28-2.80)(0.28-2.11)

Device Profile/Captivar 1 1
Exacto 1 0.355 1.3 0.47
(0.70-2.56)(0.66-2.51)

Location Left 1 1
Right 1.5 0.27 1.6 0.17
(0.76-3.06)(0.82-3.06)

Morphology Slightly elevated (IIa) 1 1
Sessile (Is)a 2.2 0.017 2.3 0.01
(1.14-4.41)(1.22-4.39)

Tumor size 1-5 mm 1 1
6-9 mm 1.1 0.87 0.9 0.73
(0.53-2.11)(0.44-1.79)

Conclusion: CSP achieved proper resection depth in only about 80% of lesions even when performed by an experienced endoscopist. Given that a few small polyps with advanced histology may be unexpectedly resected with CSP, this procedure should be evaluated further, especially for sessile polyps with advanced histology, before it becomes standard of care for excision of small colorectal polyps.

Disclosure of Interest: All authors have declared no conflicts of interest.

References


OP138 MANAGEMENT AND RISK FACTORS FOR INCOMPLETE RESECTION ASSOCIATED WITH COLD FORCES POLYPECTOMY FOR DIMINUTIVE COLORECTAL POLYPS: A SINGLE-INSTITUTION RETROSPECTIVE COHORT STUDY

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Introduction: Adequate polypectomy is important during screening colonoscopy to prevent progression of colorectal carcinoma and decrease mortality. Cold polypectomy is now widely performed. Cold forceps polypectomy (CFP) is a simple and quick technique allowing complete resection of most DPAs. However, evidence for its efficacy is lacking, precise histopathological diagnosis is difficult, and little is known about the risk factors for histologically incomplete resection.

Aims & Methods: The aim of this retrospective cohort study is to evaluate the clinicopathological characteristics and clinical outcomes of patients who underwent removal of DPs by CFP as well as predictors of incomplete resection. We retrospectively investigated 1129 DPs resected by CFP with jumbo biopsy forceps (Radial Jaw2k4; Boston Scientific, Marlborough, MA) in 587 patients (392 men, 195 women; mean age 66±9.4 years) at Hiroshima City Asa Citizens Hospital between November 2015 and December 2016. We evaluated the clinical outcomes of 999 tumours for which a precise histopathological analysis was made and investigated the relationship between incomplete resection and clinicopathological factors. Complete resection was defined as when additional bites for resection were not needed and both the lateral and vertical margins of the specimen were tumour-free resection margins.

Results: Lesions were mainly located in the transverse colon (336 lesions, 30%), ascending colon (252 lesions, 22%) and sigmoid colon (228 lesions, 20%). Of the lesions, 1013 (94%) were protruding/sessile and 65 (6%) were flat elevated. Most lesions (985[87%]) were low-grade (n = 783) or high-grade (n = 202) adenomas and 14(1%) were well-differentiated adenocarcinomas. The en bloc resection rate was 92%(198/999) and the histological en bloc resection rate was 78% (777/999). Precise histopathological diagnosis was difficult in 22% of cases. The lateral margins could not be assessed histologically for tumour involvement in 155 (16%) lesions, additional bites for resection were needed for 81 (8%) lesions, and involvement of the vertical margin could not be histologically assessed in 56 (6%) lesions. Multivariate analysis showed tumour size ≥4 mm (odds ratio [OR] 3.8; 95% confidence interval [CI] 2.65–5.37; p < 0.01), non-tangential direction of forces in relation to the tumour (OR 1.73; 95% CI 1.21–2.45; p < 0.01), and lack of muscularis mucosae mucosal in the pathological specimens (OR 15.7; 95% CI 9.16–27.7; p < 0.01) to be significant independent predictors of incomplete resection. One (0.1%) of the 999 patients had delayed bleeding that was easily managed by endoscopic clipping. There were no cases of perforation.

Conclusion: This study identified significant independent predictors of incomplete resection of diminutive colorectal polyps and may provide helpful information when planning CFP.

Disclosure of Interest: All authors have declared no conflicts of interest.
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**Conclusion:** There is high concordance between both abnormal AET and borderline AET, and low MNBI. When low, MNBI identifies patients with abnormal as well as borderline AET (but not physiologic AET) who respond to medical and surgical anti-reflux therapy. MNBI therefore complements AET in defining esophageal reflux burden, and in predicting symptom response to anti-reflux therapy.

**Disclosure of Interest:** E. Savarino: Consulting fee from: Medtronic, Sofar, Malesci, Takeda, Abbvie, MSD

S. Roman: consulting fee: Medtronic research support: Sandhill, Crossover
J. Pandolfino: Medtronic, Sandhill, Torax Consultants/Speaker Astra Zeneca, Takeda - speaker: Ironwood, Impeleo - consultant

**Abstract No:** OP140

**Response rates from anti-reflux therapy based on acid exposure time (AET) and mean nocturnal baseline impedance (MNBI)**

<table>
<thead>
<tr>
<th>MNBI (low: &lt;2292 ohms)</th>
<th>AET &gt; 6%</th>
<th>AET 4-6%</th>
<th>AET &lt; 4%</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>low</td>
<td>normal</td>
<td>low</td>
</tr>
<tr>
<td>Medical therapy</td>
<td>66/88 (75.0%)</td>
<td>0/1 (0.0%)</td>
<td>35/51 (66.8%)</td>
</tr>
<tr>
<td>Anti-reflux surgery</td>
<td>18/23 (78.3%)</td>
<td>0</td>
<td>14/16 (87.5%)</td>
</tr>
<tr>
<td>Overall</td>
<td>84/111 (75.7%)</td>
<td>0/1 (0.0%)</td>
<td>49/67 (73.1%)</td>
</tr>
</tbody>
</table>

*p < 0.05 compared to AET > 6, low MNBI, and AET 4-6%, low MNBI Response rates were similar between AET > 6 with low MNBI and AET 4-6% with low MNBI (p = ns)

**Citation:** Abnormal esophageal acid burden measured using acid exposure time (AET) from 24-hour pH-impedance monitoring predicts favorable symptom outcome from medical and surgical anti-reflux therapy. Alternative reflux evidence is deemed necessary when AET is borderline and inconclusive. Esophageal baseline mucosal impedance extracted from pH-impedance data during night-time hours (MNBI) represents a new paradigm that is co-linear with AET. The value of MNBI when AET is inconclusive has not been previously evaluated.

**Aims & Methods:** Our aim was to determine the value of MNBI in predicting symptom outcome from medical and surgical anti-reflux therapy when AET is borderline and inconclusive, in this ongoing multicenter collaboration. Esophageal function studies from patients with persisting reflux symptoms were reviewed from two centers (one each in Europe and US) for this preliminary report. For inclusion, patients with typical or atypical reflux symptoms were required to have completed ambulatory pH-impedance monitoring (Sandhill Scientific, Boulder, CO) off antisecretory therapy. AET data were extracted from ambulatory pH-impedance studies. Overall AET was abnormal when > 6%, and physiologic when < 4%; AET 4-6% was considered borderline and inconclusive. Baseline impedance was calculated at the 5 cm impedance channel (to correspond to AET) at three stable 10-min time periods (1, 2, and 3 AM) during the ambulatory pH-impedance study, and averaged to yield MNBI, abnormal if < 2292 ohms. Symptom response was assessed using change in global symptom scores from symptom questionnaires over follow-up; a 50% reduction in global symptoms constituted a response to anti-reflux therapy, both medical management and anti-reflux surgery. Data were analyzed to assess concordance between AET and MNBI, and to assess symptom response in relationship to physiologic, borderline and abnormal AET in the context of abnormal MNBI.

**Results:** A total of 371 patients (54.5 ± 0.7 yr, 60.0% female) had adequate pH-impedance studies performed off antisecretory therapy, and symptom data available for inclusion in this study. Of these, 107 (28.8%) had abnormal AET, and 264 (68.3%) had abnormal MNBI. Of 107 patients with abnormal AET, low MNBI was concordant with AET in 106 (99.1%), and discordant (abnormal AET, normal MNBI) in only 1 patient. Similarly, concordance between AET 4-6% and low MNBI was noted in 62 of 68 patients (91.2%), and discordance (AET 4-6%, normal MNBI) in only 8.8% (p = 0.011 compared to AET > 6%). In contrast, of 196 patients with physiologic AET, discordant normal MNBI was noted in only 130 (66.3%), and with the remainder 33.7% discordant with physiologic AET but low MNBI (p < 0.0001 for each comparison with AET > 6 and AET 4-6%). Of 330 patients with symptom data available from medical therapy, 142 (43.0%) had at least 50% symptom improvement over 38.7 ± 0.8 months of follow up. Symptom response following antireflux surgery was available in 63 patients, and 48 (76.2%) responded (p < 0.0001 compared to medical therapy). Response to both medical therapy and surgery were better when AET > 6% (medical therapy: 74.2% response, surgery 78.3% response) and MNBI < 2292 (medical therapy: 60.1% response, surgery: 82% response). In contrast, response to therapy was worse when AET < 4% (medical therapy: 21.1% response, surgery: 69.6% response), and MNBI < 2292 (medical therapy: 17.4% response, surgery: 53.8% response). Response to medical therapy with AET 4-6% resembled that seen when AET > 6% when MNBI was low (Table, p = 0.44), significantly different from patients with AET < 4, regardless of whether MNBI was normal or low (p < 0.0001 for each comparison).

**Conclusion:** There is high concordance between both abnormal AET and borderline AET, and low MNBI. When low, MNBI identifies patients with abnormal as well as borderline AET (but not physiologic AET) who respond to medical and surgical anti-reflux therapy. MNBI therefore complements AET in defining esophageal reflux burden, and in predicting symptom response to anti-reflux therapy.
LES-CD separation in HH patients was 2.13 cm. 47% were classified as Type I EGJ, 35% as Type II and 18% as Type III. Mean Result:

We enrolled 100 patients. During surgery, 53% had a HH. In details, 4 cm CD, Type II EGJ above CD obtained. A large endoscopic clip was applied to mark the EGJ. The distance 2 cm separation; Type III classified as Type I (normal EGJ without evidence of the B ring or gastric border of CD impression and to the top of the proximal gastric folds was displaced above the proximal border of CD. At UE the distance from proximal folds), Type II was classified as Type I (normal EGJ without evidence of the B ring or gastric folds), Type II and Type III documented patients (0.01; IQR 0–0.04) and abnormal in 12 (7.8 IQR 6.9) (p < 0.001). All details are reported in Table 1. A strong linear correlation between BR and MNBI was observed (Pearson test; r = -0.771, p < 0.001).

Table 1: Pathophysiological characteristics of patients with heartburn stratified for BR (+/-)

<table>
<thead>
<tr>
<th>BR (+)</th>
<th>BR (-)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male (n)</td>
<td>8</td>
<td>7</td>
</tr>
<tr>
<td>Mean age (mean ± sd)</td>
<td>54.7 ± 12.7</td>
<td>49.8 ± 6.2</td>
</tr>
<tr>
<td>AET (med; IQR)</td>
<td>5.6; 1.9</td>
<td>5.9; 2.2</td>
</tr>
<tr>
<td>Reflux number (med; IQR)</td>
<td>61; 19.5</td>
<td>64.5; 22.5</td>
</tr>
<tr>
<td>MNBI (med; IQR)</td>
<td>1111.7; 131.3</td>
<td>1913.5; 318.7</td>
</tr>
<tr>
<td>PSPW index (med; IQR)</td>
<td>36; 9.5</td>
<td>45; 9.5</td>
</tr>
</tbody>
</table>

Conclusion: HRM can accurately diagnose the presence of HH, with high sensitivity and specificity. In particular, HRM can better classify HH than endoscopy and radiology, reaching an optimal agreement with surgical in vivo assessment.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP141 HIGH-RESOLUTION MANOMETRY IS SUPERIOR TO ENDOSCOPY AND RADIOLOGY IN ASSESSING AND GRADING SLIDING HIATAL HERNIA: A PROSPECTIVE COMPARISON WITH SURGICAL IN VIVO

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1Surgery, University of Campania 2Luigi Vanvitelli8, Naples, Naples/Italy 3Department Of Surgery, Oncology And Gastroenterology, University of Padua, Padua/Italy 4Surgery, Imperial College - Surgery, Imperial College; London/GB, London
United Kingdom
2Division Of Gastroenterology, Department Of Internal Medicine, University of Pisa, Pisa/Italy
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5Department Of Medical And Surgical Sciences, S. Orsola-Malpighi Hospital, Bologna/Italy
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8Esophageal Surgery Unit, Pisa/Italy
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Introduction: Sliding hiatal hernia (HH) has been associated with abnormal esophageal acid exposure, prolonged esophageal clearance, increased reflux episodes and it is correlated with the severity of gastroesophageal reflux disease. The diagnosis of HH is made with a barium-swallow esophagogram (BSE), and it can be also described at upper endoscopy (UE). However, these methods are limited by the subjective and indirect evaluation of lower esophageal sphincter (LES) and crural diaphragm (CD). High resolution manometry (HRM) allows to clearly identify CD and LES. However, its diagnostic accuracy has been poorly investigated.

Aims & Methods: Aim of the study was to determine the diagnostic value of HRM in the detection of HH, compared to BSE and UE, using as reference the surgical in vivo measurement. We prospectively enrolled patients undergoing open foregut surgery between 2009 and 2014. All subjects underwent BSE, UE, HRM and in vivo evaluation of esophageal gastric junction (EGJ). At BSE EGJ was classified as Type I (normal EGJ without evidence of the B ring or gastric folds), Type II ≥2 cm and Type III ≥2 cm, when the B ring or gastric folds were displaced above the proximal border of CD. At UE the distance from proximal border of CD by compression and to the top of the proximal gastric folds was recorded. UE Type I indicated a normal EGJ; Type II and Type III documented patients (0.01; IQR 0–0.04) and abnormal in 12 (7.8 IQR 6.9) (p < 0.001). AET (med; IQR) 5.6; 1.9 5.9; 2.2 0.567. Reflux number (med; IQR) 61; 19.5 64.5; 22.5 0.668. All details are reported in Table 1. A strong linear correlation between BR and MNBI was observed (Pearson test; r = -0.771, p < 0.001).

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<td>45; 9.5</td>
</tr>
</tbody>
</table>

Conclusion: Bile refluxes strongly affected MNBI in patients with NERD. Further, they are associated to an abnormal PSPW index reflecting the relevance

Abstract No: OP141

<table>
<thead>
<tr>
<th>HRM all</th>
<th>HRM Type I</th>
<th>HRM Type II</th>
<th>HRM Type III</th>
<th>Endoscopy all</th>
<th>Endoscopy Type I</th>
<th>Endoscopy Type II</th>
<th>Endoscopy Type III</th>
<th>Barium all</th>
<th>Barium Type I</th>
<th>Barium Type II</th>
<th>Barium Type III</th>
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<tr>
<td>Sensitivity (%)</td>
<td>94.3</td>
<td>91.5</td>
<td>91.4</td>
<td>100</td>
<td>96.2</td>
<td>74.5</td>
<td>54.3</td>
<td>100</td>
<td>69.8</td>
<td>97.9</td>
<td>54.3</td>
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<tr>
<td>Specificity (%)</td>
<td>91.5</td>
<td>94.3</td>
<td>93.8</td>
<td>100</td>
<td>74.5</td>
<td>96.2</td>
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<td>82.9</td>
<td>97.9</td>
<td>69.8</td>
<td>90.8</td>
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<tr>
<td>PVPT (%)</td>
<td>92.6</td>
<td>93.5</td>
<td>89.9</td>
<td>100</td>
<td>81</td>
<td>94.6</td>
<td>61.3</td>
<td>56.3</td>
<td>97.4</td>
<td>74.2</td>
<td>76</td>
</tr>
<tr>
<td>PVNT (%)</td>
<td>93.5</td>
<td>92.6</td>
<td>95.3</td>
<td>100</td>
<td>94.6</td>
<td>81</td>
<td>76.8</td>
<td>100</td>
<td>74.2</td>
<td>97.4</td>
<td>78.7</td>
</tr>
<tr>
<td>Kappa</td>
<td>0.85</td>
<td>0.86</td>
<td>0.847</td>
<td>1.0</td>
<td>0.716</td>
<td>0.716</td>
<td>0.368</td>
<td>0.636</td>
<td>0.661</td>
<td>0.665</td>
<td>0.482</td>
</tr>
</tbody>
</table>

Conclusion: HRM can accurately diagnose the presence of HH, with high sensitivity and specificity. In particular, HRM can better classify HH than endoscopy and radiology, reaching an optimal agreement with surgical in vivo assessment.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

of this parameter in identifying patients with abnormal chemical clearance and therefore develop GERD symptoms.

Disclosure of Interest: All authors have declared no conflicts of interest.

OPI43 REDUCTION OF DAY TIME ACID GASTRO OESOPHAGEAL REFUX BY TREATING INCREASED SUPRAGASTRIC BELCHING

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3Wingate Institute, Queen Mary University London Wingate Institute Centre for Digestive Diseases, London/United Kingdom

Introduction: Supragastric belching (SGB) is considered a behavioural disorder. SGB can manifest as a large number of belch episodes during daytime, or can be associated with reflux symptoms or rumination. Supragastric belches can be immediately followed by acid reflux and in some GERD patients, SGB-associated reflux can contribute to up to 1/3 of the total acid exposure (AET) immediately followed by acid reflux and in some GERD patients, SGB-associated reflux can contribute to up to 1/3 of the total acid exposure (AET).

We hypothesized that reducing SGB might improve QOL (Koukias, 2015). Current treatments for SGB are cognitive behavioural therapy (CBT) and Baclofen. We hypothesized that reducing SGB might improve QOL and reduce acid GERD.

Aims & Methods: The aim of our study was to assess the effectiveness of CBT in patients with pathological SGB and/or increased SGB-related acid reflux exposure. Patients were recruited from the upper GI Physiology Unit after performance of pH-pHmetry (Sandill Sci, USA). Visual analysis of tracing was performed to identify SGB and patients with more than 13 SGB/day were invited to participate. A total of 45 patients were included in the SGB group. The CBT protocol was adapted from Katzka et al (2013) and consisted of teaching 1. diaphragmatic breathing, 2. mouth opening/tongue position and 3. recognition of a warning signal/feeling pre-belching. Patients exercised these manoeuvres daily and tried to apply them to prevent belching. Before and after CBT, subjective evaluation included a 4-item visual analog scale (VAS) regarding severity of belching. Objective evaluation included pH-pHmetry at baseline and after CBT therapy. Parameters were number of SGB, the acid exposure time (AET), and proportion of AET associated to SGB.

Methods: Patients were recruited since March 2016. So far, 30 patients completed the protocol (median age: 45, range 20–72, 16 females) of which 28 had a second pH study. Subjective evaluation: VAS scores decreased after CBT in 30/31 patients (before: 200 (220–320) mm vs. after: 140 (200–230) mm, p < 0.0001). 15/31 patients had VAS score improvement > 50%. Objective evaluation: Number of SGB decreased significantly after CBT in 25/28 patients [before: 89 (45–230) vs. after 42 (19–138), p < 0.0001]. 15/28 patients had reduction of SGB by more than 50%. Fifteen patients had increased AET pre-treatment, [AET 9.3 (SEM 0.84). In these patients SGB contributed to 31% of the AET. Overall, AET after CBT was: 6.2 (SEM 0.95), p = 0.0056). In 8/15 patients with baseline increased AET, we observed after CBT a reduction of number of reflux episodes driven by SGB and AET by 40%.

Conclusion: Cognitive behavioural therapy ameliorates supragastric belching. It reduces the number of belches and improves social and daily activities in 50% of patients. Careful analysis of pH-pHmetry allows identification of a subgroup of GERD patients with acid reflux predominantly driven by SGB. In these patients, CBT can reduce daytime esophageal acid exposure.

Disclosure of Interest: D. Sifrim: research grant Sandhill Sci (Denver USA)
All other authors have declared no conflicts of interest.

OPI44 POST-REFLUX SWALLOW-INDUCED PERISTALTIC WAVE INDEX AND MEAN NOCTURNAL BASELINE IMPEDANCE PREDICT HEARTBURN RESPONSE TO PROTON PUMP INHIBITORS BETTER THAN ACID EXPOSURE TIME IN GERD

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9Ae, Modena, Gastroenterology and Digestive Endoscopy Unit, Modena/Italy
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Introduction: Traditionally, acid exposure time (AET) has been regarded as the most useful parameter to predict heartburn improvement with proton pump inhibitor (PPI) therapy. However, recent studies showed high rates of heartburn response to PPIs also in patients with normal AET. Two novel impedance parameters, namely the post-reflux swallow-induced peristaltic wave (PSPW) index and mean nocturnal baseline impedance (MBI) were found useful in identifying GERD patients and distinguishing between reflux hypersensitivity and functional heartburn (FH). Therefore, they could prove useful in predicting PPI-induced heartburn relief.

Methods: We aimed to investigate demographic, endoscopic and impedance features able to predict PPI response in patients with heartburn. Off-therapy impedance-pH tracings from 425 patients, 317 with definitely PPI-responsive heartburn (i.e. heartburn repeatedly abolished by 4-week PPI-therapy and repeatedly recurring after PPI withdrawal) and 108 with PPI-refractory (i.e. >50% of symptom relief after 8-week high-dosage PPI therapy), were blindly analyzed. Baseline demographic and endoscopic characteristics, conventional impedance-pH variables including acid exposure time (AET) and number of reflux episodes, PSPW index and MBI were assessed by means of multivariable logistic regression to identify independent predictors of PPI responsiveness. Models based on independent predictors were then developed and compared for the ability to predict symptom improvement by calculating the area under the Receiver Operating Characteristic (AUC) curve. Finally, logistic regression analysis was used to adapt a prediction model.

Results: AET, MBI and PSPW index were the only factors associated with PPI responsiveness: abnormal values were found in 60%, 76% and 92% of PPI-responsive cases (P < 0.017 for all pairwise comparisons). As shown in the Table, using AUCs, PSPW index (AUC 0.794, P = 0.002) and MBI (AUC 0.741, P = 0.003), both separately and combined (AUC 0.810, P < 0.001), predicted PPI responsiveness better than AET (AUC 0.687).

Table. Baseline characteristics associated with PPI responsiveness (multivariate logistic regression analysis)

<table>
<thead>
<tr>
<th>Variable</th>
<th>OR (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male gender</td>
<td>0.623 (0.330–1.175)</td>
<td>0.144</td>
</tr>
<tr>
<td>Age (years)</td>
<td>1.009 (0.987–1.032)</td>
<td>0.393</td>
</tr>
<tr>
<td>BMI</td>
<td>0.983 (0.920–1.049)</td>
<td>0.613</td>
</tr>
<tr>
<td>History of reflux esophagitis</td>
<td>1.786 (0.604–4.693)</td>
<td>0.239</td>
</tr>
<tr>
<td>Hiatral hernia</td>
<td>0.753 (0.403–1.407)</td>
<td>0.375</td>
</tr>
<tr>
<td>Abnormal AET</td>
<td>0.379 (0.155–0.924)</td>
<td>0.033</td>
</tr>
<tr>
<td>Positive SAP</td>
<td>1.310 (0.599–2.868)</td>
<td>0.498</td>
</tr>
<tr>
<td>Positive SI</td>
<td>1.854 (0.799–4.300)</td>
<td>0.150</td>
</tr>
<tr>
<td>Abnormal number of reflux events</td>
<td>1.576 (0.733–3.295)</td>
<td>0.227</td>
</tr>
<tr>
<td>Abnormal PSPW index</td>
<td>12.499 (5.348–28.157)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Abnormal MBI</td>
<td>3.586 (1.885–6.824)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Conclusion: AET, PSPW index and MBI are independent predictors of heartburn responsiveness to PPIs. However, PSPW index and MBI can link PPI responsive heartburn to reflux better than AET and should become part of the standard analysis of impedance-pH tracings.

Disclosure of Interest: V. Savarino: Consulting fee from Malesci, Reckitt, AlfaWasserman, Abbvie E. Savarino: Consulting fee from Medtronic, Sofar, Takeda, Abbvie, MSD All other authors have declared no conflicts of interest.
OP146 IDENTIFICATION OF A MICROBIOTA BENEFICIAL AGAINST COLITIS AND COLITIS-ASSOCIATED CANCER


Introduction: Inflammatory bowel disease (IBD) is an inflammatory disease of the gastrointestinal tract. The pathogenesis of IBD is multifactorial, involving genetic, environmental, and microbial factors. Microbiome dysbiosis is a hallmark of IBD and has been associated with disease severity. The colonization of germ-free mice with the microbiota from patients with ulcerative colitis (UC) or Crohn’s disease (CD) induces colitis, suggesting a pathogenic role for specific bacterial taxa.

Aims & Methods: In this study, we aimed to investigate the role of the intestinal microbiota and its interaction with the host mucosa in mediating the protection against inflammation observed in UC and CD mice. We examined the impact of the microbiota on the development of colitis in both UC and CD mice.

Results: We observed that the colonization of germ-free mice with the microbiota from patients with UC or CD induced colitis, with significantly increased disease activity and pathological features, including increased colon weight, colon length, MPO, fecal LCN-2, tumor count, and tumor size. The microbiota from UC and CD patients induced similar pathological changes, suggesting a common pathogenic mechanism.

Conclusion: This study demonstrates that the microbiota from UC and CD mice are capable of inducing colitis in both UC and CD models. The findings suggest that specific bacterial taxa may contribute to the pathogenesis of IBD. Further studies are needed to identify the key players and mechanisms involved in the development of colitis.

Disclosure of Interest: All authors have declared no conflicts of interest.

References:

OP147 PROTECTIVE ROLE OF ESCHERICHIA COLI NISSLE 1977 ON INTESTINAL PERMEABILITY IN IRRITABLE BOWEL SYNDROME: AN IN VITRO STUDY

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Introduction: Several gastrointestinal diseases, such as inflammatory bowel diseases and Irritable Bowel Syndrome (IBS), are characterized by epithelial barrier alterations which likely play a key role in the pathogenesis. In the absence of a clear pharmacological interventions to restore intestinal permeability in IBS, an interesting perspective is represented by probiotics, live microorganisms widely used in clinical practice. Escherichia coli Nissle 1917 (EcN) is a probiotic already approved for the maintenance of remission of ulcerative colitis, although the underlying molecular mechanism remains to be clarified.

Aims & Methods: The aim of this study was to characterize the potential effect of EcN in reversing the increase of intestinal permeability caused by known stimuli and to evaluate the potential efficacy of EcN in IBS. We used an in vitro model of jejunal epithelial monolayer permeability induced by SLigR (a protease-activated receptor-2 activating peptide). Our study revealed that EcN significantly reduced intestinal permeability by decreasing the expression of ZO-1 and occludin, which are important tight junction proteins.

Results: EcN induced a dose-dependent reduction of EcN-2 monolayer of 52% (108, P < 0.05) and 32% (106) compared to untreated CaCo-2 (CTR). TCPNf and IFN-γ induced an increase in CaCo-2 permeability compared to CTR (P < 0.05). The co-incubation of EcN with IFN-γ reduced the increase of epithelial integrity by 77% and 63% for 108 and 106 respectively, compared to SLigR alone. EcN induced a significant increase in ZO-1 and occludin gene expression compared to CTR (P < 0.05). The co-incubation of EcN with IBS showed a recovery of permeability rate compared to untreated IBS (P < 0.05). In conclusion, our study demonstrated that EcN has the potential to restore intestinal permeability in IBS, which is an important target in the management of this condition.
incubation of EcN 108 with SUP of patients with IBS-D led to a significant recovery of barrier integrity (P < 0.05).

Conclusion: EcN is able to act on different tight junction proteins by reinforcing the integrity of the intestinal epithelial barrier. EcN reverts the increase of epithelial monolayer permeability induced by inflammatory stimuli and mediators spontaneously released by IBS biopsies. Further study should look at EcN potential application in IBS.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP148 IS THE MICROBIOME IMPLICATED IN THE DEVELOPMENT OF GENUINE IRRITABLE BOWEL SYNDROME-TYPE SYMPTOMS IN INFLAMMATORY BOWEL DISEASE?

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Introduction: Irritable bowel syndrome (IBS)-type symptoms affect 35% of patients with clinically quiescent inflammatory bowel disease (IBD). (1) The presence of these symptoms is associated with anxiety, depression, somatisation and reduced quality of life, (2) but their effect on disease outcomes remains uncertain. Alterations in the intestinal microbiome are implicated in pathogenesis of IBS and IBD, yet whether intestinal dysbiosis is also associated with the development of genuine IBS-type symptoms in quiescent IBD remains uncertain.

Aims & Methods: We aimed to assess the microbiome in 270 consecutive IBD patients who, using a combination of clinical disease activity indices, the Rome III criteria for IBS and faecal calprotectin (FC) (using a cut-off of 250ug/g to define active mucosal inflammation), were divided into four groups as follows: True IBS, quiescent disease, occult inflammation, active disease. Baseline demographic, disease-related and psychological data were described in Table 1.

Results: Baseline demographic, disease related and psychological data are described in Table 1.

Disclosure of Interest: All authors have declared no conflicts of interest.

Abstract No: OP148

Table 1

| IBD with true IBS (n=70) | Quiescent IBD (n=81) | P value* | IBD with occult inflammation (n=66) | P value* | Active IBD (n=53) | P value*
|-------------------------|---------------------|----------|-------------------------------------|----------|------------------|----------
| Mean age in years (SD)  | 47.1 (15.4)         | 51.4 (17.2) | 0.11                               | 50.9 (18.5) | 0.19             | 50.9 (15.8) | 0.19
| Female gender (%)       | 47 (67.1)           | 34 (42.0)  | 0.002                              | 35 (53.0)  | 0.09             | 35 (60.0)  | 0.90
| Married or co-habiting (%) | 41 (58.6)   | 52 (64.2)  | 0.48                               | 40 (60.6)  | 0.81             | 39 (73.6)  | 0.08
| University graduate/professional (%) | 16 (22.9) | 20 (24.7)  | 0.79                               | 17 (26.6)  | 0.62             | 15 (28.8)  | 0.45
| Mean BMI (SD)           | 26.1 (5.6)          | 26.4 (5.5)  | 0.73                               | 27.5 (6.7)  | 0.19             | 27.6 (4.9)  | 0.11
| Tobacco user (%)        | 15 (21.4)           | 5 (6.2)    | 0.006                              | 11 (16.9)  | 0.51             | 8 (15.1)   | 0.37
| Alcohol user (%)        | 43 (61.4)           | 34 (47.5)  | 0.44                               | 41 (62.1)  | 0.93             | 34 (64.2)  | 0.76
| Crohn’s disease (%)     | 41 (58.6)           | 42 (51.9)  | 0.41                               | 40 (60.6)  | 0.81             | 27 (50.9)  | 0.40
| 5-ASA use (%)           | 41 (58.6)           | 45 (55.6)  | 0.71                               | 33 (50.0)  | 0.32             | 21 (39.6)  | 0.04
| Immunosuppressant use (%) | 29 (41.4) | 30 (37.0)  | 0.58                               | 21 (31.8)  | 0.25             | 17 (32.1)  | 0.29
| Anti-TNFα use (%)        | 13 (18.6)           | 13 (16.0)  | 0.68                               | 8 (12.1)   | 0.30             | 8 (15.1)   | 0.61
| Glucocorticoid use (%)  | 7 (10.0)            | 5 (6.2)    | 0.39                               | 10 (15.2)  | 0.36             | 6 (11.3)   | 0.81
| Mean HADS anxiety score (SD) | 9.7 (4.7) | 6.4 (4.2)  | <0.001                             | 6.4 (4.1)  | <0.001           | 8.2 (4.5)  | 0.08
| Mean HADS depression score (SD) | 6.7 (4.7) | 3.6 (3.6)  | <0.001                             | 4.0 (3.5)  | <0.001           | 6.4 (4.2)  | 0.71
| Mean PHQ-15 score (SD)  | 12.9 (4.5)          | 8.0 (4.8)  | <0.001                             | 7.7 (3.8)  | <0.001           | 12.1 (4.2) | 0.35
| Mean SF-36 score (SD)   | 70.7 (26.6)         | 79.9 (26.1) | 0.04                               | 76.3 (28.2) | 0.25             | 66.8 (31.2) | 0.47
| Physical functioning    | 37.9 (40.3)         | 70.7 (40.1) | <0.001                             | 61.2 (42.2) | 0.001            | 40.7 (43.6) | 0.72
| Role limitations physical health | 53.2 (45.3) | 77.1 (38.7) | 0.001                              | 75.9 (39.3) | 0.003            | 59.0 (41.1) | 0.49
| Role limitations emotional | 38.4 (22.1) | 51.1 (25.1) | <0.001                             | 48.4 (20.3) | 0.01             | 34.1 (21.9) | 0.31
| Pain General health     | 40.1 (20.1)         | 56.0 (24.1) | <0.001                             | 51.4 (24.5) | 0.004            | 38.2 (22.0) | 0.63
| Mean FC (SD)            | 87.8 (68.1)         | 75.6 (61.1) | 0.24                               | 1080 (1036) | <0.001           | 1268 (1238) | <0.001

*Independent samples t-test for continuous data, and y2 for comparison of categorical data vs. IBD with true IBS.

Microbiome composition was highly variable, even within patient groupings. No major taxa were differentially abundant between the four disease status groups. Patients with quiescent disease appeared to have greater phylogenetic alpha diversity than the other three disease status groups, which were similarly diverse, though this difference was not statistically significant. Beta diversity analysis showed slight, though significant, variation between the four groups. Differences between Crohn’s disease (CD) and ulcerative colitis (UC) patients were much more marked. In CD, there was a lower proportional abundance of the genus Faecalibacterium (3.46% versus 6.97%; P < 0.001), and a higher proportional abundance of the genus Ruminococcus (3.63% versus 1.27%; P < 0.001). Phylogenetic alpha diversity was also significantly lower in CD (P < 0.001). Beta diversity analysis showed significantly greater within-group variation amongst CD patients compared to UC patients.

References
**OP149 THE COMPLEMENT SYSTEM AS A REGULATOR OF THE HOST-MICROBIOTA RELATIONSHIP IN IBD**

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**Introduction:** The complement system is the major humoral component of innate immunity. Despite its key role in sensing microbial surfaces, its impact on the equilibrium at the interface of gut immune system and microbiota in health and inflammation remains elusive. Recently, complement protein C4 was implicated in the pathogenesis of Crohn’s disease by a genome wide association study.

**Aims & Methods:** Thus, we performed a study to delineate the impact of the complement system on (i) the relationship of host and microbiota and (ii) the properties of the mucosal immune response in health and inflammation. The extent of complement opsonization of the microbiota was quantified by flow cytometry (FC): Bacteria were isolated from stool of IBD patients, stained for immunoglobulin A (IgA) and C3b/c and classified as double negative, double positive or single positive. The share of events in each of these populations was correlated with the level of inflammation, clinical disease activity, and therapeutic strategies employed. The 4 populations were sorted via fluorescence-assisted cell sorting (FACS) and metagenomic analysis of these bacterial fractions was performed. Expression of complement proteins in the intestine was analyzed by quantitative polymerase chain reaction (qPCR) of mRNA isolates from colonic biopsies in active disease. However, this was not true for all targets and the model was established to investigate complement opsonization in the intracellular handling of pathogens: Helicobacter cells were infected with GFP-tagged Salmonella typhimurium (opsonized and non-opsonized) and intracellular growth was quantified over time by culture, confocal laser scanning microscopy and flow cytometry.

**Results:** Complement proteins were markedly upregulated in ileal and colonic biopsies in active disease. However, this was not true for all targets and the observed change differed between genes. Mucosal expressions were different from the luminal environment: While most complement components were detectable in biopsies at the mRNA level, only certain complement proteins could be identified in stool. Importantly, this included C3, but not the terminal complement complex. The extent of C3b coating of bacterial surfaces correlated significantly with the level of inflammation (p = 0.003). The proportion of complement opsonized bacteria ranged from 0 % to 4 % and did not correlate with intestinal inflammation. This was also different from IgA opsonization which correlated positively with the grade of inflammation. Employing FACS and 16S-based metagenomics, we were able to identify specific microbial species within the respective sorting groups (IgA/C3c double-positive, double-negative, and single-positive fractions) which showed some association with inflammation and specific disease. The cell culture experiments showed a significant difference in intracellular Salmonella loads after 6 and 24 hours (p = 0.019), which was independent of bacterial uptake by the cells or non-specific binding.

**Conclusion:** The complement system represents a relevant player in human IBD. We show that the complement system has some specificity for commensal bacterial distinct from IgA both in the steady state and during intestinal inflammation. Moreover, we show that complement opsonization optimizes the clearance of intracellular bacteria by epithelial cells.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**References**


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**OP150 METABOLOBMIC AND MICROBIOTA PROFILE OF CROHN’S PATIENTS IS A PREDICTOR OF PRIMARY NON-RESPONSE TO ANTI-TNF THERAPY**

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**Introduction:** Biological therapy with anti-TNF blockade forms the backbone for treatment in moderate to severe Crohn’s disease (CD). Metabonomic approaches to profiling Crohn’s disease has led to numerous discoveries in disease pathogenesis and is an important in elucidating pathways responsible for interactions between human microbiota and host.

**Aims & Methods:** The aim of our longitudinal study was to identify predictive biomarkers of response to anti-TNF therapy using metabolomic and microbiome profiling. Moderate to severe CD patients with luminal disease commencing anti-TNF therapy had 3-monthly visits for 12 months with collection of biofluids (urine, faeces and serum) and disease assessment performed at each visit. Assessment of response was by biochemistry and faecal calprotectin or mucosal healing. A response index combining biochemistry (50% decrease in FC or CRP) and mucosal healing within 14 weeks was used to define therapeutic response in the presence of adequate drug level. We collected 179 urine, 210 serum and 168 faecal samples from 68 anti-TNF naive CD patients (luminal phenotype undergoing anti-TNF therapy without surgical resections) and 20 healthy controls. Liquid-Chromatography Mass Spectroscopy using Waters Xevo TQ-S and Processing using Woleryzkit, sequencing with MiSeq illumina and processing using MiseqData was performed.

**Results:** There were 18 non-responders and 9 responders to anti-TNF therapy according to our strict criteria for response. Multiple biomarkers were identified across assays to be significant for predicting anti-TNF response to therapy across all visits (Table 1). The strongest models were from serum bile acid (R2X0.29, Q2Y0.30, p = 4.97 × 10−5) and urinary HILIC (R2X0.14, Q2Y0.30, p = 1.28 × 10−3). Serum BA profiling analysis identified 2 conjugated and 1 unconjugated BAs, while urinary HILIC profiling identified cysteine as biomarker with MiSeq illumina and processing using MiseqData was performed. Lactobacillus is higher in responders while clostridiales were lower in abundance for non-responders after bonferroni correction. Lactobacillus is known to synthesise cysteine from serine and for expansion in gut microbiota. Faecalibacterium and rumonococcus increased over time in responders to anti-TNF therapy. However, the overall quantities of species did not alter significantly over time nor with therapy.

**Conclusion:** The metabonomic approach is an important tool in demonstrating the chemical profile of alterations in human microbiota resulting from inflammatory bowel disease and therefore the interaction that occurs between the microbiome and host. This prospective, longitudinal cohort study of microbiome and metabolomic analysis demonstrates that there are predictive biomarkers involved with bile acid and inflammatory pathways. The microbiome of patients with Crohn’s disease does not alter significantly despite anti-TNF therapy response which allows for prediction of therapeutic outcome.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**Abstract No:** OP150

**Table 1:** Prediction of response to anti-TNF therapy

<table>
<thead>
<tr>
<th>OPLS-DA models</th>
<th>Serum</th>
<th>Faeces</th>
<th>Urine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Responders versus Non-responders</td>
<td>R2X</td>
<td>0.0835</td>
<td>0.251</td>
</tr>
<tr>
<td>R2Y</td>
<td>0.889</td>
<td>0.183</td>
<td>0.615</td>
</tr>
<tr>
<td>Q2Y</td>
<td>0.269</td>
<td>−0.355</td>
<td>0.411</td>
</tr>
<tr>
<td>p-val</td>
<td>2.11 × 10−4</td>
<td>4.97 × 10−7</td>
<td>0.0099</td>
</tr>
</tbody>
</table>
DISEASE AND COLITIS MODELS

OP152 PANETH CELLS DYSFUNCTION AND DEATH IS DIRECTLY LINKED TO IFN-Λ-LAMBDA SIGNALING
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Introduction: The abundance of trillions of beneficial commensal microorganisms that reside in the small and large intestinal tract together with cells of the gut-associated immune system requires an effective barrier in order to preserve tissue homeostasis. There is overwhelming evidence corroborating the notion that the pathogenesis of Crohn’s disease, an idiopathic inflammatory bowel disease, is closely related to the increased immune responses presumably directed against commensal enteric bacteria in a genetically susceptible host. While lymphocyte-derived type II IFN (IFN-λ) has been implicated in the pathogenesis of Crohn’s disease, the impact of IFN-λ on small intestinal inflammation remains unknown.

Aims & Methods: The central aim of this project was the question if and by which pathways type III IFN (in particular IL28, a member of this IFN family) contribute to intestinal inflammation in mice and men. In the long run, we aim to decipher novel functions of type III IFNs on mucosal cells that could be targeted for future therapeutic intervention.

Results: Here we discovered that IL28 (belonging to the type III IFN family) is strongly upregulated on the transcriptional level in vitro and in vivo in human and murine models of ileitis. Remarkably, IL28 immunostaining was particularly enhanced in intestinal epithelial cells in areas of severe inflammation accompanied by a reduced number of Paneth cells. These data strongly implicate that IL28 expression is linked to disease activity in CD. In line with our hypothesis, we identified that IL28 promotes massive epithelial cell death and loss of immune homeostasis in mice with an epithelial cell specific deletion of a central apoptosis mediator caspase-8 (Casp8ΔIEC). While these mice are genetically sensitized to epithelial cell death, we further uncovered that IL28 overexpression in wildtype animals resulted in a nearly complete depletion of Paneth cells. These data demonstrate that IL28 signaling affects Paneth cell homeostasis and thus antimicrobial defense. Notably, this effect was independent of type I and II IFN signaling and directly mediated by STAT1 activation in intestinal epithelial cells. Moreover, we provide compelling evidence that Paneth cell death was dependent on MLKL, a master regulator of regulated necrosis and caspase-8 as a central regulator of cell death. Using the small intestinal organoid model we further uncovered that IL28 overexpression affected the expression of tight-junction molecules suggesting an impact of this cytokine on intestinal barrier function.

Conclusion: In summary, our results strongly implicate a pathophysiological role for IFN-λ during small intestinal inflammation by controlling Paneth cell homeostasis and barrier function and hence the rationale for the investigation of this pathway in other inflammatory or infectious bowel diseases.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
*shared senior authorship

OP153 THE STIMULATION OF MACROPHAGES WITH MICROBIAL-DERIVED COMPOUNDS SUPPORTS INCREASED IL-19 EXPRESSION IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE EXPERIMENTAL MODELS
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2Department Of Pathology, University of Basel, Basel/Switzerland
3Department Of Genomics And Immunoregulation, University of Bonn, Bonn/Germany
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Introduction: Interleukin (IL)-19, a member of the IL-20 cytokine family, that signals through the IL-20 receptor type I (IL-20Rα: IL-20Rβ) is a cytokine with rather unknown function. Although the expression of the type II IL-20 receptor in the colon is low compared to the IL-22 receptor (1, 2), some studies have suggested a role of IL-19 for IBD (3).

Aims & Methods: To investigate the importance of IL-19 for the development of colitis biopsies of patients with Crohn’s disease (CD) and ulcerative colitis (UC) we received from the Swiss IBD cohort study (SIBD project 2015-05). The importance of IL-19 for colitis was further studied with a newly generated Il19−/− mouse model knockout mice.

Results: The expression of IL-19 is increased in biopsies from UC patients but not CD patients with active disease as compared to quiescent disease, whereas the expression of the type II IL-20 receptor is not significantly changed in IBD patients. Furthermore, direct activation of macrophages by CD40 ligation caused colitis, but did not induce IL-19 expression indicating that a barrier breach allowing the access of bacterial-derived products as observed in the DSS model is required for the expression of IL-19 during colitis. The stimulation of macrophages with the Toll-like receptors (TLR) ligands and injection of Lipopolysacharide (LPS) into mice decreased IL-19 expression, whereas TLR3 agonists induced the expression of IL-19, which depends on Mydd8, but TLR2 – 2, – 4 and – 9 ligands but not the TLR3 ligand poly (IC) induced the expression of IL-19. Colonic macrophages but not dendritic cells were identified as a source of IL-19 production, which was further induced by lipopolysaccharide (LPS). The expression of IL-19 was also upregulated upon injection of Oligo-MCM12 and CD1d deficient animals showed a severe DSS colitis, the expression of IL-19 was not induced in Oligo-MCM12 mice after exposure to DSS. Furthermore, direct activation of macrophages by CD40 ligation caused colitis, but did not induce IL-19 expression indicating that a barrier breach allowing the access of bacterial-derived products as observed in the DSS model is required for the expression of IL-19 during colitis. The stimulation of macrophages with the Toll-like receptors (TLR) ligands and injection of Lipopolysacharide (LPS) into mice decreased IL-19 expression, whereas TLR3 agonists induced the expression of IL-19, which depends on Mydd8, but TLR2 – 2, – 4 and – 9 ligands but not the TLR3 ligand poly (IC) induced the expression of IL-19. Colonic macrophages but not dendritic cells were identified as a source of IL-19 production, which was further induced by lipopolysaccharide (LPS).

Conclusion: Microbial-derived products that have entered the host after intestinal barrier breach induce IL-19 expression by macrophages supporting the development of IBD. Although we did not observe an effect of IL-19 on signaling of BMDMs, IL-19 may have direct effects on intestinal macrophages, as we observed IL-20r in the lamina propria of humans and mice, and reduced IL-6 production by colonic macrophages of IL-19 deficient mice with colitis. The deletion of the individual members of the IL-20 cytokine family and individual receptor chains is needed to further dissect the importance of this cytokine family for IBD.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

OP154 CD1D MODULATES COLONIC INFLAMMATION IN NOD2−/− MICE BY ALTERING THE COMPOSITION OF INTESTINAL MICROBIOTA
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Introduction: NOD2 mutations are associated with the development of inflammatory bowel diseases. However, while most animal studies have reported no impact of NOD2 deficiency on experimental colitis, NOD2 deficiency only is insufficient for development of IBD and an additional hit is needed. Like NOD2, the deficiency of CD1d, non-classical MHC class I molecule, showed no impact on experimental colitis. Although we did not observe an effect of IL-19 on signaling of BMDMs, IL-19 may have direct effects on intestinal macrophages, as we observed IL-20r in the lamina propria of humans and mice, and reduced IL-6 production by colonic macrophages of IL-19 deficient mice with colitis. The deletion of the individual members of the IL-20 cytokine family and individual receptor chains is needed to further dissect the importance of this cytokine family for IBD.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
DSS-induced colitis in NOD2+/− mice compared to those of littermate cohousing NOD2+/+, CD1d+/+, and wild-type mice during DSS-induced colitis (<p<0.001 and p=0.019, respectively). The intestinal microbial composition of NOD2−/− CD1d−/− mice was different (decreased relative abundance of Bacteroidetes and increased relative abundance of Firmicutes). Paneth cell degranulation was decreased in NOD2−/− CD1d−/− mice compared to those of littermate cohousing NOD2+/+, CD1d+/+, and wild-type mice after pilocarpine administration (p<0.001).

**Conclusion:** The CD1d in NOD2−/− mice modulates colonic inflammation by altering the composition of the intestinal microbiota, which may be caused by Paneth cell dysfunction.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**References**


**OP156**

**IL-10-INDEPENDENT PROTECTIVE ACTIVITIES OF HUMAN-DERIVED CLOSTRIDIUM STRAINS IN EXPERIMENTAL COLITIS**

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**Introduction:** Previous studies show that murine- and human-derived Clostridium strains, which are decreased in active human inflammatory bowel diseases (IBD), induce colonic TGFβ and IL-10-producing Foxp3 regulatory T cells (Tregs) and attenuate experimental colitis in murine models (Atarashi K, . . . Honda K, Science 2011 and 2013). However, additional protective effects of these commensal intestinal bacterial species independent of IL-10 are unknown.

**Aims & Methods:** To investigate IL-10-independent effects of the Clostridium strains, we treated IL10−/− mice, which develop T-cell-mediated colitic, with 17 human Clostridium strains obtained from Dr. Honda and analyzed the degree of colitis and microbiota, metabolomic and immunological profiles. To establish a “humanized” colitis model, we colonized germ-free (GF) IL10−/− mice with either a mixture of three aggressive human bacteria species (Escherichia coli LF82, Enterococcus faecalis and Ruminococcus gnavus, EER) or feces from a normal human. We treated these EER- and human feces-induced colitis mice with the mixture of human-derived 17 Clostridia before or 2 weeks after bacterial colonization. The severity of colitis was examined by blinded histological scores, as well as expression of IFNγ, IL-12p40 and IL-17 in colonic tissues. Flow cytometry analysis of Foxp3 and several cell surface markers was performed using lamina propria cells, mesenteric lymph node cells and splenocytes.

**Results:** The EER- and human feces-colonized exGF IL10−/− mice developed progressive colitis with increased Th1/Th17 responses, but the 17 Clostridia significantly diminished histidine decarboxylase, a key enzyme converting histidine to histamine, in colonic tissues and fecal histamine levels compared to non-treated groups (Table).

**Abstract No:** OP156

**Mouse group**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Clostridia treatment</th>
<th>Germ-free Unites</th>
<th>Human feces-induced colitis</th>
<th>EER-induced colitis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Pre</td>
<td>Untreated</td>
<td>Post</td>
</tr>
<tr>
<td>Histological scores (0-12)</td>
<td>0</td>
<td>5.0</td>
<td>7.6</td>
<td>4.5*</td>
</tr>
<tr>
<td>Cytokines from colon tissue(pg/ml/50mg tissue)</td>
<td>IFNγ</td>
<td>ND</td>
<td>148*</td>
<td>285*</td>
</tr>
<tr>
<td>IL-12p40</td>
<td>553</td>
<td>910*</td>
<td>1692</td>
<td>1053*</td>
</tr>
<tr>
<td>qPCR (focal) (relative to donor)</td>
<td>Fasbacterium sp</td>
<td>–</td>
<td>1.5*</td>
<td>12.5</td>
</tr>
<tr>
<td>E. coli</td>
<td>–</td>
<td>0.2*</td>
<td>5.0</td>
<td>0.4*</td>
</tr>
<tr>
<td>Metabolomics (nmol/g cecal contents)</td>
<td>Histamine</td>
<td>85</td>
<td>60*</td>
<td>–</td>
</tr>
<tr>
<td>1-Methylhistamine</td>
<td>ND</td>
<td>–</td>
<td>7.3</td>
<td>4.0*</td>
</tr>
<tr>
<td>HDRC expression (colon tissue mRNA) (relative to germ-free)</td>
<td>1</td>
<td>1.25*</td>
<td>2.67</td>
<td>1.08*</td>
</tr>
</tbody>
</table>

ND, not detectable; *p<0.01, compared to untreated group, - , not tested, HDC, histidine decarboxylase. EER, human-derived E. coli LF82, E. faecalis and R. gnavus.
**Conclusion:** Our findings suggest novel IL-10-independent protective mechanisms for a resident protective bacterial cocktails in IBD patients.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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**OP157  FAECAL MICROBIOTA IN PAEDIATRIC INFLAMMATORY BOWEL DISEASE BEFORE AND AFTER THERAPY**


**Results:**

- We obtained repeated faecal analysis one year after therapy, 16 (52%) had been treated with imab or not, with less abundance of the Clostridia species (26.3%) at follow-up (overlap in 97); in total 288 subjects. In total 315 (33.4%) subjects reported AD at baseline (n = 232) or at follow-up (n = 324). There were 72 cases with pure AD at baseline and 85 subjects with pure AD at follow-up, AD symptom complex persisting in 20 subjects, p = 0.016) and female gender (15/20 vs. 350/683, p = 0.019). Persistent AD was associated with PPIs at baseline (4/20 vs. 72 cases with pure AD at baseline and 85 subjects with pure AD at follow-up, AD symptom complex persisting in 20 subjects, p = 0.016) and female gender (15/20 vs. 350/683, p = 0.019). Persistent AD was associated with PPIs at baseline (4/20 vs. 72 cases with pure AD at baseline and 85 subjects with pure AD at follow-up, AD symptom complex persisting in 20 subjects, p = 0.016) and female gender (15/20 vs. 350/683, p = 0.019).

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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**OP158  ABDOMINAL DISTENTION SYMPTOMS WITHOUT FUNCTIONAL DYSPEPSIA OR IRRITABLE BOWEL SYNDROME ARE PERSISTENT: 10 YEAR FOLLOW-UP OF THE KALIXANDA STUDY**


**Introduction:**

- Functionality Intestinal dyspepsia (FD) and irritable bowel syndrome (IBS) are common conditions in the population. Symptomatic abdominal distention (AD) coexists with FD and IBS but may also exist as a separate symptom complex.

**Disclosure of Interest:**

- All authors have declared no conflicts of interest.

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**Reference**


**Possible risk factors for FD and IBS at baseline and pure AD at baseline and at follow-up. Age dichotomized at 60-years at baseline, alcohol>100 g/week and H. pylori positive by histology or culture.**

**Conclusion:** Although FD, IBS and AD coexist, one third of those with AD present without FD or IBS. Furthermore, it is persistent and there was no association with immune activating disorders such as Helicobacter pylori infection, asthma or allergy, suggesting that the AD symptom complex is a functional disorder and the pathogenesis is as yet unexplained.

**Disclosure of Interest:** All authors have declared no conflicts of interest.
OP159 THE PREVALENCE OF ROME IV FUNCTIONAL DYSPEPSIA AND ITS IMPACT ON HEALTH IMPAIRMENT; RESULTS FROM A THREE-COUNTRY GENERAL POPULATION STUDY

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2Dept. Of Medicine, University of North Carolina, Chapel Hill, NC/United States of America
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4Dept Of Internal Medicine, Sahlgrenska University Hospital - Dept of Internal Medicine, Sahlgrenska University Hospital; Gothe, Gothenburg/Sweden

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Introduction: The population prevalence of Rome IV functional dyspepsia and its effect on health impairment is unknown. We used data from a population-based study to address this, and compared somatisation, quality of life, healthcare utilisation, and presence of overlapping irritable syndrome and functional heartburn in individuals fulfilling criteria for Rome IV functional dyspepsia against non-dyspeptic controls.

Aims & Methods: An internet-based health survey was completed by 6300 general population adults from three English-speaking countries (2100 each from United States, Canada, and United Kingdom). Quota-based sampling was used to ensure equal sex, age, and education distribution across the countries. The survey included questions on demographics, healthcare visits, medication use, criteria for the Rome IV functional dyspepsia as well as for irritable bowel syndrome and functional heartburn, the patient health questionnaire-12 somatisation measure, and the Short Form-8 quality of life questionnaire.

Results: Data was available for analysis from 5931 subjects (49.2% female; mean age 47.4 years, range 18-92). Overall, 551 (9.3%) of the population fulfilled criteria for Rome IV functional dyspepsia. This comprised 339 (61.5%) with postprandial distress syndrome-PDS, 97 (17.6%) with epigastric pain syndrome-EPS, and 115 (20.9%) with overlapping PDS-EPS. Subjects with functional dyspepsia had significantly greater health impairment than non-dyspeptic controls, with on average 73% seeking healthcare more than once yearly and 59% taking GI-relevant medication (i.e. GI-specific, psychotropics, analgesia, or complementary medicine). Notably, those with overlapping Rome IV PDS and EPS had higher frequency of co-existing irritable bowel syndrome and functional heartburn, worse somatisation, and poorer mental and physical quality of life scores, compared to EPS- or PDS-alone (see table). Somatisation and quality of life scores were similar between EPS- and PDS-alone.

Conclusion: Almost 10% of the population fulfil criteria for Rome IV functional dyspepsia, subjects with Rome IV functional dyspepsia, in particular those with overlapping PDS and EPS, have considerable health impairment. This is despite frequent healthcare visits and use of GI-relevant medication. Study support: The Rome Foundation

Disclosure of Interest: All authors have declared no conflicts of interest.

References

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Disclosure of Interest: All authors have declared no conflicts of interest.

Disclosure of Interest: All authors have declared no conflicts of interest.
Introduction: Previous studies have defined irritable bowel syndrome (IBS), as well as distinct upper and lower gastrointestinal (GI) symptom groupings, by factor analysis. However, most previous studies have not used population-based samples, and none have used the most recent validated diagnostic questionnaire to define functional GI disorders. The Rome IV criteria define these disorders based on specific symptom combinations. We investigated how these symptom combinations group together in a factor analysis.

Aims & Methods: The Rome IV questionnaire was completed online in English by a population-based sample of 5931 respondents from the United Kingdom, United States, and Canada (49% female, age range 18 to 92 years). We performed an exploratory factor analysis on a selection of questions from the validated Rome IV diagnostic questionnaire, including all symptoms used to define functional GI disorders. The number of factors was decided based on eigenvalues (> 1.0), and varimax rotation was used to simplify the structures. Factor loadings greater than 0.4 were deemed relevant.

Results: Four factors were identified, which we characterised as upper GI symptoms (1), IBS (2), constipation (3), and diarrhoea (4). The upper GI symptoms factor contained a large number of items, including both oesophageal and gastroduodenal symptoms, and had no further breakdown. The IBS factor was defined by the key components in the Rome IV diagnostic criteria for IBS: abdominal pain associated with defecation and abnormal bowel habits (r > 0.75). Faecal incontinence was part of the diarrhoea factor, albeit with a lower loading (r = 0.41). The fourth factor included all six symptoms in the diagnostic criteria for functional constipation. Not fitted were pain "anywhere in the abdomen" (complex structure), bloating/abdominal distension (unique), and anorectal pain (unique). Rotated factor loadings are listed in table 1.

Conclusion: Distinct upper and lower GI symptom groupings exist in the general population, and can be identified using the English Rome IV questionnaire in a large sample from three English-speaking countries.

Disclosure of Interest: W.E. Whitehead received research grants from Ironwood Pharmaceuticals, Takeda Pharmaceuticals, and Salix Pharmaceuticals and the Rome Foundation, and is a consultant to Ono Pharma USA. O.S. Palsson: Olafur Palsson received research grants from Ironwood Pharmaceuticals, Takeda Pharmaceuticals, and Salix Pharmaceuticals and the Rome Foundation. H. Törnblom: Håkan Törnblom has served as Consultant/Advisory Board member for Almirall and Allergan as a speaker for Tillotts, Takeda, Shire and Almirall. L. Van Oudenhove: Lukas Van Oudenhove has received grant support from Abide Therapeutics and Nestlé and has given scientific advice to Grünenthal. J. Tack: Jan Tack has given scientific advice to Abide Therapeutics, AlfaWassermann, Allergan, Christian Hansen, Danone, Genfit, Ironwood, Janssen, Kiowa Kirin, Menarini, Mylan, Novartis, Nutricia, Ono Pharma, Rhythm, Shionogi, Shire, SK Life Sciences, Takeda, . . . Magnus Simrén: Magnus Simrén has received unrestricted research grants from Danone and Ferring Pharmaceuticals, and served as a Consultant/Advisory Board member for AstraZeneca, Danone, Nestlé, Menarini, Almirall, Allergan, Albireo, Glycom and Shire, and as a spe… All other authors have declared no conflicts of interest.
Constipation is a common side effect of opioid use, and can affect

Table Continued

<table>
<thead>
<tr>
<th>Respondents, %</th>
<th>Rome IV with OIC (n = 951)</th>
<th>Non-Rome IV with constipation (n = 1065)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Feeling of incomplete bowel movement</td>
<td>82* (24)</td>
<td>48</td>
</tr>
<tr>
<td>Stomach cramps</td>
<td>65* (44)</td>
<td>44</td>
</tr>
<tr>
<td>Rectal burning during/after bowel movement</td>
<td>59* (40)</td>
<td>40</td>
</tr>
<tr>
<td>Haemorrhoids</td>
<td>53* (40)</td>
<td>40</td>
</tr>
<tr>
<td>Nausea</td>
<td>46* (32)</td>
<td>32</td>
</tr>
<tr>
<td>Non-haemorrhoidal rectal bleeding</td>
<td>34* (24)</td>
<td>24</td>
</tr>
<tr>
<td>Vomiting</td>
<td>29* (18)</td>
<td>18</td>
</tr>
<tr>
<td>Emotional- psychological symptoms</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Frustrated</td>
<td>28* (16)</td>
<td>16</td>
</tr>
<tr>
<td>Dependent and ‘not free’</td>
<td>27* (15)</td>
<td>15</td>
</tr>
<tr>
<td>Anxious or worried</td>
<td>23* (14)</td>
<td>14</td>
</tr>
<tr>
<td>Depressed</td>
<td>21* (14)</td>
<td>14</td>
</tr>
<tr>
<td>Helpless</td>
<td>21* (13)</td>
<td>13</td>
</tr>
<tr>
<td>Obsessed</td>
<td>20* (12)</td>
<td>12</td>
</tr>
<tr>
<td>Disgusted</td>
<td>16 (11)</td>
<td>11</td>
</tr>
<tr>
<td>Effects on quality of life/social symptoms</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Excessive time spent in the bathroom</td>
<td>54* (38)</td>
<td>38</td>
</tr>
<tr>
<td>Difficulty following normal routine</td>
<td>45* (30)</td>
<td>30</td>
</tr>
<tr>
<td>Difficulty being intimate with others</td>
<td>30* (29)</td>
<td>29</td>
</tr>
<tr>
<td>Difficulty pursuing hobbies</td>
<td>39* (27)</td>
<td>27</td>
</tr>
<tr>
<td>Difficulty working/doing household chores</td>
<td>38* (26)</td>
<td>26</td>
</tr>
<tr>
<td>Difficulty socialising</td>
<td>33* (23)</td>
<td>23</td>
</tr>
<tr>
<td>Difficulty taking opioid drugs as normal</td>
<td>30* (21)</td>
<td>21</td>
</tr>
</tbody>
</table>

*p < 0.05 vs non-Rome IV group

Conclusion: Comparing respondents meeting Rome IV OIC criteria with those who did not, they appeared to experience greater symptom and biopsychosocial burden. This study suggests that Rome IV criteria can identify more severe OIC patients, but may underdiagnose OIC patients who do not demonstrate the full scale of symptoms.

Disclosure of Interest: A. Lass: Contractor to Shionogi Ltd. All other authors have declared no conflicts of interest.

OP163 USERS OF WEAK OPIOIDS HAVE A SMALLER SPECTRUM OF CONSTIPATION SYMPTOMS, BUT A SIMILAR DEGREE OF BOTHER FROM CONSTIPATION, AS USERS OF POTENT OPIOIDS

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2Medical, Shionogi Limited, London/United Kingdom
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Introduction: Constipation is a common side effect of opioid use, and can affect up to 81% of patients, despite concomitant use of laxatives. However, it is not clear whether there is any difference in biopsychosocial disease burden of constipation in patients using strong or weak opioids. Aims & Methods: To assess the impact of strong (e.g. buprenorphine, fentanyl) or weak (e.g. codeine, dihydrocodeine) opioids in patients with chronic pain who have constipation. This was a quantitative, questionnaire-based, online survey of respondents aged ≥40 years with largely non-cancer-related chronic pain, treated long-term with strong opioids (N = 1210) or using weak opioids (n = 605) in Germany, Spain and UK. Past medical history, treatment, symptoms, disease burden, and effects on quality of life were assessed. Results: A comparable degree of bother from constipation symptoms was felt by both weak- and strong-opioid users, with 38% and 40% of respondents, respectively, stating that constipation bothered them quite a lot/a great deal (between-group comparison, p = 0.40). This pattern was reflected in the main psychological symptoms experienced due to constipation (frustration, dependence, anxiety; Table). Both groups were similar in incidence of more common physical symptoms (straining to pass stools, abdominal bloating, sensation of bowel blockage/obstruction; Table). However, weak-opioid users experienced significantly fewer less-common physical symptoms of constipation vs strong-opioid users, including stomach cramps, rectal burning and haemorrhoids (all p < 0.02; Table). Moreover, the impact on quality of life/social symptoms was felt significantly less by weak- vs strong-opioid users (Table).

Table: Study findings in strong- and weak-opioid users who report constipation.

<table>
<thead>
<tr>
<th>Respondents, %</th>
<th>Strong-opioid users (n = 1210)</th>
<th>Weak-opioid users (n = 605)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Higher physical symptoms</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Straining to try to pass stools</td>
<td>74</td>
<td>77</td>
</tr>
<tr>
<td>Difficulty socialising</td>
<td>66</td>
<td>67</td>
</tr>
<tr>
<td>Abdominal bloating</td>
<td>69</td>
<td>68</td>
</tr>
<tr>
<td>Feeling of incomplete bowel movement</td>
<td>64</td>
<td>67</td>
</tr>
<tr>
<td>Difficulty working/doing household chores</td>
<td>47* (40)</td>
<td>40</td>
</tr>
<tr>
<td>Nausea</td>
<td>46* (39)</td>
<td>39</td>
</tr>
<tr>
<td>Non-haemorrhoidal rectal bleeding</td>
<td>29* (19)</td>
<td>19</td>
</tr>
<tr>
<td>Vomiting</td>
<td>21* (11)</td>
<td>11</td>
</tr>
<tr>
<td>Emotional-psychological symptoms</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Frustrated</td>
<td>24</td>
<td>24</td>
</tr>
<tr>
<td>Dependent and ‘not free’</td>
<td>21</td>
<td>18</td>
</tr>
<tr>
<td>Anxious or worried</td>
<td>18</td>
<td>15</td>
</tr>
<tr>
<td>Helpless</td>
<td>18</td>
<td>16</td>
</tr>
<tr>
<td>Depressed</td>
<td>19* (14)</td>
<td>14</td>
</tr>
<tr>
<td>Obsessed (unable to stop thinking about it)</td>
<td>16</td>
<td>14</td>
</tr>
<tr>
<td>Disgusted</td>
<td>13</td>
<td>11</td>
</tr>
<tr>
<td>Effects on quality of life/social symptoms</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Excessive time spent in the bathroom</td>
<td>45* (38)</td>
<td>38</td>
</tr>
<tr>
<td>Difficulty following normal routine</td>
<td>35* (25)</td>
<td>25</td>
</tr>
<tr>
<td>Difficulty being intimate with others</td>
<td>33* (21)</td>
<td>21</td>
</tr>
<tr>
<td>Difficulty pursuing hobbies</td>
<td>31* (19)</td>
<td>19</td>
</tr>
<tr>
<td>Difficulty working/doing household chores</td>
<td>31* (19)</td>
<td>19</td>
</tr>
<tr>
<td>Difficulty socialising</td>
<td>27* (16)</td>
<td>16</td>
</tr>
<tr>
<td>Difficulty taking opioid drugs as normal</td>
<td>22* (9)</td>
<td>9</td>
</tr>
</tbody>
</table>

*p < 0.05 vs weak-opioid users

Conclusion: Both weak- and strong-opioid users experience considerable biopsychosocial burden caused by constipation. Weak-opioid users appear to be subjectively as bothered by their constipation as strong-opioid users, despite experiencing less severe physical symptoms and a less drastic impact on quality of life. This may reflect the latter group having more serious underlying pain conditions and/or requiring other concomitant therapies that cause debilitating side effects of greater concern than constipation, compared with the former group.

Disclosure of Interest: A. Lass: Contractor to Shionogi Ltd. All other authors have declared no conflicts of interest.

Reference

TUESDAY, OCTOBER 31, 2017 08:30-10:00

ACUTE AND CHRONIC PANCREATITIS: RISK FACTORS AND PREVENTION - ROOM E2

OP164 ENDOSCOPIC ULTRASOUND-BASED MULTIMODAL EVALUATION OF THE PANCREAS FOR THE DIAGNOSIS OF EARLY CHRONICPancreatitis

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Introduction: Early diagnosis of chronic pancreatitis (CP) is hindered by the limited accuracy of diagnostic methods. Endoscopic ultrasound (EUS) and the endoscopic pancreatic function test (ePFT) are the most sensitive morphological...
and functional method respectively. The multimodal EUS-based pancreatic evaluation provides dynamic morphological and functional information of the pancreas supporting the diagnosis of CP.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP165 THE IMPACT OF BARIATRIC SURGERY ON ACUTE PANCREATITIS MORTALITY AND OTHER OUTCOMES: A NATIONWIDE ANALYSIS

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Introduction: Rapid weight loss after bariatric surgery (BS) has been associated with the formation of gallstones, and subsequent acute cholecystitis and pancreatitis (AP). However, the complex post-surgical anatomy limits the possibility of performing an ERCP as part of AP treatment. Therefore, the aim of this study was to assess the impact of bariatric surgery on mortality, morbidity and resource utilization among patients with AP using a national database.

Aims & Methods: This was a case-control study using the National Inpatient Sample (NIS), a publicly available inpatient database in the United States. All patients with an ICD-9 CM code for a principal diagnosis of AP were included. There were no exclusion criteria. Patients with a past history of BS were included. No significant differences in mortality between the different weight categories presented. Results: The search yielded 1163 studies. After critical review, 4 studies with 1139 patients were included. Mean age was 52 years (SD 18), 546 (52%) patients were men, BMI was 26.3 (SD 6.8), 294 (26%) patients were obese. The most prevalent aetiologies were biliary (n = 439, 39%) and alcohol (n = 195; 17%). 551 (48%) patients had predicted SAP, 299 (26%) had necrosis, 247 (22%) had organ dysfunction. The secondary outcomes were: 1-Morbidity: Intensive care unit (ICU) admission, shock and multi-organ failure. 2- Resource utilization: use of ERCP, cholecystectomy, total parenteral nutrition (TPN), length of hospital stay (LOS), total hospital costs. Multivariate regression analyses were used to adjust for the following confounders: Age, sex, race, income in patients’ zip code, Charlson Comorbidity Index, hospital region, location, size and teaching status.

Result: A total of 274,775 patients with AP were included in the study, of which 4240 (1.7%) had undergone bariatric surgery. The mean patient age was 51 years and 48% were female. After adjusting for confounders, patients with and without a history of bariatric surgery had similar adjusted odds of mortality (adjusted Odds Ratio (OR) 1.37, 95% CI: 0.51–3.65, p < 0.02). Looking at morbidity, patients with and without a history of bariatric surgery had similar adjusted odds of shock (aOR: 0.71, 95% CI: 0.23 – 2.24, p = 0.57), multiple organ failure (aOR: 0.61, 95% CI: 0.08–4.37, p = 0.62), and ICU admission (aOR: 0.34, 95% CI: 0.11 – 1.06, p = 0.06). As for resource utilization data, patients with bariatric surgery had lower adjusted odds of ERCP (aOR: 0.55, 95% CI: 0.38 – 0.79, p < 0.01), but both patient groups had similar adjusted odds of cholecystectomy (aOR: 1.21, 95% CI: 0.98 – 1.49, p = 0.07) and TPN use (aOR: 1.21, 95% CI: 0.77 – 1.90, p = 0.41). Interestingly, although patients with bariatric surgery had shorter adjusted length of stay (adjusted mean difference: -0.48 days, 95% CI: -0.74 to -0.23, p < 0.01) and total hospitalization costs (adjusted mean difference: - $755, 95% CI: - $1295 to - $215, p < 0.01), both patient groups had similar total hospitalization charges (adjusted mean difference: $1949, 95% CI: $4366 to $467, p = 0.11).

Conclusion: Bariatric surgery has no impact on inpatient all-cause mortality among patients who develop acute pancreatitis, despite its association gallstone acute pancreatitis and limited ERCP performance. In addition, bariatric surgery does not affect morbidity in this patient population as measured by rate of shock, multiple organ failure and ICU admission. However, a history of bariatric surgery is associated with decreased rates of ERCP, shorter length of stay and lower hospital costs.

Disclosure of Interest: All authors have declared no conflicts of interest.
A73

United European Gastroenterology Journal 5(5S)

**OP167 STATIN CONSUMPTION IS ASSOCIATED TO A LOWER RISK OF POSTENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY PANCREATITIS**


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**Introduction:** The most frequent complication of endoscopic retrograde cholangiopancreatography (ERP) is post-ERP acute pancreatitis (PEP), which is associated to increased morbidity, mortality and costs. Statin consumption seems to lower the incidence of acute pancreatitis due to other etiologies, according to previous studies. The relationship between statin use and the incidence of PEP has not been studied before.

**Aims & Methods:** We aimed to investigate the relationship between the use of statins and the incidence of PEP. Methods: multicenter (4 Spanish tertiary-care public hospitals) retrospective cohort study. Adult patients undergoing an ERP between January 2015 and January 2016 were included in the study. We excluded patients with chronic pancreatitis, with ongoing acute pancreatitis and those who developed other complications after ERP. Patients were classified into 2 groups: under statin treatment (group S) and controls (group C). A multivariate analysis was performed (binary logistic regression) including possible confounding variables: center, female gender, previous pancreatitis, suspected sphincter of Oddi dysfunction, difficult cannulation (>10 minutes), pancreatic guidewire passages >1, pancreatic injection, pancreatic stent, presence of malignant biliary stenosis and presence of cholelithiasis.

**Results:** Six hundred and ninety-four patients were included, median age 76 (63–85), 324 (41%) females, 209 (30%) in group S. Thirty (0.5%) patients developed PEP, 4 (2%) in group S and 28 (6%) in group C. Univariate analysis yielded an Odds Ratio (OR) for developing PEP for group S of 0.3 (0.1–0.9), p = 0.034; multivariate analysis showed an adjusted OR of 0.3 (0.1–0.8), p = 0.020. Only 1 patient died (overall: 0.1%, within patients with PEP: 4%), who was in group C.

**Conclusion:** We conclude that in our sample of patients, statin consumption was independently associated to a 70% risk reduction of PEP.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**References**


**OP168 THE RISK FOR POST-ERCP PANCREATITIS AFTER INADVERTENT PANCREATIC DUCT CANNULATION CAN BE PREVENTED BY TEMPORARY PROPHYLACTIC PANCREATIC STENT:**

A MULTICENTRE, PROSPECTIVE, RANDOMIZED TRIAL

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**Introduction:** The incidence of acute pancreatitis (AP) is the most frequent complication of endoscopic retrograde cholangiopancreatography (ERP) and the most frequent cause of iatrogenic AR. The rate of post-ERP-Pancreatitis (PEP) is about 3.5% of all ERCPs, in high-risk patients up to 25% [1, 2]. Due to the lack of specific therapy of AP, prevention of PEP should be a crucial goal. The most promising prophylactic approaches are non-steroidal anti-inflammatory drugs (NSAID) and pancreatic stents [3]. Although several studies showed a decreased risk of PEP for NSAID and pancreatic stents, the results of these studies are inconsistent [4]. All these studies included only high-risk patients and do not represent the cross-section of ERCPs typically performed [5]. Further, definition of high risk is inconsistent [6]. One of the described risk factors is inadvertent cannulation of the pancreatic duct [3, 5].

**Aims & Methods:** Aim of the study was to evaluate the effect regarding the rate of PEP after prophylactic pancreatic stent in an unselected patient population with inadvertent cannulation of the pancreatic duct. Multicentre, prospective, randomized study. Patients undergoing first time ERCP were eligible. In case of inadvertent cannulation of the pancreatic duct patients were randomized for prophylactic pancreatic stent or no prophylactic pancreatic stent.

**Results:** 169 patients were randomized (87 stent, 82 no stent). PEP occurred in 33/169 patients (19.5%). Rate of PEP was statistically significantly lower in the stent group (12.6%) compared to the no stent group (26.8%); odds ratio 0.395; 95% confidence interval: 0.178–0.878. Inclusion of patients with inadvertent cannulation of the pancreatic duct during first time ERCP can be significantly reduced by a temporary prophylactic pancreatic stent.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**References**

**OP170** TERMINOLOGY AND DESCRIPTION OF VASCULAR LESIONS IN SMALL BOWEL CAPSULE ENDOSCOPY: AN INTERNATIONAL DELPHI CONSSENSUS STATEMENT


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Introduction: The terminology and description of small bowel (SB) vascular lesions in capsule endoscopy (CE) are scarce in the medical literature. They are mostly based on the reader’s background and opinion, and therefore remain mainly subjective, with a potential negative impact on clinical care, teaching and research regarding SB-CE. Our aim was to define and to describe the most frequent vascular lesions in SB-CE.

Aims & Methods: A panel of 18 European expert SB-CE readers, teachers and researchers was built aside the UEGW 2016 meeting. Three of these experts animated an internet-based, three-round Delphi consensus, but did not participate to any vote. They built questionnaires that included various still frames of vascular lesions from third-generation SB-CE videos. The remaining 15 experts were asked to rate different proposals for diagnostic, terminology, and description of various SB vascular lesions. Rare or protruding SB vascular lesions (Kaposi’s sarcoma, Dieulafoy ulceration simplex, varices, vascular tumors) were not considered for the study. A 6-point Likert rating scale (varying from strongly disagree to strongly agree) was used for all proposal in the 3 successive questionnaires. A consensus was considered to be reached when at least 80% voting members scored the statement within the “[dis]agree” or “[strongly] disagree”.

Results: Consensual terms and descriptions of angiodyplasia, erythematous patch, red spot or red spot, and phlebectasia were reached (table 1). No consensus was reached for definition or description of more subtle or small vascular mucosal abnormalities.mucosal layer (surrounded with intestinal villi).

**Table 1:** Results

<table>
<thead>
<tr>
<th>Terminology</th>
<th>Definition</th>
<th>Agreement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Angiodyplasia</td>
<td>A clearly demarcated, bright-red, flat lesion, consisting of tortuous and clustered capillary dilatations, within the mucosal layer (surrounded with intestinal villi). Can be small (few mm) to large (few cm).</td>
<td>93.3%</td>
</tr>
<tr>
<td>Erythematous patch</td>
<td>A small (few mm) and flat reddish area, without any vessel appearance, within the mucosal layer (surrounded with intestinal villi).</td>
<td>80%</td>
</tr>
<tr>
<td>Red spot or red spot</td>
<td>A miniscale (less than 1 mm), punctuate, and flat lesion with a bright-red area, without linear or vessel appearance, within the mucosal layer (surrounded with intestinal villi).</td>
<td>80%</td>
</tr>
<tr>
<td>Phlebectasia</td>
<td>A small (few mm), flat to slightly elevated, bluish venous dilatation running below the mucosa (covered by intestinal villi).</td>
<td>86.6%</td>
</tr>
</tbody>
</table>

Conclusion: An international group has reached a consensus on the terminology and the description of the most frequent and relevant SB vascular lesions in CE. These terms and descriptions will be useful for daily practice but also for teaching and for medical research. Publication: United European Gastroenterology Journal 5(5S)

**Disclosure of Interest:** All authors have declared no conflicts of interest.


**OP171** A PROSPECTIVE MULTICENTER SINGLE-BLEND RANDOMIZED CONTROLLED TRIAL COMPARING FNA AND FNB IN THE DIAGNOSES OF SOLID MASSESA PROSPECTIVE MULTICENTER SINGLE-BLEND RANDOMIZED CONTROLLED TRIAL COMPARING FNA AND FNB IN THE DIAGNOSIS OF SOLID MASSES


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2Center For Interventional Endoscopy, Tongji Hospital affiliated to Tongji Medical College, HUST, Wuhan/China
3Shanghai Institute of Digestive Surgery and Gastroenterology, B.J. Medical College, Beijing/China
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5Fudan University: Shanghai Cancer Center, Fudan University, Shanghai/China
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Introduction: Endoscopic ultrasound (EUS) guided fine needle biopsy (FNB) with side fenestration on the needle was developed aiming to obtain both cytological aspirates and histological core samples. To reveal the diagnostic yield of FNB sampling solid mass compared to standard fine needle aspiration (FNA), we conducted a large-scale multicenter study in patients with pancreatic and non-pancreatic masses. We also aimed to establish optimal techniques in EUS tissue acquisition.

Aims & Methods: This was a prospective multicenter single-blind randomized controlled trial. Between December 2014 and January 2016, 408 patients were enrolled from five tertiary-care academic medical centers and randomized at a 1:1 ratio to receive either 22G FNA or 22G FNB. Two tissue acquisition (TA) techniques (1st and 2nd passes using slow pull vs. 3rd and 4th passes using suction methods) were performed on all EUS needles. The primary outcome was the diagnostic yield comparing FNA and FNB on all solid lesions, pancreatic and non-pancreatic masses, respectively (except for the analysis of the histologic specimen quantity of cell, tissue integrity, and blood contamination).

Results: Among all lesions, FNB group (n = 190) compared to FNA group (n = 187) gained superior histological diagnostic yield (91.44% vs. 80%; p = 0.0015), and higher cytopathological diagnostic yield (85.56% vs. 78.95%; p = 0.093). For pancreatic mass, FNB group (n = 123) achieved better histological diagnostic yield compared to FNA group (n = 126) (92.68% vs. 81.75%; p = 0.0099), and also higher cytopathological diagnostic yield (88.62% vs. 79.37%; p = 0.00468), respectively. For non-pancreatic mass, there was no difference between FNB and FNA on diagnostic accuracy. Furthermore for pancreatic mass, when slow pull technique was applied in the first and second passes, FNB was superior to FNA on specimen quality and diagnostic yield.

Conclusion: Overall diagnostic yield of EUS-FNB needle acquisition was better compared to FNA needle among all studied solid lesions. For pancreatic masses, the 22G FNB needle also gained superior histological diagnostic accuracy and higher cytological diagnostic yield compared to 22G FNA. We further suggest choosing FNB over FNA on pancreatic lesion for TA when slow pull technique was applied in the first two passes.

Disclosure of Interest: All authors have declared no conflicts of interest.

order to measure tissue volume and isolate malignant cells from desmoplastic stroma. Sample size based on 50% difference in the presence of desmoplastic stroma at 80% power was estimated at 34 patients.

**Results:** Of the 46 patients randomized to undergo EUS-guided sampling, the final diagnosis was pancreatic cancer in 36, neuroendocrine tumor in 2, sarcoma in 1 and benign disease in 7. The median total tissue volume, 6.1 mm³ (IQR 2.2–9.9) vs. 0.28 mm³ (IQR 0.045–0.93) (p < 0.001) and presence of desmoplastic stroma in tumor, 84.6 vs. 33.3% (p < 0.001) were significantly higher in the FNB cohort. Also, the diagnostic yield at cell block was significantly higher for the FNB cohort, 97.8 vs. 82.6% (p = 0.003). There was no difference in diagnostic adequacy at ROSE between the FNB and FNA cohorts, 100 vs. 95.7% (p = 0.50).

**Table:** Comparing diagnostic characteristics between FNB and FNA needles

<table>
<thead>
<tr>
<th></th>
<th>FNB</th>
<th>FNA</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ROSE - diagnostic adequacy: n (%)</td>
<td>46 (100)</td>
<td>44 (95.7)</td>
<td>0.495</td>
</tr>
<tr>
<td>ROSE - diagnostic accuracy: n (%)</td>
<td>45 (97.8)</td>
<td>43 (93.5)</td>
<td>0.617</td>
</tr>
<tr>
<td>Diagnostic cell block: n (%)</td>
<td>45 (97.8)</td>
<td>38 (82.6)</td>
<td>0.030</td>
</tr>
<tr>
<td>Total tissue area (mm²): Mean (SD)</td>
<td>11.1 (2.6)</td>
<td>9.0 (1.9)</td>
<td>0.001</td>
</tr>
<tr>
<td>Median</td>
<td>6.1</td>
<td>0.28</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>IQR</td>
<td>2.2–9.9</td>
<td>0.045–0.93</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Range</td>
<td>0.025–181.1</td>
<td>0.0044–0.30</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Total tumor area (mm²): Mean (SD)</td>
<td>1.7 (2.3)</td>
<td>0.50 (1.86)</td>
<td>0.001</td>
</tr>
<tr>
<td>Median</td>
<td>0.68</td>
<td>0.099</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>IQR</td>
<td>0.23–2.8</td>
<td>0.0044–0.30</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Range</td>
<td>0–12.4</td>
<td>0–11.6</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Desmoplastic fibrosis present: n (%)</td>
<td>33 (84.6)</td>
<td>13 (33.3)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

**Conclusion:** The Fransen biopsy needle yields significantly more tissue with superior histology than the FNA needle. This development is likely to advance the role of EUS in facilitating molecular-based anti-cancer therapy.

**Disclosure of Interest:** R. Hawes: Consultant for Olympus America inc. and Boston Scientific Corporation

S.Varadarajulu: Consultant for Olympus America Inc. and Boston Scientific Corporation

All other authors have declared no conflicts of interest.

**OP73 CAN ARTIFICIAL INTELLIGENCE FOR ENDOCOSCOPY PROVIDES FULLY AUTOMATED DIAGNOSIS OF HISTOLOGICAL HEALING IN ULCERATIVE COLITIS?**

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**Introduction:** Recent studies suggest that histological remission is a treatment goal in ulcerative colitis (UC). However, there is a discrepancy between histological remission and conventional endoscopic mucosal healing. We have already reported two useful aspects of EC that is the next-generation ultra-magnifying endoscopy allowing visualization of microvessels; one is that findings of EC are more numbers of images for machine learning.

**Aims & Methods:** The aim of this study is to develop a new CAD system for the histological remission in UC, with use of EC combined with NBI mode. Histological assessment was based on Geboes index. Geboes index ≥3.0 and absence of basal plasmacytosis was considered as histological remission, while Geboes index >3.0 or presence of basal plasmacytosis was as active. The algorithm of this CAD system was programmed based on texture analysis, which can quantify the pattern of endoscopic image and vessel features. Support vector machine was used as a classifier for two-category diagnostic output (histological remission or active status). A total of 1935 images (histological remission, 1042; active status, 893) were used for machine learning process. The overall accuracy to distinguish histological remission from active status was assessed by using leave-one-out cross validation. In this validation, randomly selected one image was evaluated by using the developed CAD system which was trained by using the remaining 1934 images.

**Results:** According to the leave-one-out cross validation which was repeatedly calculated for 1935 times, the average accuracy of the developed CAD system (identification of histological remission was 81.7%. The accuracy with high confidence (probability ≥90%) was 98.9%. The high confidence rate was 32.4%.

**Conclusion:** The diagnostic ability of artificial intelligence in classification of EC image for assessment of histological activeness of UC was substantially good, although it was tentative model. Higher accuracy could be expected with much more numbers of images for machine learning.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**OP74 A PILOT INTERNATIONAL MULTICENTER RANDOMIZED CONTROLLED TRIAL OF CHROMOENDOSCOPY VERSUS AUTOFLUORESCENCE IMAGING FOR NEOPLASIA DETECTION IN PATIENTS WITH LONGSTANDING ULCERATIVE COLITIS (FIND-UC)**


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**Introduction:** Patients with longstanding ulcerative colitis (UC) are at increased risk for developing colorectal cancer and regular surveillance is advised. Previous studies demonstrated that both surveillance with chromoendoscopy (CE) and autofluorescence imaging (AFI) increased dysplasia detection rates in patients with longstanding UC when compared to standard white light endoscopy. Chromoendoscopy is currently recommended in national guidelines, but is poorly adopted in clinical practice because it is time-consuming. AFI is a push-button technique in which endogenous autofluorescence is used to highlight neoplastic tissue. The aim of this pilot trial was to determine whether AFI should be further studied as an alternative method for dysplasia surveillance in patients with longstanding UC.

**Aims & Methods:** In this prospective, non-inferiority pilot randomized trial with fixed design, patients undergoing colonoscopy surveillance for longstanding UC (Montreal E2 > 15 years or Montreal E3 > 8 years) in 5 centers in the Netherlands and the UK were randomized for inspection with either CE or AFI (1:1). Patients with active colitis (MAYO > 1 in at least 1 segment) or Barrett’s Bowel Preparation Scale ≤ 6 were excluded. Randomization was stratified for presence of previous dysplasia and/or primary sclerosing cholangitis (PSC). Targeted biopsies of visible lesions and random biopsies of each segment were collected. The main outcome was the relative dysplasia detection rate calculated by the quotient of CE over AFI. This relative detection rate was determined for the proportion of UC patients in which at least one dysplastic lesion was detected and for the mean number of dysplastic lesions per patient. A relative detection rate below 1.50 for both outcomes would support performing a subsequent large non-inferiority trial. For this study, 210 UC patients were needed to achieve a relative detection rate of 1.50 with an 80% confidence interval between 1.00 and 2.25. Dysplasia was diagnosed by an expert gastrointestinal pathologist in consensus with a second expert pathologist.

**Results:** Between August 2013 and March 2017, 210 UC patients were randomized to undergo surveillance with CE (N = 105) or AFI (N = 105). The mean age of patients at colonoscopy was 56.1 (SD 12.7) years, 58.1% were male and the median time since previous surveillance colonoscopy was 3 years (IQR 1–4) (Table 1). During CE, dysplasia was detected in 20 (19.0%) patients, while 14 patients (13.3%) were diagnosed with dysplasia during AFI. The relative dysplasia detection rate was calculated by the quotient of CE over AFI. This relative detection rate for CE versus AFI for the proportion of UC patients with at least one dysplastic lesion was 1.43 (95% CI; 0.76–2.68). The mean number of detected dysplastic lesions per patient was 0.37 for CE compared to 0.13 for AFI (relative dysplasia detection rate 2.79, 95% CI; 1.61–4.82). During CE, the proportion of patients in whom targeted biopsies were taken (65.7% vs. 47.6%, p < 0.001) was larger and total extubation times were longer (25.1 min vs. 18.0 min, p < 0.01).

**Table 1:** Patient characteristics of randomized patients with longstanding ulcerative colitis.

<table>
<thead>
<tr>
<th></th>
<th>Chromoendoscopy (N = 105)</th>
<th>Autofluorescence imaging (N = 105)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age, years (SD)</td>
<td>56.1 (12.3)</td>
<td>56.3 (13.1)</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>44 (41.9%)</td>
<td>44 (41.9%)</td>
</tr>
<tr>
<td>UC duration in years, median (IQR)</td>
<td>19.0 (13.0–27.3)</td>
<td>22.5 (15.0–32.8)</td>
</tr>
</tbody>
</table>
Conclusion: In this pilot randomized study with fixed design comparing CE with AFI for dysplasia surveillance in patients with longstanding UC, AFI was non-inferior to CE on a dysplasia per patient basis, but was inferior on the basis of mean number of dysplastic lesions detected. These results argue against a future large prospective randomized trial comparing these methods for dysplasia surveillance in patients with longstanding UC (NTR4062).

Disclosure of Interest: J.L.A. Vleugels’ research department is receiving research support from Olympus and Fujifilm. J.L. Aerts has received speaker fees from Olympus; research support and consultancy fees from Cosmo Technologies; is a member of the clinical advisory board of Lumendi.

M.D. Rutter: Rutter’s department is receiving research support from Olympus, Allergan, Pentax and Norgine.

K. Ragunath: Ragunath has received educational grants from Olympus, Cook and Covidien; speaker honorarium from Olympus; consultancy fees from Olympus and Boston Scientific; research support from COOK, Covidien, AstraZeneca and Pentax.

C.I. Reeve: Reeve’s department receives research funding from Olympus Medical, ARC Medical, Aqualand Endoscopy, Almirall, and Cook (from 2010 to present). C.Y. Ponsioen: Ponsioen’s department is receiving research support from Olympus and Fujifilm.

S. Samuel: Samuel has received speaker fees from Abbvie, MSD and Pharmacosmos; consultancy fees from Pfizer and Falk and educational grant from Abbvie, MSD and Ferring.

F. Butt: Butt’s department receives research funding from Olympus Medical, ARC Medical, Aqualand Endoscopy, Almirall, and Cook (from 2010 to present). E. Dekker: Dekker has equipment on loan from Olympus Europe and Fujifilm, has received a research grant from Olympus Europe and Fujifilm, and consulted for Tollotts Pharma (one time).

All other authors have declared no conflicts of interest.

Disclosure of Interest: All other authors have declared no conflicts of interest.

Reference

TUESDAY, OCTOBER 31, 2017 08:30-10:00 NEW INSIGHTS IN MICROBIOTA: GUT AND LIVER ASPECTS - ROOM B5

OP176 GUT MICROBIOTA INVOLVES IN NON-ALCOHOLIC FATTY LIVER DISEASE VIA AFFECTING INTRA-HEPATIC CD4+ T LYMPHOCYTE
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Op176 Abstract: Introduction: Gut microbiota plays an important role in the pathogenesis of non-alcoholic fatty liver disease (NAFLD). CD4+T lymphocytes have also emerged as an important player in NAFLD since the function of their immune was realized. But the effects of gut bacteria on intra-hepatic T lymphocytes are not very clear.

Aims & Methods: To investigate the impact of gut microbiota on hepatic CD4+T lymphocyte in the pathogenesis of non-alcoholic fatty liver disease. High fat diet (HFD) was used to induce NAFLD. After 8 weeks of HFD feeding, mice were given PBS, Antibiotics (neomycin and polymixin B) or Lactobacillus by gavage once a day for 4 weeks and sacrificed. Primary hepatocytes isolated from livers of normal diet feeding mice were co-cultured with CD4+ T lymphocytes or its cultured supernatants, of which CD4+ T lymphocytes were isolated from mesenteric lymph nodes of mice fed 12 weeks of HFD or normal diet.

Results: Compared with the PBS group, lymphocytic infiltration in livers of antibiotics group and lactobacillus group are less, as well as lower ALT and AST. But the effects of gut bacteria on intra-hepatic T lymphocytes are not very clear.

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Disclosure of Interest: All authors have declared no conflicts of interest.

Disclosure of Interest: All authors have declared no conflicts of interest.

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Introduction: The advent of image-enhanced endoscopic modalities have paved the way for better optical diagnosis of colorectal polyps. Fujifilm recently introduced a new technology – Blue Light Imaging (BLI) that utilises powerful light emitting diode (LED) technology and short wavelength absorption of haemoglobin with no post processor digital reconstruction to enhance mucosal surface and vessel patterns. This is a novel concept.

Aims & Methods: The aim of this study was to investigate the diagnostic ability of BLI in the optical diagnosis of diminutive colorectal polyps. Images from a pilot study with 64 images from normal subjects were given PBS, Antibiotics (neomycin and polymixin B) or Lactobacillus by gavage once a day for 4 weeks and sacrificed. Primary hepatocytes isolated from livers of normal diet feeding mice were co-cultured with CD4+ T lymphocytes or its cultured supernatants, of which CD4+ T lymphocytes were isolated from mesenteric lymph nodes of mice fed 12 weeks of HFD or normal diet.

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maintaining ileal CD. AIEC bacteria adhere to the enterocytes through high-affinity interactions with their variant FimH and abnormally expressed CEACAM6 protein on host cells. Decreasing CEACAM6 expression in CD intestinal cells is one strategy that could prevent AIEC bacteria colonization of the intestinal mucosa and subsequent inflammation. This work aims at studying the role of the collagenous and LPS-binding domains (HMD High Methyl Diet) on AIEC colonization, on DNA methylation, and on genes expression with a specific focus on CEACAM6.

Aims & Methods: CEABAC10 female mice were fed a HMD (supplemented in folate, ferrous, zinc and methionine) for 2 weeks before being sacrificed. After weaning, the colonic epithelial cells from offspring were purified using EDTA. We analyzed different physiological parameters such as the lipocalin-2 level in stools and intestinal permeability. E. coli population was quantified using a cultural and qPCR approaches. DNA methylation of CEACAM6 promoter was measured using bisulfite-sequencing and qPCR was used to quantify CEACAM6 mRNA in colonic epithelial cells. RNA-seq was used to highlight transcriptomic changes in colonic cells and ELISA was used to quantify IgA concentration in the stools.

Results: Mice fed a HMD did not present any sign of spontaneous inflammation or altered intestinal permeability when compared to mice fed a conventional diet. Microbiota analysis revealed a 1000-fold decrease in E. coli population in mice fed HMD compared to mice receiving a conventional diet. As expected, bisulfite sequencing showed a hyper-methylation of the CEACAM6 promoter, associated with a significant decrease in CEACAM6 expression as measured by qPCR, following HMD treatment. RNA-seq data confirmed the decrease in CEACAM6 expression and highlighted 309 up-regulated genes following HMD. Among them, 88 were involved in adaptive immunity and 15 took part into the IgA synthesis pathway. Further analysis revealed an increase in E. coli-specific IgA concentration in intestinal lumen of mice treated with HMD compared to control diet group.

Conclusion: This work shows that the addition of a few vitamins and oligo-elements to the diet could interfere with the DNA-methylation metabolism leading to changes in the methylation such as a decrease in CEACAM6 and to activation of genes involved in IgA synthesis. The excessive specific E. coli-IgA quantity secreted into the lumen during HMD could explain the decrease in E. coli colonization. A diet-based strategy could help decreasing E. coli colonization in CD patients by modulating DNA methylation and favoring IgA production.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

expression of MCP-1 (P < 0.01) and TNF-a (P < 0.05), and B lymphocytes decompensated stage. Four metabolites (creatinine, triglyceride 20:5/20:4; acid 18-hydroxyarachidonic; epoxy-8, 11, 14-eicosatrienoic acid) reached the threshold (fold changes analysis) as possible candidates for infection biomarkers. However, in univariate analysis by principal component analysis none of the markers reached statistical significance difference between infected and non-infected groups.

Conclusion: There is a different metabolic profile for patients with decompensated cirrhosis, expressed primarily through phosphatidylcholine metabolism disorder. Metabolomic analysis is a promising method to find new markers of infections in decompensated patients but targeted metabolitcal studies are required.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

TUESDAY, OCTOBER 31, 2017
10:30-12:00
PERINAL FISTULISING CROHN’S DISEASE: FROM PATHOPHYSIOLOGY TO MANAGEMENT - ROOM C1

OP182 ANTI-TNF THERAPY FOR RECTOVAGINAL FISTULAS COMPLICATING CROHN’S DISEASE: A GETAID STUDY
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5Gastroenterology, CHU de Bordeaux, Bordeaux/France
6Hopital Saint Eloi Hepatologie Gastro enterologie, Montpellier/France
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8Hepato-gastroenterology Unit, hospital, Nantes/France
9Dept. Of Gastroenterology, Besançon university hospital gastroenterology, Bourbeuf/Crete France
10Institut Mutualiste Montsouris, Paris/France
11Hopital Rangueil, Toulouse/France
12Gastroenterology, hospital, Nimes/France
13CHU Salpetriere, Saint-Etienne/France
14Hospital Colmar, Colmar/France
15CHRU Tours, Tours/France
16Gastroenterology Unit, Inserm U934, Nancy University and Hospital, Nancy/France
17Caen Hospital, Caen/France

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Introduction: Anti-TNF therapy is effective for fistulising Crohn’s disease (CD). However, persistence or recurrence of rectovaginal fistulas can represent a devastating condition in CD patients and a challenge for gastroenterologists and surgeons. Given the small size of available studies, it is difficult to draw definite conclusions regarding the efficacy of anti-TNF therapy in treating rectovaginal fistulas complicating CD. We thus evaluated the efficacy of anti-TNFs for the treatment of rectovaginal fistulas in a large cohort of CD patients.

Aims & Methods: This GETAID multicenter retrospective study included all adult patients from 16 French tertiary centers who were treated with anti-TNF therapy for rectovaginal fistula complicating CD. Only patients who received anti-TNF induction treatment (adalimumab, infliximab or certolizumab) and at least one maintenance injection/infusion were analyzed. Clinical response

Abstract No: OP179

Table 1: Hemodynamic and liver function parameters in groups of animals.

<table>
<thead>
<tr>
<th>SHAM-operated rats (n = 10)</th>
<th>BDLS rats (n = 10)</th>
<th>BDLS + CECT7765 (n = 10)</th>
<th>Kruskal-Wallis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median (P25-P75)</td>
<td>Median (P25-P75)</td>
<td>Median (P25-P75)</td>
<td></td>
</tr>
<tr>
<td>Velocity (mm/sec)</td>
<td>38.0 (37.0–42.0)</td>
<td>25.0 (25.0–30.0)</td>
<td>0.005</td>
</tr>
<tr>
<td>Portal Vein Area (mm2)</td>
<td>0.95 (0.87–0.99)</td>
<td>2.06 (1.79–2.30)</td>
<td>0.003</td>
</tr>
<tr>
<td>Diameter (mm)</td>
<td>1.1 (1.05–1.12)</td>
<td>1.62 (1.51–1.71)</td>
<td>0.003</td>
</tr>
<tr>
<td>Portal Flow (ml/sec)</td>
<td>37.11 (36.11–38.97)</td>
<td>61.84 (44.77–62.63)</td>
<td>0.045</td>
</tr>
<tr>
<td>Congestion Index</td>
<td>0.02 (0.02–0.03)</td>
<td>0.07 (0.07–0.08)</td>
<td>0.03</td>
</tr>
<tr>
<td>ALP (U/L)</td>
<td>49.0 (30.0–64.0)</td>
<td>271.5 (198.5–283.5)</td>
<td>0.010</td>
</tr>
<tr>
<td>ALT (U/L)</td>
<td>45.0 (45.0–52.0)</td>
<td>26.0 (25.0–32.0)</td>
<td>0.017</td>
</tr>
<tr>
<td>Urea (mg/dL)</td>
<td>14.0 (12.0–15.0)</td>
<td>7.65 (4.30–11.50)</td>
<td>0.044</td>
</tr>
<tr>
<td>Albumin (g/dL)</td>
<td>4.3 (3.50–5.70)</td>
<td>5.80 (5.70–6.20)</td>
<td>0.023</td>
</tr>
<tr>
<td>Total Bilirubin (mg/dL)</td>
<td>0.40 (0.30–0.50)</td>
<td>12.0 (11.0–12.0)</td>
<td>0.002</td>
</tr>
</tbody>
</table>

1P < 0.016 compared with sham-operated rats 2P < 0.016 compared with BDLS rats BDLS: bile-duct ligation; CECT7765: B. Pseudocatenulatum CECT7765; ALP: alkaline phosphatase; ALT: alanineaminotransferase.
was evaluated at 1 year and at date of latest news. The main endpoint was complete clinical fistula closure at 1 year. We also looked at predictors of anti-TNF therapeutic response.

Results: One hundred and six patients were treated at least one anti-TNF injection/infusion. Nine patients stopped anti-TNF therapy during induction due to lack of efficacy. Ninety-seven patients were in clinical remission 7 months after anti-TNF maintenance therapy were included in the analysis. Median follow-up was 76 months. Four types of fistulas were reported: 34 recto-vaginal fistulas (35%), 7 enterovaginal fistulas (7%), 36 ano-vaginal fistulas (37%), and 20 ano-vulvar fistulas (21%). In 15% of patients, only 25% had a response at one year in case of lack of response at 6 months. Patients with active smokers. Ten percent of patients were previously exposed to anti-TNF therapy. Seventy-two patients were treated with infliximab (74%), 23 with adalimumab (24%), 2 with certolizumab (2%). Only 5% of patients received concomitant use of other immunosuppressive agents. In this large cohort of CD patients, anti-TNF therapy induced a complete clinical response at 1 year. A partial clinical response was seen in 25% of patients and a lack of response in 37% of the patients. Between one surgery for fistula was performed in 37% of patients. In the cohort of patients with complete clinical response at one year, only 25% had a response at one year in case of lack of response at 6 months. For this analysis, no factor was associated with a clinical response at one year. Among patients with a clinical response at 6 months, 91% maintained a complete clinical response at one year, whereas only 25% had a response at one year in case of lack of response at 6 months. Patients with active smokers. Ten percent of patients were previously exposed to anti-TNF therapy. Seventy-two patients were treated with infliximab (74%), 23 with adalimumab (24%), 2 with certolizumab (2%). Only 5% of patients received concomitant use of other immunosuppressive agents. In this large cohort of CD patients, anti-TNF therapy induced a complete clinical response at 1 year in 63% of patients and 38% had a complete fistula closure following induction therapy. Anti-TNF therapy seems to be a good option for the treatment of rectovaginal fistulas complicating CD in clinical practice in both the short- and long-term.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP183 HIGHER INFLIXIMAB AND ADALIMUMAB SERUM LEVELS CORRELATE WITH PERIANAL FISTULA CLOSURE IN CROHN’S DISEASE PATIENTS


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Introduction: The four necrosis factor (TNF)-TNF agents are effective to treat perianal Crohn’s disease (CD). It has been suggested that CD patients with perianal fistulas need higher serum concentrations of infliximab compared to patients with pure luminal disease in order to attain remission.

Aims & Methods: For this analysis, we identified all CD patients with perianal fistulas receiving active treatment with infliximab or adalimumab at our centre. Serum drug concentrations of infliximab and adalimumab in CD patients with perianal fistula were collected. Anti-TNF antibody concentrations in patients with closed fistula, defined by the absence of active draining fistula at physical examination and/or confirmed by magnetic resonance imaging were compared to drug levels in patients with persistently draining perianal fistulas. Only patients receiving anti-TNF maintenance treatment were included and if the time interval between the final observation and last drug level measurement did not exceed four weeks. Patients who underwent surgical interventions (ie. ligation of intersphincteric fistula tract surgery or fecal diversion procedure) between physical examination and measurement of anti-TNF serum levels were excluded, as well as patients with internal fistulas.

Results: We identified 66 CD patients (out of a total cohort of 352) that received active treatment with infliximab or adalimumab and had perianal fistula(s). For seven patients treated with adalimumab and 19 with infliximab. The median serum concentrations of infliximab at trough (interquartile range) were significantly higher in patients with closed fistula(s) (n=32) compared to patients with actively draining fistula (n=15): 6.0 µg/ml [5.4–6.9] versus 2.3 µg/ml [1.1–4.0], respectively (p<0.001). The same outcome was seen in 19 patients treated with adalimumab (13 with closed fistula and 6 with active fistula) with a median serum concentration of 7.4 µg/ml [6.5–10.8] versus 4.8 µg/ml [1.7–6.2] respectively; p=0.003. ROC analysis of anti-TNF serum measurements showed high accuracy for both infliximab and adalimumab with an AUC of respectively 0.92 (95% CI: 0.82–1.00) and 0.89 (95% CI: 0.71–1.00). An infliximab trough serum concentration ≥ 5 µg/ml yielded the optimal results in terms of combined sensitivity of 86.67% (95% CI: 59.5–98.3) and specificity of 84.38% (95% CI: 67.2–94.7). An adalimumab serum concentration ≥ 5.9 µg/ml was associated with fistula closure with a sensitivity of 83.3% (95% CI: 35.9–99.6) and specificity of 92.3% (95% CI: 64.0–99.8). There were no differences seen in infliximab and adalimumab dose and intervals between patients with active draining fistula and closed fistula.

Conclusion: An association was found between the level of anti-TNF serum concentrations and fistula closure in CD patients. Pursuing higher serum anti-TNF levels in CD patients with perianal fistula might improve fistula closure rates.

Disclosure of Interest: A. Strik: has received lecture fees from Mercik Sharp & Dohme, Takeda, AbbVie, Johnson and Johnson, Biogen and Mundipharma.
M. Lowenberg: has received speaking fees from Abbvie, Covidian, Dr. Falk, Ferring Pharmaceuticals, Mercik Sharp & Dohme, Receptos, Takesa, Tiliotts and Tramedico. He has received research grants from AbbVie, Mercik Sharp & Dohme, Achmea healthcare and ZonMW.

C.Y. Ponsioen: has received grant support from Takeda, Dr. Falk Pharma, lecture fees from Abbvie, Takeda, Ferring, Dr. Falk Pharma and consultancy fees from AbbVie and Takeda.
G.R. D’Haens: received speaker fees from Abbvie, Ferring, Johnson and Johnson, Merck Sharp & Dohme, Mundipharma, Norgine, Pfizer, Shire, Millennium/Takeda, Tiliotts and Vifor.
All other authors have declared no conflicts of interest.
were associated with ustekinumab failure-free survival at 24 months, but not significantly, when compared to those with lower CRP levels (1.2-24.8) and especially patients with a previous history of infliximab failure (p<0.05).

In multivariate analysis, no predictive factor of ustekinumab failure-free survival was identified in more than 2 years. More than 50% of patients maintained ustekinumab during follow-up without loss of response, intolerance or surgery, with a good safety profile. No predictive factor of ustekinumab failure-free survival was identified in multivariate analysis.

Disclosure of Interest: P. Wils: Janssen
All other authors have declared no conflicts of interest.

OPI87 USEFULNESS OF COMBINATION THERAPY WITH ADAHIMAB AND IMMUNOMODULATORS IN PATIENTS WITH CROHN’S DISEASE: A LARGE, MULTI-CENTRE COHORT STUDY
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9Department Of Internal Medicine, Division Of Ibd, Yamato Yamanote Medical Center, Tokyo/Japan
10Department Of Internal Medicine, Division Of Gastroenterology, Kawasaki Medical School, Kawasaki/Japan
11Department Of Gastroenterology And Hepatology, Osaka University Graduate School of Medicine, Suita/Japan
12Division Of Gastroenterology, School of Medicine, lwate Medical University, Mito/Japan
13Department Of Gastroenterology, Oita Red Cross Hospital, Oita/Japan
14Division Of Internal Medicine, Department Of Inflammatory Bowel Disease, Hyogo College of Medicine, Nishinomiya/Japan
15Department Of Gastroenterology And Clinical Science, Graduate School of Medical Sciences, Kyushu University, Fukuoka/Japan
16Second Department Of Internal Medicine, Osaka Medical College, Takatsuki/Japan
17Center For Advanced IBD Research And Treatment, Kitasato University, Kitasato Institute Hospital, Tokyo/Japan
18Center For Translational Research, The Institute Of Medical Science, The University of Tokyo, Tokyo/Japan

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Introduction: The benefits of combination therapy with adalimumab and immunomodulators in patients with Crohn’s disease (CD) is still open to debate. The ADJUST study is a retrospective multi-centre cohort study conducted at 41 institutions in Japan. Data were retrospectively collected from all patients with CD who had received at least one induction dose of 160mg of adalimumab between October 2010 and December 2013. Patients with active CD who received adalimumab for induction of remission were included, while those with inactive CD who started on adalimumab for prevention of postoperative recurrence or for unknown reasons were excluded. The cumulative rates of retention of adalimumab were estimated by the Kaplan–Meier method. Prognostic factors related to the cumulative rates of adalimumab were evaluated by multivariate Cox regression analysis. We also compared the cumulative rates of retention between the groups with/without immunomodulators stratified by potential confounding factors.

Results: A total of 970 patients (median age, 33.6 years; female, 31%) were included in the study. The median duration of CD was 7.5 years. Forty-three percent of the patients had undergone at least 1 intestinal resection. The median prednisolone dose and albumin levels of the patients were 0.90 mg/dL and 4.9 at one and two years, respectively. Concomitant treatment with immunomodulators and prednisolone was administered to 37% and 16% of the patients, respectively. Forty-nine percent of the patients had been previously treated with infliximab. The 1-, 2- and 4-year cumulative retention rates of adalimumab were 69%, 62% and 58%, respectively. In the multivariate Cox regression analysis, female sex, perianal disease, lower albumin levels, concomitant treatment with prednisolone and previous infliximab use were identified as independent predictors for discontinuation of adalimumab, whereas concomitant treatment with immunomodulators was a prognostic factor for higher retention rate of adalimumab. According to the stratified analyses, combination therapy with adalimumab and immunomodulators significantly improved the cumulative retention rates in patients with CRP levels of ≥4.00 mg/dL and those receiving concomitant treatment with prednisolone or previously treated with infliximab.

Conclusion: Our data suggested that combination therapy of adalimumab and immunomodulators significantly increased the retention of adalimumab, especially in infliximab-treated CD patients with higher CRP levels and those who received concomitant treatment with prednisolone at initiation of adalimumab treatment.

Disclosure of Interest: H. Tanaka: H. Tanaka has received lecture fees from Mitsubishi Tanabe Pharma, AbbVie, EA Pharma and Eisai.
A. Yamada: A. Yamada has received research grants from AbbVie and EA Pharma.
T. Fujii: T. Fujii has received a research grant from Eisai.
S. Shinnazi: S. Shinnazi has received lecture fees from Mitsubishi Tanabe Pharma, AbbVie, EA Pharma and Eisai.
T. Kobayashi: T. Kobayashi has received research grant and lecture fee from EA Pharma; lecture fee from AbbVie.
T. Hibi: T. Hibi has received research grants and lecture fees from AbbVie and EA Pharma.
All other authors have declared no conflicts of interest.

OPI88 SPACING OF INFlixIMAB THERAPY IN PATIENTS WITH INFLAMMATORY BOWEL DISEASES IN CLINICAL REMISSION: PRELIMINARY RESULTS OF A RETROSPECTIVE MULTI-CENTRE FRENCH NATIONAL COHORT
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Introduction: Infliximab (IFX) is efficient to maintain clinical remission in patients with inflammatory bowel diseases (IBD) refractory to conventional therapies. To date, there is no clear guideline regarding the withdrawal of anti-TNF agents and the majority of IBD patients are treated with IFX for long-term medical management. An alternative to withdrawal of IFX may be the spacing of IFX infusion interval. This strategy was only evaluated in a large prospective controlled trial in rheumatoid arthritis patients with interesting results (Fautrel B, Ann Rheum Dis, 51(1)).

Aims & Methods: The primary aim of this study was to evaluate the effect of a spacing of IFX infusion interval on the maintenance of clinical remission in IBD patients. Secondary aims of this study were to evaluate the occurrence of allergic reactions to IFX after spacing and the efficacy of IFX intensification after clinical relapse. This was a retrospective multicentre French national cohort including all IBD patients treated with infliximab who were in clinical remission according to the referring physician and a had a spacing of their infusion interval over 9 weeks for at least two consecutive infusions. Clinical relapse was defined according to referring physician and leading to IFX intensification was considered as primary endpoint. The clinical efficacy of IFX intensification after spacing and occurrence of drug reactions were also monitored.

Results: Eighty-nine patients were included in the study (61 patients with Crohn’s disease [CD] and 28 with an ulcerative colitis [UC]). Median delay between IFX introduction and spacing was 35.6 months (IQR: 17.6–64). Thirty-five (39%) patients were already treated with an immunosuppressive drug (methotrexate) at the time of IFX spacing. Maximum infusion interval spacing was of 13 weeks and 41 patients (46%) had infusion interval spacing ≥12 weeks. Cumulative probability of clinical relapse-free survival after spacing was 82.7% ± 4.1 and 72.6% ± 4.9 at one and two years, respectively. All IBD patients with a clinical relapse after spacing had an intensification of IFX therapy (n = 27) with a clinical response in 89% of patients. Only one patient had to withdraw IFX therapy after clinical relapse due to IFX allergic reaction occurring three years after spacing. Regarding clinical relapse, the median delay between IFX introduction and spacing of infusion interval was significantly shorter in IBD patients with clinical relapse compared to patients without clinical relapse (22.9 months [IQR: 13.3–42] vs. 41.3 months [IQR: 22.5–67.1], respectively, p = 0.027). CD patients, in univariate analysis, a delay >4 years between IFX introduction and spacing was significantly associated to the maintenance of clinical remission after spacing (RR = 0.26; CI 95%: 0.07–0.89, p = 0.032). For UC patients, radiologic inflammatory activity before spacing was associated to clinical relapse after spacing (RR = 13.9; CI 95%: 1.24–157.1, p = 0.033). In multivariate analysis, a delay >4 years between IFX introduction and spacing (RR 0.36, CI 95%: 0.19–0.68, p = 0.002), concomitant treatment with an immunosuppressant (RR = 0.31; CI 95%: 0.11–0.85, p = 0.022) and penetrating phenotype (CI 95%: 0.34–0.89, p = 0.039) were significantly associated to the maintenance of clinical remission after spacing in CD patients.

Conclusion: After spacing of IFX infusions over 9 weeks more than 70% of IBD patients remained in clinical remission over two years. Only one patient stopped IFX therapy after withdrawal of IFX. A short delay between IFX introduction and spacing seems to be a good predictive factor of clinical relapse after spacing, at least in CD. The collection and analysis of data from a larger national cohort is ongoing.

Disclosure of Interest: L. Peyrin-Biroulet: Mereck, Abbvie, Janssen, Ferrering, Norgine, Tillots, Vifor, Therakos, Pharmacosmos, Piéleg, BMS, ucbharma, Hospira, Takeda, Biogaran, Pfizer, HAC-Pharma
OP189 HIGHER RATE OF CORRECTCOEURTESE AND CORRECTCOEURTEISE DEPENDENCE IN ELDERLY-ONSET UC PATIENTS DIAGNOSED 70 YEARS COMPARED TO 70 YEARS OF AGE: A POPULATION-BASED STUDY

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Introduction: Recent French population-based study reported that elderly-onset UC patients with Crohn’s disease diagnosed over age of 70 years have different disease course regarding localization, disease progression and exposure to medication than patients aged 60–69 years (1).

Aims & Methods: The aims of this study was to assess whether the disease phenotype and long-term outcome also differs in elderly-onset (ulcerative colitis) UC diagnosed before and after the age of 70 years. Elderly-onset UC patients (â60 years at diagnosis) from a French prospective population-based Registry (EPIMAD) were included. Demographic and clinical data at diagnosis and at maximal follow-up were collected using a predefined questionnaire.

Results: 468 elderly-onset UC patients were included (median follow-up 6.2 years) of whom 277 (59%) were <70 years and 191 (41%) ≥70 years at diagnosis. Male gender was more frequent in patients <70 years than in older individuals (54% vs. 65%; p=0.01) while patients >70 years had higher rate of left-sided colitis than younger ones (63% vs. 49%; p=0.02). The 1 and 5-year cumulative probabilities of medication exposure were similar between the two age groups (5-aminosalicylic acid: 60% vs. 70% and 77% vs. 77%, p=0.75; corticosteroids: 19% vs. 23% and 30% vs. 34%, p=0.54; immunosuppressants: 3% vs. 2% and 10% vs. 9%, p=0.78). However, patients <70 years compared to older individuals experienced significantly more corticosteroid (12% vs. 3%, p=0.03) and tended to be more corticosteroid (24% vs. 16%, p=0.08). Only 4 patients received anti-TNFα therapy, 3 of them diagnosed <70 years. The rate of surgery was not influenced by age at diagnosis (1 and 5-year risk: 6% vs. 4% and 10% vs. 6%, p=0.39).

Conclusion: Elderly-onset UC is heterogeneous group of patients with respect to disease phenotypes and disease progression. Patients ≥70 years at diagnosis had higher frequency of left-sided colitis than younger ones. Importantly, patients diagnosed ≥70 years had more severe disease course in terms of higher rate of corticostereine and corticosterone dependence than those ≥70 years.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

TUESDAY, OCTOBER 31, 2017 10:30-12:00 EVIDENCE-BASED MANAGEMENT OF BARRETT’S AND OESOPHAEGAL ADENOCARCINOMA - ROOM B2

OP190 EVIDENCE OF MAJOR MALIGNANT PROGRESSION IN PERSISTENT NONDYSPLASTIC BARRETTS ESOPHAGUS - A DUTCH NATIONWIDE COHORT STUDY

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Introduction: The risk of esophageal adenocarcinoma (EAC) in patients with non-dysplastic Barrett’s esophagus (NDBE) may have been overestimated in some studies. Lower progression rates could lead to changes in the current surveillance strategy, thereby reducing its associated risks and costs.

Aims & Methods: The aim of this study was to evaluate whether persistence of NDBE among consecutive surveillance endoscopy identifies patients at a very low risk for malignant progression. In this population-based retrospective study, patients with a first diagnosis of NDBE between 2003 and 2012 were selected using the Dutch nationwide registry of histopathology (PALGA). Patients were followed until the development of EAC or high-grade dysplasia or up to the last endoscopy contact with biopsy sampling (through May 2016). Incidence rates and rate ratios for EAC and HGD/EAC combined were calculated to evaluate whether persistence of NDBE during consecutive endoscopies and progression time reduce the risk of malignant progression.

Results: In this study, 12,729 patients with NDBE were included, with a total follow-up of 64,563 (median 4.4 [IQR 3.0 – 6.8]) years. Malignant progression was seen in 437 patients (3.4%) after a median follow-up of 5.1 years (IQR 3.2 – 7.4). This rate resulted in an overall age-adjusted rate to EAC of 0.53 per 100 person-years and a rate to EAC of 0.68 (95% CI: 0.62 – 0.74) per 100 person-years. At first follow-up endoscopy after a median of 2.3 years (IQR 1.8 – 3.2), 11,782 patients (93%) were found to have non-dysplastic NDBE. 727 (57%) and 223 (18%) patients progressed to low-grade dysplasia and HGD/EAC, respectively. In patients with both consecutive endoscopies showing NDBE after a median of 2.8 years (IQR 4 – 4.0), the malignant progression rate was 0.52 (95% CI: 0.40 – 0.67) per 100 person-years (RR 0.63 (95% CI: 0.45 – 0.83)) versus 0.86 in patients after one endoscopy. Patients with five consecutive non-progressive endoscopies had a 60% rate reduction (RR 0.40 (95% CI: 0.13 – 0.97)) for development of EAC (progression rate: 0.34 (95% CI: 0.11 – 0.41) per 100 person-years). The incidence of EAC decreased with 30% (adjusted HR 0.71, 95% CI: 0.67 – 0.75) for each year of FU without progression (progression-free time).

Conclusion: Persistent NDBE at two consecutive surveillance endoscopies reduces the risk of malignant progression towards HGD/EAC or EAC by twofold. As progression risk reduces even further after more consecutive negative follow-up endoscopies, this study contributes to the growing evidence that surveillance intervals in subgroups of patients with persistent BE might be lengthened.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference
fever \( n = 9 \) and 1 perforation treated conservatively by clipping. Strictures requiring dilatation: \( n = 5 \).

**Conclusion:** H-APC appears to be feasible and safe and has a short-term efficacy of 92% in this interim analysis; final results of this large prospective study have to be awaited. The comparative value of H-APC to alternative methods such as RFA is then to be assessed in a prospective randomized trial.

**Disclosure of Interest:** T. Rösch: Erbe Co. supported the study and Nurse Support. T. Rösch has a cooperation contract for Research Support covering this and other projects

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H. L.A.M. Wensink: supported the performance of this study

O. Pech: Erbe Co. supported the performance of this study

S. Faiss: Erbe Comp. supported the Performance of the study

M. Anders: Erbe Comp. supported the EES study

C. Eld: Erbe Comp. supported the performance of this study

**References**


OP194 NEUTROPHIL LYMPHOCYTE RATIO AS PREDICTIVE MARKER OF SURVIVAL IN ESOPHAGEAL CANCER: SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: Several studies showed that a high preoperative Neutrophil-Lymphocyte Ratio (NLR) is a predictor of worse survival in many solid tumors, including esophageal cancer. Neutrophils are a consistent part of the tumor microenvironment. It has been previously reported that TANs are related to tumor growth. The aim of this systematic review and meta-analysis is to collect all the data about this marker in order to quantify its strength in esophageal cancer prognostication.

Aims & Methods: The meta-analysis was performed using the Preferred reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines. We used inclusion criteria adapted from the REPporting recommendations for tumor MARKER prognostic studies criteria. We conducted a comprehensive search of all prospective or observational studies reporting NLR prognostic data in esophageal cancer patients. The primary outcome measure was Overall Survival (OS) while Disease Free Survival (DFS) and Progression Free Survival (PFS) were secondary outcome measures. All included studies had a directly or indirectly available HR. We analyzed data using fixed effect model or random effect model depending on heterogeneity.

Results: We included in the quantitative synthesis 17 studies published between 2011 and 2017, comprising 5672 patients. The NLR cut-off value ranged from 2 to 5. Our analysis about OS of all included studies showed that a high preoperative NLR is an effective predictor of a worse survival (HR 1.72, p = 0.0001). Similar results were obtained about DFS (HR 1.94, p = 0.0003) and PFS (HR 1.66, p = 0.0001). We conducted sub-analysis both for cut-off ranges subgroups and treatment modality subgroups obtaining the same prognostic relevance.

Conclusion: Retrospective design of included study is the major bias. There is high heterogeneity among studies in terms of patients characteristics, duration of follow-up and cut-off threshold. Moreover, NLR has been proposed in several studies as a prognostic marker for non-oncological diseases, mostly heart disease.

Disclosure of Interest: All authors have declared no conflicts of interest.

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Introduction: The most optimal timing of esophagectomy after neoadjuvant chemoradiotherapy (nCRT) is unknown. Theoretically, an extended interval between nCRT and surgery might increase the chance of the best pathological response: pathological complete response (pCR) because of a prolonged effect of the nCRT and this might possibly improve disease-free and overall survival.

Conversely, it is thought that an extended interval might lead to residual tumor outgrowth, a more difficult surgical resection, with a higher complication rate, and possibly a worse survival. The aim of this study was to assess the time interval between nCRT and surgery in the Netherlands and to correlate this with pathological cell infiltrate of the tumor and surgical morbidity and mortality.

Aims & Methods: Patients with esophageal cancer treated with nCRT and surgery between 2011 and 2016 were selected from a national database of the Dutch Upper Gastrointestinal Cancer Audit. (1) Differences in patient and treatment characteristics, stage and type of surgery, surgical complications and postoperative mortality are compared across six subgroups discriminated by the length between end of nCRT and surgery. To evaluate the association between the interval and pathohistological complete response (pCR), intraoperative, postoperative complications and mortality, multivariable logistic regression analysis was used.

Results: In total 3102 patients were included. The median [interquartile range] time interval between the end of nCRT and surgery was 8 [7-10] weeks. The interval between end of nCRT and surgery was divided into six (A-F) groups: 0-5 weeks (A; n = 157), 6-7 weeks (B; n = 878), 8-9 weeks (C; n = 992), 10-12 weeks (D; n = 720), 13-14 weeks (E; n = 195) and 15 or more weeks (F; n = 180). In intervals E and F, there were significantly more patients with ASA III+ and 40 years (SIR 3.18, 95% CI 0.04–17.69), 40–49 years (SIR 3.78, 95% CI 1.43–9.83), 50–59 years (SIR 2.36, 95% CI 1.22–4.11), and not consistently present across all subgroups.

Conclusion: An extended interval (≥10 weeks for adenocarcinoma and ≥12 weeks for squamous cell carcinoma) was associated with a higher probability of a pCR. These groups had the same probability for intraoperative and severe postoperative complications. The extended interval groups were associated with higher total postoperative complications (E and F) and mortality (D and F).

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference


TUESDAY, OCTOBER 31, 2017 10:30-12:00
H. PYLORI: TREATMENT AND ANTIBIOTIC RESISTANCE - ROOM 7.1

OP195 HELICOBACTER PYLORI ERADICATION AND THE RISK OF GASTRIC CANCER: A POPULATION-BASED COHORT STUDY

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Introduction: Helicobacter pylori is a stomach bacterium associated with an increased risk for gastric cancer. We aimed to assess if the risk of gastric cancer remains increased after H. pylori eradication.

Aims & Methods: This was a population-based, nationwide cohort study in Sweden conducted between 1 July 2005 and 31 December 2012. Data on H. pylori eradication were retrieved from the Swedish Prescribed Drug Registry and eradication consisted of triple therapy with a proton pump inhibitor and 2 antibiotics (clarithromycin and amoxicillin or metronidazole). The cancer incidence in the cohort was compared to that of the corresponding background population using standardized incidence ratios (SIRs) with 95% confidence intervals (CIs).

Results: In total, 92, 852 individuals (46.3% men) received eradication therapy during the study period. The total follow-up time after eradication was 331, 694 person-years (mean 3.6 years). Of the eradicated participants, 76 (0.08%) developed gastric cancer, corresponding with an incidence of 22.9/100, 000 person years. The SIR of gastric cancer after eradication was increased (SIR 1.46, 95% CI 1.15–1.83). The SIR for men was 1.30 (95% CI 0.94–1.77) and for women (SIR 1.67, 95% CI 1.15–2.35). The SIRs were higher in the age groups <40 years (SIR 3.18, 95% CI 0.04–17.69), 40–49 years (SIR 3.78, 95% CI 1.38–8.22), 50–59 years (SIR 2.36, 95% CI 1.22–4.11), and not consistently increased in the age groups 60–69 years (SIR 0.97, 95% CI 0.50–1.69) and ≥70 years (SIR 1.38, 95% CI 1.00–1.84).

Conclusion: The overall risk for gastric cancer after eradication for H. pylori remained increased compared to the general population.

Disclosure of Interest: All authors have declared no conflicts of interest.
**Abstract No: OP197**

### Treatment

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**Results:**

- Up to now, 20,175 patients (60% women) have finished follow up. Mean age was 49 years. Of all patients, 4.2% had drug allergies (81% to penicillin), 56% of had dyspepsia, 18% had gastric duodenal ulcer. Two-thirds (66%) were managed by gastroenterologists in Europe is extremely diverse and the overall eradication rate is suboptimal, mainly due to the frequent use of triple therapies where they are ineffective (most European regions).

- In order to achieve >90% eradication, physicians are encouraged to use quadruple therapies.

**Disclosure of Interest:**

- A.G. McNicholl: Dr. McNicholl has received retribution from Allergan for formative actions.
- D.S. Bordin: Dr. Bordin has served as lecturer for Astellas, AstraZeneca, KRKA and Abbott.
- Perez-Asa: Dr. Perez-Asa has received retribution from Allergan and Mylan for formative actions.
- B. Vaira: has received retribution from Allergan for formative actions.
- M. Castro Fernandez: Dr. Castro-Fernandez has received retribution from Allergan for formative actions.
- J. Molina Infante: Dr. Molina-Infante has served as a consultant for Casen Recordati and has received retribution from Allergan for formative actions.
- P. Byzantine: has served as speaker, consultant and advisory member for or has received research funding from Almirall, Allergan and Reckitt Benckiser.

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**Introduction:** Due to the diversity of strains, resistances and geographical particularities, the best approach for *Helicobacter pylori* management remains unclear.

**Aims & Methods:** We aimed to assess the management of *H. pylori* infection by gastroenterologists in Europe and to evaluate the efficacy of first-line treatments. A systematic prospective registry of the clinical practice of European gastroenterologists regarding *H. pylori* infection and treatment (30 countries and 250 recruiting investigators). A local coordinator was selected from each country with more than 10 *H. pylori* references on PubMed. Each coordinator selected a representative group of recruiting investigators from its country. An electronic clinical research file was created on AEG-REDCap to systematically register all adult patients infected with *H. pylori*. Variables included: Patients' demographics, previous eradication attempts, prescribed eradication treatment, adverse events, and outcomes (cure rates, compliance, follow up, etc.).

**Results:** Up to now, 20,175 patients (60% women) have finished follow up. Mean age was 49 years. Of all patients, 4.2% had drug allergies (81% to penicillin), 56% of had dyspepsia, 18% had gastric duodenal ulcer. Two-thirds (66%) were managed by gastroenterologists in Europe is extremely diverse and the overall eradication rate is suboptimal, mainly due to the frequent use of triple therapies where they are ineffective (most European regions). In order to achieve >90% eradication, physicians are encouraged to use quadruple therapies.

**Disclosure of Interest:** A.G. McNicholl: Dr. McNicholl has received retribution from Allergan for formative actions.

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B. Vaira: has received retribution from Allergan for formative actions.

M. Castro Fernandez: Dr. Castro-Fernandez has received retribution from Allergan for formative actions.

J. Molina Infante: Dr. Molina-Infante has served as a consultant for Casen Recordati and has received retribution from Allergan for formative actions.

P. Byzantine: has served as speaker, consultant and advisory member for or has received research funding from Almirall, Allergan and Reckitt Benckiser.

J.P. Gisbert: Dr. Gisbert has served as speaker, consultant and advisory member for or has received research funding from Almirall, Nycomed, AstraZeneca, Casen Recordati, and Allergan. All other authors have declared no conflicts of interest.

**Reference:**

On behalf of the European Helicobacter and Microbiota and the HpEuReg investigators.
OF198 HELICOBACTER PYLORI ERADICATION THERAPY WITH VONOPRAZAN WAS MORE EFFECTIVE THAN COMBINED EFFECTIVE PUMP INHIBITORS, AND THE EFFECT WAS NOT DISTURBED IN THE PATIENTS WITH LIFE STYLE-RELATED DISEASES

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Introduction: Vonoprazan (VPZ) combined with two anti-biotics therapy has been used for Helicobacter pylori (HP) eradication in Japan, and there is still little information of the detailed eradication results. The aim of the present study was to retrospectively compare the HP eradication outcomes between proton pump inhibitors (PPI) and VPZ with 1,774 subjects of our hospital in 2017 - 2019. To evaluate which factors affected the eradication effect with VPZ was affected by lifestyle-related diseases including obesity, hypertension (HT) and diabetes mellitus (DM).

Aims & Methods: In total, 1774 subjects (primary eradication: 1485, secondary: 289) received HP eradication therapy in our hospital in 2012 - 2016. The eradication judgment was performed by C-urea breath test (UBT), and the eradication rate (%), per-protocol analysis) was calculated. Eradication therapy was performed with PPI (lansoprazole (LPZ) 30 mg or esomeprazole (EPZ) 20 mg) or VPZ 20 mg + clarithromycin (CAM) 200 mg + amoxicillin (AMPC) 750 mg twice/day for 7 days as primary eradication. Failure of the primary eradication was followed by the secondary eradication with PPI or VPZ 20 mg + metronidazole (MNZ) 250 mg + AMPC 750 mg twice/day for 7 days.

Results: The primary eradication rates were VPZ 90.5% (371/410, LPZ 73.7% (246/334), RPZ 75.5% (366/482), and EPZ 83.0% (215/259). The eradication rate of VPZ 90.5% was higher compared to that of the other three PPIs (828/1076) (<0.001) and each PPI. The secondary eradication rate was VPZ 93.1% (54/58), LPZ 87.7% (50/57), RPZ 90.5% (67/74), EPZ 91.0% (91/100). Secondary eradication rate tended to be high in VPZ (93.1%) but not significant compared to that in all other PPIs (90.0%) (208/231) (P = 0.47). Next, we analyzed the influence of the lifestyle-related diseases on eradication. The primary HP eradication rate did not depend on the body weight: obese subjects (BMI > 25, n = 262. VPZ 97.0% vs PPI 72.4%) and no obese subjects (n = 771: VPZ 90.5% vs PPI 77.3%). As indicated, VPZ worked better in the obese subjects compared to the other non-obese subjects (BMI > 25: 97.0% vs BMI < 25: 90.5%). P = 0.089), suggesting the effect of VPZ was not influenced by the body weight. Regarding HT, primary eradication rate was better in VPZ compared to PPI (76.8%). The eradication rate was 97.9% for 178 patients with DM (VPZ 89.3%, PPI 68.9%) was not different from 1368 non-DM subjects (VPZ 90.6%, PPI 77.7%). There was not the serious adverse event with VPZ and PPI during the investigation period.

Conclusion: Therapy using VPZ was effective compared to that of PPI, and life-style related diseases including obesity, hypertension, DM, had no influence on the HP eradication with VPZ.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP199 OPTIMIZED 14-DAY SEQUENTIAL VERSUS 10-DAY BISMUTH QUADRUPLE THERAPY CONTAINING HIGH DOSE ESOMEPRAZOLE IN THE FIRST-LINE TREATMENT OF H. PYLORI INFECTION

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Introduction: Our previous trial and meta-analysis showed that 14-day sequential eradication therapy consisting of treatment by several antimicrobial drugs is a good model for studying the effect of antibiotics on the abundance of antibiotic resistance genes in the gut.

Aims & Methods: The aim of the study was to explore the gut resistome before and after antibiotic therapy by shotgun metagenomic sequencing. Seventy stool samples were used for analysis: 35 samples from H. pylori-positive patients before eradication therapy, 35 - from the same subjects after the completion of eradication therapy consisted of treatment by amoxicillin (1000 mg), clarithromycin (500 mg), proton pump inhibitor in a standard dose, bismuth subsalicylate (240 mg) bid for 14 days, lactulose was added as a prebiotic. Total DNA was isolated from the stool samples using beat beating method and sequenced on Solid 5500xW platform. Reads were aligned to the Comprehensive Antibiotic Resistance Database (CARD). The largest significant fold changes were found for beta-lactams antibiotic resistance genes abundances in the microbiomes of patients before and after eradication were assessed using Wilcoxon signed-rank test (p-value < 0.05 was considered significant).

Conclusion: Eradication therapy of H. pylori infection leads to increasing of abundance of different antibiotic resistance genes. Significant changes of abundance were shown for genes conferring resistance to 12 from 27 groups of antibiotics (CARD). The largest significant fold changes were found for beta-lactams (for some patients quantity of TEM beta-lactamases increased up to 125-fold), for macrolides (mrx and mphA genes up to 288- and 360-fold, respectively), for amoxicillin (aph, aadA, increase up to 297, 352-fold), for fluoroquinolones (spxB up to 133-fold increase). Moreover significant expansion of genes coding for beta-lactam and efflux pathways was also detected. Notably, a large number of antibiotic resistance genes were found to appear in the microbiome after therapy. Most of these genes confer resistance to beta-lactams (TEM beta-lactamases and shv genes), amnoglycoside (aad, aad), vancomycin (vanXVC), fluoroquinolones (gmr genes). This eradication therapy leads to the accumulation of genes promoting the resistance to antibiotics, that were not part of the treatment.

Disclosure of Interest: All authors have declared no conflicts of interest.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference
This work was financially supported by the Ministry of Education and Science of Russian Federation (agreement #14.575.21.0076, ID RFMEF15714X0076).
**Aims & Methods:** We aimed to evaluate the resistance rates encountered by European gastroenterologists in their routine clinical practice. A Local Coordinator was selected from each country with more than 10 H. pylori references in PubMed. Each Coordinator selected a representative group of recruiting gastroenterologists.

**Results:** Overall, 39 gastroenterologists from their country participated in the study. An e-CRF was created on AEG-REDCap for data collection. Each Coordinator selected a representative group of recruiting gastroenterologists.

**Conclusion:** The mean rate of H. pylori clarithromycin resistance in European nations has surpassed the threshold established by consensus conferences (15%) in which empirical use of standard triple therapy should be discarded. Dual resistance to clarithromycin and metronidazole is close to reach the 15% prevalence in which non-bisnath quadruple therapies efficacy is significantly challenged. There is a strong acquisition of antibiotic resistance after failed treatments.

**Disclosure of Interest:** A.G. McNicholl: Dr. McNicholl has received retribution from Allergan for formative actions.

P. Bytzer: Dr. Bytzer has served as speaker, consultant and advisory member for or has received research funding from Almirall, Allergan and Reckitt Benckiser. J. Molina Infante: Dr. Molina-Infante has served as a consultant for Casen Recordati and has received retribution from Allergan for formative actions. J.P. Gisbert: Dr. Gisbert has served as speaker, consultant and advisory member for or has received research funding from Almirall, Nycomed, AstraZeneca, Casen Recordati, and Allergan.

All authors have declared no conflicts of interest.
Disclosure of Interest: All authors have declared no conflicts of interest.

Table 1: Cytokine expression in affected vs healthy colonic tissue in patients post complicated AD versus uncomplicated AD

<table>
<thead>
<tr>
<th>Cytokine</th>
<th>Healthy complicated</th>
<th>Diverticular uncomplicated</th>
<th>Healthy healthy</th>
<th>Diverticular uncomplicated</th>
<th>P for diverticular vs healthy uncomplicated</th>
<th>p for diverticular vs healthy healthy</th>
<th>P for diverticular complication</th>
<th>P for healthy complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>TNFα</td>
<td>1.06 ± 1.57</td>
<td>5.4 ± 4.4</td>
<td>0.45 ± 0.35</td>
<td>0.19 ± 0.11</td>
<td>0.0127</td>
<td>0.46</td>
<td>0.004</td>
<td>0.56</td>
</tr>
<tr>
<td>IL-6</td>
<td>1.56 ± 2.1</td>
<td>5.14 ± 10</td>
<td>0.34 ± 0.34</td>
<td>0.13 ± 0.07</td>
<td>0.05</td>
<td>0.25</td>
<td>0.008</td>
<td>0.46</td>
</tr>
<tr>
<td>IL-1β</td>
<td>0.35 ± 0.5</td>
<td>0.8 ± 0.82</td>
<td>0.12 ± 0.05</td>
<td>0.13 ± 0.13</td>
<td>0.14</td>
<td>0.77</td>
<td>0.522</td>
<td>0.66</td>
</tr>
</tbody>
</table>
Aims & Methods: We aimed to determine whether colonic diverticula are associated with chronic gastrointestinal symptoms and diverticula, we found no mucosal inflammation. Our work challenges the theory that colonic diverticula are associated with mucosal inflammation or chronic gastrointestinal symptoms.

Discourse of Interest: All authors have declared no conflicts of interest.

References

OP207 UTILITY TO ENDOSCOPIC SUBMUCOSAL DISSECTION FOR THE COLORECTAL TUMORS NEAR OR WITHIN DIVERTICULUM: CASE SERIES
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Introduction: Surgery is standard treatment for colon tumors coexistence with diverticulum. However, it is currently controversial whether colon tumors near or within diverticulum can be treated by endoscopic submucosal dissection (ESD).

Aims & Methods: The aim of this retrospective case series was to clarify feasibility of ESD for superficial colorectal tumors near or within diverticulum. Consecutive patients with colorectal tumors near or within diverticulum removed by ESD in two referral centers were included. Clinicopathological characteristics and clinical outcomes were analyzed.

Results: There were 11 patients including 6 cases of the near-type and 5 cases of within-type diverticulum. The tumor showed type 2 in NBI International Colorectal Endoscopic (NICE) Classification in 10 cases [1, 2]. Pit pattern diagnosis in Kudo’s classification was type III. In one case, type IV without serration features in 2 cases and type VI in 7 cases [3]. In 4 of them the diverticulum could not be recognized in the tumor before the ESD. En-bloc R0 resection was achieved in 7 patients (64%). Median tumor size and procedure time were 23 mm (15–80) and 120 min (50–210), respectively. The ESD could not be continued in four cases due to the intra-diverticulum tumor extension and required strip biopsy, band ligation, polypectomy and/or argon plasma coagulation. Traction device using the “clip-and-line method” [4] was used in one case having two diverticula within the tumor and had kept global traction during ESD. One case with pin-hole perforation was occurred at the diverticulum and was endoscopically managed by immediate closure by endoclips. Emergency surgery was not required in any cases. During median 12 month follow-up period, only two cases detected residual tumors. One case was successfully ablated and other case required additional surgery.

Conclusion: The present study demonstrated that ESD was effective and safe for the treatment of colorectal tumors near or within diverticulum. The use of traction device may be helpful to see the cutting site at the diverticulum and to achieve en-bloc R0 resection.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

Table 1. Incidence of complicated diverticular disease by age group and calendar year.

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Year</th>
<th>Events</th>
<th>Rate per 100,000 pyrs (95% CI)</th>
<th>IRR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>18–44</td>
<td>2000</td>
<td>7</td>
<td>0.6 (0.2–1.2)</td>
<td>1</td>
</tr>
<tr>
<td>2013</td>
<td>29</td>
<td>2.0</td>
<td>1.4 (2.9–7.8)</td>
<td>3.4 (1.5-7.8)</td>
</tr>
<tr>
<td>45–54</td>
<td>2000</td>
<td>15</td>
<td>5.1 (2.8–8.3)</td>
<td>1</td>
</tr>
<tr>
<td>2013</td>
<td>41</td>
<td>10.8</td>
<td>7.7 (4.6–14.6)</td>
<td>2.1 (1.3–3.7)</td>
</tr>
<tr>
<td>55–64</td>
<td>2000</td>
<td>22</td>
<td>9.5 (5.9–14.4)</td>
<td>1</td>
</tr>
<tr>
<td>2013</td>
<td>50</td>
<td>16.7</td>
<td>12.4 (22.1)</td>
<td>1.9 (1.3–3.7)</td>
</tr>
<tr>
<td>64–74</td>
<td>2000</td>
<td>39</td>
<td>21.2 (15.0–28.9)</td>
<td>1</td>
</tr>
<tr>
<td>2013</td>
<td>70</td>
<td>28.1</td>
<td>21.9 (35.5)</td>
<td>1.3 (0.9–1.9)</td>
</tr>
<tr>
<td>75–84</td>
<td>2000</td>
<td>51</td>
<td>39.8 (29.7–52.4)</td>
<td>1</td>
</tr>
<tr>
<td>2013</td>
<td>61</td>
<td>39.9</td>
<td>30.6 (51.3)</td>
<td>1.1 (0.7–1.6)</td>
</tr>
<tr>
<td>85+</td>
<td>2000</td>
<td>22</td>
<td>46.0 (38.6–69.7)</td>
<td>1</td>
</tr>
<tr>
<td>2013</td>
<td>30</td>
<td>44.6</td>
<td>30.1 (63.6)</td>
<td>0.9 (0.6–1.7)</td>
</tr>
</tbody>
</table>

Conclusion: The incidence of complicated diverticular disease has increased by 1.4 fold from 2000 to 2013 and this increase in incidence appears to be in those under the age of 65 years. This could be due to the increase in known risk factors for complicated diverticulosis such as obesity and physical inactivity or the increased use of prescription medications such as steroids or opiate analgesics which are associated with an increased risk of perforation. It is also possible part of this increase may be due to increased ascertainment of cases due to increased use of diagnostic imaging and endoscopy.

Discussion of Interest: All authors have declared no conflicts of interest.
TUESDAY, OCTOBER 31, 2017

10:30-12:00

MECHANISMS OF CARCINOGENESIS IN THE PANCREAS - ROOM E3

**OP208** ENHANCED EXPRESSION OF K-RAS PROTEIN IN PANCREAS PROMOTES DEVELOPMENT OF CIGARETTE SMOKE-INDUCED CHRONIC PANCREATITIS IN MICE

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2Department Of Pediatrics, Gastroenterology And Allergology, Medical University of Bialystok, Bialystok/Poland
3Department Of Medical Pathomorphology, Medical University of Bialystok, Bialystok/Poland

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**Introduction:** Epidemiological studies have demonstrated a strong association between smoking and the increased risk for developing chronic pancreatitis (CP) and pancreatic ductal adenocarcinoma (PDAC). The exact mechanism underlying the effects of cigarette smoke (CS) on pancreatic injury remains unknown. We have previously showed that increased Ras activity is a key element in development of pancreatic inflammation and its progression to PDAC. However, it is not clear if similar phenomenon is involved in CS-induced CP.

**Aims & Methods:** Therefore, the aim of our study was to determine if CS will promote development of CP in mice exposed to repeated episodes of acute pancreatitis (AP). Our secondary aim was to evaluate the involvement of K-Ras protein in this process. Mice were exposed to CS or a sham treatment (no smoke exposure) using a cigarette smoking inhalation system for 12 weeks. After 2 weeks of experiment, half of the animals from the CS and sham exposure groups were additionally subjected to a repeated caerulein treatment (7-hourly i.p. 50 μg/kg/dose, once a week, for 10 consecutive weeks) to mimic recurrent episodes of AP. At the end of experiment the extension of pancreatic damage was determined by H&E and Trichrome staining. The expression of K-Ras protein was evaluated by immunohistochemistry (K-Ras:2B Antibody (C-19); sc-521).

**Results:** C57BL/cdmbmice exposed to CS or caerulein injections alone did not develop any pancreatic damage determined by histopathology examination. However, concomitant treatment with both of these agents caused focal acinar atrophy, with slight intralobular and perivascular areas of fibrosis, resembling mild CP. Moreover, immunohistochemistry examinations revealed increased expression of K-Ras only in mice treated with both CS and caerulein.

**Conclusion:** CS promotes development of CP in mice exposed to repeated episodes of AP. This process may be, at least partially, related to increased expression of K-Ras protein. Further studies are needed to determine the exact role of K-Ras and downstream signaling pathways in CS-induced CP.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**References**

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**Abstract No: OP207**

<table>
<thead>
<tr>
<th>Case Location</th>
<th>Tumor Size (mm)</th>
<th>Diverticulum size (mm)*</th>
<th>Treatment</th>
<th>Traction</th>
<th>Complications **</th>
<th>Complete resection ***</th>
<th>Histology</th>
<th>Depth of tumor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Near tumor diverticulum</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>Sigmoid 40</td>
<td>IIA (LST-NG)</td>
<td>3</td>
<td>ESD</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Dysplasia</td>
</tr>
<tr>
<td>2</td>
<td>Sigmoid 23</td>
<td>IIA (LST-NG)</td>
<td>5</td>
<td>ESD</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Dysplasia</td>
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<tr>
<td>3</td>
<td>Sigmoid 15</td>
<td>IIA (LST-NG)</td>
<td>4</td>
<td>ESD</td>
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<td>No</td>
<td>Yes</td>
<td>Dysplasia</td>
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<tr>
<td>4</td>
<td>T/C 16</td>
<td>Recurrent</td>
<td>4</td>
<td>ESD</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Dysplasia</td>
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<tr>
<td>5</td>
<td>A/C 21</td>
<td>IIA (LST-NG)</td>
<td>5</td>
<td>ESD</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Adenoma</td>
</tr>
<tr>
<td>6</td>
<td>Cucum 20</td>
<td>IIA (LST-NG)</td>
<td>5</td>
<td>ESD</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Dysplasia</td>
</tr>
<tr>
<td>Within tumor diverticulum</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>Sigmoid 80</td>
<td>Is + IIA (LST-G)</td>
<td>4</td>
<td>ESD</td>
<td>Yes</td>
<td>Perforation</td>
<td>Yes</td>
<td>Adeno-carcinoma</td>
</tr>
<tr>
<td>8</td>
<td>Sigmoid 30</td>
<td>IIA (LST-G)</td>
<td>6</td>
<td>Hybrid ESD &amp; band ligation</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Dysplasia</td>
</tr>
<tr>
<td>9</td>
<td>Sigmoid 40</td>
<td>Is + IIA (LST-G)</td>
<td>6</td>
<td>Hybrid ESD &amp; polypectomy</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Dysplasia</td>
</tr>
<tr>
<td>10</td>
<td>A/C 30</td>
<td>Is + IIA (LST-G)</td>
<td>10</td>
<td>ESD &amp;polypectomy &amp; APC</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Dysplasia</td>
</tr>
<tr>
<td>11</td>
<td>Cucum 20</td>
<td>IIA (LST-NG)</td>
<td>6</td>
<td>Hybrid ESD &amp; strip biopsy</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Dysplasia</td>
</tr>
</tbody>
</table>

ESD, endoscopic submucosal dissection; mm, millimeters; LST, lateral spreading tumor; G, granular; NG, non-granular; SM, submucosal invasive cancer; M, mucosa; T/C transverse colon; A/C, ascending colon; APC, argon plasma coagulation * Diverticulum size was measured by comparing top of the attachment. ** Complications including bleeding and perforation *** Complete resection means en-bloc resection with pathological margin negative (R0) resection.
OP210 LIPOXIN A4 INHIBITS PANCREATIC STELLATE CELL DIFFERENTIATION INTO PANCREATIC TUMOR STROMAL MYOFIBROBLASTS AND PANCREATIC TUMOR GROWTH IN VIVO

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Introduction: The pancreatic tumor stroma has shown to strongly support tumor growth and metastasis. Human pancreatic stellate cells (hPSCs), as precursors of cancer-associated fibroblasts like myofibroblasts (CAF), are a main component of the tumor stroma of pancreatic ductal adenocarcinoma (PDAC). Upon activation, human hPSCs differentiate into CAF and promote tumor growth, invasion and metastasis in PDAC [1]. Lipoxin A4 (LXA4), a natural bioactive lipid, has shown to inhibit fibroblast activation [2]. This makes LXA4 a potential therapeutical strategy to diminish the pro-tumorigenic effects of the pancreatic tumor stroma, by inhibiting hPSC activation into CAF. The aim of the present study was to investigate whether LXA4 can inhibit the differentiation of human pancreatic stellate cells (hPSCs) into CAF and thereby inhibit hPSC-induced tumor growth in 3D culture. LXA4 is capable to inhibit the hPSC differentiation into CAF and thereby inhibit hPSC-induced tumor growth in 3D culture. LXA4 is capable to inhibit the hPSC differentiation into CAF and thereby inhibit hPSC-induced tumor growth in 3D culture.

Results: The LXA4-specific surface receptor FRP2/ALX was found to be upregulated in hPSCs. LXA4 significantly inhibited TGF-β induced activation markers (e.g. αSMA, collagen, PDGF-Rβ), migration and morphological changes in hPSCs. These inhibition of hPSC differentiation were caused by inhibition of Smad2/3 phosphorylation by LXA4. Conditioned medium experiments showed that LXA4 activated hPSCs, which reduced the migratory behavior of hPSCs. Conditioned medium experiments showed that LXA4 activated hPSCs, which reduced the migratory behavior of hPSCs.

Conclusion: The LXA4-specific surface receptor FRP2/ALX was found to be upregulated in hPSCs. LXA4 significantly inhibited TGF-β induced activation markers (e.g. αSMA, collagen, PDGF-Rβ), migration and morphological changes in hPSCs. These inhibition of hPSC differentiation were caused by inhibition of Smad2/3 phosphorylation by LXA4. Conditioned medium experiments showed that LXA4 activated hPSCs, which reduced the migratory behavior of hPSCs.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
1. Apte MV, Wilson JS, Lugea A, Pandol SJ. A starring role for stellate cells in mice making it a potential therapeutic agent to modulate hPSC induced tumor promoting effects and the growth of stroma containing LXA4 is capable to inhibit the hPSC differentiation into CAF and thereby inhibit hPSC-induced tumor growth in 3D culture.

OP211 PROTEIN FACTORS PRESENTED IN SERUM OF PANCREATIC CANCER PATIENTS ENHANCES THE MOTILITY OF CANCER CELLS - A NOVEL VIEW OF PANCREATIC CANCER CELL METASTASIS

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3Regenerative Medicine, Warsaw Medical University, Warsaw/Poland

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Introduction: Pancreatic cancer remains a serious clinical problem and a challenge for doctors and scientists. Despite the new possibilities in the diagnosis and treatment of cancer, 5-year survival rate applies to less than 5% of patients. Although many studies pathogenesis of pancreatic cancer, as well as other cancer models, this cancer needs further investigation. The process of cancer metastasis is a cascade of events involving proteolysis, cell motility and migration, proliferation and neangiogenesis. Cells released from the primary tumor must penetrate into the lymphatic vessels and/or blood vessels, which occurs by spreading. Circulating cells can then migrate through the walls of blood into surrounding tissues, where they settle, proliferate and form a new outbreak of disease. Understanding cellular processes responsible for the spread of cancer can be useful to improve the diagnosis and prognosis of the disease in patients diagnosed with pancreatic cancer.

Aims & Methods: The aim of study was to supplement the knowledge about the metastasis process of pancreatic cancer and to understand the role of protein factors presented in serum of pancreatic cancer patients that enhances the motility of cancer cells. The effect of pancreatic cancer patients were compared to the serum of control group and were added to pancreatic cancer cell line BxPC-3 (adenocarcinoma, ATCC® cell bank CRL-1687 TM). We evaluated cell migration, proliferation, adhesion response, activation of MAPK44/42 and Akt kinase, and invasion into Matrigel of pancreatic cancer patients (including HGF, VEGF and SDF-1) in the blood of patients, by ELISA test.

Results: We report that 1) serum from patients group and control group, and much stronger as SDF-1, HGF and VEGF can activate migration, adhesion and proliferation of pancreatic cancer cell line CRL1687; 2) we discovered higher metastatic potential of serum from patients with pancreatic cancer compared to control serum; 3) we report higher concentration of SDF-1, HGF, and VEGF in the serum of patients with pancreatic cancer. We report for the first time that diluted (1%) serum and plasma induces migration of malignant pancreatic cancer cell line much more strongly than any others knowns potent pro-metastatic factors. We found that this remarkable pro-migratory activity of diluted plasma is associated with a ~50-100-KD protein that interacts with Gz protein-coupled receptors and activates p42/44 MAPK and AKT signaling in target cells. We report for the first time that this pro-migratory factor, chaperoned by fibrinogen, is vitronectin and that this effect can be inhibited by fibrinogen.

Conclusion: The results prove a strong metastatic activity of blood serum and a significant role of HGF/SF, VEGF and SDF-1 factors in pancreatic cancer cell migration. Our results prove a mechanism for enhancing motility of pancreatic cancer cells to lymphatic vessels and blood vessels, in which the concentration of fibrinogen is low, and thus suggests that free vitronectin stimulates migration of tumor cells.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
We treated Mist1 CreERT2/Aims & Methods: selected cell signaling pathways. creatic ductal adenocarcinoma (PDAC) to a more acinar phenotype by blocking possible to redifferentiate pancreatic intraepithelial neoplasia (PanIN) and pan-
suggest that ductal neoplasia predominantly initiates from acinar cells after
Contact E-mail Address:
Department Of Gastroenterology, Nanjing Drum Tower Hospital, Nanjing/China
Nature Communications
Recent studies in genetically engineered mouse models (GEMMs)
AND SIRTUIN 1 LEADS TO PARTIAL REDIFFERENTIATION OF
5
markers including Amylase and CPA1 by a factor of more than 10-fold, and
SOX9, HNF1B, and Muc5ac. We then performed a kinetic analysis in ''KPC''
the expression of typical acinar and ductal markers using immunoblot, reverse
DNA methyltransferase inhibitor (5-Aza), and sirtuin 1 (SIRT1) inhibitor
compounds in vitro, including histone deacetylase (HDAC) inhibitor SAHA,
mucosal homeostasis in the gut. In fact, IgA deficiency has been associated with
3
addition and in line with our hypothesis, we found synthetic lethality between
geted therapeutic intervention. Indeed, DDR defects sensitize ATM-deficient
altered genome integrity might allow synthetic lethality-based options for tar-
show that ATM deficiency leads to chromosomal instability with recurrent and
PDAC reminiscent of human counterparts. Array CGH and SKY analysis
1
A92
Loss of ATM accelerates pancreatic cancer formation and Epithelial-
OPI213 COMBINED INHIBITION OF HISTONE DEACTYLASES AND SIRTUIN 1 LEADS TO PARTIAL REDIFFERENTIATION OF PDAC TO A MORE ACINAR PHENOTYPE BY LIMITING ENTERIC NEURAL FUNCTION.
S. Zhang, X. Zou
Department Of Gastroenterology, Nanjing Drum Tower Hospital, Nanjing/China
Contact E-mail Address: 13770771661@163.com
Introduction: Recent studies in genetically engineered mouse models (GEMMs) suggest that ductal neoplasia predominantly initiates from acinar cells after transdifferentiation to a ductal phenotype. We hypothesized that it might be possible to redifferentiate pancreatic intraepithelial neoplasia (PanIN) and pancreatic ductal adenocarcinoma (PDAC) to a more acinar phenotype by blocking selected cell signaling pathways.
Aims & Methods: We treated Mist1<sup>creERT<sup>2</sup></sup>/Aims & Methods: selected cell signaling pathways. creatic ductal adenocarcinoma (PDAC) to a more acinar phenotype by blocking possible to redifferentiate pancreatic intraepithelial neoplasia (PanIN) and pancreatic ductal adenocarcinoma (PDAC) to a more acinar phenotype by blocking selected cell signaling pathways.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**Reference**

OPI215 MONOCYTE-DERIVED MACROPHAGES RESTORE GUT MOTILITY IN POSTOPERATIVE ILEUS BY LIMITING ENTERIC NEURAL DAMAGE.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**Reference**

OPI213 COMBINED INHIBITION OF HISTONE DEACTYLASES AND SIRTUIN 1 LEADS TO PARTIAL REDIFFERENTIATION OF PDAC TO A MORE ACINAR PHENOTYPE BY LIMITING ENTERIC NEURAL FUNCTION.
S. Zhang, X. Zou
Department Of Gastroenterology, Nanjing Drum Tower Hospital, Nanjing/China
Contact E-mail Address: 13770771661@163.com
Introduction: Recent studies in genetically engineered mouse models (GEMMs) suggest that ductal neoplasia predominantly initiates from acinar cells after transdifferentiation to a ductal phenotype. We hypothesized that it might be possible to redifferentiate pancreatic intraepithelial neoplasia (PanIN) and pancreatic ductal adenocarcinoma (PDAC) to a more acinar phenotype by blocking selected cell signaling pathways.
Aims & Methods: We treated Mist1<sup>creERT<sup>2</sup></sup>/Aims & Methods: selected cell signaling pathways. creatic ductal adenocarcinoma (PDAC) to a more acinar phenotype by blocking possible to redifferentiate pancreatic intraepithelial neoplasia (PanIN) and pancreatic ductal adenocarcinoma (PDAC) to a more acinar phenotype by blocking selected cell signaling pathways.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**Reference**
Conclusion: Our study reveals a critical role for vonoprazan-derived M cells in supporting neuromuscular function and restoring intestinal homeostasis after surgical trauma. From a therapeutic point of view, our data indicate that inappropriate targeting of monocytes may increase neutrophil-mediated innophathology and prolong the clinical outcome of POI, while future therapies should be aimed at enhancing M cell repair functions.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP216 VONOPRAZAN, A NOVEL ACTIVE POTASSIUM-COMPETITIVE ACID BLOCKER, AND RABEPRAZOLE INDUCE SMALL INTESTINAL DYSBIOSIS AND EXACERBATE THE NON-STERoidal ANTI-INFLAMMATORY DRUG-INDUCED SMALL INTESTINAL ENTEROPATHY

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Introduction: Vonoprazan fumarate, a novel active potassium-competitive acid blocker, was launched in Japan before it entered the world market. Vonoprazan and rabeprazole are both competitive inhibitors (PPIs) such as rabeprazole and esomeprazole. Recent studies show which exacerbated the NSAID-induced small intestinal enteropathy. In this study, we examine the effect of vonoprazan or rabeprazole on the composition of the microbiota in the small intestine and NSAID-induced small intestinal enteropathy.

Aims & Methods: Aim of this study is to investigate the effect of vonoprazan on the microbiota in the small intestine and NSAID-induced small intestinal enteropathy in mice. C57BL/6J mice received intraperitoneal administration of vonoprazan, rabeprazole, or vehicle for 7 days, and were administered indomethacin to gavage to induce damage to the small intestine. Some mice administered either the vehicle- and vonoprazan- or rabeprazole-treated groups showed 2.8-fold and 1.7-fold increases in indomethacin-induced damage to the small intestine, respectively. This high sensitivity to indomethacin-induced damage was caused by the intestinal microbiota obtained from the mice treated with either vonoprazan or rabeprazole.

Conclusion: Vonoprazan and rabeprazole induced small intestinal dysbiosis, which exacerbated the NSAID-induced small intestinal enteropathy.

Disclosure of Interest: All authors have declared no conflicts of interest.

References


OP218 HYPOXIA DISRUPTS INTESTINAL BARRIER VIA REGULATING NHE9-TIGHT JUNCTION IN SEVERE ACUTE PANCREATITIS RAT MODELS

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Introduction: Intestinal barrier dysfunction is attributed to various diseases, including inflammation, hypoxia, ischemia, intoxication, and considered as an important pathogenic factor for many diseases. In severe acute pancreatitis (SAP), it is well established that intestinal barrier dysfunction is a major element to promote SAP development and hypoxia plays a crucial role in infectious complications. Thus, deeply comprehending the mechanisms of intestine barrier dysfunction is indeed required for SAP treatment. Extensive evidences has indicated that intestine hypoxia triggered by SAP disrupting tight junction (TJ) is responsible for barrier dysfunction. Recently, the protective role of sodium/hydrogen exchanger 8 (NHE8) in intestine in various conditions has been well documented. We have previously demonstrated that inflammation reduced intestinal NHE8 expression. However, the role of NHE8 in SAP induced intestine barrier dysfunction has not been reported.

Aims & Methods: The aim of this study is to explore the intestinal expression of NHE8 in SAP rat model, and further explore the effects of hypoxia on NHE8 expression and potential mechanisms in Caco-2 cells hypoxia model. To induce SAP, SD rats were retrograde injected with 3% sodium taurocholate into the pancreatic duct, and ileum mucosal tissues were collected 24 hours later. For mechanism study, Caco-2 cells were incubated with 200µM cobalt chloride (CoCl2) for 6 hours to induce acute hypoxia model. Hypoxia-inducible factor alpha (HIF-1α) specific inhibitor 2-Methoxyestradiol (2-MeOE2) was incubated with Caco-2 cells for 6 hours under hypoxia. To further investigate the
relationship between NHE8 and TJ proteins, NHE8-shRNA plasmid (shNHE8) was constructed.

Results: In SAP group, NHE8 protein expression was significantly decreased compared with the control group (0.5 ± 0.04 vs. 1.2 ± 0.04, n = 12, P < 0.05). For CoCl2-intervened Caco-2 cells, HIF-1α protein expression were significantly stimulated compared with the control (1.5 ± 0.02 vs. 1.21 ± 0.15, P < 0.05), whereas NHE8 proteins expression were significantly reduced compared with the control (0.58 ± 0.06 vs. 1.02 ± 0.09, n = 3, P < 0.05). Additionally, CoCl2 treatment significantly reduced Claudin-1 and ZO-1 proteins expression when compared with control (1.05 ± 0.02 vs. 1.3 ± 0.06 vs. 1.53 ± 0.06, n = 3, P < 0.05). 2-MeOE2 treatment obviously blocked CoCl2 induced HIF-1α protein expression (3.59 ± 0.29 vs. 4.53 ± 0.25, n = 3, P < 0.05). Furthermore, 2-MeOE2 treatment dramatically increased the expressions of NHE8 (0.05 ± 0.07 vs. 0.58 ± 0.06, n = 3, P < 0.05). Claudin-1 (1.6 ± 0.16 vs. 1.05 ± 0.02, n = 3, P < 0.05) and ZO-1 (1.56 ± 0.08 vs. 1.33 ± 0.06, n = 3, P < 0.05) compared with CoCl2 pretreated cells (P < 0.05). Interestingly, compared with the mock shRNA transfected cells, the expressions of Claudin-1 and ZO-1 proteins transferred with shRNA NHE8 were significantly decreased (1.87 ± 0.15 vs. 2.38 ± 0.12; 1.06 ± 0.06 vs. 1.44 ± 0.06, n = 3, P < 0.05).

Conclusion: In SAP, the decrease of intestinal NHE8 expression is responsible for intestine barrier dysfunction. Moreover, intestinal hypoxia caused by SAP might also influence the expression of NHE8 via HIF-1α.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP219 MODULATION OF THE ENDOCANNABINOID SYSTEM BY FATTY ACID AMIDE HYDROLASE, MONO- AND DIACYLGLYCEROL LIPASE INHIBITORS AS AN ATTRACTIVE TARGET FOR SECRETORY DIARRHEA THERAPY

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Introduction: Secretory diarrhea remains a major global public health problem and a 10X-fold leading cause of death, particularly in children and the elderly. Thus, it is clear that there is an urgent need for developing effective anti-diarrhetic strategies. Many disorders can disrupt intestinal fluid and electrolyte absorption, including Crohn’s disease, ulcerative colitis, and diarrhoea-predominant irritable bowel syndrome. More recently, the concept of the enteroendocannabinoids was introduced. They are considered as a mediator of the effect of inhibition of selected enzymes involved in the synthesis and degradation of endocannabinoids on electrolyte equilibrium in the mouse colonic tissue.

Aims & Methods: Male Swiss-Webster mice were used in this study. The effects of PF-3845, JZL-184 and RHC-80267 (inhibitors for fatty acid amide hydrolase (FAAH), mono- (MAGL) and diacylglycerol lipase (DAGL), respectively) on epithelial ion transport were characterized in isolated mouse colon stimulated by PF-3845, JZL-184 and RHC-80267 (inhibitors for fatty acid amide hydrolase (FAAH), mono- (MAGL) and diacylglycerol lipase (DAGL), respectively) on epithelial ion transport were characterized in isolated mouse colon stimulated by forskolin (FSK), veratridine (VER) and bethanecol (BET). Next, colonic tissue was co-incubated with selected inhibitors and cannabinoid receptor antagonists, AM 251 and AM 630 (CB, and CB antagonists, respectively). To assess changes in the active ion transport in response to addition of tested drugs, the measurements of short-circuit current (Isc) in mouse colon and illeum in vitro were performed.

Results: We observed that basolateral addition of PF-3845 induced antiseruic effect in FSK-stimulated colonic tissue (p < 0.01), which was significantly reversed by JZL-184 (p < 0.01) and AM 630 (p < 0.01). JZL-184 significantly reduced epithelial ion transport (p < 0.05) under FSK-stimulated conditions. Furthermore, co-incubation with AM 630 reversed this effect leading to an increase in ion transport when compared to JZL-184 alone (p < 0.05). After administration of JZL-184, we did not observe any significant effect on colonic Isc. However, application of AM 630 to colonic tissue treated subsequently with JZL-184 led to a pronounced increase in Isc compared with JZL-184 alone (p < 0.01). In turn, basolateral addition of PF-3845, JZL-184 or RHC-80267 was without any statistically significant effect on BET-evoked ion transport when compared to control.

Conclusion: For the first time, we report that the modulation of the endocannabinoid system may play a crucial role in providing a novel effective secretory diarrhea therapy. To confirm our findings, in vivo studies are necessary to evaluate the effect of inhibition of selected enzymes involved in the synthesis and degradation of endocannabinoids on electrolyte equilibrium in murine models of secretory diarrhea.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP221 INFliximab Trough Levels Above 7 mg/ml in Inflammatory Bowel Disease Treated With Infliximab: Better Control of Inflammation Without Increased Risk of Infection

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Introduction: Target infliximab trough level for optimal control of inflammation in Inflammatory Bowel Disease treated with Infliximab is 3 – 7 g/ml. A higher target infliximab trough level of 3 – 7 g/ml are more effective and still safe regarding the risk of infection compared to levels below this threshold. In this single-centre cohort study we included 183 IBD patients (109 Crohn’s disease, 74 ulcerative colitis including IBD - unclassified disease). All patients received infliximab treatment between 2002 and 2015 at tertiary referral university IBD Centre (162 adults, 21 children) with available infliximab trough level data. Effectiveness and safety of high trough levels of > 7 g/ml was compared to trough levels below 7 g/ml. Effectiveness was assessed by correlating fecal Calprotectin (141 matched samples), CRP (376 matched samples) and endoscopy (69 colonoscopies) data to infliximab trough levels (426 samples, ELISA assay). Safety was assessed by comparing rates of infections in semesters (defined by 3-month periods) with high trough levels (> 7 g/ml) compared to semesters with infliximab trough levels below this threshold. Data on trough levels were available in 473/1681 (28%) semesters. Continuous variables were described using the median and interquartile range

Disclosure of Interest: None

Results: Among the whole cohort, 34 (30%) out of 113 patients relapsed within the follow-up period. The prevalence of circulating IFNg-secreting CD4+ T cells (Th1), IL-17-secreting CD4+ T cells (Th17) and Foxp3-expressing CD4+ T cells (Treg) as well as the concentrations of a wide broad of cytokines (IL-6, IL-8, IL-10, IL-13, IL-17A, INFγ, TNFa, IFNg) were measured in the serum were significantly different all over the time between patients who relapsed and those who stay in clinical remission. Various circulating double positive CD4+ T-cell subsets co-expressing Foxp3 and IL-17 and Foxp3 and INFγ were detectable in CD patients in remission. The subset of CD4+ T cells co-expressing IL-17 and Foxp3 was found significantly enriched (2-fold increase) in the circulating compartment in the cohort of patients in remission who experienced a clinical relapse 3 months later compared with that of CD patients who stayed in remission all over the follow-up period. In a multi-variate analysis, elevated serum ucCRP, low serum IL-10 and high number of double positive IL-17 and Foxp3 T cells were 3 independent factors significantly associated with the risk of further clinical relapse in CD patients in remission.

Conclusion: Detectable circulating cross-over immune CD4+ T-cell subsets co-expressing Foxp3, IL-17 and INFγ in CD patients in remission argues in the presence of a unique CD4+ T-cell subset co-expressing Foxp3 and IL-17 that preceding the occurrence of a flare suggests the potential contribution of this double positive T-cell subset in the pathogenesis of CD.

Disclosure of Interest: C. Jossen: Cendrine Jossen is an employee of Indicia Legastelois: Ste´ phane Legastelois is an employee of Indicia All other authors have declared no conflicts of interest.

TUESDAY, OCTOBER 31, 2017 10:30-12:00 ABSTRACTS ON FIRE: PREDICTING AND OPTIMIZING IBD OUTCOME - HOTSPOT
and filgotinib (200 mg QD; 474 nM) and its metabolite (7438 nM) and converted used as reported for tofacitinib (5 mg BID; 68 nM), baricitinib (4 mg QD; 27 nM) (Table).<ref>1</ref>

**Table:** Overall % cytokine inhibition in the context of clinical concentrations for various JAK inhibitors

<table>
<thead>
<tr>
<th>Cytokine</th>
<th>Tofacitinib 5 mg BID</th>
<th>Baricitinib 4 mg QD</th>
<th>Filgotinib and its metabolite 200 mg QD</th>
</tr>
</thead>
<tbody>
<tr>
<td>IL-15</td>
<td>J1/T2/S3</td>
<td>68</td>
<td>55</td>
</tr>
<tr>
<td>IL-10</td>
<td>J1/T2/S3</td>
<td>61</td>
<td>53</td>
</tr>
<tr>
<td>IL-6</td>
<td>J1/J2/S1</td>
<td>60</td>
<td>63</td>
</tr>
<tr>
<td>IL-12</td>
<td>J1/J3/S5</td>
<td>58</td>
<td>28</td>
</tr>
<tr>
<td>IL-21</td>
<td>J1/J3/S3</td>
<td>61</td>
<td>39</td>
</tr>
<tr>
<td>IL-23</td>
<td>J2/T2/S4</td>
<td>20</td>
<td>19</td>
</tr>
<tr>
<td>EPO</td>
<td>J2/J5/S5</td>
<td>24</td>
<td>29</td>
</tr>
</tbody>
</table>

Conclusion: These analyses illustrate the importance of studying a broad range of JAK pairing potencies and clinical concentrations when comparing JAK inhibitor compounds. Calculated profiles of cytokine inhibition for a number of JAK inhibitors were generally similar when efficacious doses are considered, with only minor differences in percentage cytokine inhibition, suggesting limited differentiation of these JAK inhibitors based on JAK pharmacology. Ultimately, only robust clinical testing will determine whether there are clinical differences between JAK inhibitors.


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**OP223: IDENTIFICATION OF GENETIC SIGNATURES AND IMMUNE MECHANISMS THAT DEFINE THERAPEUTIC RESPONSE AND FAILURE TO ANTI-INTEGRIN THERAPY WITH VEDOLIZUMAB IN IBD PATIENTS**

Introduction: Vedolizumab (VDZ), a humanized monoclonal antibody targeting the α4β7 integrin, was approved for the treatment of Crohn’s disease (CD) and ulcerative colitis (UC). Despite proven clinical efficacy for inducing and maintaining remission, subgroups of patients have no clinical benefit from anti-adhesion therapy with VDZ.

Aims & Methods: Within this study, we aimed to identify genetic, cellular and immunological mechanisms that define and predict response and failure of VDZ therapy. For this purpose, intestinal RNA Sequencing was performed in UC and...
CD patients (remitters and non-remitters) before and at week 14 of VDZ therapy. 

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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Aims & Methods: Adult pts naive to immunosuppressive and biologic therapy included in CALM had: 1) baseline (BL) CDAI > 150 and ≤ 450 (for receiving prednisone ≥ 20 mg or equivalent) or ≥ 220 and ≤ 450 (for receiving no or < 20 mg prednisone or equivalent); 2) active endoscopic CD, defined as total CD endoscopic index of severity (CDEIS) > 6 and sum of CDEIS subscores ≥ 6 in ≥ 1 segment with ulcers; 3) CRP < 5 mg/L and/or FC < 250 μg/g. Pts were randomly assigned 1:1 to T2T or CM groups, following up to an 8 week (wk) of 40 mg/day prednisone burst and taper. Pts were eligible for early randomization between BL (wk 0) and wk 8 if CDAI > 220 and were either on corticosteroids for 4 wks, or had intolerance/contraindication for prednisone therapy or per investigator assessment. Pts received the following treatment options (TO) 1-4 administered in a stepwise manner: TO1 = no treatment; TO2 = 180/80 mg aludinum (ADA) wks 0/2; 40 mg every other wk; TO3 = ADA 40 mg wks; TO4 = ADA 40 mg wks + azathioprine [AZA] 2.5 mg/kg/day. Early randomized pts were assigned to TO2. Treatment at randomization and 3 following visits was based on failure to fulfill success criteria: CDAI < 150, CRP < 5 mg/L, FC < 250 μg/g, and absence of deep ulcers for the T2T group and CDAI decrease ≥ 70 or 100 (at randomization or post-randomization, respectively) or CDAI < 200 and no prednisone for the CM group. The primary endpoint was CDEIS < 4 and absence of deep ulcers at wk 48. Secondary endpoints at wk 48 included deep remission (CDEIS < 150), discontinuation of steroids ≥ 8 wks, absence of draining fistulae (CDEIS < 4, and no deep ulcers), biologic remission (FC < 250 μg/g, CRP < 5 mg/L, and CDEIS < 4), CDEIS < 4, and absence of deep ulcers in each segment, and CDEIS = 0. Missing data were imputed using non-responder imputation.

Introduction: The concept of "treat to target" (T2T) implies that close serial monitoring of patients (pts) with Crohn’s disease (CD) using biomarkers of inflammation, serum C-reactive protein (CRP) and fecal calprotectin (FC), assists in timely treatment escalation in order to improve outcome. CALM, a prospective, open-label, multicenter, active-controlled, Phase 3 study, assessed the benefit of T2T versus standard clinical management (CM) of CD.

**Results:** A total of 244 pts were randomized. At BL, the mean ± SD age was 31.6 ± 11.7 years, mean ± SD CD duration was 95.9 ± 19.8 years and 57.8% were female. BL characteristics between T2T and CM groups were similar. Results are shown in the Table. No new safety signals with ADA were observed. The overall rate of adverse events was similar between T2T and CM groups.

**Table. Summary of primary and select secondary endpoints of CALM study**

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>T2T group</th>
<th>CM group</th>
<th>Adjusted risk difference* (%)</th>
<th>P value**</th>
</tr>
</thead>
<tbody>
<tr>
<td>CDEIS &lt; 4 and absence of deep ulcers</td>
<td>56 (45.9)</td>
<td>37 (30.3)</td>
<td>16.1 (3.9, 28.3)</td>
<td>0.010</td>
</tr>
<tr>
<td>CDEIS &lt; 4 and absence of deep ulcers</td>
<td>45 (36.9)</td>
<td>28 (23.0)</td>
<td>14.5 (2.9, 26.0)</td>
<td>0.014</td>
</tr>
<tr>
<td>CDEIS &lt; 4, no steroids for ≥ 8 wks, no fistulae, CDEIS &lt; 4, and no deep ulcers</td>
<td>36 (29.5)</td>
<td>29 (23.8)</td>
<td>5.9 ( -5.2, 17.0)</td>
<td>0.299</td>
</tr>
</tbody>
</table>

*Risk difference (T2T – CM) was stratified by screening smoking status and weight. **P values for the difference between the groups were based on Cochran-Mantel-Haenszel test stratified by screening smoking status and weight.
Conclusion: This is the first study showing that the treat-to-target approach leads to superior endoscopic and deep remission outcomes in CD compared with symptom-driven care.

Disclosure of Interest: J. Colombel: Consultant, advisory board member or speaker for AbbVie, Bristol-Myers Squibb, Ferring Pharmaceuticals, Genentech, Gilead, Immunogard, Merck, Millennium Pharmaceuticals, Pfizer, Prometheus Laboratories, Sanofi, and others. R. Panaccione: Consultant and/or lecture fees from AbbVie; speaker fees from AbbVie, Takeda, and Vifor Pharma; and advisory board fees from Hospira, Janssen, MSD, Mundipharma, Roche, Pfizer, and Dr Falk Benelux. M. Lukas: Served as a consultant or speaker or advisory member for Abbvie, MSD, Takeda, Eghis, Hospira, Celltrion, Janssen, and Vifor. F. Baert: Received research grants from AbbVie, Chiesi, Ipsen, MSD, Roche, sponsors of clinical studies in CD (AbbVie, Falk, Ferring, Janssen, Mundipharma, MSD, Pfizer, Takeda, Vifor). T. Vanišek: Served as advisory member for Hospira, Pfizer and Takeda, has received lecture fees from Takeda. C. 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Sandborn: Consultant: AbbVie; ActoGeniX NV, AGI Therapeutics, Alba Therapeutics; receipt of honoraria fees from AbbVie; Bristol-Myers Squibb, and Janssen; Research support: AbbVie, Bristol-Myers Squibb, Genentech, GlaxoSmithKline, Janssen, and others. P. Rutgeerts: Consultancy fees from AbbVie, Bristol-Myers Squibb, Centocor, Merck, Takeda, and UCB Pharma; speaker fees and research support from AbbVie, Centocor, MSD, and UCB Pharma. D. Hommes: Consulting fees, lecture fees and/or research support: AbbVie, AstraZeneca, Bristol-Myers Squibb, Cellerio, Centocor, ChemoCentryx, Gilead, Johnson & Johnson, Leo Pharma, MSD, Otsuka, Novimmune, Tramedico, UCB Pharma and others. S. Schreiber: Consultancy and lecture fees from AbbVie, Falk Pharma, Ferring, Genentech, GSK, MSD, Pfizer, Shire, Takeda. J. Peterson: Abbvie employee; may own AbbVie stock and/or options. B. Huang: Abbvie employee; may own AbbVie stock and/or options. Q. Zhou: Abbvie employee; may own AbbVie stock and/or options. J. Peterson: Abbvie employee; may own AbbVie stock and/or options. K. Wallace: Abbvie employee; may own AbbVie stock and/or options. K. Markham: Abbvie employee; may own AbbVie stock and/or options. A.M. Robinson: Abbvie employee; may own AbbVie stock and/or options. R. Thakkar: Abbvie employee; may own AbbVie stock and/or options. K. Wallace: Abbvie employee; may own AbbVie stock and/or options. A.M. Robinson: Abbvie employee; may own AbbVie stock and/or options. R. Thakkar: Abbvie employee; may own AbbVie stock and/or options. G.R. D’Haens: Consulting and/or lecture fees: AbbVie, ActoGeniX, AIM Centocor, Ferring, GlaxoSmithKline, MSD, Pfizer and others; Research grants: AbbVie, Janssen, Given Imaging, MSD, and others; Speaking honoraria: AbbVie, Tiffolits, Tifamedco, Norgine, and others. All other authors have declared no conflicts of interest.
adverse outcomes, such as hospitalizations, surgical procedures, including major surgeries, and serious disease-related complications in patients enrolled in CALM.

**Aims & Methods:** Immunosuppressive and biologic-naive adult patients with CD treated with or without corticosteroids (CS), and with baseline (BL; week 0) CRP >5 mg/L (low-dose CS) or >20 mg/L (no CS), active endoscopic CD (overall CD Endoscopic Severity [CDEIS]>6 and sum of CDEIS subscores >6 in ≥1 segment with ulcers), and CDR >5 mg/L and/or FC >250 g/L were treated with prednisone burst and taper, then randomized to the TO2T or CM arms at week 9. Some patients with CDCAI >220 and CS for >4 weeks or intolerance/contraindication for CS or per investigator assessment were able to be randomized early. Patients received up to four treatment options (TO) administered in a stepwise fashion: 1) prednisone bolus (pre-defined therapeutic target: TO1: 160/80 mg adalimumab (Humira®); ADEAS weeks 0, 2, 40 mg every other week; TO3 = ADEA 40 mg weekly; TO4 = ADEA 40 mg weekly + azathioprine 2.5 mg/kg/dy. CD-related hospitalizations, CD-related surgical procedures (median bowel resection±irrigation, abscess drainage, seton placement, fistulotomy, placement of a TPN access line]) after randomization and a composite endpoint of CD-related hospitalization or serious complication (presence of abscess, fistula or stricture, skin and ocular extra-intestinal manifestation, and serious adverse drug reaction) from randomization to up to week 48 or last dose date, whichever was later, were summarized as incidences or rates (events [E]/100 Patient Years [PY]). Differences between treatment groups in rates of CD-related hospitalizations and surgical procedures or in incidences of the composite endpoint were analyzed using a Chi-square test. Hazard ratio (95% CI) of the composite endpoint and Cox proportional hazard model. Any no treatment, on or after randomization and up to 70 days after last dosing were summarized in all randomized patients.

**Results:** A total of 244 patients were randomized 1:1 to the TO2T and CM arms. Mean age at BL was 31.6 ± 11.7 and 57.8% were female. The rate of CD-related hospitalizations after randomization was significantly lower in the TO2T compared to CM arm: 14 events (13.2/E/100 PY) vs 29 events (28.0/E/100 PY), \(P = 0.021\). The rates of CD-related surgical procedures between treatment arms were 7 events (6.7/E/100 PY) in TO2T and 9 events (8.7/E/100 PY) in CM, \(P = 0.582\). The proportion of patients with CD-related hospitalization or serious complication was numerically lower in TO2T compared with CM: 18 patients (14.8%) vs 25 patients (20.5%), \(P = 0.240\). TO2T was associated with numerically lower risk of CD-related hospitalization or serious complication than CM: hazard ratio 0.7, 95% CI 0.4–1.3, \(P = 0.249\).

**Conclusion:** The TO2T approach using tight control of inflammation by biomarkers lead to a reduction of major adverse outcomes indicative for a detrimental course, including CD-related hospitalizations. A longer study would be needed to confirm these findings.

**Disclosure of Interest:** J. Colombo: Consult/ad board/speaker: AbbVie, Bristol-Myers Squibb, Ferring Pharmaceuticals, Genentech, Giuliani SPA, Given Imaging, Merck, Millennium Pharmaceuticals, Pfizer, Prometheus Laboratories, Sanofi, Schering-Plough, Takeda, Teva Pharmaceuticals, UCB Pharma

R. Panaccione: Consult/lecture: AbbVie, Amgen, AstraZenea, Axcan, Biogen, Bristol-Myers Squibb, ChemoCentryx, Eisai, Eli Lilly, Genentech, GSK, Janssen, Merck, Takeda, Otera, Otsuka, Pfizer, Shire, Prometheus, Schering-Plough, Synta, Teva, UCB, Warner Chilcott

B. Huang: Abbvie employee; may own AbbVie stock and/or options

G. D’Haens: Consulting/speaker/research: AbbVie, ActoGeniX, AIM, Boehringer Ingelheim, Centocor, Chemo Centrosy, Cosmo Tech, Dr Falk Pharma, Elian, Genentech, GSK, Janssen, Kiesel, MSD, Neovacs, Norgine, Nycomed, Schiff, Shire, UCB, Vifor

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**Contact E-mail Address:** nn281@cam.ac.uk

**Introduction:** The course of Crohn’s disease (CD) varies substantially between affected individuals, but reliable prognostic markers are not available in clinical practice. This hinders disease management because patients with aggressive disease will be undertreated by conventional “step-up” therapy, while those with indolent disease would be exposed to the risks of unnecessary immunosuppression of a “top-down” approach. Previously, we described a transcriptional signature that is detectable within peripheral blood CD8 T cells at diagnosis and which correlates with subsequent disease course. To translate this work to the bedside and overcome the technical challenges of separating cell populations, we sought to develop a whole blood qPCR-based biomarker that can re-capitulate the CD8 subgroups without the need for cell separation. Here we describe the development and validation of this biomarker and the upcoming biomarker-stratified trial that will test whether it can deliver personalised medicine in CD.

**Aims & Methods:** From a training cohort of 69 newly diagnosed IBD patients, we simultaneously obtained a whole blood PAxgene RNA tube and peripheral blood T-cell suspension. After confirming that the CD transcripional signature was detectable and correlated with prognosis, we used machine learning to identify a transcriptional classifier in whole blood gene expression data that would re-capitulate the CD transcripional signature. Model selection was performed using a Bayesian Information Criterion (BIC) and the genes identified were subsequently tested by qPCR and optimised to produce an 18 gene qPCR assay. Using the independent validation of this biomarker was established using a second, independent cohort of 85 newly diagnosed patients with CD from 4 sites around the United Kingdom. This validated the biomarker and confirmed that the subgroups identified had significantly different disease courses (analogous to those observed with the CD8 T-cell subgroups). The hazard ratio for time to treatment escalation in this validation cohort was 3.52 (1.84–6.76, 95% confidence intervals, \(P = 0.0002\)). We now propose to conduct the first ever biomarker-stratified trial in any inflammatory disease to determine whether this biomarker can deliver personalised medicine in CD.

**Conclusion:** We have developed, optimised and validated a whole blood qPCR classifier that is able to predict disease course from diagnosis in IBD patients. This represents a major step towards personalised treatment in IBD, and we will then assess whether this could make personalised medicine a reality in CD.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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**Conclusion:** We have developed, optimised and validated a whole blood qPCR classifier that is able to predict disease course from diagnosis in IBD patients. This represents a major step towards personalised treatment in IBD, and we will then assess whether this could make personalised medicine a reality in CD.

**Disclosure of Interest:** All authors have declared no conflicts of interest.
The rate of nodal metastasis in dissected lymph nodes was 52.3% (34/65). The rate of residual cancer in endoscopically treated lesions, except those considered non-curative, was 4% (2/65), and all 2 lesions had vascular invasion (negative/positive), and curability (R0 resection/R1 resection). We retrospectively assessed the surgical cases following non-curative endoscopic resection. We identified 1137 patients who underwent ESD from August 2006 to December 2016. Of these, pathological diagnosis was non-curative resection in 350 patients (30.7%), with at least one adenoma at the time of diagnosis (115), and dyspepsia (6%). At initial endoscopy, 11 patients (2.2%) had AG, atrophic gastritis (AG), or intestinal metaplasia (IM), or dysplasia (D) was diagnosed by histology, were identified in the hospital pathology database. The clinical, endoscopic, histological and follow-up data were collected from the electronic files for these patients. They were analysed using SAS 9.4 software (Cary, NC, USA).

Results: During a 15-year period, out of 16,764 patients having undergone upper endoscopy with gastric biopsies, 485 patients (60% of men, median age 68 years, min 11 - max 97) with GPL, were identified (detection rate 2.9%). The most frequent indications for endoscopy were anaemia (38%), digestive bleeding (22%), abdominal pain (17%), surveillance (15%), alteration of general status (11%), and dyspepsia (6%). At initial endoscopy, 11 patients (2.2%) had AG, 362 (75%) IM, 80 (16%) low grade dysplasia (LGD), 10 (2%) high grade dysplasia (HGD), and 22 (4.5%) had GADK with concomitant GPL (IM or D). H. pylori infection was found by histology in 204 patients (42%). Endoscopic aspect was considered normal in 17.5% of patients with IM, in 6% of patients with LGD, and in 20% of patients with HGD. The median number of biopsies obtained during initial endoscopy was 4 (min 0 - max 190). Patients with HGD, were significantly older than those with IM and LGD (median age 75 vs 68 years, p = 0.006). From 485 patients, 326 (67%) had at least one follow-up endoscopy (median: 1, min 0 - max 24, Q1-Q3: 0 - 2), after the initial biopsy period of 2.9 months (max 124, Q1-Q3: 1-14) since the initial diagnosis of GPL. During a median follow-up of 40 months (min 0.3 - max 137 months), out of 362 patients with IM, 18 (5%) showed progression to HGD, and 5 (1.4%) to GADK. Among 485 patients, 8 developed GADK during follow-up (annual incidence rate 0.11%). Altogether, with the 22 patients in whom GADK was found already at the time of the diagnosis of GPL, 30 GADK were identified in the studied population (6.2%).

Conclusion: This study showed that in France: I) Most of GPL were diagnosed in patients referred for endoscopy for anaemia or digestive bleeding. II Patients with HGD were older than those with LGD and IM. III The progression from IM to more severe lesions (LGD, HGD, GADK) was observed in 7% of patients during a median follow-up of 33.3 months, and the annual incidence of GADK in this population was 0.11%. IV) Modalities of surveillance of GPL were heterogeneous, V) New endoscopic techniques may improve the endoscopic diagnosis of GPL in the future.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP231 WATER EXCHANGE SIGNIFICANTLY IMPROVED ADENOMA DETECTION RATE AND RELATED MEASURES AND COLON CLEANLINESS IN PROPOFOL-SEDATED PATIENTS


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Dalin Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation, Chiayi/Taiwan

Hualien Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation, Hualien/Taiwan

Xijing Hospital of Digestive Diseases, Fourth Military Medical U, Xian/China

Contact E-mail Address: felixleung@socal.rr.com

Introduction: Increase in adenoma detection rate (ADR), proportion of patients with at least one adenoma) decreased risks of interval colorectal cancer and related deaths after usual air insufflation (AI) colonoscopy. In randomized controlled trials (RCTs) of unsedated and minimally sedated patients, compared with AI, water exchange (WE) significantly decreased insertion time (primary outcome) and increased ADR (secondary outcome). We recently completed two RCTs each with ADR as the primary outcome comparing WE vs. AI in Chinese patients, some of whom were sedated with propofol.

Aims & Methods: We pooled the data of two RCTs (NCT02135601, 0189491) to assess the hypothesis that WE could significantly increase ADR and secondary outcomes of adenoma-related measures in propofol sedated patients. 510 patients were randomly assigned to either AI (n = 258) or WE (n = 252).

Results: Demographic data were comparable. Despite a significantly shorter inspection time, ADR (38% vs. 26.7%), flat (32.5% vs. 19.4%), combined advanced & sessile serrated ADR (13.1% vs. 7.4%), adenoma/colonic polyp, and right colon ADR of WE were significantly higher than those of AI. WE showed significantly cleaner colons and longer insertion time. Comparable withdrawal time without polypectomy and adenoma/positive colonoscopy suggested equivalent withdrawal techniques were used (Table).

<table>
<thead>
<tr>
<th>Method</th>
<th>N (n = 258)</th>
<th>WE (n = 252)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Site</td>
<td></td>
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</tr>
<tr>
<td>Site</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sex, n(%)</td>
<td>107 (41.5)</td>
<td>103 (40.9)</td>
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<tr>
<td>Age</td>
<td>52.7 (10.8)</td>
<td>53.8 (11.7)</td>
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<tr>
<td>Body mass index, kg/m²</td>
<td>23.5 (3.2)</td>
<td>23.7 (3.3)</td>
</tr>
<tr>
<td>Results</td>
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<td></td>
</tr>
<tr>
<td>ADR</td>
<td>0.006</td>
<td></td>
</tr>
<tr>
<td>Insertion time</td>
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</tbody>
</table>

Disclosure of Interest: All authors have declared no conflicts of interest.

OP230 CLINICAL CHARACTERISTICS AND MANAGEMENT OF PATIENTS WITH GASTRIC PRECURSORS LESIONS IN FRANCE: A LARGE 15-YEAR SINGLE CENTER RETROSPECTIVE STUDY

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Introduction: Early detection and adequate surveillance of gastric precancerous lesions (GPL) may prevent the development of gastric adenocarcinoma (GADK) and GADK-related mortality. The epidemiological and clinical data on GPL lesions in France are missing.

Aims & Methods: Our aim was to analyse, in a large retrospective study, the frequency, clinical characteristics, evolution, and modalities of surveillance of GPL in France. All the patients having undergone endoscopy with gastric biopsies between 2000 and 2015 in one academic center, and in whom GPL [atrophic gastritis (AG), or intestinal metaplasia (IM), or dysplasia (D)] was diagnosed by histology, were identified in the hospital pathology database. The clinical, demographic and procedural data of the two pooled randomized controlled trials (N = 510).

Contact E-mail Address: felixleung@socal.rr.com

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<tr>
<td>Site, n(%)</td>
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</tr>
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<td>Sex, n(%)</td>
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</tr>
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<td>Age</td>
<td>52.7 (10.8)</td>
<td>53.8 (11.7)</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>23.5 (3.2)</td>
<td>23.7 (3.3)</td>
</tr>
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</table>

Disclosure of Interest: All authors have declared no conflicts of interest.
Demographic and procedural data of the two pooled randomized controlled trials (N = 510).

Method

<table>
<thead>
<tr>
<th>A1(n = 258)</th>
<th>WE(n = 252)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indications, n(%)</td>
<td>107(41.5)</td>
<td>105(41.7)</td>
</tr>
<tr>
<td>Diagnostic Positive fecal occult blood</td>
<td>22(8.5)</td>
<td>29(11.5)</td>
</tr>
<tr>
<td>Surveillance Screening</td>
<td>35(13.6)</td>
<td>32(12.7)</td>
</tr>
<tr>
<td>Volume of water infused during insertion, mL</td>
<td>94(36.4)</td>
<td>86(34.1)</td>
</tr>
<tr>
<td>Volume of water aspirated during insertion, mL</td>
<td>0 [0-0]</td>
<td>700 [200-1200]</td>
</tr>
<tr>
<td>Boston bowel preparation score - total</td>
<td>6.49(1.15)</td>
<td>6.92(1.18)</td>
</tr>
<tr>
<td>Insertion time, min</td>
<td>6.00(4.1)</td>
<td>7.25(4)</td>
</tr>
<tr>
<td>Withdrawal time, without polypectomy, min</td>
<td>9.45(5.2)</td>
<td>9.48(5.0)</td>
</tr>
<tr>
<td>Inspection time, min</td>
<td>7.4(2.5)</td>
<td>6.8 (1.9)</td>
</tr>
<tr>
<td>ADR, n (%) [95% CI]</td>
<td>69 (26.7)</td>
<td>98 (38.9)</td>
</tr>
<tr>
<td>[21.7–32.5]</td>
<td>[33.1–45.0]</td>
<td></td>
</tr>
<tr>
<td>Adenoma/colonyoscopy</td>
<td>0.51(1.40)</td>
<td>0.72(1.07)</td>
</tr>
<tr>
<td>[0-0]</td>
<td>[0-0]</td>
<td></td>
</tr>
<tr>
<td>Adenoma/positive colonooscopy</td>
<td>1.74(2.13)</td>
<td>1.68(1.02)</td>
</tr>
<tr>
<td>Combined advanced &amp; sessile serrated ADR, n(%) [95% CI]</td>
<td>19 (7.4)</td>
<td>33 (13.1)</td>
</tr>
<tr>
<td>[4.7–11.3]</td>
<td>[9.4–17.9]</td>
<td></td>
</tr>
<tr>
<td>Flat (non-polypoid) ADR, n(%) [95% CI]</td>
<td>50 (19.4)</td>
<td>81 (32.3)</td>
</tr>
<tr>
<td>[15.0–24.7]</td>
<td>[26.7–38.3]</td>
<td></td>
</tr>
<tr>
<td>Right colon ADR, n(%) [95% CI]</td>
<td>27 (10.5)</td>
<td>44 (17.5)</td>
</tr>
<tr>
<td>[7.2–14.8]</td>
<td>[13.2–22.7]</td>
<td></td>
</tr>
</tbody>
</table>

Data: Mean(SD); median [IQR]. For continuous variables, P values were obtained using t-test. For categorical variables, P values were obtained by Chi Square test. P < .05 was considered significant.

Conclusion: WE enhanced quality of colonoscopy in propofol-sedated patients by significantly improving ADR, adenoma-related measures and colon cleanliness, even when its pain-allieving effect was not critical.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP232 COLONIC POST-POLYPECTOMY BLEEDING IN PATIENTS ON NEW ORAL ANTI-COAGULANT – A CASE CONTROL STUDY

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Introduction: Anticoagulants are commonly used to treat patients with cardiovascular and cerebrovascular diseases. Recently developed new oral anticoagulants (NOAC) that are direct thrombin inhibitor and direct factor Xa inhibitor overcome some limitations of vitamin K antagonist, including drug drug interaction and regular dose adjustments on the basis of laboratory monitoring. The risk of post-polypectomy bleeding (PPB) in patients on anti-platelet therapy and vitamin K antagonist has been well studied (1, 5). However, data on the risk of post polypectomy bleeding in patients on NOAC are scanty.

Aims & Methods: This aim of this study was to determine if the risk of colorectal post-polypectomy bleeding in patients on NOAC. Data of consecutive inpatients with age between 18 – 89 in five year period (from 2012 to 2016), who underwent colonoscopy with NOAC therapy (dabigatran, rivaroxaban and apixaban) were collected in 16 Hong Kong Public Hospitals by Clinical Data Analysis and Reporting System (CDARS). NOAC were stopped 1–2 days before colonoscopy and resumed after procedure according to the local hospital practice.

Results: Among 272 patients on NOAC underwent colonoscopy, 106 patients underwent colon polypectomy. Colonoscopy was performed in 16 Hong Kong Public Hospitals by Clinical Data Analysis and Reporting System (CDARS). NOAC were stopped 1–2 days before colonoscopy and resumed after procedure according to the local hospital practice. The relative risk and characteristics of PPB were analysed.

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TUESDAY, OCTOBER 31, 2017 14:30-15:30

IMPLICATIONS OF BIOLOGICS IN IBD - ROOM B2

OP233 MRI IMPROVEMENT AFTER ANTI-TNF THERAPY IS PREDICTIVE OF SUSTAINED CLINICAL REMISSION AND IS A POTENTIAL THERAPEUTIC TARGET IN CROHN'S DISEASE

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2Dept. Of Radiology, CHU Estuing Clermont-Ferrand, Clermont-ferrand;France
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Introduction: MRI has been suggested as a potential alternative to endoscopy to evaluate therapeutic efficacy in ileocolonic Crohn's disease (CD).

Aims & Methods: We aimed to determine if MRI endpoints at week 12 (W12) are able to predict corticosteroids-free deep remission (CFREM) and MRI remission at W52 in patients treated with anti-TNF. CD adult patients needing anti-TNF agents and no bowel resection. MRI remission was defined as no active MRI lesions. Deep remission was defined as no corticosteroids-free deep remission and MRI remission at W12.

Results: Overall, 64 CD patients were enrolled in the study. Nine patients were primary non-responders and left the study before the second MRI. Among the included patients, 41.4% were active smokers and 22.0% previously underwent intestinal resection. CD location was ileal, colonic and ileocolonic in 48.3%, 8.6% and 43.1%, respectively. Overall, 65.5% received concomitant immunosuppressive therapies. In addition, 46.6% and 53.4% of the patients were treated

Conclusion: The risk of colorectal post-polypectomy bleeding in patients with NOAC is high and often delayed in presentation. Resuming NOAC 4 days after colonoscopy may reduce the bleeding risk by half. However, this strategy should be studied in prospective trial to address the bleeding and thrombotic risk.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
with infliximab and adalimumab, respectively. We assessed the variation of MRI parameters between baseline and W12 in patients achieving CFREM at W52 compared to those who did not among 55 CD patients. In univariate analysis, five factors evaluated at W12 were predictors of CFREM at W52: disappearances of ulcerations (OR = 6.4, p = 0.05), of oedema (OR = 3.3, p = 0.05), of enlarged mesenteric lymph nodes (OR = 5.9, 0.041), of or slerotolipomatosis (OR = 12, p = 0.03), and 10% increase of ADC (OR = 4.3, p = 0.02). Using several multivariate models, we defined transmural response at W12 as at least one factor among the three following factors: disappearance of ulcerations, increase of ADC (\(\text{ADC} > 10\%\)), and disappearance of at least one extra-enteric sign (slerotolipomatosis OR enlarged mesenteric lymph nodes). Transmural response predicted CFREM at W52 in 18%, 53%, 67% and 100% of the patients when respectively none, one, two or three criteria were achieved at W12. ROC curves, we identified that 25%-decrease of C1 score or MaRIA index at W12 were the best variations of these scores to predict CFREM at W52. All the MRI endpoints (Table 1) evaluated at W12 were highly predictive of CFREM at W52. In addition, transmural response (AUC = 0.66, Se = 71.4%, Spe = 60%, PPV = 75.0%, NPV = 55.6%) and MRI response according to Clermont score (AUC = 0.77, Se = 64.3%, Spe = 90.0%, PPV = 78.3%, PPV = 81.3%) or MaRIA (AUC = 0.84, Se = 78.6%, Spe = 90.0%, PPV = 85.7%, PPV = 85.7%) evaluated at W12 were highly predictive of deep MRI remission at W52.

**Table 1**: Performances of MRI endpoints evaluated after 12 weeks of treatment with anti-TNF to predict sustained corticosteroids-free clinical remission at week 52.

<table>
<thead>
<tr>
<th>MRI endpoints evaluated at W12</th>
<th>AUC</th>
<th>Se</th>
<th>Spe</th>
<th>NPV</th>
<th>PPV</th>
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<tr>
<td>Transmural response</td>
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<tr>
<td>At least one criteria among:</td>
<td>0.73</td>
<td>80%</td>
<td>67%</td>
<td>82%</td>
<td>64%</td>
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<tr>
<td>- disappearance of ulcerations</td>
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<td>(\Delta\text{ADC} &gt; 10%)</td>
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<tr>
<td>- disappearance of at least one extra-enteric sign (slerotolipomatosis OR enlarged mesenteric lymph nodes)</td>
<td>0.76</td>
<td>86%</td>
<td>66%</td>
<td>75%</td>
<td>75%</td>
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<td>MRI Response</td>
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<tr>
<td>(\Delta\text{Clemont score} &gt; 25%)</td>
<td>0.68</td>
<td>76%</td>
<td>60%</td>
<td>75%</td>
<td>75%</td>
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<tr>
<td>(\Delta\text{MaRIA} &gt; 25%)</td>
<td>0.64</td>
<td>37%</td>
<td>91%</td>
<td>64%</td>
<td>78%</td>
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<tr>
<td>Complete remission</td>
<td>0.66</td>
<td>37%</td>
<td>96%</td>
<td>65%</td>
<td>88%</td>
</tr>
<tr>
<td>No segmental Clermont score &gt; 12.5</td>
<td>0.64</td>
<td>32%</td>
<td>96%</td>
<td>63%</td>
<td>86%</td>
</tr>
<tr>
<td>No segmental MaRIA &gt; 11</td>
<td>0.66</td>
<td>32%</td>
<td>96%</td>
<td>63%</td>
<td>100%</td>
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<tr>
<td>No segmental Clermont score &gt; 8.4</td>
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<tr>
<td>No segmental MaRIA &gt; 7</td>
<td>0.66</td>
<td>32%</td>
<td>100%</td>
<td>64%</td>
<td>100%</td>
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</table>

**Conclusion**: MRI is a reliable tool to monitor therapeutic response in ileocolonic CD. Our short-term MRI endpoints are highly predictive of CFREM or transmural healing at W52, supporting their use in daily practice and clinical trials.

**Disclosure of Interest**: A. Buisson: No conflict of interest related to this work. I declare consulting fees for Takeda, Abbvie and Hospira; lecture fees for Takeda, Abbvie, Hospira, MSD, Ferring, Vifor pharma, Sanofi-Aventis. M. Reymond: None related to this work. Lecture fees for Abbvie. All other authors have declared no conflicts of interest.

**References**


**OP234 EFFICACY OF ENDOCUTaneous PLACEMENT OF A DRUG-ELUTING PLATFORM WITH INFlixIMAB FOR THE TREATMENT OF MUCOSAL LESIONS IN A RAT MODEL OF EXPERIMENTAL COLITIS**

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**Introduction**: Refractory mucosal lesions in Inflammatory Bowel Disease (IBD) patients are an important clinical challenge. Biological therapies have changed the way of treating these patients. Endoscopic administration of these drugs (targeted therapy) could decrease this refractory active inflammation by providing important clinical benefits. We have developed a novel hydrogel (TriBio) with triple biological activity (bioadhesive, biocompatible and bioactive) that can act as drug-eluting platform (patent pending).

**Aims & Methods**: The aim of this study was to evaluate the utility of endoscopic administration of 2 mL of TriBio platform with infliximab (0.5 mg/mL) as a shield, in a rat model of TNBS-induced colitis. Colitis was induced by intrarectal administration of 30 mg TNBS to 24 Sprague-Dawley male rats (Day 0). At day 3, animals were randomized in three groups (n = 8, each) to receive: a) TriBio-infliximab, b) Tribio or c) saline. Macroscopic follow-up (colonoscopy) was assessed at days 6 and 12. Afterwards, animals were sacrificed and colon was resected, weighted and histologically evaluated (1-4 scale). Ponderal evolution and appearance of stool were recorded.

**Results**: The treatment with TriBio-Infliximab significantly improved the clinical condition of the animals (weight evolution, and stool appearance). Similarly, the weight of the colon was also lower in animals treated with TriBio-infliximab when compared to controls (TriBio & saline). Histologic score also showed that TriBio-infliximab treatment significantly reduced the ulcer and the presence of necrosis and fibrosis.

**Table 1**

<table>
<thead>
<tr>
<th>Time</th>
<th>Tribio-Infliximab</th>
<th>Tribio</th>
<th>Saline</th>
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<tr>
<td>Day 3</td>
<td>-7.9 ± 2.1</td>
<td>-6.4 ± 1.8</td>
<td>-9.4 ± 1.8</td>
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<td>Day 6</td>
<td>-5.2 ± 2.7b</td>
<td>-11.4 ± 5.2</td>
<td>-15.7 ± 3.6</td>
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<td>Day 12</td>
<td>-2.2 ± 3.3b</td>
<td>-8.9 ± 4.1,17</td>
<td>-11 ± 7.5</td>
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</table>

**Macroscopic features**

<table>
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<tr>
<th>Stool appearance</th>
<th>Normal</th>
<th>Liquid</th>
<th>Presence of blood</th>
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<tr>
<td>Colon weight (mg/cm)</td>
<td>229 ± 43b</td>
<td>376 ± 93</td>
<td>131 ± 324</td>
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<tr>
<td>Ulceration (area)</td>
<td>2.1 ± 2.0b</td>
<td>9.8 ± 4.6</td>
<td>14.2 ± 11.1</td>
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<tr>
<td>Necrosis</td>
<td>0.6 ± 0.8b</td>
<td>1.8 ± 0.4</td>
<td>2.0 ± 0.0</td>
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<tr>
<td>Fibrosis</td>
<td>0.5 ± 0.8b</td>
<td>1.4 ± 0.3</td>
<td>1.3 ± 0.6</td>
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</table>

bp < 0.05 vs. saline, bp < 0.05 TriBio

**Conclusion**: Endoscopic placement of infliximab associated to a drug-eluting platform solves inflammatory lesions in experimental colitis. These results may open a new way to manage patients with refractory lesions.

**Disclosure of Interest**: R. Bartoli: The author declares the authorship of the patent. J. Boix: The authors declares the authorship of the patent V. Lorenzo-Zúñiga: The authors declares the authorship of the patent All other authors have declared no conflicts of interest.

**OP235 FINAL RESULTS ON EFFICACY AND SAFETY OF BIOSIMILAR INFlixIMab AFTER ONE-YEAR: RESULTS FROM A PROSPECTIVE NATIONWIDE COHORT**

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11st Department Of Medicine, Semmelweis University, Budapest/Hungary
21st Department Of Internal Medicine, University of Szeged, Szeged/Hungary
3Military Hospital – State Health Centre, Budapest/Hungary
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52nd Department Of Medicine, Zala County Hospital, Zalaegerszeg/Hungary
62nd Department Of Medicine, B-A-Z County and University Teaching Hospital, Miskolc/Hungary
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9Department Of Gastroenterology, University of Debrecen, Debrecen/Hungary
10Department Of Medicine And Gastroenterology, Markusovszky Hospital, Szombathely/Hungary
11Department Of Gastroenterology, Tolna County Teaching Hospital, Szekszard/Hungary
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**Introduction**: Biosimilar infliximab CT-P13 received positive CHMP recommendation in June 2013 for all indications of the originator product. It has been previously shown that CT-P13 is effective and safe in inducing remission in inflammatory bowel diseases (IBD). Demographic data were collected and a harmonized monitoring strategy was applied. Clinical remission, response and biochemical response was evaluated at week 14, 30 and 54. None of the patients had received infliximab
within 12 months prior to initiation of the biosimilar infliximab. Safety data was registered.

Results: 353 consecutive IBD (209 CD and 144 UC) patients were included of which 229 patients reached the week 54 endpoint. The age at disease onset was 24/28 years (median, IQR: 19–34) and 22–39) in CD and UC patients, respectively. 31/41% of CD patients had colonic/ileocolonic disease location, 43.5% had complicated disease behaviour, 39% had perianal disease, while 56.2% of UC patients had extensive colitis. 23/19% of patients had received previous anti-TNF therapy in CD and UC, respectively. 60/51% of CD/UC patients received concomitant therapies at baseline. 49, 53, 48% and 80, 81 and 65% of CD/UC patients reached clinical remission and response by week 14, 30 and 54, respectively. Remission and response rates were 56, 41, 43% and 74, 66 and 50% in UC patients. Previous anti-TNF exposure was associated with decreased clinical remission in both CD and UC. Mean CRP decreased significantly both in CD and UC by week 14, which was maintained throughout the 1-year follow-up. 31 (8.8%) patients had infusion reactions, 32 (9%) patients had infections and 1 death occurred.

Conclusion: Final results from this prospective nationwide cohort confirm that CT-P13 is effective and safe in inducing and maintaining remission in both CD and UC. Efficacy was influenced by previous anti-TNF exposure, no new safety signals were detected.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP236 EFFICACY OF HEPATITIS B VIRUS VACCINATION IN NEWBORN EXPOSED TO ANTI-TNF ALPHA IN UTERO

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Introduction: Neonates exposed to maternal anti-TNF alpha therapy in utero are born with clinically significant anti-TNF alpha levels that can still be detected throughout the first months of life. 1, 2 Adults treated with anti-TNF alpha agents have been reported to react inadequately to the hepatitis B virus (HBV) vaccine compared to adults not treated with anti-TNF alpha. 3, 5 Since 2011, HBV vaccination is included in the Dutch National Vaccination Programme. The efficacy of the HBV vaccination is unclear in children that have been exposed to anti-TNF alpha in utero. The objective of this study was to compare anti-HBs levels following routine HBV vaccination in anti-TNF alpha-exposed children versus non-exposed children.

Aims & Methods: We performed a cross-sectional, controlled cohort study at a single, tertiary referral center. Study enrollment took place from 2014 until 2017. Pregnant women treated with anti-TNF alpha until at least the second trimester for Inflammatory Bowel Disease (IBD) and their subsequent children were recruited from the IBD preconception outpatient clinic. Pregnant women treated with other medication than anti-TNF alpha for IBD and their subsequent children were eligible as controls. Women were not eligible for participation in case of HBV infection. Adherence to the Dutch National Vaccination Programme was mandatory for participation in this study (Routine HBV vaccination (Engerix-B Junior, RNA vaccine at 6 weeks, 3, 4 and 11 months). A venous blood sample was obtained from the children one month after final HBV vaccination. Anti-HBs levels were measured in all children by ELISA.

Results: Anti-HBs levels at 12 months did not differ between the anti-TNF alpha exposed (n = 15) and the control group (n = 12) (>1000 IU/L vs >1000 IU/L, p = 0.85). All children successfully immunised against HBV, defined as anti-HBs >10 IU/L. Median anti-HBs levels determined in cord blood at birth were 2.5 ug/mL (IQR: 0.40–11.01 ug/mL). There were no differences in birth outcomes, growth and infections in the first year of life between the anti-TNF alpha exposed and the control group.

Conclusion: This study suggests that children born with detectable anti-TNF alpha levels can be effectively vaccinated against HBV.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
Conclusion: The indication of colonoscopy, sex, age, and time between the last dose of bowel preparation and colonoscopy longer than 7 h are factors that are independently related to the quality of colon cleansing.

Disclosure of Interest: All authors have declared no conflicts of interest.

Table 1: Risk Factors of Inadequate Colonic Cleansing

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<tr>
<th>OR</th>
<th>95% CI</th>
<th>p-value</th>
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<td>1.8</td>
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Introduction: Participation in colon-cancer screening is still low in Europe and worldwide. Especially bowel preparation is reported to be the most unpleasant burden. Despite the fact that bowel preparation is a major cornerstone of quality of colonoscopy, in a certain proportion of patients bowel preparation is still insufficient. Problems with dietary recommendations and problems taking the preparation orally very often in these cases. Among our patients use of cell phone has increased rapidly in the last years. Therefore using this new medium for improvement of colonoscopy preparation has to be considered.

Aims & Methods: To optimize patients’ guidance in colonoscopy preparation an easy-to-use solution for all mobile phones by short message service (SMS) covering the 4 days prior colonoscopy was used in a prospective, randomized multicenter study. In comparison to other approaches not only laxative intake but also patient guidance over the last four days before colonoscopy was served by SMS. 500 (250/250) participants with appointment for outpatient colonoscopy were randomized to regular colonoscopy preparation (control group) or SMS supported colonoscopy preparation. The control group received information about colonoscopy preparation orally and by a leaflet as regularly done by gastroenterologists. The SMS supported group additionally received information regarding dietary and general recommendations time axis adjusted to the colonoscopy appointment by an automated SMS system starting 4 days prior colonoscopy preparation. Level of bowel cleanliness was measured by BBPS. Patients’ satisfaction with bowel preparation procedure was analyzed by a questionnaire.

Results: Participants of the SMS supported colonoscopy preparation had a significantly higher BBPS score (7.6 ± 0.6 vs. 5.9 ± 0.01) in comparison to regular colonoscopy preparation. All regions of the colon had higher BBPS scores in SMS supported patients. Overall patient satisfaction with bowel preparation was higher in the SMS supported group.

Conclusion: Water-assisted colonoscopy preparation by an automated 4-day guidance improved bowel cleanliness. Patient guidance covering the last four days before colonoscopy was highly accepted by the patients. We conclude further that the usage of a simple tool as SMS for optimizing colonoscopy preparation could improve CRC-screening participation.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

OP2042 NEW GENERATION FULL-SPECTRUM VERSUS STANDARD FORWARD-VIEWING COLONOSCOPY: A RANDOMIZED CONTROLLED TRIAL
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Introduction: Technology of colonoscopy is constantly evolving. New full-spectrum (FVE) endoscopes (FUSE) offer 70° and 120° angle of view compared to the standard forward-viewing endoscopes (FVE). From March 2015 trough December 2016 patients referred to colonoscopy screening, positive fecal immunological test, or polyp surveillance underwent colonoscopy with FVE Pentax i10 or FUSE instruments. 974 patients were allocated to receive FUSE first, and 160 (50%) to receive SFV first. Per-lesion analysis, the adenoma miss rate was significantly lower in patients in the FUSE first than in those in the SFV first: 11.7 vs. 13.6% (P = .001) and 49.4 (41.4–57.9) % (P < .001). The polyp miss rate vs. patient analysis was also significantly lower in the FUSE first than in the SFV first: 11.9 (8.0–15.4) % vs 22.9 (17.5–28.3) % (P < .001). The polyp miss rate vs. patient analysis was also significantly lower in the FUSE first than in the SFV first: 13.9 (10.0–17.7) % vs 26.8 (21.3–32.4) % (P < .001). The adenoma detection rate was significantly higher in patients in the FUSE first than in those in the SFV first: 11.7 vs. 9.8% (P = .04). The adenoma detection rate was significantly higher in patients in the FUSE first than in those in the SFV first: 6.29 (5.49–70.4) % vs 49.4 (41.4–57.9) % (P = .018). Cecal intubation rates (%), mean cecal intubation and withdrawal time (min) of FUSE and SFV colonoscopy (140–170 min). Randomization was stratified by sex, age, indication and institution. Primary endpoint was the adenoma detection rate vs-protocol, per-patient analysis. Secondary endpoints included the polyp miss rate and the adenoma detection rate. This trial is registered with UMIN00002448.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
OP244 IMPLEMENTATION OF AN OPTICAL DIAGNOSIS STRATEGY FOR DIMINUTIVE POLYPS INCLUDING SESSILE SERRATED LESIONS: TRAINING AND LONG-TERM QUALITY ASSURANCE

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Introduction: Narrow band imaging (NBI) allows real-time differentiation of diminutive polyps with a histology determination. Before this practice can be implemented in daily practice, guidelines endorse ≥90% negative predictive value (NPV) for neoplastic rectosigmoid histology in the rectosigmoid and ≥90% agreement in surveillance intervals for high-confidence predictions. This study aimed to evaluate the diagnostic accuracy of diminutive polyps and to determine whether these endoscopists can achieve and maintain the prior thresholds.

Aims & Methods: In this prospective multicentre study, endoscopists accredited for colonoscopies in FIT-positives within the Dutch bowel cancer screening program were trained in optical diagnosis with our validated NICE-WASP module [1]. This module includes optical differentiation of sessile serrated lesions. Trained endoscopists were required to reliably diagnose defined thresholds in Imaging-based and real-time tests before entering the continuation phase. In this phase, endoscopists recorded histology predictions and confidence levels of all polyps in consecutive FIT-positives colonoscopies for 1 year. Endoscopists were randomised to receive feedback or no feedback on their performance. Primary outcome was whether endoscopists could maintain a NPV ≥90% for neoplastic histology in the rectosigmoid for high-confidence predictions, either with or without regular interim performance feedback. NPV was determined by comparing predictive value against histology outcome. Sensitivity was defined as adenomatous and sessile serrated lesion histology. For surveillance interval agreement, prediction was based on the combination of high-confidence predictions and histology outcome of low-confidence predictions and polyps sized ≥5 mm. The related equation thresholds were used and adjusted for clustering of polyps per patient and per endoscopist.

Results: Of 39 endoscopists initially attending the training sessions, 27 (69%) qualified after a median number of 3 tests (range 2–5). The pooled NPV for predicting neoplastic histology during the real-time phase was 94.1% (95% confidence interval (CI) 86.1–97.6). In the continuation phase, these 27 endoscopists performed 3, 144 colonoscopies in which 4, 504 diminutive polyps were removed. Of these, 73.5% were predicted with high-confidence and 40% with low-confidence (CI 69.8–77.3). In the rectosigmoid, the pooled NPV for predicting neoplastic histology in the rectosigmoid at the end of the continuation phase was 90.8% (95% CI 88.6–92.6). The NPV in the feedback group was 91.7% (95% CI 88.2–94.2) and 99.6% (95% CI 85.2–92.8) in the observation group (p = 0.93). The pooled surveillance interval agreement was 95.4% (95% CI 94.9–96.6), and did not differ between the feedback and observation group (96.4% versus 94.1%, p = 0.10). Individually, 17 (63%) endoscopists achieved ≥90% NPV for predicting neoplastic rectosigmoid histology, 24 (89%) achieved ≥90% surveillance interval agreement and 16 (59%) achieved both. High-confidence predictions for adenomatous and sessile serrated adenomas/polyps were independently associated with accurate histology prediction.

Conclusion: Using a validated training module including sessile serrated lesions, a selected group of endoscopists achieved and maintained a pooled NPV and high-confidence prediction agreement of at least 90% over the period of 1 year. Providing regular interim feedback did not lead to differences in those endpoints. This study design can be used as a template for safe implementation of an optical diagnosis strategy in daily practice (NCT02516748).

Disclosure of Interest: P. Fockens provides ongoing consultancy to Cook, Olympus, Medtronic, and Fujifilm. E. Dekker has equipment on loan from Olympus Europe and Fujifilm, has received a research grant from Olympus Europe and Fujifilm, and consulted for Tillotts Pharma (one time). All other authors have declared no conflicts of interest.
Introduction: Helicobacter pylori (H. pylori) infection is strongly associated with development of non-cardiac gastric cancer, and gastric adenocarcinoma occurred in patients naïve to H. pylori infection is very rare. In this study, we investigated the clinical characteristics of non-cardiac gastric adenocarcinoma that developed in H. pylori uninfected patients who underwent endoscopic resection.

Aims & Methods: A total of 2221 gastric neoplasia in 1707 patients that were removed by ESD or EMR between January 2010 and May 2016 at our hospital were included. If H. pylori infection status was not evaluated or if H. pylori infection status was not determined, patients were excluded. Patients were excluded if they were not evaluated by H. pylori-serum antibody test: serum antibodies (<3U/ml), urea breath test and stool antigen tests.

Results: Finally, 1, 430 non-cardiac gastric adenocarcinoma in 1111 patients were analyzed in this study. 18 (1.3%) out of 1430 lesions were diagnosed as H. pylori uninfected gastric adenocarcinoma. Among patients with H. pylori-infected gastric adenocarcinoma, 58.4% were younger than 70 years old, and 41.6% were 70 years old or older. The differences in incidence between the two groups were significant (p < 0.001).

Conclusion: We determined the effect of co-incubation of cultured rat gastric fibroblasts with Hp strain encoding for cagA-, vacA- strain on the transdifferentiation of fibroblasts into myofibroblasts associated with Hp-infected inflammation and neoplasia. We also attempted to examine whether differentiated fibroblasts possess characteristics of cancer associated fibroblasts (CAF) able to induce epithelial mesenchymal transition (EMT) of normal rat gastric epithelial cells (RGM-1 cell line). Gastric mucosal samples were harvested from 8-week-old Spraque-Dowley rats and cultured to obtain the sub-confluent fibroblasts. The isolated fibroblasts were infected with 1 × 10⁵ per dish of live Hp (ATCC 700824, cagA-, vacA-) and incubated in humidified atmosphere for 3h, 24h and 48h. At respective times, Hp (cagA- vacA-) increased mRNA expression of α-SMA, collagen I, and HSP-70 and HIF1α. After co-incubation with live Hp, fibroblasts were harvested for determination of the protein expressions of α-SMA and HSP70, by Western Blot analysis.

Results: We found that fibroblasts co-cultured with Hp (cagA- vacA-) strongly upregulated protein expression α-SMA and HSP70. In contrast, the co-incubation with Hp (cagA- vacA-) failed to significantly alter the expression of mRNA for N-cadherin, vimentin, b Twist and Snail mRNAs was observed already after 24h, along with the over-expression of Twist and Snail mRNAs was observed already after 24h, along with the over-expression of Twist and Snail mRNAs was observed already after 24h.
immunoglobulin G antibody test and colonoscopy, was conducted to evaluate the association between Helicobacter pylori and colorectal neoplasm.

**Results:** Multivariable analyses adjusted for age, body mass index, smoking status, alcohol intake, regular exercise, regular aspirin use, and family history of colorectal cancer showed that the odds ratio (OR) [95% confidence interval (CI)] for any adenoma and advanced neoplasm was 1.32 (1.07–1.61) and 1.90 (1.05–3.56) in participants with H. pylori infection and without H. pylori infection, respectively. The association persisted after further adjustment for inflammatory markers or metabolic variables including fasting blood glucose and high-density lipoprotein-cholesterol, and low-density lipoprotein-cholesterol. Regarding the location, a positive association was confined to cases with proximal adenomas, and was observed similarly in all the evaluated subgroups.

**Conclusion:** In a large-scale study, carefully controlled for confounding factors, involving asymptomatic participants without a history of colorectal cancer, H. pylori infection was significantly associated with the risk of any colorectal adenoma and advanced colorectal neoplasm. Prospective studies are necessary to determine whether H. pylori eradication can reduce this risk.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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**References**

8. All authors have declared no conflicts of interest.
OP252 ADHERENCE TO FOOD GUIDELINES OF THE WORLD CANCER RESEARCH FUND & AMERICAN INSTITUTE FOR CANCER RESEARCH AND PANCREATIC CANCER RISK

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Introduction: Pancreatic cancer is one of the most lethal cancers, it has an increasing incidence and limited treatment options. Prevention of this cancer might be the key in lowering the burden of this disease. Two well-known modifiable risk factors are smoking and BMI. For other lifestyle factors, such as diet, there is limited or inconsistent evidence for the association with pancreatic cancer. The World Cancer Research Fund (WCRF) and American Institute for Cancer Research (AICR) have developed guidelines for the prevention of cancer in general. It is known that adherence to these guidelines results in a lower risk of colorectal and breast cancer, however to what extend this applies to pancreatic cancer is unknown.

Aims & Methods: The aim of this study was to assess whether adherence to the WCRF/AICR guidelines is associated with a lower risk of pancreatic cancer. This study was embedded in the Rotterdam Study, a longstanding, prospective and population-based cohort study. Data on dietary intake were collected at baseline, through a frequent food questionnaire and interview by a dietician. We constructed an adherence score, based on the WCRF/AICR recommendations on weight management, foods and drinks that promote weight gain, plant and animal foods, alcoholic drinks, and use of dietary supplements. A higher score corresponds with greater adherence and an hypothesised lower risk of pancreatic cancer. We used Cox Proportional Hazard Models to estimate the association between the adherence score and pancreatic cancer risk.

Results: For 9778 (65.5%) participants dietary data was available. During a median follow-up time of 11.9 years, 77 patients developed pancreatic cancer. Adherence to the WCRF/AICR recommendations was analysed continuously and after stratification into quartiles. Greater adherence was associated with a reduced risk of pancreatic cancer, however not significantly (HRcontinuous: 0.82, 95%(CI: 0.64–1.04)). Stratified analysis showed a significant effect for the third quartile (HR: 0.44, 95%(CI: 0.22–0.88)) with a P-value for trend over the quartiles of 0.028. This effect persisted after excluding all participants with less than two years of follow-up, ensuring the effect was not due to yet undetected disease. Further analysis of the separate recommendations showed that the overall effect was driven by refraining from taking dietary supplements (HR: 0.54, 95%(CI: 0.34–0.84)).

Conclusion: Greater adherence to the World Cancer Research Fund and American Institute for Cancer Research guidelines for diet and lifestyle might be associated with lower risk of pancreatic cancer. Promoting these recommendations to the general population could help reduce pancreatic cancer incidence. However definitive results should follow from pooled analyses of multiple, large and longstanding prospective cohorts to secure more power.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP253 SURVEILLANCE FOR PANCREATIC CANCER IN HIGH-RISK INDIVIDUALS: FIRST-ROUND SCREENING RESULTS OF A MULTICENTRIC ITALIAN PROGRAM

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Introduction: The early diagnosis of cancer can help reduce mortality. Surveillance programs on high-risk individuals (HRI) proved to be able to detect premalignant lesions or early pancreatic adenocarcinoma (PDAC). Currently, surveillance programmes on HRI are based on findings from endoultrasoundography and/or MRI. These imaging techniques proved to be able to diagnose malignant or pre-malignant both on syndromic and familiar cases. The aim of our study was to provide the first registry-based Italian experience on HRI enrolled in a surveillance program for pancreatic cancer.
Aims & Methods: The multicentric surveillance program includes: individuals with familial pancreatic cancer (FPC), defined as those with 3 first, second- or third-degree relatives with PDAC or individuals with 2 relatives with PDAC with at least 1 first-degree relative; BRCA 1/2 or p16 mutation carriers with at least 1 first- or second-degree relative diagnosed with PDAC; subjects suffering from hereditary pancreatitis, Peutz-Jeghers syndrome. The surveillance program consists of an annual magnetic resonance cholangiopancreatography (MRCP). Results: Seventy-eight subjects were enrolled from September 2015 to February 2017, by six high-volume pancreatic Institutions. The mean age was 50 years (range 25–79). Sixty-seven (86%) subjects had FPC, 9 were syndrome HRI (11.5%) and 2 (2.5%) subjects suffered from hereditary pancreatitis. MRCP detected pancreatic cysts in 14 HRI (17.9%, 12 FPC- and 2 syndromic-HRI) and 2 (2.5%) subjects suffered from hereditary pancreatitis. MRCP detected pancreatic cysts in 14 HRI (17.9%, 12 FPC- and 2 syndromic-HRI) and 2 (2.5%) subjects suffered from hereditary pancreatitis. Of note, a patient with a MD-IPMN with high-grade dysplasia (Figure) has been considered for surgical resection. Two suspected solid lesions were identified at MRCP, not further confirmed at endoluathonscopic. Conclusion: The first-round of the Bariatric screening program in Italy, the rate of diagnosed malignant or pre-malignant lesions on HRI is lower than expected. The multicentric surveillance program includes: individuals with familial pancreatic cancer, GUT 2013. Bartsch D, Refinement of screening for familial pancreatic cancer, GUT 2016.

References

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Introduction: CDKN2A-p16-Leiden mutation carriers have a 15–20% risk of developing pancreatic ductal adenocarcinoma (PDAC). Surveillance of these carriers increased the survival but did not prevent all cancer deaths. Understanding of the natural course of PDAC might further improve the surveillance program.

Aims & Methods: The aim of the study was to evaluate the role of cystic precursor lesions (PRL) and the growth rate of PDAC. Since 2000, a large cohort of CDKN2A-p16-Leiden mutation carriers has participated in the annual MRI-surveillance program. We compared the frequency of cystic PRL in this group with that of controls who underwent MRI-scanning for symptoms of liver-biliary tract disorders. We also evaluated whether cystic PRL increase in size and develop into PDAC. Finally, we calculated the growth rate of screen-detected PDAC.

Results: Cystic PRL were found in 52 (25%) of 205 mutation carriers compared to 19 (19%) of 100 controls (P = 0.22). Growth of PRL was observed in six mutation carriers (12%). Five (9.7%) of 52 mutation carriers with PRL and eight (7.0%) of 114 mutation carriers without PRL developed PDAC (P = 0.56). The growth rate of PDAC was 21 mm per year. A reduction of the surveillance interval to 6 months would increase the detection of early tumors from 58% to 92%.

Conclusion: Cystic PRL play a minor role in the development of PDAC in CDKN2A-p16-Leiden mutation carriers. More intensive surveillance is only recommended for patients with large cystic PRL. Independent of the presence of cystic PRL, the surveillance interval may be reduced to 6 months, if studies show this approach to be cost-effective.

Disclosure of Interest: All authors have declared no conflicts of interest.

References


OP255 CHARACTERIZATION OF GENETIC ALTERATIONS IN Pancreatic CANCER HIGH-RISK POPULATION G. Rosan, E. Scapa, E. Santo, M. Ben-Yehoyada

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Introduction: Pancreatic cancer (PC) is a leading cause of cancer death worldwide. Despite modern treatments, 90% of patients die within one year of diagnosis. At early stages, surgical treatment is most beneficial, however, early diagnosis is rare, and most PC cases are confirmed as being locally invasive or metastatic. Inherited predisposition to pancreatic cancer is prevalent in 10% of PC cases. These include characterized genetic conditions such as the hereditary breast and ovarian cancer syndrome (HBOC), Lynch syndrome, familial adenomatous polyposis (FAP), Peutz-Jeghers syndrome (PJS), familial atypical multiple mole melanoma syndrome (FAMMM), and hereditary pancreatitis (HP). However, about 85% of PC cases with strong family history are still uncharacterized.

Aims & Methods: We have recruited 120 high-risk PC individuals for genetic screening and clinical surveillance to identify new criteria for familial pancreatic. For all individuals, germ line DNA was extracted from whole blood and analyzed for the BRCA1 and 2 mutations. Whole Exome Sequencing (WES) technique (Illumina HiSeq platform) was used to screen families with high prevalence to PC for pathogenic germline mutations. Candidate genetic variants were analyzed for their pathogenic potential through familial genetic segregation analysis. Endoscopic ultrasound (EUS) was used to correlate the genetic findings to the clinical phenotype.

Results: We screened 10 informative families and performed segregation analysis. Out of these families, we have discovered several possible pancreatic cancer candidates’ point mutations in well-established as well as in unreported genes. Whole exome sequencing (WES) revealed wide variety of genetic changes in cancer related genes including KLRK1, CLN5, GNAS, GNAS, MSH2, GATA4, GATA3, and KDR genes.

Conclusion: PC development is relatively slow, making it ideal for screening of high-risk individuals. Therefore, identifying this high-risk population is crucial for better surveillance and early detection of pancreatic cancer.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
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Introduction: The prognosis of early stage pancreatic cancer has improved yet there is no feasible screening tool in clinical use. Recent studies have shown that an electronic nose can detect volatile organic compounds from urine and can discriminate between cancer patients and healthy controls.

Methods: The aim of this study was to determine if pancreatic cancer can be detected non-invasively from a urine sample by an electric nose (FAIMS, Field Asymmetric Ion Mobility Spectrometer). Pancreatic cancer patients were recruited in two centers, Sendiöki Central Hospital and Kuopio University Hospital. In January 2011, 64 patients provided a urine sample at the time of the diagnosis. Controls were patients undergoing hernia reparation or cholecystectomy and were recruited in the same centers during the same time period. They provided a urine sample before their operation. 100 ml of midstream urine was stored in −70°C and thawed and warmed up to room temperature for analysis in random order with FAIMS. FAIMS analysis volatile compounds released from the sample, producing an ion mobility spectrum. The resulting spectra were analyzed by linear discriminant analysis and cross-validated by leave-one-out cross-validation (LOOCV).

Results: 80 patients with pancreatic cancer, 40 with acute pancreatitis, 16 with chronic pancreatitis and 14 patients with suspected pancreatic lesion and 44 controls were recruited. The mean age of the pancreatic cancer patients was 70. 49% were females, 29% had stage IB-IIb, 71% stage III-IV cancer and 26% underwent the Whipple procedure or radical pancreactectomy. Patients who died had 16.9 months mean survival time and the mean follow-up time for survivors was 57 months (25–87 months). FAIMS signal data was identified to detect differences between cancer and control samples. The test detected pancreatic cancer with 81% sensitivity and 68% specificity. We combined patients with familial pancreatic cancer, GUT 2013. Bartsch D, Refinement of screening for familial pancreatic cancer, GUT 2016.

References

with pancreatic cancer and premalign pancreatic lesions into one group and controls. Sensitivity was 83% and specificity 63%.

Conclusion: We found that the urine of pancreatic cancer patients has distinct volatile compounds that can be detected by FAIMS, which can distinguish pancreatic cancer patients from controls. It may also be able to detect premalign pancreatic lesions. This investigation was the first to test the ability of electronic nose to detect pancreatic cancer from urine samples. Measurement is quick and easy to perform, its costs are low and most importantly it is non-invasive. AIMS/FAIMS has potential to be a screening tool for pancreatic cancer.

Disclosure of Interest: A. Roine: Owner of Olfactomics Ltd, a company that develops clinical applications of eNose technology

N. Oksala: Owner of Olfactomics Ltd, a company that develops clinical applications of eNose technology

All other authors have declared no conflicts of interest.

TUESDAY, OCTOBER 31, 2017 14:00-15:30

Carcinogenesis and Tumor Progression in GI Cancer - Room B5

OP257 HINOS PROMOTES A CD24+CD133+ LIVER CANCER STEM CELL PHENOTYPE AND TUMOR PROGRESSION THROUGH A TACE/ADAM17 DEPENDENT NOTCH SIGNALING PATHWAY

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Introduction: Hepatocellular carcinoma (HCC) is closely associated with chronic inflammation caused by viral hepatitis, alcoholic or non-alcoholic steatohepatitis, and other conditions leading to chronic inflammation and hepatocyte regeneration. These long-term processes include an accumulation of genetic and/or epigenetic changes of the liver microenvironment and evolution of liver cancer stem cells (LSCs). Growing evidence supports the concept that tumor initiation can be driven by cancer stem cell (CSCs) subsets that are responsible for tumor relapse, metastasis, and chemotherapy-resistance. Therefore, identification of CSC markers as well as signaling pathways activated in LSCs could advance the development of liver cancer diagnosis and treatment strategies. The inducible nitric oxide synthase (iNOS) is associated with more aggressive solid tumors, including hepatocellular carcinoma (HCC). Notch signaling in cancer stem cells promotes cancer progression and requires Notch cleavage by ADAM (a disintegrin and metalloproteinase) proteases. We hypothesized that iNOS/NO promotes Notch1 activation through ADAM17/TACE activation in liver cancer stem cells (LCS) leading to a more aggressive cancer phenotype.

Aims & Methods: Primary human HCC were subjected to immunohistochemistry (IHC) for the expression CD24, CD133, iNOS, activated ADAM17/TACE or activated Notch. CD24+CD133+ cells isolated from HCC cell lines or from human tumors were assessed in vitro and in vivo (Xenograft tumor model in mice) for stem-like properties and growth characteristics. Lentiviral-based short hairpin RNA (LV-shRNA) and LV-iNOS were used to knockdown or overexpress hNOS in LSCs, respectively. Activation of the Notch signal pathway was determined in reporter CD24+/CD133+ cells after (i) LV-shRNA expression, or the inhibition of iNOS (1400W) or TACE (TAPI-2). Immunoprecipitation experiments were carried to assess the interaction between TACE and iRhom2 or TACE and Notch intracellular domain (NICD). We evaluated the effect of iNOS and TACE with clinic-pathological features using a liver cancer tissue microarray (TMA).

Results: Expression of stem cell markers, CD24 and CD133 in the tumors of patients with HCC was found to be independent of gender, age, tumor size, and metastasis. The expression of iNOS in CD24+CD133+ liver cancer stem cells (LSCs), but not CD23-CD133- LSCs, promoted Notch1 signaling and stemness characteristics in vitro and in vivo as well as accelerated HCC initiation and tumor formation in the mouse xenograft tumor model. Lentiviral-based short hairpin RNA (shRNA)-mediated iNOS knockdown or iNOS activity inhibition using BYK191023 significantly suppressed CD24+CD133+ LSCs stemness characteristics in vitro and in vivo. Furthermore, up-regulation of iNOS expression in LSCs led to TACE and iRhom2 phosphorylation in a cyclic GMP (cGMP)-protein kinase G (PKG)-dependent manner. Immunoprecipitation experiments show that the physical binding between TACE and iRhom2 increased significantly when iNOS was overexpressed. Kaplan-Meier analysis showed that high hNOS and NICD expression was significantly associated with aggressive behavior of HCC and decreased survival in patients.

Conclusion: These findings link NOTCH to Notch1 signaling in CD24+CD133+ LSCs through the activation of ADAM17/TACE and identify a new mechanism for how iNOS contributes to progression of CD24+CD133+ HCC.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

OP258 AUTOPIHGY INHIBITS PROTUMORAL EFFECTS INDUCED BY COLIBACTIN-PRODUCING COLORECTAL CANCER ASSOCIATED ESCHERICHIA COLI

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Introduction: The mucosa of patients with colorectal cancer (CRC) is abnormally colonized by Escherichia coli strains, which frequently harbor the pathogenic pks gene cluster responsible for the synthesis of the genotoxin colibactin. Colibactin-producing E. coli induce DNA damage and enhance tumorigenesis in CRC mouse models. Autophagy, cellular process allowing the degradation of cytoplasmic contents via the lysosomal pathway, plays a crucial role in the maintenance of homeostasis and is implicated in various human diseases including cancer.

Aims & Methods: This study aimed at investigating the role of autophagy in host responses to infection with the CRC-associated E. coli strains. mRNA expression levels of autophagy genes in the colonic mucosal biopsies from CRC patients were determined by qRT-PCR. Autophagy induction was assessed by Western blot and immunofluorescence labelling of LC3. DNA damage was assessed by Western blot analysis and immunofluorescence labelling of phospho-H2AX.

Recruitment of the DNA repair protein RAD51 into the nucleus, which is required for DNA repair damage, was examined by Western blot analysis of nuclear and immunofluorescence staining. Intestinal epithelial HCT116 cells infected with intestinal epithelial cells (APC(−)/ATG16L1(−/−)) and the control mice (APC(+/+)APC(+/+)1400W) were infected with the pks-harboring E. coli strain (pks+ E. coli).

Results: mRNA expression levels of many autophagy genes were increased in the tumor tissue compared to the control tissue. A special emphasis was given to the expression in the mucosa colonized with pks+ E. coli compared with those colonized with E. coli strain without pks island (pks- E. coli). Infection of HCT116 cells with the pks+ E. coli strain resulted in autophagy activation, and this was dependent on the presence of the pks island. Autophagy deficiency increased the incidence of colonic tumorigenesis induced by infection with the pks+ E. coli 11G5 strain in APCMin−/− mice.

Conclusion: Autophagy is induced in intestinal epithelial cells infected with the pks+ E. coli, and a functional autophagy is necessary to limit the protumoral effects of pks+ E. coli on infected cells.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
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Introduction: Several studies and meta-analysis demonstrated that patients with mismatch repair (MMR) genes deficient colorectal cancer (CRC) have a more favorable stage-adjusted outcome compared to CRC with MMR defects T-cells, macrophages, and natural killers, infiltration might be increased enhancing immune surveillance mechanisms [1]. In fact, a higher densit of tumor infiltrating lymphocytes was associated with better disease free survival in MMR defective cases with defective pks in CRC with MMR genes deficiency showed a higher CD80 expression, and in vitro silencing of MSH2, MLH1 and MSH6 significantly increased CD80+ cell rate [4]. However, the precise role of CD80 signalling and its effect on MMR genes expression in colonic carcinogenesis remain unclear.

Aims & Methods: The aim of this work was to investigate whether the modulation of CD80 signalling may influence the expression of MMR genes in a mouse model of early colorectal carcinogenesis. C57BL/6 mice received azoxymethane (AOM) at a dose of 10mg/kg body weight weekly for 4 weeks to induce dysplasia and then sacrificed four to six months after the first AOM injection to perform histology, flow cytometry analysis and immunohistochemistry of colonic mucosa. Some WT mice received i.p. a monoclonal antiCD80 or antiCTLA4 antibody following AOM administration. Immunohistochemistry for MLH1, MSH2 and MSH6 was carried on. Non parametric statistics was performed.

Results: Low-grade dysplasia (LGD) extension was to about 20% of the colonic mucosa at 4 and 6 months after AOM treatment in the AOM group and in the
AOM-antiCD80 antibody while it dropped at less than 5% in the AOM-antiCD80 antibody group. By comparing ITGB6 and CEA levels we found that ITGB6 levels in patients with metastatic disease were significantly higher than in patients with non-metastatic disease. In a separate follow-up cohort (n=19), after surgical R0 resection of the colon tumor and concomitant liver metastases, ITGB6 serum levels declined to zero. Of note, we found that ITGB6 serum levels also declined after removal of the liver metastases. However, ITGB6 serum levels rise again when liver metastases were newly diagnosed or tumor progression occurred. In this regard, ITGB6 serum levels were much more reliable as CEA levels. By immunohistochemistry, ITGB6 staining was stronger in metastatic compared to non-metastatic tumors. However, ITGB6 was also found strongly expressed in the tumor microenvironment and could be a more reliable marker for cancer stem-like cells (CSC), which are more aggressive and resistant to therapy.

Conclusion: This is the first study showing ITGB6 levels in patients sera. Our findings provide evidence that ITGB6 can serve as a novel serum biomarker for diagnosis and prognostic of colorectal cancer (CRC), as a marker for tumor surveillance and help in early detection and treatment response as well as a therapeutic target for CRC treatment. In summary, our findings suggest that using targeted therapy in patients with high levels of ITGB6 may be a novel treatment option for CRC patients.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

OP260 BETA-6-INTEGRIN SERVES AS A NOVEL SERUM TUMOR MARKER AND THERAPEUTIC TARGET FOR COLORECTAL CANCER (CRC)
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Introduction: Colorectal cancer (CRC) is the third most common malignancy and one of the leading causes of cancer-related deaths worldwide. The need for novel biomarkers and therapeutic strategies for CRC is obvious and the identification of such markers and targets might significantly improve prognosis of CRC patients. β3-integrin (ITGB6) is a marker for cells undergoing epithelial-to-
mesenchymal transition and has been associated with many epithelial tumors, such as breast cancer. Therefore, ITGB6 serves as a cell surface receptor for matrix proteins, such as fibronectin, and activates matrix degrading enzymes, such as matrix metalloproteinases 2 and 9 as well as TGF-

Aims & Methods: The aim of this study was to investigate whether ITGB6 might serve as a novel serum maker and therapeutic target in CRC patients. We used serum samples of 19 healthy volunteers and 269 CRC patients including 53 patients with metastatic CRC. A follow-up cohort consisted of 19 CRC patients (n=11 without lymph node metastasis, n=4 with lymph node metastasis and n=4 with liver metastasis) serum samples were collected pre-surgery (~3 to ~1 days, post-surgery (2 to 6 days) and during follow-up visits (visit 1: 3 to 20 weeks, visit 2: 20 to 30 weeks, visit 3: 30 to 60 weeks). Wild-type and ITGB6-deficient mice were treated with 0.5-1.0% DDS for 7 days in drinking water followed by a recovery period of 14 days over three cycles. 10 mg azoxymethane (AOM) was administered by i.p. injection six times. ITGB6 serum levels were determined by ELISA.

Results: We detected ITGB6 in the serum of CRC patients (range 0–10 ng/mL) and found that a cut-off of ≥28.8/μl ITGB6 predicts metastatic disease in 100% of respective patients. An ITGB6 serum level above 2 ng/ml was also associated with a significantly worse prognosis compared to patients with a ITGB6 serum level below 2 ng/ml. By comparing ITGB6 and CEA levels we found that ITGB6 levels in patients with metastatic disease were significantly higher than in patients with non-metastatic disease. In a separate follow-up cohort (n=19), after surgical R0 resection of the colon tumor and concomitant liver metastases, ITGB6 serum levels declined to zero. Of note, we found that ITGB6 serum levels also declined after removal of the liver metastases. However, ITGB6 serum levels rise again when liver metastases were newly diagnosed or tumor progression occurred. In this regard, ITGB6 serum levels were much more reliable as CEA levels. By immunohistochemistry, ITGB6 staining was stronger in metastatic compared to non-metastatic tumors. However, ITGB6 was also found strongly expressed in the tumor microenvironment and could be a more reliable marker for cancer stem-like cells (CSC), which are more aggressive and resistant to therapy.

Conclusion: This is the first study showing ITGB6 levels in patients sera. Our findings provide evidence that ITGB6 can serve as a novel serum biomarker for diagnosis and prognostic of colorectal cancer (CRC), as a marker for tumor surveillance and help in early detection and treatment response as well as a therapeutic target for CRC treatment. In summary, our findings suggest that using targeted therapy in patients with high levels of ITGB6 may be a novel treatment option for CRC patients.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

OP261 RESPONSIBLE GENES FOR CHARACTERISTICS OF THE INDUCED CANCER STEM-LIKE SPHERE CELLS OF HEPATOCELLULAR CARCINOMA (HCC)
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Introduction: Cancer stem cells are thought to play important roles in carcinogene-
sis, recurrence, metastasis, and poor prognosis. They are the primary tumor survivors and are responsible for metastasis and chemoresistance.

Aims & Methods: In this study, we examined the target to develop the therapy against intrapathic recurrence of HCC after surgery. A unique medium supple-

Disclosure of Interest: All authors have declared no conflicts of interest.

References
OP262 IN VIVO EFFICACY OF LOCAL THERAPY WITH ADHESIVE WAFER CONTAINING ANTI-CANCER DRUG IN AN ORTHOTOPIC PanCREATIC CANCER MOUSE MODEL

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Introduction: Pancreatic cancer (PC) has the highest mortality rate of all the major cancers. It is the only leading cancer killer with a 5-year survival rate still in the single digits and the survival rate has not improved in the last 40 years. Less than 15% of patients are candidates for surgical resection at the time of diagnosis. Endoscopic ultrasonography-guided fine-needle injection (EUS-FNI) is an attractive minimally invasive delivery system with potential applications in local (intratumoral) against PC. EUS-FNI has demonstrated its feasibility and safety in delivery of medications, however, the procedure has attained attention as a method of antitumor-agent delivery such as anticancer drug, alcohol, gene, and dendritic cells as well as radioactive seeds. Recently Levy et al. in Mayo Clinic reported EUS-guided fine-needle injection of gemcitabine for locally advanced and metastatic pancreatic cancer.

Aims & Methods: The objectives of this study are to confirm in vivo efficiency of adhesive wafer containing chemotherapeutic agent (gemcitabine or paclitaxel). Adhesive wafer consists of the two kinds of polymer matrix of CMC-glycerol and polyvinyl alcohol and chemotherapeutic agent are distributed in this wafer. Orthotopic PC model induced by local injection of AsPC-1 tumor cells into the tail of the pancreas. Adhesive wafer containing gemcitabine or paclitaxel was directly applied in the surface of pancreatic cancer and free gemcitabine or paclitaxel was administered by intratumoral (I.T.) injection as positive control. We compared the anti-tumor efficiency of adhesive wafer containing gemcitabine or paclitaxel and that of intratumoral injection of free drug (positive control) in the orthotopic PC mouse model.

Results: The volume of adhesive wafer containing gemcitabine or paclitaxel treating groups shows significantly supersedes than positive control group. The metastasis scores of non-treating group, vehicle, adhesive wafer containing gemcitabine or paclitaxel, and positive control groups were 1.80, 1.83, 1.87 and 1.00, respectively. These results demonstrate that adhesive wafer containing gemcitabine or paclitaxel for local chemotherapy is more effective than intratumoral injection of free drug in orthotopic PC mouse model.

Conclusion: This study provides the first in vivo application of the adhesive wafer containing paclitaxel for the treatment of pancreatic cancer. We confirmed that higher antitumor effects of adhesive wafer containing paclitaxel and gemcitabine than intratumoral injection of free drug in orthotopic PC mouse model. These results indicate that adhesive wafer containing chemotherapeutic agents is one of new candidates for local chemotherapy of PC.

Disclosure of Interest: All authors have declared no conflicts of interest.

TUESDAY, OCTOBER 31, 2017 15:45-17:15 MULTIDISCIPLINARY MANAGEMENT OF COMPLICATED LUMINAL CROHN’S DISEASE - HALL 6

OP263 PATIENT-REPORTED OUTCOMES WITH UPADACITINIB IN SUBJECTS WITH MODERATELY TO SEVERELY ACTIVE CROHN’S DISEASE: PHASE 2 RESULTS FROM CELEST STUDY L. Peyrin-Biroulet1, E. Louis2, E.V. Loftus Jr3, N. Tundia4, M. Fuldeore4, A. Lacerda4, J. Enejosa4, A. Pangan4
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Introduction: Upadacitinib (UPA) is an oral selective Janus kinase 1 inhibitor that is being assessed for treatment in subjects with Crohn’s disease (CD). The effects of UPA on patient-reported outcomes (PROs) were evaluated in a phase 2 dose-ranging study.

Aims & Methods: A total of 113-740 (Celest study; NCT02363649) was designed to evaluate the efficacy and safety of multiple doses of UPA. Subjects with moderately to severely active CD with inadequate response or intolerance to immunosuppressants or tumour necrosis factor alpha inhibitors were randomly assigned in a 1:1:1:1:1:1 ratio to double-blind induction therapy with placebo (PBO) or UPA at 3, 6, 12 or 24 mg twice daily (BID) or 24 mg once daily (QD) for 16 weeks, followed by a blinded extension therapy for 36 weeks. PROs assessed were the Inflammatory Bowel Disease Questionnaire (IBDQ) and EuroQuol (EQ-5D) and Work Productivity and Activity Impairment (WPAI) questionnaires. Herein, analyses of within-group changes from baseline to week 16 are presented. Percentage of subjects whose improvements met or exceeded the minimum clinically important difference (MCID) in IBDQ score (defined as increase ≥ 15 points or ≥ 4 SD units) was calculated using mixed-effects model for IBDQ total score and analysis of covariance for EQ-5D visual analogue scale score (VAS) and WPAI score. Missing data were reported using non-responder imputation (NRI) and last observation carried forward (LOCF) methods.

Results: Celest enrolled 220 subjects with mean age of 41 years, mean CD duration of 13 years and mean CDAI of 303; 57% were female and 96% had failed or were intolerant to tumour necrosis factor alpha inhibitors. At baseline, overall mean IBDQ score was 116, EQ-5D VAS was 48.9, and WPAI was 61.%. At week 8, clinically meaningful improvements in IBDQ MCID were observed in 53-62% of subjects in all UPA dose groups, except the 3 mg BID group. At week 16, UPA was associated with dose-related increases in the percentage of patients achieving IBDQ response (Table). Significantly more subjects achieved the MCID for the IBDQ score in all UPA dose groups vs PBO with a plateaued response to UPA at 6 mg BID. Significant improvement from baseline in mean EQ-5D VAS at week 16 was observed for both the 6 mg and 24 mg BID doses vs PBO. Activity impairment was significantly reduced for the 6 mg and 24 mg BID doses vs PBO. Overall work impairment was significantly reduced for the 24 mg dose vs PBO.

Table: Patient-Reported Outcome Results

| UPA Dose | IBDQ at week 16 (NRI), % | Remission | MCID ≥ 16 | WPAI: % overall work impairment
<table>
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<tbody>
<tr>
<td>PBO</td>
<td>9</td>
<td>12</td>
<td>13</td>
<td>16</td>
</tr>
<tr>
<td>3 mg BID</td>
<td>(n = 39)</td>
<td>(n = 33)</td>
<td>(n = 28)</td>
<td>(n = 32)</td>
</tr>
<tr>
<td>6 mg BID</td>
<td>(n = 36)</td>
<td>(n = 39)</td>
<td>(n = 32)</td>
<td>(n = 33)</td>
</tr>
<tr>
<td>12 mg BID</td>
<td>14.5</td>
<td>41.8**</td>
<td>32.5*</td>
<td>44.4***</td>
</tr>
<tr>
<td>24 mg BID</td>
<td>18.0</td>
<td>17.2*</td>
<td>9.8</td>
<td>15.3*</td>
</tr>
<tr>
<td>EQ-5D VAS</td>
<td>6.6</td>
<td>9.4</td>
<td>17.2*</td>
<td>4.5</td>
</tr>
<tr>
<td>WPAI: % activity</td>
<td>4.4</td>
<td>11.3*</td>
<td>13.6</td>
<td>28.6*</td>
</tr>
<tr>
<td>WPAI: % overall work impairment</td>
<td>2.4</td>
<td>17.2*</td>
<td>20.9</td>
<td>15.9* (n = 18) - 3.9</td>
</tr>
</tbody>
</table>

Conclusion: Subjects with active and refractory CD treated with 16 weeks of UPA showed clinically meaningful and early improvements in health-related quality of life, had better work performance, and were better able to perform daily activities compared with subjects on PBO.


Acknowledgements & Funding Statement: Financial support for the study and medical writing services (Joann Hettsch, Fishawack Group, Conschohocken, PA) was provided by AbbVie. AbbVie participated in interpretation of data, review, and approval of the abstract. All authors contributed to development of the abstract and maintained control over final content.

OP264 FECAL MICROBIOTA TRANSPLANT FOR CROHN’S DISEASE: A PROSPECTIVE, RANDOMIZED STUDY IN CHINESE POPULATION Z. Yang, X. Wang, C. Bu Department Of Gastroenterology, Third Xiangya Hospital, Central South University, Changsha/China

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Introduction: Crohn’s disease (CD) is an inflammatory bowel disease (IBD), characterized by chronic, recurrent, uncontrolled and idiopathic immune-mediated inflammation that can affect any sites along the whole length of the gastrointestinal tract. CD impairs health-related quality of life (HRQoL) and the incidence of CD continues to rise in low-incidence areas, including China. The precise aetiology of IBD is unclear; however, the intestinal microbiota has been proposed to play an important role in the pathogenesis of IBD. Patients with CD usually present with an overall drop in gastrointestinal microbiota species richness and alternation in the abundance of several taxa. Such conditions are potentially amenable to biologic therapies. Fecal microbiota transplant (FMT) infusion of a fecal suspension from a healthy individual into the gastrointestinal tract of a patient to restore the intestinal homeostasis. During the past several years FMT is a highly effective therapy for recurrent Crohnid Stricture infection (CDI). However, few case series have reported the effects of FMT for CD and the results...
were mixed. We carried out this trial to investigate the outcomes of FMT for CD and to analyse the factors correlated with curative effect.

Aims & Methods: Several case series have reported the effects of FMT for CD. We assessed the efficacy and safety of FMT for patients with CD in a prospective, randomized study trial. Patients with active CD (n = 31) were assigned to groups. Procedures were conducted at The Third Xiangya Hospital of Central South University form January 2014 through March 2016. Patients with active CD (n = 31) were randomized assigned to receive FMT by either gastroscopy or colonoscopy (200 g Qualified stool sample was mixed with sterile saline solution). Fresh fecal suspension was generated from a related healthy volunteer or a prescreened standard donor. Patients were followed by physical examination and laboratory tests of peripheral blood on weeks 1, 2, 4, 6 and 8 after the transplant. Extraction donor and CD patient fecal in DNA, analysis by Illumina MiSeq platform. For patients who didn’t get clinical remission after a single FMT, a second transplant will be taken one week later. The primary end point was clinical remission of CD (Crohn’s disease activity index less than 150 score or CDAI decrease more than 100 score) at week 8. Secondary endpoint was the adverse effects related to the therapy.

Results: In 14 of 31 patients received FMT by colonoscopy and 13 by gastroscopy. Clinical remission was achieved in 15 patients (55.6%) after a single FMT. 12 patients received a second transplant and 3 obtaining clinical remission. Resulting in an overall clinical remission rate of 66.7%. At week 8 compared to who didn’t get a clinical remission, patients with clinical remission have lower CDAI (420 vs 200, P < 0.05), less times of daily diarrhea (6 vs 4, P < 0.05). Adverse effects of FMT were all mild and self-limited. There was no significant difference in adverse events between groups. Operational Taxonomic Units (OTU) analysis shows that CD patient have a lower OTU number than donor (117 vs 238, P < 0.05). CD patients also have a lower abundance of Bacteroides, Roseburia, Turicibacter, Faecalibacterium and higher abundance of Bilophila, Streptococcus, Clostridium, Paraprevotella.

Conclusion: FMT is effective in treating CD, with satisfactory short-term effects and no severe adverse effect. CD patients have a drop of microbiota species richness and alternation in the abundance.

Disclosure of Interest: All authors have declared no conflicts of interest.

References:

TUESDAY, OCTOBER 31, 2017 13:45-17:15 CASE FINDING AND SURVEILLANCE OF BARRETT’S OESOPHAGUS - ROOM C1

OP265 A NOVEL, INTERACTIVE WEB-BASED EDUCATIONAL TOOL IMPROVES DETECTION AND DELINEATION OF BARRETT’S OESOPHAGUS RELATED NEOPLASIA (BORN): THE BORN PROJECT

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Introduction: Endoscopic detection and delineation of neoplasia is crucial for the surveillance and treatment of Barrett's oesophagus.

Aims & Methods: High-quality HD-videos were obtained from pts with BORN (endoscopically visible lesion with HGD/EAC) or without dysplasia (ND) BD. For BORN videos, 3 experts independently delineated lesions throughout the video using software developed specifically for the project. The mean AND/OR-ratio of each pair of experts was used to denote agreement on delineated frames. All videos and frames with an agreement ratio ≥0.25 were reviewed in consensus after which the experts repeated delineation independently. In Phase I, 6 assessors scored 4 sets of 20 videos. The order of the sets and the order of videos within each set were randomized for each assessor.

Assessors were classed as: Trainees: fellows in training; Junior: board certified ≤3 yrs of practice; Senior: board certified ≥3 yrs in practice. Assessors paused the video when a BORN lesion was visible, marked their preferred biopsy position and then delineated the entire lesion using the BORN software. After each set, assessors were guided through mandatory, tailored feedback based on their scores and the experts’ delineations. After Phase I, BORN videos with no apparent contribution to the learning process (either a perfect score at baseline (“too easy”)) or poor performance throughout the 4 sets (“too difficult”) were excluded. This condensed version of the training module, again consisting of 4 sets, was then validated in Phase II by 121 new assessors from Canada (19), Germany (20), the Netherlands (33), United Kingdom (28), and United States (31). Only the parameters 1) Detection score: percentage of BORN lesions with a biopsy mark positioned within “the sweet spot” (i.e. area delineated by all 3 experts). 2) Delineation score: percentage of the sweet spot delineated by the assessor. 3) Relative delineation score: mean agreement of the assessor with the 3 experts divided by the mean agreement amongst experts.

Results: In Phase I, detection scores and delineation scores significantly increased over the 4 sets. There were no significant differences between trainees, juniors and seniors. In Phase II, detection and delineation again significantly increased over the 4 sets with an even higher increase in outcome parameters compared to Phase I (Table 1). Again, there were no significant differences between trainees, juniors and seniors or between countries.

Table 1: Phase I (80 videos by 68 assessors) and phase II (25 videos by 121 assessors)

<table>
<thead>
<tr>
<th>Set</th>
<th>Phase 1</th>
<th>Phase II</th>
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<tbody>
<tr>
<td>1</td>
<td>Detection score (%)</td>
<td>64%</td>
</tr>
<tr>
<td>2</td>
<td>Median delineation score (%)</td>
<td>41%</td>
</tr>
<tr>
<td>3</td>
<td>Relative delineation score (%)</td>
<td>45%</td>
</tr>
<tr>
<td>4</td>
<td>Median relative agreement score (%)</td>
<td>44%</td>
</tr>
<tr>
<td>5</td>
<td>Relative increase set 1/set 4</td>
<td>94%</td>
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</tbody>
</table>

Conclusion: We have developed and validated a unique interactive web-based teaching tool that significantly improves the detection and delineation of BORN. This improvement was found to be robust and significant in endoscopists with a range of experience and country of practice.


OP266 MANAGEMENT OF PATIENTS WITH BARRETT'S OESOPHAGUS: A COST-EFFECTIVENESS ANALYSIS

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Introduction: Barrett's oesophagus (BO) is a known precursor to oesophageal adenocarcinoma (OAC). Surveillance and/or treatment of BO patients is recommended by various clinical practice guidelines, but prior analyses indicated that surveillance of non-dysplastic BO is not cost-effective. However, those studies largely predated the advent of widespread use of endoscopic therapy.
Aims & Methods: This study aimed to determine the optimal management strategy of BO patients through a cost-effectiveness analysis. We used the Microsimulation Screening Analysis (MISCAN) model of OAC to simulate a hypothetical cohort of US males with BO at age 60 who were followed over their life-time under 203 different management strategies. In the first strategy (natural history), no BO patients received endoscopic surveillance or treatment. In all other strategies, BO patients with high-grade dysplasia received endoscopic therapy and then underwent intensive surveillance. For patients with low-grade or no dysplasia, treatment and/or surveillance strategies were varied. An incremental cost-effectiveness analysis was performed to specify the optimal management strategy using a willingness-to-pay threshold of $100,000 per quality-adjusted life-year (QALY).

Results: In the natural history strategy, 68 OAC cases were diagnosed and 50 patients died of OAC per 1000 BO patients. The total cost in this strategy was $3,995,560. Surveillance with endoscopic therapy for BO patients with high-grade dysplasia reduced OAC incidence to 19–54 cases depending on the intensity of surveillance but also increased costs to $4,292,995–15,531,773. Strategies that also involved endoscopic therapy of patients with low-grade dysplasia reduced OAC cases to 17–55, however total costs increased to $4,396,760–15,906,455. The optimal management strategy was to offer surveillance every 3 years to BO patients without dysplasia; surveillance every 6 months within the first year of diagnosis of patients with low-grade dysplasia and annually thereafter; and endoscopic therapy of patients with high-grade dysplasia. The surveillance stop age of BO patients in the optimal strategy was 80 years. This strategy prevented 64% of OAC cases at an incremental cost-effectiveness ratio of $97,918 per QALY (Table 1).

Table 1: The results of incremental cost-effectiveness analysis (CEA) per 1000 BO patients

<table>
<thead>
<tr>
<th>Surveillance interval/Treatment**</th>
<th>CEA result</th>
</tr>
</thead>
<tbody>
<tr>
<td>ND LGD HGD</td>
<td>Surveillance stop age (y)</td>
</tr>
<tr>
<td>none none none</td>
<td>-</td>
</tr>
<tr>
<td>none 1y, then 2y Tx</td>
<td>70</td>
</tr>
<tr>
<td>10y 1y, then 2y Tx</td>
<td>70</td>
</tr>
<tr>
<td>10y 6m, then 1y Tx</td>
<td>70</td>
</tr>
<tr>
<td>5y 1y Tx</td>
<td>70</td>
</tr>
<tr>
<td>4y 1y Tx</td>
<td>75</td>
</tr>
<tr>
<td>3y 6m, then 1y Tx</td>
<td>75</td>
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<tr>
<td>3y 3m, then 1y Tx</td>
<td>80</td>
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<td>3y 6m, then 1y Tx</td>
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<td>2y 6m, then 1y Tx</td>
<td>90</td>
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</tbody>
</table>

References:

Disclosure of Interest: All authors have declared no conflicts of interest.

Aims & Methods: In this study, we further investigated the impact of miR-9 in maintaining intact of intestinal epithelial during the pathogenic process of CD. miR-9 expression was assayed in isolated IECs and inflamed colon samples of 2, 4, 6-trinitrobenzene sulfonic acid (TNBS)-induced and CD patients by qRT-PCR and miRNA in situ hybridization. The levels of SMAD nuclear interacting protein 1 (SNIP1) and CDH1, was investigated in colonic epithelia cells and colorectal tumor models. The role of miR-9 was further studied in the experimental colitis mice by intracolonial administration of miR-9 precursors or inhibitors.

Results: We found that miR-9 expression was significantly upregulated in IECs isolated from inflamed colon tissues of CD patients compared to control and 2, 4, 6-trinitrobenzene sulfonic acid (TNBS)-induced colitis mice, when compared with negative controls. Interestingly, the genes of SNIP1, cyclin D1 and E-cadherin were downregulated significantly and correlated inversely to miR-9, while the genes of E-cadherin, cyclin D1 and E-cadherin were upregulated in CD patients. Furthermore, we demonstrated that miR-9 cooperatively suppressed SNIP1 and CDH1 expression at posttranscriptional levels in colonic cells. In addition, upregulation of miR-9 suppressed colonic cell proliferation via suppressing SNIP1-mediated cyclin D1 expression, induced EMT by targeting CDH1, and vice versa. Moreover, downregulation of upregulation of miR-9 in TNBS-induced colitic colon alleviated or aggravated experimental colitis, respectively.

Conclusion: Our study reveals the mechanism that miR-9 inhibits growth of IECs, promotes EMT and thereby affects intestinal epithelial homeostasis. Blockade of miR-9 in vivo may serve as a potential therapeutic intervention for CD.

Disclosure of Interest: All authors have declared no conflicts of interest.

Aims & Methods: In this study, we investigated the efficacy of NAMPT inhibition by the small molecule inhibitor FK866 as a novel treatment strategy in intestinal inflammation. NAMPT enzymatic activity was blocked in the dextran sulfate sodium (DSS) model of colitis in mice and in the azoxymethane (AOM)/DSS model of colitis-associated cancer. Mucosal NAD levels and its metabolites were determined by HPLC. FK866 was tested on the differentiation and polarization of human and mouse primary macrophages. Further, lamina propria mononuclear cells (LPMC) from IBD patients were treated ex vivo with FK866, dexamethasone or infliximab and assayed for cytokine release.

Results: FK866 treatment was associated with an altered monocyte/macrophage biology which was characterized by NAD-depleting enzymes. These display an important mechanistic link with a dysfunctional NAD metabolism. NAMPT upregulation counteracts an increased cellular NAD turnover mediated by NAD-depleting enzymes. These display an important mechanistic link between inflammatory, metabolic and transcriptional pathways and NAD metabolism. NAMPT is strongly upregulated in IBD patients, however, its functional impact still remains unclear.

References:

Disclosure of Interest: All authors have declared no conflicts of interest.
**OP269** BALANCING JAK/STAT-SIGNALING WITH TOFACITINIB IN MONOCYTES OF HEALTHY CONTROLS AND IBD PATIENTS

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**Introduction:** Monocytes are bridging natural and acquired immunity. Information about JAK signaling in monocytes is scarce especially in an inflammatory milieu. JAK-inhibition is a promising new anti-inflammatory treatment option. However, JAK/STAT activation may be involved both in anti-inflammatory and anti-inflammatory monocyte programs. We have shown that GM-CSF-activated regulatory monocytes (GMaM) induce Treg-differentiation in co-cultures with naive T-cells in vitro. Inflammatory T-cells produce high amounts of GM-CSF in vivo, not leading to anti-inflammatory monocytes, likely because of pro-inflammatory cytokines in the environment. We used JAK-inhibitor Tofacitinib to explore mechanisms that block pro-inflammatory pathways and still allow anti-inflammatory functions in monocytes.

**Aims & Methods:** Primary monocytes from peripheral blood of healthy human donors were isolated and phenotyped by FACS analysis after treatment with GM-CSF and JAK-inhibitor Tofacitinib. Monocytes were co-cultured with autologous naive T-cells and differentiation of Foxp3⁺ regulatory T-cells was evaluated by FACS. Furthermore, primary monocytes from IBD patients with active disease were used to investigate JAK STAT signaling and inhibition. JAK1 activation (represented by IFNγ-induced phospho-STAT1), JAK2 activation (represented by GM-CSF-induced phospho-STAT5), and JAK3 activation (represented by gp130-phosphoS727) was analysed by FACS. Non-toxic doses of 1 to 1000 nM of Tofacitinib were used.

**Results:** We aimed to define the dose of JAK inhibition that keeps JAK2 activity (GM-CSF-induced pSTAT5) intact. Upon stimulation with 10–100 nM Tofacitinib, we detected GM-CSF-induced phospho-STAT5 while phospho-STAT1 and phospho-STAT6 were blocked. Concentrations above 100 nM Tofacitinib led to inhibition of GM-CSF-induced CD39⁺, CD206⁺, CD209⁺ expression. 10–100 nM Tofacitinib allowed CD39⁻, CD206⁻, CD209⁻ expression and IL-10 release while TNFα was still blocked. Co-culture of GM-CSF and T-cells resulted in increased differentiation of Foxp3⁺ Treg that was even enhanced when 10 nM Tofacitinib was used. Investigation of JAK STAT activation in monocytes from IBD patients revealed a lower increase after stimulation compared to healthy controls. Furthermore, TNFα expression was not inhibited in monocytes obtained from IBD patients using the same dosage of Tofacitinib which significantly inhibited TNFα expression in healthy controls (10–100 nM).

**Conclusion:** JAK inhibition in monocytes from IBD patients revealed a lower increase after stimulation compared to healthy controls. Moreover, TNFα expression was not inhibited in monocytes obtained from IBD patients using the same dosage of Tofacitinib which significantly inhibited TNFα expression in healthy controls (10–100 nM). Tofacitinib reduced the proliferation and migration and upregulated the expression levels of TJ proteins. Interestingly, CHG specificity and activity were verified by finding that scrambled CHG peptide did not modify the course of colonic inflammation.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**References**


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**OP270** CHROMOFUNGIN, CGA47-66 DERIVED PEPTIDE, SUPPRESSES CLASSICALLY ACTIVATED MACROPHAGES AND IMPROVES EPITHELIAL BARRIER FUNCTIONS DURING COLITIS

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**Introduction:** Chromogranin-A (ChgA) is a prohormone secreted by neuroendocrine and immune cells and is elevated in inflammatory bowel disease (IBD) and can generate several peptides. ChgA has eight exons and Chromofungin (CHR: ChgA47–66), a peptide with cardioprotective and antinociceptive effects, is encoded on exon Exon-IV. IBD involves characterized by Gram-negative macrophages and the activation of proinflammatory and anti-inflammatory signaling pathways, altered functions of macrophages, intestinal tight junction (TJ) barrier and intestinal epithelial cells. Moreover, the nuclear transcription factor kappa B (NF-kB) signaling, a master regulator of genes transcription, is dysregulated leading to perpetuate inflammation.

**Aims & Methods:** We aimed to study the activity of CHR, ChgA Exon-IV, in colonic tissues of patients with active ulcerative colitis (UC) and undergoing with immunosuppressive therapy (Infliximab: DSS-colitis), as well as in colonic epithelial cells. Expression of Exon-IV and its correlation with classical activated macrophages (CAMs) markers (IL1B, IL6, TNFA, SLAM7, TLRA, CD120B, alternative activated macrophages (MACs) markers (IL10, TGFβ, MR, CMYC, CD14, NFκB, and TJ proteins (Claudin-1 (CLDN1), zonula occludens-1 (ZO1), E-cadherin (EcadCH), occludin (OCLD)) were determined in human colonic tissues. Colitis was induced in C57BL/6 mice by administration of DSS (5%, 5 days). Preventive CHR (2.5 mg/kg/day) treatment or vehicle stomach feeding before colitis induction and lasted for 5 days. Disease activity index, macroscopic score, histological score and serum C-reactive protein were evaluated. Mouse colonic CAMs, AAMS and TJ proteins were assessed using ELISA RT-qPCR. CHR (200 ng/ml) treated naïve peritoneal macrophages were exposed for 6 h to LPS (100 ng/ml) to promote CAMs, or to IL-4 (10 ng/ml) to promote AAMS. CAMs and AAMS markers were quantified. To gain more mechanistic insights, phosphorylated NF-κB levels were quantified in mouse colonic mucosa and CAs using Western Blot. In vitro chemokinesis assay of CHR (200 ng/ml) on naïve macrophages were assessed by transwell migration assay using MCP-1 (30 ng/ml) as a chemotactant. Caco-2 epithelial cells were treated with CHR (1, 10, 100 nM/ml) for 24 h in the presence or absence of LPS (100 ng/ml) when compared to LPS condition. JAK/STAT activation in colitic mice and CAMs compared to controls. Moreover, CHR treatment decreased the expression levels of E-selectin (E-selectin), TNFα, IL-6, CCL2, CCL5, and IL-1β and increased the expression levels of CD14, IL10, TGFB, and CLDN1. Interestingly, expression levels of NF-κB were upregulated by CHR treatment and significantly increased the expression levels of CAMs compared to control condition. CHR-conditioned AAMS expressed more Arg1 and CD14 when compared to IL-4/IL-13 condition. CHR treatment reduced intracellular NF-κB activation in colitic mice and CAMs compared to controls. Moreover, CHR treatment downregulated macrophages migration, increased epithelial cells' proliferation, viability, and upregulated the expression levels of TJ proteins. Interestingly, CHG specificity and activity were verified by finding that scrambled CHG peptide did not modify the course of colonic inflammation. NF-κB activation, and CAMs and epithelial cell barrier functions.

**Conclusion:** CHR treatment attenuates the severity of colitis and the inflammation process via the modulation of macrophages' functions, maintaining TJ barrier integrity and diminishing NF-κB activation. Targeting CHG may represent a promising new direction in the search for therapeutic targets and biomarkers associated with IBD.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**References**

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**OP271** A ROLE FOR THE NADPH OXIDASES NOX1 AND P22PHOX IN VEO-IBD

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**Introduction:** NOD2 is one of the most known IBD risk factors which has been well characterized genetically and functionally. In brief, NOD2 is a PAMP-recognition receptor which mediates NK-kB-dependent signals upon stimulation with muramyl dipeptide (MDP). In previous studies we have shown that the production of ROS as a host defense mechanism is controlled by NOD2. Further, members of the group of the ROS-producing NADPH oxidases seem to play a critical role as they have been identified as novel molecular interactors of NOD2. Interestingly, in a pediatric patient early onset IBD, we identified the gene mutation in NOX1 and CYBA, we generated plasmids harbouring NOX1 and CYBA. In previous studies we have shown that the production of ROS as a host defense mechanism is controlled by NOD2. Further, members of the group of the ROS-producing NADPH oxidases seem to play a critical role as they have been identified as novel molecular interactors of NOD2. Interestingly, in a pediatric patient early onset IBD, we identified the gene mutation in NOX1 and CYBA, we generated plasmids harbouring NOX1 and CYBA. These two genes code for two NADPH oxidases. In previous studies we have shown that the production of ROS as a host defense mechanism is controlled by NOD2. Further, members of the group of the ROS-producing NADPH oxidases seem to play a critical role as they have been identified as novel molecular interactors of NOD2. Interestingly, in a pediatric patient early onset IBD, we identified the gene mutation in NOX1 and CYBA, we generated plasmids harbouring NOX1 and CYBA. These two genes code for two NADPH oxidases.
OP272 - A NOVEL ORAL DOMAIN ANTIBODY TO TUMOUR NECROSIS FACTOR (TNF), ENGINEERED TO BE STABLE TO INTESTINAL PROTEASES, RESULTS IN HIGH CONCENTRATIONS OF ACTIVE COMPOUND DETECTED IN FAECES OF CROHN’S PATIENTS AFTER ORAL DOSING

**Introduction:** Monoclonal antibodies to TNF have transformed the treatment options for patients with Inflammatory Bowel Disease (IBD). V565 is a novel oral domain antibody (Vorabody) to TNF engineered to be resistant to intestinal proteases. It is 115 amino acids (12.6 kDa) in size and neutralizes TNF in vitro.

**Aims & Methods:** Following earlier demonstration of the safety and tolerability of high single and multiple doses of V565 in healthy volunteers, this study aimed to assess V565 pharmacokinetics following a single oral dose to patients with Crohn’s disease (CD). Six subjects with CD received a single dose of open label V565. Prior to dosing, the diagnosis of CD was confirmed by a gastroenterologist and a clinical assessment of severity was carried out. As this was primarily a pharmacokinetic study, patients were excluded if they required surgery, had a current abscess, a non-infectious stricture, or a history of obstruction. Serial blood samples were taken to assess systemic V565 exposure, and all stool samples were collected for up to three days after dosing for detection of faecal V565. In addition, urine was collected from all patients over periods 0–4 h, 4–8 h, 8–12 h and 12–24 h post dose.

**Results:** Two subjects with CD were dosed with a single 555 mg dose of V565. Following review by the study safety committee a further four subjects were dosed with a single 1665 mg dose of V565. Active V565 was detected in the faeces of all subjects. In the stool samples around 24 h after dosing V565 was detected at concentrations up to 84 μM.

**Conclusion:** V565, an oral domain antibody to TNF engineered to be resistant to intestinal proteases, resulted in high concentrations of active drug in the faeces of all Crohn’s patients following a single oral dose, demonstrating survival in the human GI tract. No drug was detected in any serum sample from any patient (LLoQ 62.5 ng/ml).

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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**OP273 - SUSTAINED INCREASE IN COLONOSCOPY PRACTICE 3 YEARS AFTER INTRODUCTION OF QUALITY IMPROVEMENT IN COLONOSCOPY (QIC) BUNDLE**

**Aims & Methods:** We identified if changes in colonoscopy practice were sustained three years following the initial “bundle” implementation. Data were collected from the original study sites, including ADR and histamine butylbromide use. Histamine butylbromide usage rate was used as a marker for uptake of the bundle implementation. Comparisons were made with baseline data collected for 3 months prior to bundle implementation and for a duration of 9 months following completion. Sustainability data were collected for 6 months, 3 years following implementation. Data were compared globally by endoscopy unit and by quartile, where colonoscopists were ranked by baseline ADR. Multilevel logistic regression analyses were undertaken.

**Results:** 12 endoscopy units housed within 8 UK NHS Trusts participated. Global analyses included data from a total of 184 colonoscopists and 28615 procedures. Quartile analyses included data from 50 colonoscopists and 14435 procedures.
procedures. Hyoscine butylbromide use significantly rose and was sustained almost at baseline globally in all endoscopy units and quartiles. A sustained ADR increase (18.2%) was observed globally. Quartile analyses demonstrated that improvement was most marked in the lowest colonoscopy quartile (Table 1).

Conclusion: A simple, evidence-based intervention changed colonoscopy practice, as evidenced by increased Hyoscine Butylbromide use in all quartiles and endoscopy units. As a result ADR was improved. These effects were sustained 3 years following implementation, suggesting this approach is a feasible and durable means of improving ADR, particularly in groups with lower ADRs, with minimal resources.

J.E. East: Clinical advisory board: Lumendi, Boston Scientific Research support: Olympus, Cosmo Pharmaceuticals.
P.T. Rajasekhar: Previous travel and speaking grant for Olympus invited talk
S. Dunn: Dr Dunn previously undertook a research post funded by Aquilant Endoscopy.
R. Bevan: Dr Bevan has previously been awarded a competitive travel grant by Cook Endoscopy.
C.J. Rees: Colin Rees has received research grants from ARC medical, Olympus Medical, Aquilant endoscopy, Norgine, travel grants from Boston scientific and Cook medical and speaking grants from Norgine and Olympus.
All other authors have declared no conflicts of interest.

References

OP274 VARIATION BETWEEN PATHOLOGICAL MEASUREMENT AND ENDOSCOPIC ESTIMATED SIZE OF COLONIC POLYPS
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Introduction: Current guidelines about post-polypectomy colonoscopy surveillance take in count size, number, villous component and high-grade dysplasia of resected polyps to stratify patients’ risk and determine surveillance intervals. Regarding size, 10 millimeters is the cut-off to classify a polyp as an advanced adenoma. Polyp size is visually estimated during the colonoscopy. Is a two-dimensional subjective evaluation with significant variability among endoscopists. The pathological size results from the measurement with a ruler after excision and fixation with formalin. Is not consensual what measurement should be consider to determine surveillance colonoscopy: endoscopic or pathological.

Aims & Methods: The aim of this study was to evaluate variation between colon polyp size reported by the endoscopist and its pathological size. All colonoscopy performed by 7 experienced colonoscopists during a 12-month period in our center were retrospectively analyzed. The inclusion criteria were (1) adenomatous polyps excised in a single specimen; (2) not fragmented during retrieval; (3) exact documentation of endoscopic estimated size and resection method. The exclusion criteria (1) polyps greater than 25 millimeters; (2) unclear size (not reported or reported imprecisely); (3) more than one polyp placed in the same recipient after fragmentation; (4) polyps excised in a single specimen; (2) not fragmented during retrieval; (3) exact documentation of endoscopic estimated size and resection method. The exclusion criteria (1) polyps greater than 25 millimeters; (2) unclear size (not reported or reported imprecisely); (3) more than one polyp placed in the same recipient after fragmentation; (4) polyps excised in a single specimen; (5) polyps are probably more overestimated than smaller ones. The pathological-endoscopic variation is significantly correlated with each endoscopist.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

OP275 SHOULD WE RESECT AND DISCARD SMALL AND DIMINUTIVE POLYPS?
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Introduction: Small (6–9 mm) and diminutive (1–5 mm) colonic polyps are frequently encountered during colonoscopy. Diminutive polyps rarely have advanced histological features.1 To date histology is the gold standard for evaluation of polyp size and their potential impact upon surveillance. The aim of this study was to evaluate the variation between endoscopic estimated size of colorectal polyps and their reported size.

Aims & Methods: The aim of this study was to evaluate variation between endoscopic estimated size of colorectal polyps and their potential impact upon surveillance. The variation based on the method of excision.

Disclosure of Interest: There is a considerable variability between the endoscopic estimated size and pathological size. In our study endoscopists tend to overestimate the polyp size. The overestimation was more evident in EMR, suggesting that larger polyps are probably more overestimated than smaller ones. The pathological-endoscopic variation is significantly correlated with each endoscopist.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

Abstract No: OP273

Table 1

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<tr>
<th>Quartile</th>
<th>Buscopan Rate Pre-QIC</th>
<th>Buscopan Rate Post-QIC</th>
<th>Buscopan Rate Sustainability</th>
<th>Overall P Value</th>
<th>ADR Pre-QIC</th>
<th>ADR Post-QIC</th>
<th>ADR Sustainability</th>
<th>Overall P Value</th>
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<tr>
<td>Upper</td>
<td>19.1</td>
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<td>77.2</td>
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Disclosure of Interest: All authors have declared no conflicts of interest.

References


OP277 OPTICAL DIAGNOSIS OF T1 COLORECTAL CANCER AMONGST ACREDITED ENDOSCOPY CENTERS IN A NATIONWIDE BOWEL CANCER SCREENING PROGRAM

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Introduction: Endoscopic recognition of early stage colorectal cancer (CRC) is of paramount importance in the management of colonic polyps. Accurate optical diagnosis of early stage CRCs (T1 CRCs) can guide treatment strategies. So far, little is known about the identification and endoscopic removal of T1 CRCs in a faecal immunochemical test (FIT)-based screening program. The aim of this study was to examine whether endoscopists performing colonoscopies in a FIT-based screening program are able to identify T1 CRCs correctly and to describe the treatment approaches towards these T1 CRCs.

Aims & Methods: In a prospective multicentre study, endoscopists accredited for FIT-positive colonoscopies within the Dutch bowel cancer screening program were trained in optical diagnosis with our validated NICE-WASP module. A total of 27 endoscopists completed the training successfully and entered the prospective study, in which the endoscopists as well as pathologists reported their findings in a predefined structure. Endoscopists recorded endoscopic diagnosis (adenoma, hyperplastic polyp, sessile serrated lesion and CRC) of every lesion in all consecutive FIT-positive colonoscopies for the Dutch screening program during one year. Two by two contingency tables were created to calculate sensitivity and specificity. T1 CRC was defined as CRC confined to the submucosa without invasion of the muscularis propria at histopathological evaluation.

Results: Between February 2015 and February 2017, 27 endoscopists recorded histology predictions during 3, 622 FIT-positive colonoscopies. During these colonoscopies, 287 patients (7.9%) were diagnosed with CRC. Overall, sensitivity of optical diagnosis of CRC was 76.0% (95% CI; 70.7–80.8) and specificity 99.7% (95% CI 99.6–99.8). In 107 (37%) patients with CRC, a total of 110 T1 cancers were detected (table 1). T1 CRCs had a median size of 20 mm (range 6–100 mm) and were predominantly located in the rectosigmoid (83%). Of these 110 T1 cancers, 41 (37%) were correctly predicted as CRC. Of these 41 correctly diagnosed CRCs, 18 were removed endoscopically en bloc were referred for surgical treatment because of suspicion of invasive cancer (N = 16), non-lifting sign (N = 4) or preference for TEM (N = 3). Of the 69 non-recognized T1 CRCs, 67 were endoscopically removed and 2 were referred for surgical treatment because of their size. Piecemeal removal was performed in 15 unrecognized T1 cancers and the remaining 52 were removed en-bloc. After histopathological evaluation, resection margins showed invasive growth in 13 non-recognized T1 cancers and in 17 cases resection margins could not be assessed. In 43 patients, an additional colonoscopy had to be performed to mark the previous endoscopic resection site of the T1 cancer after histological outcome. In total, adjuvant surgical treatment was required in 3 (7%) patients with recognized T1 CRCs compared to 29 (42%) of patients with non-recognized early stage cancers.

Table: Clinicopathological features of detected T1 CRCs.

<table>
<thead>
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<th>No.</th>
<th>%</th>
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<td>11</td>
<td>12%</td>
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<table>
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<tr>
<th>Location</th>
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<tbody>
<tr>
<td>Proximal to rectosigmoid</td>
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<tr>
<td>Rectosigmoid</td>
<td>91 (83%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Morphology</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sessile</td>
<td>47 (43%)</td>
</tr>
<tr>
<td>Pedunculated</td>
<td>40 (36%)</td>
</tr>
<tr>
<td>Flat (elevated)</td>
<td>7 (6%)</td>
</tr>
<tr>
<td>Other or missing</td>
<td>16 (15%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Endoscopic diagnosis</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adenoma</td>
<td>67 (61%)</td>
</tr>
<tr>
<td>Hyperplastic</td>
<td>1 (1%)</td>
</tr>
<tr>
<td>CRC</td>
<td>41 (37%)</td>
</tr>
<tr>
<td>Missing</td>
<td>1 (1%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Kikuchi/Haggit level</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>SM1/Haggit 1</td>
<td>2/12 (13%)</td>
</tr>
<tr>
<td>SM2/Haggit 2</td>
<td>2/15 (15%)</td>
</tr>
<tr>
<td>SM3/Haggit 3</td>
<td>1/13 (13%)</td>
</tr>
<tr>
<td>Not determined</td>
<td>65 (59%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Lymphangio-invasion</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Suspect/Yes</td>
<td>2 (2%) 8 (7%)</td>
</tr>
<tr>
<td>No</td>
<td>88 (80%)</td>
</tr>
<tr>
<td>Unknown</td>
<td>12 (11%)</td>
</tr>
</tbody>
</table>
Radical resection margin pathology after endoscopic treatment

<table>
<thead>
<tr>
<th></th>
<th>Yes</th>
<th>No</th>
<th>Unable to determine</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1 CRCs (N = 110)</td>
<td>53 (62%)</td>
<td>14 (17%)</td>
<td>18 (21%)</td>
</tr>
</tbody>
</table>

Conclusion: In a prospective study in which endoscopists were trained in optical diagnosis, approximately two-thirds of the T1 CRCs were not recognized during consecutive FIT-positive colonscopes leading to suboptimal use of endoscopic and surgical treatment options. Training in structured lesion assessment is needed to improve endoscopic recognition of T1 CRCs and ensure optimal treatment strategies (NCT02516748).

Disclosure of Interest: P. Fockens: P. Fockens provides ongoing consultancy to Cook, Olympus, Medtronic, and Fujifilm. E. Dekker: Dekker has equipment on loan from Olympus Europe and Fujifilm. This study was funded by the Dutch Cancer Society (grant no. 2008-4407) and the Japan Society for Gastroenterology. T. Ochiai: T. Ochiai received an equipment loan from Olympus Europe and Fujifilm.

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Disclosure of Interest: P. Fockens: P. Fockens provides ongoing consultancy to Cook, Olympus, Medtronic, and Fujifilm. E. Dekker: Dekker has equipment on loan from Olympus Europe and Fujifilm. This study was funded by the Dutch Cancer Society (grant no. 2008-4407) and the Japan Society for Gastroenterology. T. Ochiai: T. Ochiai received an equipment loan from Olympus Europe and Fujifilm.

Contact E-mail Address: seabie@ncc.go.jp

Disclosure of Interest: A combination of detection serum anti-Helicobacter pylori antibody and measurement of the level of serum pepsinogens has been used in screening for early gastric cancer (EGC). However, there are several issues which need to be improved. MicroRNAs (miRNAs) circulating in peripheral blood have been reported to be potentially useful for detecting cancer. The aims of this study are 1) to identify specific serum miRNAs and establish the discriminant model for EGC detection, 2) to validate the miRNAs and the discriminant model using a large cohort.

Aims & Methods: This retrospective study included 1417 serum samples of patients with EGC stored at the National Cancer Center Biobank between 2008 and 2012. In addition, 3051 serum samples of non-cancer patients stored at the National Center for Geriatrics and Gerontology Biobank and healthy volunteers who were recruited in the Toray Industries and the Yokohama Minoura Clinic between 2010 and 2015 were used as control. miRNA expression profiles of whole serum samples were comprehensively evaluated using highly sensitive microarray analysis. A chip (3D-Geno8) which was designed to detect 2555 miRNA sequences registered in miRBase release 20. Diagnostic models were constructed using the expression levels of several miRNAs in the discovery cohort and the diagnostic performances of the model were evaluated in the validation cohort.

Results: Patients and lesions characteristics of gastric cancer were as follows; male/female = 1001/416, median age (range) = 66 (20-90), stage 1A/1B/II = 1349/58/10, differentiated-type/undifferentiated-type/special type = 811/580/18. The discovery cohort included 708 patients with EGC and 4343 non-cancer controls. A diagnostic model for EGC detection constructed by a combination of the five miRNAs (miRNA A, B, C, D, and E) had a sensitivity of 99% and specificity of 97% with 0.99 area under curve (AUC). The validation cohort included 708 patients with EGC and 708 non-cancer controls. The diagnostic model could accurately discriminate EGC from the three kinds of non-cancer cohorts with a sensitivity of 99% and a specificity of 97% with 0.99 of AUC. The diagnostic accuracies of the model were equivalent among the stage (sensitivities of 99%, 100% and 100% in IA, IB and II respectively) and major histological types (sensitivities of 98%, 99%, and 100% in differentiated-type, undifferentiated-type, and special types, respectively).

Conclusion: Novel combination of serum miRNAs could be useful diagnostic biomarkers to detect EGC with high accuracy. Further prospective studies are warranted to confirm the diagnostic performance of the model.

Disclosure of Interest: K. Kato: I have the following financial relationships to disclose. corporate-sponsored research, ONO, Shionogi, MSD J. Kawauchi: Employee of Toray Industries, Inc. S. Takizawa: Employee of Toray Industries, Inc. T. Ochiai: I have the following financial relationships to disclose. Kyowa Medex, Aspenex Corporation, Takeda, Rohto Pharmaceutical Co., Ltd., Aichi Japan Atherosclerosis Research Foundation, Inter Stem, BioMimetics

Sympathies

All other authors have declared no conflicts of interest.

References

surgically removed cancer and adjacent non-neoplastic tissue. Modelling by local experts was used to compare patient and cancer characteristics, including location, size, stage, and morphology, as well as surgical pathology, between those positive or negative for either marker in plasma. The primary outcome for comparison was complete surgical resection (clear margins, absence of distant metastases and lack of apical node involvement as a strong suspicion of residual disease).

**Results:** Of 189 cases with peri-diagnostic blood collected, 91 cases also had matched tissue samples and 93 cases had at least one post-surgical blood sample available for assay. ctDNA was detected in the blood of 119/189 (63.0%) of cases at diagnosis and was significantly more likely to be detected with later stage and distal location (all p < 0.01). The mean BCAT1 and IKZF1 methylation in cancer tissues were 48.0% and 60.5% (respectively), compared to 6.8% and 0.4% in non-neoplastic tissues (each p < 0.0001). Detectable methylation of either marker was seen in 90/91 (98.9%) cancer tissues. Tissue methylation levels in cancer were not concordant with detection in blood or affected by any of the aforementioned variables affecting ctDNA detection. A finding of a positive ctDNA result was most strongly associated with complete surgical resection (OR 31.2, 95% CI 3.4–291.2). Thirty-five of the 47 (74.5%) ctDNA-positive CRC patients at diagnosis who provided a post-surgical sample became negative after surgery, most within 3–4 months. Of the 12/47 cases who retained ctDNA positive after surgery, incomplete surgical resection was observed in 5/12 (41.7%) compared to 1/35 (2.9%) who became negative (p = 0.003, Fisher Exact test). In all 93 cases providing a post-surgery blood sample, incomplete surgical resection or strong suspicion of residual disease was more likely in those returning a positive ctDNA result than in those with a negative result (5/17, 29.4%, vs 1/17, 1.3%, p = 0.001).

**Conclusion:** BCAT1 and IKZF1 methylation are common events in CRC and post-surgical blood samples in CRC are possible on cancer stage (AJCC and TNM) at diagnosis rather than whether or not these markers are methylated in cancer tissue, which is near ubiquitous. Following primary cancer resection, a positive ctDNA result is associated with a significantly higher likelihood of incomplete surgical resection. Consequently, this test has the potential to allow dynamic monitoring of tumour bulk. Detection of methylated BCAT1/IKZF1 DNA in blood appears clinically useful for assessing adequacy of initial therapy and potential for recurrence.

**Disclosure of Interest:** G. Young: Paid consultant of Clinical Genomics P/L.
D. Murray: I am a paid employee of Clinical Genomics P/L.
S. Pedersen: I am a paid employee of Clinical Genomics P/L.
R. Baker: I was a paid employee of Clinical Genomics P/L at the time the study was conducted.

All other authors have declared no conflicts of interest.

**Reference**

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**TUESDAY, OCTOBER 31, 2017 1545-17:15**
**RANDOMISED CONTROLLED TRIALS IN FUNCTIONAL LOWER GI DISORDERS - ROOM 7.1**

**OP281 PRELIMINARY RESULTS OF A RANDOMISED CONTROLLED TRIAL ON HYPNOTHERAPY FOR IRRITABLE BOWEL SYNDROME (THE IMAGINE STUDY)**

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2Psychiatric Policlinic, Leids University Medical Centre, Leiden/Netherlands
3Department Of Gastroenterology And Hepatology, Academic Medical Center - Department of Gastroenterology and Hepatology, Academic Medical Center; Amst, Amsterdam/Netherlands
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**Introduction:** Irritable Bowel Syndrome (IBS) is a common functional gastrointestinal disorder, characterized by abdominal pain, discomfort and altered bowel habits, often accompanied by symptoms of bloating and distension. In general the efficacy of drug therapies is limited. Although individual hypnotherapy was demonstrated to be cost-effective for secondary care patients with IBS, implementation in primary care is limited due to lack of therapists. Therefore group sessions of hypnotherapy may be a more feasible large scale implementation, but the non-inferiority of group application needs to be established first.

**Aims & Methods:** We designed the IMAGINE-study to assess the overall benefit of hypnotherapy as well as to compare the efficacy of individual versus group hypnotherapy in the treatment of IBS. We designed a randomized placebo-controlled trial with 354 primary and secondary care patients (ages 18–65) with IBS (Rome-III criteria). Patients were randomly allocated to either 6 bi-weekly sessions of individual hypnotherapy, 6 bi-weekly sessions of group hypnotherapy or 6 bi-weekly sessions of educational supportive therapy in a group (placebo), with a follow-up of 9 months post treatment for all patients. Thirteen hospitals in different parts of The Netherlands collaborated in this study. The primary endpoint was the percentage of patients with adequate relief (AR) of IBS symptoms after 12 months. AR was defined as 3 or 4 weeks out of 4 weeks adequate relief from IBS symptom severity. Secondary efficacy parameters were changes in the IBS symptom severity, quality of life, cognitions, psychological complaints, self-efficacy as well as direct and indirect costs of the condition. Hypnotherapy was expected to be more effective than the control therapy, and group hypnotherapy was expected not to be inferior to individual hypnotherapy (p < 0.15 difference).

**Results:** Follow-up will be finished by the end of 2017. We present the preliminary results after three months. Of the 354 randomized patients, 150 patients were allocated to individual hypnotherapy, 150 to group hypnotherapy and 54 from the educational support group. Of these patients 79.6% 81.3% and 84% respectively completed 6 sessions of therapy, all within 3 months after start. Of those who completed the therapy 40.4% of the patients in the individual hypnotherapy, 33.7% of the patients in the group-hypnotherapy and 27.5% of those in the educational support group had adequate relief of symptoms after 3 months.

**Conclusion:** After 3 months of treatment hypnotherapy is more effective in patients with IBS than placebo. Group administration of hypnotherapy is not inferior to individual hypnotherapy. Group sessions may stimulate large-scale implementation.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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**OP282 INDIVIDUAL VERSUS GROUP HYPNOTHERAPY FOR IBS: A RANDOMIZED CONTROLLED TRIAL**

J. Lövdahl, 1 O. S. Palsson, 2 G. Ringström, 3 H. Törnblom, 3 M. Simrén 4

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2Dept. Of Medicine, University of North Carolina, Chapel Hill, Chapel Hill, NC United States of America/NC
3Dept Of Gastroenterology And Hepatology, Sahlgrenska Academy Faculty of Medicine, Gothenburg/Sweden
4Dept Of Internal Medicine, Sahlgrenska University Hospital - Dept of Internal Medicine, Sahlgrenska University Hospital; Gothe, Gothenburg/Sweden

**Contact E-mail Address:** jenny.lovdlah@vgregion.se

**Introduction:** Gut-directed hypnotherapy, delivered individually or in groups, improve symptoms in patients with irritable bowel syndrome (IBS). Using group hypnotherapy for IBS would increase cost-effectiveness of this treatment, but only very small parallel comparison between individual and group hypnotherapy has been published.

**Aims & Methods:** We aimed to evaluate and compare the effectiveness of hypnotherapy for IBS delivered in individual versus group format. We included 119 patients (mean age 41.19–70 years; 87 women) with symptoms referable to standard management, who were randomized to receive individual or group hypnotherapy. They attended eight sessions based on the North Carolina Hypnotherapy Protocol (Palsson) delivered by one nurse specialized in hypnotherapy, during a period of two weeks. The group consisted of 5–8 patients. IBS symptom severity was assessed by the IBS Severity Scoring System (IBS-SSS), and subjective health was evaluated by the Short Health Scale (SHS), at baseline and after the 12 week hypnotherapy treatment period, at visit 8. A reduction of IBS-SSS ≥ 50 compared with baseline at visit 8 was considered a response to treatment.

**Table 1:** IBS symptoms and Subjective Health before and after Hypnotherapy (median, IQR)

<table>
<thead>
<tr>
<th></th>
<th>Individual</th>
<th>Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>V.8</td>
<td>Baseline</td>
</tr>
<tr>
<td>IBS-SSS</td>
<td></td>
<td>V.8</td>
</tr>
<tr>
<td>total score</td>
<td>(237–400)</td>
<td>(140–308)</td>
</tr>
<tr>
<td>(239–382)</td>
<td>233</td>
<td>(149–314)</td>
</tr>
<tr>
<td>SHS total</td>
<td>(204–305)</td>
<td>168</td>
</tr>
<tr>
<td>score</td>
<td>(184–231)</td>
<td>191</td>
</tr>
<tr>
<td>p-value</td>
<td>p &lt; 0.001</td>
<td>p &lt; 0.001</td>
</tr>
</tbody>
</table>

**Results:** Sixty-one patients received individual treatment, 58 patients hypnotherapy in groups. Eleven patients (4 individual, 7 group) did not complete the treatment, but were included in the ITT-analysis. Groups were comparable at baseline according age, gender and IBS symptom severity (IBS-SSS) and subjective health (SHS). At the end of the treatment (visit 8) the patients in both groups reported improvement of IBS symptoms, as well as subjective health (SHS) (table 1). Improvement was observed for all five IBS-SSS domains (pain intensity, pain frequency, bloating severity, bowel habit dissatisfaction and daily life interference) (p < 0.001), as well as for all four subjective health domains of SHS (symptom burden, daily function, disease-related worry and general well-being) (p < 0.001). There were no differences between the treatment arms in regard to improvement in IBS-symptoms (p = 0.16) or subjective health (p = 0.17). Sixty-nine percent of the individual hypnotherapy patients met the responder criterion at the end of treatment, compared to 57% of group hypnotherapy patients (p = 0.25).

**Conclusion:** Both individual and group hypnotherapy is effective and relieves IBS symptoms and improves subjective health in patients with IBS. Although the proportion of responders was larger among the patients who received individual therapy, no statistically significant differences in overall improvement in GI symptoms were seen between treatment arms. Group hypnotherapy may therefore be a way to deliver effective IBS hypnotherapy at less cost. Further investigation regarding possible predictors of response to the different treatments could facilitate the choice of the most adequate treatment for each patient.
Disclosure of Interest: O.S. Paolson: Received research grants from Ironwood Pharmaceuticals, Takeda Pharmaceuticals, and Salix Pharmaceuticals and the Rome Foundation.

H. Törnblom: Has served as Consultant/Advisory Board member for Almirall and Allergan as a speaker for Tillotts, Takeda, Shire and Almirall.

M. Simren: Has received unrestricted research grants from Danone and Ferring Pharmaceuticals, and served as a Consultant/Advisory Board member for AstraZeneca, Danone, Nestlé, Menarini, Almirall, Allergan, Albireo, Glycom and Shire

All other authors have declared no conflicts of interest.

OP283 EFFECT OF LACTOBACILLUS PARACASEI CNCM I-1572 ON SYMPTOMS, GUT MICROBIOTA, SHORT CHAIN FATTY ACIDS, AND INTESTINAL MICROBIOTA ACTIVATION IN PATIENTS WITH IRREVERSIBLE BOWEL SYNDROME: A RANDOMIZED CLINICAL TRIAL

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2Department Of Food, Environmental And Nutritional Sciences, University of Milan, Milan/Italy
3University of Pavia, Pavia/Italy
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5Ospedale Di Cisanello Pisa, Pisa/Italy
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Introduction: Several lines of evidence suggest the contribution of intestinal microbiota in the pathophysiology of irritable bowel syndrome (IBS). This provides a proof of concept evidence of an implication of bacterial-host interactions in the pathophysiology and symptom generation of IBS.

Aims & Methods: To assess the effects of Lactobacillus paracasei CNCM I-1572 on clinical and gut microbiota-related factors in irritable bowel syndrome (IBS). We conducted a multicenter, randomized, double-blind, cross-over, 18-week, placebo-controlled, pilot trial assessing the effect of Lactobacillus paracasei CNCM I-1572 on symptoms, gut microbiota composition, fecal short chain fatty acids (SCFA), and on clinical and gut microbiota-related factors in irritable bowel syndrome (IBS).

Results: A total of 40 patients with IBS were enrolled from five Italian centers. Although better results were obtained with Lactobacillus paracasei CNCM I-1572, there was not a statistically significant improvement with active probiotic vs placebo, in the patients with the efficacy variables investigated. Interestingly, active probiotic, but not placebo, induced a significant increase in Lactobacillus (P = 0.011) and a significant reduction in Ruminococcus (P = 0.042), dominated by taxa related to Ruminococcus bromii and Ruminococcus albus. Lactobacillus paracasei CNCM I-1572, but not placebo, induced a significant increase in the SCFAs acetate (P = 0.021) and butyrate (P = 0.047) and a significant reduction in the pro-inflammatory cytokine interleukin-15 (P = 0.012).

Conclusion: This pilot study shows that Lactobacillus paracasei CNCM I-1572 is able to modulate gut microbiota structure and function and reduce immune activation in IBS, even if it was not statistically superior to placebo in symptom reduction. However, this study was characterized by 16S rRNA gene profiling.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP285 RANDOMIZED CLINICAL TRIAL OF FOUR TREATMENTS FOR FAecal INCONTInence AMONG ADULT COMMUNITY-DEWLLING WOMEN: ASSESSMENT OF INDIVIDUAL EFFICACY OF INORECTAL PHYSIOLOGY, THE IMPACT ON CLINICAL SEVERITY AND ON QUALITY Of LIFE

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Introduction: Faecal incontinence (FI) is a prevalent condition with a major impact on quality of life (QoL). Currently four treatments are being used in clinical practice: Kegel exercises (K), biofeedback (BF) electrostimulation (ES) and pelvic floor surgery (NM). Results of each treatment are discordant and lack methodological rigour making scientific evidence weak 1,2.

Aims & Methods: The aim of this study is to assess the efficacy of these four treatments on community-dwelling women and their impact on anorectal physiology, on clinical severity and on QoL. This is a randomized control trial. Patient physiology was studied with anorectal manometry and endoanal ultrasound-sonography; clinical severity was assessed with Cleveland and St. Mark’s scales, and QoL with the Faecal Incontinence Quality of Life (FIQQL) and the EuroQol’s EQ-5D-3L instrument. FIQQL was also evaluated by means of International Consultation on Incontinence (ICIQ) score. Patients were randomized and assigned to K (control), BF + K, ES + K or NM + K, given active treatment for a 3-month period, and then evaluated again with identical tests and questionnaires to identify changes.

Results: Sample was of 152 women with a mean age of 61.09 ± 12.17 years. Clinical severity improved for all treatment arms (Cleveland score pre and post-treatment: 10.92 ± 7.08 vs 4.42 ± 2.95 respectively for the management of IBS symptoms, this should be demonstrated in well-powered ad hoc studies.

ClinicalTrials.gov Identifier: NCT02371499.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP284 PATIENT-REPORTED OUTCOMES WITH NALDEMIDE: NEW LONG-TERM TREATMENT OF OPIOID-INDUCED CONSTIPATION (OIC) IN SUBJECTS WITH CHRONIC NON-CANCER PAIN

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Introduction: Opioid use for the treatment of chronic pain is associated with constipation. Symptoms of OIC significantly affect quality of life. The efficacy and safety profile of nalmepride (NAL), a peripherally-acting μ-opioid receptor antagonist, as a treatment for OIC has been demonstrated in multiple phase 3 studies of up to 52-week duration.

Aims & Methods: To assess the long-term effect of NAL on Patient Assessment of Constipation Symptoms (PAC-SYM) and Quality of Life (PAC-QOL). Methods: In a randomized double-blind placebo (PBO)-controlled 52-week study, subjects 18 to 80 years of age, having ≤4 spontaneous bowel movements (SBM) over 2 weeks and ≤3 SBM in a given week, were randomized 1:1 to received NAL 0.2 mg once daily or PBO for 52 weeks. Subjects were either not on laxatives or on a stable laxative regimen for the study duration. Subjects with gastrointestinal (GI) abnormalities or taking drugs that could affect GI motility were excluded.

Primary endpoints were change from baseline in the frequency of BM over the 52-week treatment period determined by PAC-SYM and quality of life as assessed by PAC-QOL, relative to PBO, and was generally well tolerated for up to 52 weeks.


T. Yamada: employee of Shionogi Inc

J.C. Arjona Ferreira: employee of Shionogi Inc
Disclosure of Interest: All authors have declared no conflicts of interest.

References

Serum and biliary surrogate markers for disease progression (ERC score >4 vs >5 based on sequential ERC findings)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Univariate</th>
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<th>Upper Value</th>
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</thead>
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<td>18.2</td>
<td>0.0000</td>
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<tr>
<td>Calpro-load &gt; 30</td>
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<td>21.0</td>
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<tr>
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<td>19.1</td>
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<tr>
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<td>1.9</td>
<td>4.7</td>
<td>&gt;105</td>
<td>0.0000</td>
</tr>
<tr>
<td>log[AST] load</td>
<td>6.9</td>
<td>2.6</td>
<td>18.7</td>
<td>continuous</td>
<td>0.0001</td>
</tr>
<tr>
<td>log[ALT] load</td>
<td>3.7</td>
<td>1.9</td>
<td>7.2</td>
<td>continuous</td>
<td>0.0001</td>
</tr>
<tr>
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<td>2.5</td>
<td>14.1</td>
<td>continuous</td>
<td>0.0001</td>
</tr>
<tr>
<td>IgG-load</td>
<td>1.4</td>
<td>0.9</td>
<td>2.4</td>
<td>ULN &gt; 1.4</td>
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<tr>
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<td>1.2</td>
<td>4.2</td>
<td>ULN &gt; 15</td>
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</tr>
<tr>
<td>APRIL-load</td>
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<td>6.4</td>
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<tr>
<td>APRIL-load</td>
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<td>1.4</td>
<td>4.6</td>
<td>&gt;0.667</td>
<td>0.0013</td>
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<tr>
<td>Sum log[GTL+ ALP+ ALT+ AST]</td>
<td>6.5</td>
<td>2.9</td>
<td>14.3</td>
<td>continuous</td>
<td>0.0000</td>
</tr>
</tbody>
</table>
| Serum and biliary surrogate markers predicting development of biliary dysplasia and CCA are shown in table.

Serum and biliary markers for disease progression (ERC score >4 vs >5 based on sequential ERC findings)

95%CI

| p |
| Calpro-load >20 | 0.0000 |
| Calpro-load > 30 | 0.0000 |
| BC-Neutroph-load | 0.0000 |
| GT-load | 0.0000 |
| log[AST] load | 0.0001 |
| log[ALT] load | 0.0001 |
| log[ALP] load | 0.0001 |
| IgG-load | 0.0113 |
| IgG-load | 0.0006 |

Conclusion: Of serum surrogate markers, log[AST], log[ALP], the sum of log[ALT+ AST + ALP+ GT] and biliary calprotectin > 20 and neutrophils in BC (>1) turned out to be best predictors for PSC progression based on ERC score in sequential examinations. Risk for development of biliary dysplasia or CCA is associated with ERC score load, biliary calprotectin (>20) and log[AST] and log[ALP], and also the sum of log[ALT+ AST + ALP+ GT]. These variables are useful for monitoring progression of bile duct changes, response for therapy and individual risk stratification for dysplasia in PSC patients.

Disclosure of Interest: All authors have declared no conflicts of interest.
OP288 DURABLE RESPONSE IN THE MARKERS OF CHOLESTASIS THROUGH 24 MONTHS OF OPEN-LABEL EXTENSION STUDY OF OBETICHOLIC ACID IN PRIMARY BILIARY CHOLANGITIS


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9. Surgery, Oncology And Gastroenterology, Università di Padova, Padova/Italy
10. Department Of Medicine II, Liver Center Munich, Munich/Germany
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12. Liver Institute of Virginia, Newport News/United States of America/VA
13. UMC Utrecht, Utrecht/Netherlands
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Introduction: Obeticholic Acid (OCA) is a selective and potent farnesoid X receptor agonist in clinical development for treatment of primary biliary cholangitis (PBC). PBC is a 12-month double-blind (DB), placebo (PBO)-controlled, Phase 3 PBC study including an open-label extension (OLE). Patients who completed the DB phase were eligible to participate in the OLE.

Aims & Methods: The purpose of the OLE is to assess safety and the durability of OCA on markers of cholestasis. Key POISE inclusion criteria: PBC diagnosis, ALP ≥1.67x ULN and/or total bilirubin >ULN to <2x ULN, stable UDCA dose or unable to tolerate UDCA. During the DB phase, 216 patients were randomized and dosed to: daily PBO, n = 73; OCA 5–10 mg (titration after 6 months to 10 mg) when compared to PBO. Patients who received PBO during the DB phase and who initiated OCA during the OLE had significant reductions in markers of cholestasis at 24 months, with the exception of total bilirubin. Pruritus was the most common adverse event (AE) associated with OCA. Overall incidence of pruritus in OCA groups during the DB phase (55–68%) was reduced during the OLE (21–37%), with comparable incidence to that in DB PBO patients (38%). During the OLE, 22 (11%) patients discontinued treatment: 4 (2%) for pruritus; 7 (4%) for other AEs; 11 (6%) for death unrelated to OCA, and 10 (5%) for other reasons.

Conclusions: OCA treatment improves liver biochemistry, most notably ALP and GGT, which is sustained through 24 months of treatment in the OLE. Pruritus was the most common AE, but its occurrence appeared to lessen with longer treatment.

Table 1: Laboratory changes through the DB and OLE study phases

<table>
<thead>
<tr>
<th>Group</th>
<th>ALP (U/L)</th>
<th>OLE 24 mo*</th>
<th>Δ ALP 12 mo/ALP Baseline</th>
<th>Δ OLE 24 mo/OLE Baseline</th>
<th>Total Bilirubin (μmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PBO</td>
<td>309.6</td>
<td>252.8</td>
<td>-8.2 (168.0)</td>
<td>-138.2 (145.5)</td>
<td>172.3 (150.7)</td>
</tr>
<tr>
<td>OCA 5–10 mg</td>
<td>18.9</td>
<td>24.6</td>
<td>-24.4 (23.5)***</td>
<td>-25.6 (26.0)***</td>
<td>18.9 (29.9)***</td>
</tr>
<tr>
<td>OCA 10 mg</td>
<td>147.1</td>
<td>214.1</td>
<td>-14.7 (17.8)***</td>
<td>-9.4 (21.7)***</td>
<td>14.0 (19.3)***</td>
</tr>
</tbody>
</table>

*p < 0.05, **p < 0.01, ***p < 0.001. Values are Mean (SD). *P-value for comparing active treatments to PBO is obtained using an ANCOVA model using DB Baseline value as a covariate and fixed effects for treatment and randomization strata factor. **P-value for the within treatment comparisons are obtained using the Student’s t-test.


L. Shapiro: Dr. Shapiro is an employee and stock shareholder of Intercept Pharmaceuticals.

All other authors have declared no conflicts of interest.
J.J. Marin4, C.J. O’Rourke5, J.B. Andersen5, J. Llop6, V. Gomez-Vallejo6,
TGR5 was evaluated in CCA progression.

Aims & Methods: The differential activation of the bile acid receptors FXR or TGR5 was determined in CCA progression. FXR and TGR5 expression was determined in two different cohorts of CCA patients (i.e. Denmark and Spain), as well as in in vitro CCA cell lines and in human cholangiocytes in culture. A third cohort of human CCA was established in immunodeficient mice and tumor growth was monitored by magnetic resonance imaging (MRI). Under chronic administration of selective TGR5 agonists, no bile acid or cholate biosynthesis were observed in the liver.

Methods: The differential effects of FXR or TGR5 activation were evaluated on proliferation, apoptosis, migration and mitochondrial energetic metabolism (i.e. Seahorse Bioscience) in CCA cells in vitro. The differential effects of FXR or TGR5 activation were evaluated on proliferation, apoptosis, migration and mitochondrial energetic metabolism (i.e. Seahorse Bioscience) in CCA cells.

Results: FXR is downregulated and TGR5 upregulated in human CCA tissue compared to normal surrounding liver tissue in both cohorts. FXR correlates with tumor differentiation, whereas TGR5 correlates with perineural invasion. TGR5 expression is increased in perihilar vs intrahepatic CCA. In vitro, FXR is downregulated and TGR5 upregulated in human CCA cells compared to normal human cholangiocytes. In mice with orthotopic implants of human CCA tumors, chronic administration of OCA inhibited the tumor growth compared to untreated control animals. This was accompanied by decreased expression of proliferation (i.e. PCNA, Ki-67), biliary (i.e. CK19) and epithelial (i.e. ZO-1) markers within the tumors. In chronic administration of INT-777 in vivo showed no effects on CCA tumor growth. In vitro, OCA inhibited CCA cell proliferation and migration, associated with decreased mitochondrial energetic metabolism. In contrast, INT-777 stimulated proliferation and migration of CCA cells, associated with increased mitochondrial energetic metabolism.

Conclusion: The differential activation of FXR or TGR5 can regulate cell proliferation, migration and mitochondrial energetic metabolism. Regulation of FXR and/or TGR5 activities may represent potential novel therapeutic strategies for CCA.

Discourse of Interest: All authors have declared no conflicts of interest.

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Disclosure of Interest: All authors have declared no conflicts of interest.

References

OP291 CLINICAL EFFECT AND SAFETY OF ENDOSCOPIC RADIOFREQUENCY ABLATION FOR UNRESECTABLE EXTRAHEPATIC CHOLANGIOCARCINOMA, A PROSPECTIVE STUDY

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Introduction: Endoscopic transpapillary placement of biliary stents to relieve jaundice is the main palliative treatment for unresectable extrahepatic cholangiocarcinoma (EHC)2,3. It was reported endoscopic biliary radiofrequency ablation (RFA) could prolong the stent patency, which may also be beneficial to improve the patient survival. However, the available evidence is still insufficient for majority of studies were retrospective case series2,3. Aims & Methods: The aim of this study is to explore the clinical effect and safety of RFA in patients with unresectable EHC. 59 Patients with unresectable

Table. Clinical characteristics and bile acid composition in PSC patients in relation to allele dose of PNPLA3 variant.

<table>
<thead>
<tr>
<th>Variable</th>
<th>CC, N = 122</th>
<th>GG, N = 18</th>
<th>p for linearity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Males, (%)</td>
<td>67 (55)</td>
<td>71 (71)</td>
<td>14 (78)</td>
</tr>
<tr>
<td>Age at diagnosis of PSC, mean (SD), years</td>
<td>41 (15)</td>
<td>39 (13)</td>
<td>36 (11)</td>
</tr>
<tr>
<td>IBD, n (%)</td>
<td>86 (70)</td>
<td>63 (79)</td>
<td>11 (61)</td>
</tr>
<tr>
<td>ERC score, mean (SD)</td>
<td>5.5 (3.3)</td>
<td>5.2 (3.3)</td>
<td>3.8 (3.6)</td>
</tr>
<tr>
<td>P-ALP, U/l</td>
<td>130 (102)</td>
<td>143 (142)</td>
<td>192 (148)</td>
</tr>
<tr>
<td>P-AST, U/l</td>
<td>42 (26)</td>
<td>53 (24)</td>
<td>0.052</td>
</tr>
<tr>
<td>B-Platelets</td>
<td>260 (97)</td>
<td>254 (95)</td>
<td>267 (133)</td>
</tr>
<tr>
<td>APRI</td>
<td>0.44 (0.35)</td>
<td>0.57 (1.25)</td>
<td>0.66 (0.60)</td>
</tr>
<tr>
<td>Bile composition</td>
<td>UDCA naive, N = 27</td>
<td>23</td>
<td>6</td>
</tr>
<tr>
<td>Cholesterol_mg</td>
<td>8.42 (3.85)</td>
<td>9.79 (4.90)</td>
<td>9.65 (4.62)</td>
</tr>
<tr>
<td>Total bile acids_mg</td>
<td>66.3 (5.6)</td>
<td>66.0 (7.1)</td>
<td>61.2 (10.8)</td>
</tr>
<tr>
<td>Cholesterol_mg</td>
<td>25.3 (3.6)</td>
<td>24.2 (3.7)</td>
<td>29.2 (6.6)</td>
</tr>
<tr>
<td>Lithocholic acid_mg</td>
<td>13.3 (10.2)</td>
<td>8.3 (5.2)</td>
<td>7.5 (3.8)</td>
</tr>
<tr>
<td>Deoxycholic acid_mg</td>
<td>154 (187)</td>
<td>104 (100)</td>
<td>53 (41)</td>
</tr>
<tr>
<td>Cholesterol_mg</td>
<td>289 (145)</td>
<td>286 (119)</td>
<td>296 (224)</td>
</tr>
<tr>
<td>Cholesterol_mg</td>
<td>473 (314)</td>
<td>512 (278)</td>
<td>469 (291)</td>
</tr>
<tr>
<td>UDCA_mg</td>
<td>17.1 (22.4)</td>
<td>14.5 (14.9)</td>
<td>7.7 (6.8)</td>
</tr>
<tr>
<td>UDCA users, N = 95</td>
<td>57</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>Lithocholic acid_mg</td>
<td>18.8 (20.0)</td>
<td>15.7 (17.9)</td>
<td>15.7 (18.6)</td>
</tr>
<tr>
<td>Deoxycholic acid_mg</td>
<td>56.2 (6.6)</td>
<td>45.9 (53.5)</td>
<td>67.3 (100.0)</td>
</tr>
<tr>
<td>Cholesterol_mg</td>
<td>144 (77)</td>
<td>146 (82)</td>
<td>153 (90)</td>
</tr>
<tr>
<td>Cholesterol_mg</td>
<td>164 (111)</td>
<td>164 (134)</td>
<td>187 (141)</td>
</tr>
<tr>
<td>UDCA_mg</td>
<td>472 (187)</td>
<td>433 (190)</td>
<td>394 (171)</td>
</tr>
</tbody>
</table>

Conclusion: The allele dose of PNPLA3 did not have any significant impact on cholesterol or phospholipid composition of bile acids in UDCA-naïve patients. However, in patients homogeneous for the mutation (GG), there was a statistically significant linearity for lower content of secondary bile acids: deoxy- and lithocholic acid, the most toxic ones, reversed by UDCA therapy.

Discourse of Interest: All authors have declared no conflicts of interest.

References
OP292 PREDNISONE DOSAGE AND CHANCE OF REMISSION IN PATIENTS WITH AUTOIMMUNE HEPATITIS: AN INTERNATIONAL MULTICENTER COHORT STUDY

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Introduction: Current treatment of autoimmune hepatitis (AIH) consists of induction therapy with prednisone followed by azathioprine maintenance therapy. The EASL (European Association for Study of the Liver) Clinical Practice Guidelines on AIH advise a prednisone dose ranging from 0.5 to 1 mg/kg/day. It is not known whether lower doses might be equally effective. We hypothesized that lower doses of prednisone would not lower the chance of achieving biochemical remission.

Disclosure of Interest: All authors have declared no conflicts of interest.

Aims: We investigated the effect of low-dose versus high-dose prednisone induction therapy in AIH on biochemical remission in a multicenter cohort, using chart review data from centers in Amsterdam, Nijmegen, Arnhem (The Netherlands) and Hamburg (Germany). Patients were eligible in case of an established AIH diagnosis according to the International Autoimmune Hepatitis Group criteria, ≥18 years old at time of diagnosis and received induction treatment with prednisone. The primary outcome was biochemical remission, defined as a normal alanine transferase (ALT) serum level (<45 U/l) at 24 weeks after initiation of therapy. Patients were split into a high- and a low-dose group using the EASL guideline cut-off of 0.50 mg/kg/day.

Methods: We performed log-binomial regression to determine differences in biochemical remission between the high and low-dose prednisone group, with correction for center and confounders: baseline ALT, maintenance therapy and use of prednisone. Biochemical remission at week 24 (median 25.9 weeks (range 16 – 36)) was similar in the low- and high-dose group: 66.3% versus 66.9% and remained similar after correction for confounders (RR 1.01 (0.81 – 1.27) p = 0.91).

Table 1: baseline characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>N = 234</th>
<th>Group p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>98</td>
<td>136</td>
</tr>
<tr>
<td>Female gender</td>
<td>72 (74%)</td>
<td>107 (79%)</td>
</tr>
<tr>
<td>Age, years</td>
<td>53.6 (±16.4)</td>
<td>51.8 (±18.3)</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>73.6 (±12.8)</td>
<td>71.0 (±17.7)</td>
</tr>
<tr>
<td>Mean prednisone dosage at start (mg/kg/day)</td>
<td>0.82</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

ANA+ | 78 (79%) | 91 (82%) | 0.67
anti-SMA+ | 56 (57%) | 84 (62%) | 0.48
LKM1+ | 3 (3%) | 3 (2%) | 0.21
anti-SLA/LP+ | 8 (8%) | 12 (9%) | 0.69
ALT (U/l) (±SD) | 403 (±443) | 717 (±744) | <0.01
AST (U/l) (±SD) | 387 (±593) | 611 (±675) | <0.01
Bilirubin (umol/l) (±SD) | 52.1 (±88.7) | 85.2 (±113.5) | 0.04

AMA+ | 78 (79%) | 91 (82%) | 0.67
anti-SMA+ | 56 (57%) | 84 (62%) | 0.48
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AST (U/l) (±SD) | 387 (±593) | 611 (±675) | <0.01
Bilirubin (umol/l) (±SD) | 52.1 (±88.7) | 85.2 (±113.5) | 0.04


Conclusion: Our data shows that prednisone starting dosages below the EASL guideline threshold of 0.50 mg/kg/day can be effective in achieving biochemical remission in AIH.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

Tuesday, October 31, 2017 15:45-17:15
From Prevention to Therapy of Oesophago-Gastric Cancer - Room E3

OP293 LONG-TERM ASPIRIN AND RISK OF GASTRIC CANCER AFTER H. PYLORI ERADICATION: A POPULATION-BASED STUDY WITH PROPENSITY SCORE ANALYSIS

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2Department Of Medicine, The University of Hong Kong, Hong Kong/Hong Kong PRC
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Results: With follow-up of 45 months, the mean overall survival was significantly longer for patients treated by RFA+ stent group than in the stent group (13.8 vs. 8.4 months, P < 0.001). The mean stent patency period of the RFA + stent group was also significantly longer than that of the stent group (6.9 vs. 3.5 months, P = 0.02). There was no significant difference in the incidence of postoperative complications between the two groups [6.9% (2/29) vs 10% (3/30), P = 0.67].

Conclusion: Endoscopic RFA combined with stenting can significantly prolong the EHCC patients' survival and stent patency period without increasing the incidence of adverse events. This approach can be considered as a safe and effective palliative treatment for unresectable EHCC.

Disclosure of Interest: All authors have declared no conflicts of interest.
Introduction: Individuals are still at risk of gastric cancer (GC) development despite successful eradication of H. pylori (HP) infection. Although aspirin has been shown to reduce the GC risk in previous studies, the results were not stratified by HP status and the role of aspirin in subjects with prior HP eradication remains unknown.

Aims & Methods: We determined the effects of long-term aspirin on GC risk in a large population-based cohort of subjects who had received HP eradication. This was a retrospective cohort study based on a territory-wide healthcare database of Hong Kong. All adult subjects who had received an outpatient prescription of clarithromycin-based HP therapy between January 2003 and December 2012 were included. The observation period commenced from the date of triple therapy prescription and was censored at the date of diagnosis of gastric cancer, death, or end of the study. Prescriptions of aspirin before HP eradication or after the censored date were excluded in the analysis. We also excluded subjects with failed HP eradication and those with GC diagnosis within 12 months of HP therapy. We determined the hazard ratio (HR) of GC with aspirin use by Cox proportional hazards model with propensity score adjustment of different baseline characteristics, comorbidities and use of concurrent medications.

Results: During a median follow-up of 7.4 years, 169 (0.27%) of the 63,605 eligible HP infected patients who had successful HP eradication developed GC (median time from HP therapy to GC development: 4.7 years). Aspirin use, defined as ≥ weekly use, was associated with a significantly reduced risk of GC development (HR 0.30, 95% CI: 0.15–0.61). Subgroup analysis showed the risk reduction was confined to non-cardia (HR 0.25, 95% CI: 0.11–0.58) but not cardia GC. The risk of GC decreased with increasing frequency, duration and dose of aspirin use (all p-trend < 0.001) (Table). Conclusion: Long-term aspirin use was associated with a frequency-, dose- and duration-related decrease in GC risk in subjects after successful HP eradication.

Table: HRs and 95% CIs for the association between frequency, duration and dose of aspirin use and risk of gastric cancer (propensity score adjustment)

<table>
<thead>
<tr>
<th>Frequency</th>
<th>HR</th>
<th>95% CI</th>
<th>p-value</th>
<th>p-trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>Never user</td>
<td>Ref</td>
<td>–</td>
<td>–</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>&lt; Monthly use</td>
<td>0.90</td>
<td>0.44–1.84</td>
<td>0.771</td>
<td></td>
</tr>
<tr>
<td>Monthly to &lt; weekly use</td>
<td>0.35</td>
<td>0.05–2.53</td>
<td>0.296</td>
<td></td>
</tr>
<tr>
<td>Weekly to &lt; daily use</td>
<td>0.30</td>
<td>0.14–0.63</td>
<td>0.002</td>
<td></td>
</tr>
<tr>
<td>Daily use</td>
<td>0.21</td>
<td>0.05–0.94</td>
<td>0.041</td>
<td></td>
</tr>
<tr>
<td>Duration</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never user</td>
<td>Ref</td>
<td>–</td>
<td>–</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>&lt;2 years</td>
<td>0.92</td>
<td>0.51–1.64</td>
<td>0.780</td>
<td></td>
</tr>
<tr>
<td>2 years to &lt;5 years</td>
<td>0.27</td>
<td>0.09–0.80</td>
<td>0.017</td>
<td></td>
</tr>
<tr>
<td>≥5 years</td>
<td>0.07</td>
<td>0.02–0.31</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Dose</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never user</td>
<td>Ref</td>
<td>–</td>
<td>–</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>&lt;150 mg</td>
<td>0.38</td>
<td>0.18–0.79</td>
<td>0.009</td>
<td></td>
</tr>
<tr>
<td>≥150 mg</td>
<td>0.15</td>
<td>0.03–0.65</td>
<td>0.011</td>
<td></td>
</tr>
</tbody>
</table>

HR, hazard ratio; 95% CI, 95% confidence interval

Disclosure of Interest: W. K. Leung: WKL has received honorarium for attending advisory board meetings of Takeda and Abbott Laboratories. All other authors have declared no conflicts of interest.

OP294 GASTRIC INTESTINAL METAPLASIA IS SIGNIFICANTLY ASSOCIATED WITH POST ENDOSCOPY NON-CARDIA GASTRIC CANCER

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Introduction: Evidence suggests that the presence of gastric intestinal metaplasia (GIM) is involved in the pathogenesis of Non-Cardia Gastric Cancer (NGC). Although GIM is associated with the occurrence of post endoscopy cancer is scarce. Aims & Methods: We attempted to determine the incidence of post endoscopy NGC and assess whether the presence of GIM is associated with its occurrence. Subjects with no previous cancer undergoing upper endoscopy at a tertiary referral center of the Clalit Health Services (CHS) HMO were included. NGC was detected through the National Cancer Registry. Demographic data was extracted from the CHS database and pathology data including presence of GC (with or without dysplasia) and extent (focal/extensive) were reviewed. Contact E-mail Address: greta.streleckiene@gmail.com

Disclosure of Interest: All authors have declared no conflicts of interest.
Introduction: AMOTL1 (Angiomotin-like protein 1), a member of Motin family, has been reported contradictorily in multiple cancer types and its Hippo-involve- ment during gastric carcinogenesis remains uninvestigated.

Aims & Methods: We seek to elucidate the functional role of AMOTL1 and comprehensively reveal its regulatory mechanisms during gastric carcinogenesis. Mass spectrometry analysis was applied to identify AMOTL1 as one of the YAP1 binding partners, which was further confirmed by co-immunoprecipitation. Immunohistochemistry was performed to confirm the localization of YAPI after AMOTL1 knockdown or overexpression. The mRNA and protein expression levels of AMOTL1 were examined by qRT-PCR and Western blot. The correlation of AMOTL1 expression with other clinical parameters was checked by immunohistochemistry on the tissue microarray. The biological function of AMOTL1 in GC was determined by MTT proliferation, monolayer colony for- mation, cell invasion assays through sRNA-mediated knockdown.

Results: What we observed as a bait, mass spectrometry revealed that AMOTL1 was listed in the key binding partners of YAPI. Knocking down AMOTL1 inhibited YAPI translocation from cytoplasm to the nucleus and promoted YAPI degradation through ubiquitinilation. In primary samples, AMOTL1 is found to be highly expressed in primary GC (P<0.001), GT (P<0.005), GC3 (P<0.006) as well as in paired GC tissues compared with adjacent non-tumorous controls (P<0.012, NCBI/GEO/GSE63089). AMOTL1 upregulation also indicated poor survival among GC patients (overall survival, HR=1.542, P<0.001, n=512, NCBI/GEO/GSE14210, GSE15459, GSE22377, GSE29272, GSE51105 and GSE62254). More importantly, overexpression of AMOTL1 was correlated with worse clinical outcomes of patients in advanced stage (overall survival, HR=1.555, P<0.001) (Supplementary Table 1). AMOTL1 further validated by gene set enrich- ment analysis (GSEA) that AMOTL1 expression was positively associated with upregulation of advanced-GC-related genes (ES=0.775, NES=1.953, P=0.025, n=300, NCBI/GEO/GSE22654). Both univariate and multivariate Cox Regression analyses suggested that AMOTL1 upregulation predicted poor sur- vival independently (univariate analysis, P=0.016; multivariate analysis, P=0.022). In vitro experiments revealed that siAMOTL1 led to reduced cell growth (P<0.001), colony formation (P<0.001) and invasion (P<0.0001), suggesting its oncogenic role during gastric carcinogenesis. Finally, AKT and MAPK signalling pathways were confirmed to be the main downstream of AMOTL1 in GC, which showed good concordant with the driver oncogenic role of YAPI.

Conclusion: AMOTL1 is abundantly expressed in GC tissues and its overexpres- sion indicates poor outcomes. The accumulation of AMOTL1 in GC promotes the growth and invasive ability of tumour cells. AMOTL1 exhibits an oncogenic role in gastric carcinogenesis through stabilization and facilitating the nucleus translocation of YAPI to activate AKT and MAPK singleing. Our findings demonstrate that AMOTL1 is involved in Hippo pathway and it might serve as a potential therapeutic target for GC.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP297 PERIOPERATIVE CHEMOTHERAPY WITH DOCETAXEL, OXALIPLATIN AND FLUOROURACIL/LEUCOVORIN (FLOT) VERSUS EPIRUBICIN, CISPLATIN AND FLUOROURACIL OR CAPECITABINE (ECF/ECX) FOR RESECTABLE GASTRIC OR GEJ ADENOCARCINOMA (FLOT4-AIO): A RANDOMIZED PHASE 3 TRIAL

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Introduction: The MAGIC trial established perioperative (periop) epirubicin, cisplatin, and 5-FU (ECF) as a standard treatment for patients (pts) with operable esophageogastric cancer, but survival continues to remain poor. FLOT4 (NCT01216644) is a multicenter, randomized, investigator-initiated, phase 3 trial. It compares the docetaxel-based triplet FLOT with the anthracycline- based triplet ECF/ECX as a periop treatment for pts with resectable gastric or GEJ adenocarcinoma.

Aims & Methods: Eligible pts of stage ≥T2 and/or cN+ were randomized to either 3 preoperative and 3 postoperative 3-week cycles of ECF/ECX (epirubicin 50mg/m2, cisplatin 60mg/m2, both d1, and 5-FU 200mg/m2 as continuous infusion or capecitabine 1250mg/m2 orally d1-21) or 4 preoperative and 4 post- operative 2-week cycles of FLOT (docetaxel 50mg/m2, oxaliplatin 85mg/m2, leucovorin 200mg/m2, and 5-FU 200mg/m2 as 24-hour infusion, all d1). The primary endpoint was overall survival (OS; 80% power; HR of 0.76; 2-sided log- rank test at 5% type I error). Funded by Deutsche Krebshilfe.

Results: Between Aug 2010 and Feb 2015, 716 pts (360 ECF/ECX; 356 FLOT) were randomly allocated. Baseline characteristics were similar between arms (overall, male 74%; median age 62; cT3/T4 81%; cN+ 80%; GEJ 56%). 91% and 57% of pts with ECF/ECX and 90% and 50% with FLOT completed planned cycles preoperative-and perioperative, respectively. Median follow up was up 43 mon. 369 pts died (203 ECF/ECX; 166 FLOT). FLOT improved OS (n=35, 35 mon with ECF/ECX vs. 50 mon with FLOT; HR 0.77 [0.63-0.94]; p=0.012). 3y OS rate was 48% with ECF/ECX and 57% with FLOT. FLOT also improved PFS (mPFS, 18 mon with ECF/ECX vs. 30 mon with FLOT; HR 0.75 [0.62-0.91]; p=0.004). No DTR (50%) was 50% with ECF/ECX and 51% with FLOT, 30- and 90-day mortality was 3% and 8% with ECF/ECX and 2% and 5% with FLOT. There was more G3/4 nausea phase 1-2 (P=0.04) and ECF/ECX vs. FLOT 5.3% and 0.5% with FLOT. Conclusion: Perip FLOT improved outcome in patients with resectable gastric and GEJ cancer compared to periop FLOT/ECX and is new standard therapy in this setting.

Disclosure of Interest: N. Homann: consulting/advisory role Sanofi, Roche, Amgen, Cellgene, Lilly H. Schmalenberg: Consulting/Advisory Role: Lilly, Baxter; Research Funding: Sanofi, Travel: Merck; G.M. Haag: advisory role: Sanofi, K.B. Kuley: travel, accommodation, expenses: Ipsen, Novartis, Sanofi W. Schmiegel: adviser: Aciaris, Amgen, Apeuct, AstraZeneca, Indivudium, Merck Serono, and Roche; speaker’s fees: Alboit, Falk Foundation, GSB, Lilly, MCI, MCK, Express, Pfizer, Sanofi Aventis, Siemens Healthcare, Merck Serono, and Roche P. Thaus-Patience: consulting: Roche, Lilly, BMS, MSD, Nordic, Pfizer; research grants: Novartis; accommodation, expenses: Roche; Merck, TEVA M. Koenigsmann: honoraria: Novartis, Cellgene, consulting: Novartis, Cellgene, travel, accommodation, expenses: Novartis M. Schuler: adviser: AstraZeneca, Boehringer Ingelheim, BMS, Cellgene, Lilly, Novartis and Roche; speaker’s fees: Novartis, Cellgene, Lilly, and Novartis; research grants Boehringer Ingelheim, BMS, and Novartis S. Al-Batran: adviser for Merck, Roche, Cellgene, Lilly, and Nordic Pharma; speaker’s fees from Roche, Cellgene, Lilly, and Nordic Pharma; research grants from Sanofi, Merck, Roche, Cellgene, Vifor, Medac, Hospira, and Lilly All other authors have declared no conflicts of interest.

OP298 TUMOR-ASSOCIATED MACROPHAGES AS NOVEL TARGETS FOR IMMUNOTHERAPY IN ESOPHAGEAL ADENOCARCINOMA

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Introduction: It has been shown that immune modulation e.g., by inhibition of the tumor-cell interaction, can greatly improve cancer response. Tumor-associated-macrophages (TAMs) are other key immunological players within the tumor microenvironment which can present both tumor-promoting and tumor-suppressive functions (1). Although several anti-TAM therapies reduce tumor growth and metastasis in preclinical cancer models (2), strategies that aim at specifically eliminating the protumoral TAMs are lacking.

Aims & Methods: This study aimed at identifying specific pro-tumoral TAM populations within the tumor microenvironment of esophageal adenocarcinoma
(EAC) and elucidate their potential therapeutic value. EAC is a highly aggressive cancer and is often associated with an anti-inflammatory microenvironment and dismal survival. It is important to determine whether TAM infiltration is associated to low survival and high recurrence in EAC, as we analyzed the transcriptomes of 73 EAC by RNAseq of pre-treatment biopsy specimens. As opposed to the publicly available TCGA database, this unique database is composed of a cohort of patients homogeneous-ly treated with standardized treatment, which facilitates the identification of novel treatment targets as well as predictive biomarkers. The ConsensusClusterPlus tool and Gene set enrichment analyses within the compu-tational pipeline used to determine whether markers that define specific TAM subpopulations could be used as prognostic factors, therapeutic targets and/or identify different EAC subgroups.

Results: Clustering of the EAC tumors using specific TAM markers, resulted in the identification of two molecular subtypes of EAC tumors. Gene Set enrich-ment analyses demonstrated that whereas one group was enriched by metabolic genes, the other group presented an “immune-like” signature and correlated significantly with worse survival. Markers that specifically define immunosup-pressive, angiogenic, and stem cell promoting TAMs were highly expressed in these cancers, together with genes involved in leukocyte migration as well as the STAT-JAK signaling pathways. Not surprisingly, this group was also significa-tively enriched with malignant genes involved in stem cell and epithelial prolif-eration, epithelial cell migration, EMT and angiogenic factors. In particular, three TAM-specific markers were identified within this “immune-like” group: MARCO, CD80 and ANG2. Immunohistochemistry analyses validated their expression at the protein level. Most importantly, patients with elevated expres-sion of one of these genes presented significantly worse survival.

Conclusion: In sum, we have demonstrated that a subset of EAC patients present an “immune-like” molecular signature which is associated to poor survival. This is characterized by the presence of various subpopulations of pro-tumoral TAMs that promote malignancy such as epithelial proliferation and migration as well as angiogenesis. In particular, three TAM genes (MARCO, CD80 and ANG2) were elevated in these patients and found to be significantly associated to worse survival. Although further experiments are warranted to define their exact prognostic and therapeutic value, our findings might have important clinical implications for EAC. They have illustrated the importance of the role of pro-tumoral TAMs in EAC and have identified a subgroup of patients with tumors that might benefit from novel tailored immu-notherapies directed against pro-tumoral TAMs.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

TUESDAY, OCTOBER 31, 2017 15:45-17:15

NERVES & BARRIER FUNCTION IN HEALTH & DISEASE - ROOM B5

OP299 ESTROGEN RECEPTOR BETA STIMULATION CONTROLS ENTERIC NEURON AND GLIAL CELL PROLIFERATION IN VITRO AND IN VIVO

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Introduction: A subpopulation of enteric glial cells has the capacity to behave like enteric neuronal stem/progenitor cells (ENSCs) and can reconstitute the enteric neuron pool upon damage. Thus, favoring ENSC differentiation can be consid-ered as a novel therapeutic approach to treat gastrointestinal motility disorders resulting from neuronal loss. In this context, accumulating evidence has shown that estrogens via the activation of the estrogen receptor beta (ER-β) may play a role in stimulating neuronal proliferation and survival in the central nervous system. Although it has been shown ER-β is expressed in the myenteric plexus both by enteric neurons and glial cells, there is no data concerning its possible role in intestinal neurogenesis.

Aims & Methods: Therefore, the aim of this study was to demonstrate if the selective ER-β agonist, LY3201, can act on ENSC-like glial cells to enhance their capacity to generate neurons in case of neuronal damage or loss. To study the effect of LY3201 on murine enteric ganglia in vitro, the muscularis externa of C57Bl/6J mice (8-10 weeks old) was enzymatically digested to isolate myenteric plexus and cultured for 5 days of incubation with placebo or different concentra-tions of LY3201 (1, 10, 100 and 1000 nM), cells were stained for glial cell (SOX10, GFAP), progenitor (SOX10, SOX2) and neuronal markers (HuC/D, NF). Moreover, the effect of LY3201 was evaluated in vivo by implanting pellets releasing 0, 119 and 1190 mg of LY3201 over a period of 7 days in two models of enteric neuronal damage: topical application of 0.1% benzalconium chloride (BAC) on the serosa of the ileum and high fat diet (HFD; 60% kcal from fat) for 12 weeks. The number of HuC/D+ neurons in the myenteric plexus was assessed by immunofluorescence.

Results: In vitro, different concentrations of LY3201 were tested in myenteric ganglionic cultures showing an increased number of glial cells (SOX10+ + GFAP + SOX2- cells) mainly at a concentration of 100 nM (Vehicle: 1130 ± 234; LY3201: 5444 ± 528 pmn/mm²). Interestingly, after blocking glial cell proliferation with an antiproliferative agent (ActD), LY3201 significantly increased the percentage of differentiated neurons (HuC/D + NF + SOX10- cells) (Vehicle 18 ± 3%; LY3201 41 ± 7%) suggesting that in response to LY3201 some glial cells with preserved ENSC capacity are able to give rise to neurons. In vivo, LY3201 treatment for 7 days was able to signifi-cantly reduced the myenteric plexus area with neuronal loss compared to the vehicle after BAC treatment (Vehicle: 2.5 ± 2 mm² versus LY3201: 8, ± 3 mm²). In line, LY3201 treatment for 7 days after a HFD resulted in an increased number of myenteric neurons compared to the control group (Vehicle: 310 ± 55; LY3201: 776 ± 49 pm²).

Conclusion: Here, we demonstrated that the selective ER-β agonist, LY3201, can promote neurogenesis in the damaged myenteric plexus by favoring differen-tiation of ENSCs. Overall, our results suggest that selective ER-β agonists may hold potential as a novel therapeutic approach to treat gastrointestinal motility disorders.

Disclosure of Interest: All authors have declared no conflicts of interest.

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Aims & Methods: We aimed to find a specific fibroblast subpopulation in mouse colon that is able to support stem cell growth and can be visualized by a monoclonal antibody. Primary fibroblasts isolated from GlitCre-ZfaGreen mouse colon were flow-sorted based on gp38 positivity and Gli1 expression (Gli1+, Gli1++ and Gli1+++). The ability to support organoid growth by fibroblasts was accessed by measurement of organoids perimeter in co-cultures of flow-sorted fibroblasts and organoids. Growth factors reduced medium. Sorted cells were further charac-terized by microarray analysis and results were confirmed by qPCR. Based on microarray results few membrane markers were chosen and an expression pattern of these markers was studied by immunofluorescent and in situ hybridization tissue staining. New candidate subpopulations were flow-sorted again and char-acterized by qPCR and co-cultures with organoids.

Introduction: The intestinal epithelium renews every 3–5 days and this process is fully dependent on stem cells. Stem cell potential is strictly defined by its micro-environment – the stem cell niche – which provide all signals required for stem cell maintenance and differentiation. Cell cultures developed from a single stem cell – so called organoids – still requires addition of growth factors such as EGF, R-spondin1 and Noggin. Local fibroblasts may help to support stem cells by producing these missing factors. Heterogeneity of organoids can be explained by various organs and these subpopulations exert different functions. Not much is known about markers for fibroblast subpopulations in intestine. Recent studies showed expression of the membrane marker podoplanin (gp38) (1) and transcripti-onal expression of Gli1 (2) by all intestinal fibroblasts.

Results: We observed differential expression of Gli1 in gp38+ intestinal fibroblasts. gp38+Gli1++fibroblasts were able to support stem cell growth in vitro. Unsorted primary markers unexpressed in GlitCre-ZfaGreen fibroblasts identified several new markers expressed by all colon fibroblasts (such as Iga9, Sdc2 and Sdc3) and two markers that showed a differential expression (Iga8 and CD90). Iga8 stained mostly smooth muscle cell layer in a colon and does not contribute to the stem cell niche. CD90+ cells located in close proximity to stem cells, supported stem cell growth and express crucial stem cell growth factors such as Grem1, Wnt2b and R-spondin3. We also identified semaphorins class 3 (Sema3) mem- bers - Sema3a, Sema3b, Sema3c, Sema3d - expressed by CD90+ fibroblasts. We identified several new markers for organoid growth in co-cultures with CD90+ fibroblasts.

Conclusion: We identified CD90 as a marker for mouse colon fibroblasts located in close proximity to stem cells. This subpopulation supported stem cell growth and expressed crucial stem cell growth factors such as Grem1, Wnt2b and R-spondin3. Moreover we found an additional protein family, class 3 semaphorins (Sema3), which is expressed by CD90+ fibroblasts and able to increase organoid growth.

Disclosure of Interest: All authors have declared no conflicts of interest.

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OP301 INDIAN HEDGEHOG SUPPRESSES A STROMAL CELL-DERIVED IMMUNE RESPONSE IN PATIENTS WITH ACTIVE ULCERATIVE COLITIS


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Introduction: Upon intestinal epithelial damage, a dual response is required to re-establish intestinal homeostasis. While ensuring repair of the epithelial integrity, rapid recruitment and activation of the immune system is essential to limit impact of harmful luminal content. Indian Hedgehog (Ihh) is an epithelial factor that functions as a critical sensor in this process, and loss of Ihh activity, which is essential to limit impact of harmful luminal content, occurs in a disease context, as the receptor for Ihh is only expressed in the mesenchyme, but the exact Hedgehog target cell has remained elusive.

Aims & Methods: The aim of this study was to further elucidate the nature of this target cell in the context of intestinal inflammation. Gene expression profiles were determined in Villin-CreERT2-Ihfl/fl and Rosa26-CreERT2-Ptchfl/fl animals. Sensitivity to DSS induced colitis was tested in Villin-CreERT2-Ihfl/fl, C. Smal-CreERT2-Ihfl/fl and C. Smal-CreERT2-Ptchfl/fl mice. Ihh signaling was characterized by Hedgehog responsive cells in vivo and in vitro, thereby impairing the recruitment of immune cells. Animals deficient in general intestinal Hedgehog signaling (Villin-CreERT2-Ihfl/fl and Ghil-CreERT2-Smo6/fl) were more sensitive to DSS colitis. In contrast, animals lacking the receptor Smo6 were more resistant to DSS colitis.

Conclusion: We show that epithelium-derived Indian Hedgehog signals exclusively to fibroblasts in the intestine. Loss of Ihh leads to a rapid immune response with upregulation of fibroblast-derived CXCL12, and migration of immune cells into the lamina propria.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP302 SEMAPHORIN-3E PLAYS A ROLE IN TIGHT JUNCTION FUNCTION IN PATIENTS WITH ACTIVE ULCERATIVE COLITIS

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Introduction: Patients with ulcerative colitis (UC) patients reveal a dysfunction of tight junction barrier and immune dysregulation. A defective tight junction (TJ) barrier is a key pathogenic factor in the causation and progression of UC by allowing increased antigenic permeation especially gut-derived bacterial lipopolysaccharides (LPS). Semaphorins (Sema) and their receptors plexins (PLX) are important regulators of epithelial barrier and immune dysregulation, while, IL-8 increase was aggravated. In Caco-2 cells, mRNA expression of PAR2 and 4 was increased after thapsigargin-induced ERS, and PAR4 levels were restored to basal in the presence of AEBSF and -4 were used to elucidate the mechanism of action of epithelial proteases. Results: Trypsin-Like Activity was significantly higher in biopsies from UC patients compared to controls, p = 0.0157. Thapsigargin enhanced trypsin-like activity in Caco2 cells at 6 hours at the apical side of the transwell. ABP assay identified a unique band at 33 KDa in ERS-induced Caco-2 supernatants. Paracellular permeability, IL-8 and antimicrobial peptides (AMP) genes were measured to study the impact of proteases on intestinal barrier function. Serine protease inhibitor (AEBSF), and antagonists of protease-activated receptors (PAR) -2 and -4 were used to elucidate the mechanism of action of epithelial proteases.

Conclusion: Our data showed that in intestinal epithelial cells, ERS increased serine protease activity, which is responsible for increased barrier function and dys-regulated AMP expression. We identified PAR2 and PAR4 activation as mechanisms of ERS-induced barrier dysfunction, and Trypsin-3 as a candidate protease overexpressed upon ERS, and in UC patients epithelium.

Disclosure of Interest: All authors have declared no conflicts of interest.

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OP303 ENDOPLASMIC RETICULUM STRESS INCREASES TRYPSIN-3 ACTIVITY IN ENTEROCYTES AND ALTERS BARRIER FUNCTION


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Introduction: Ulcerative Colitis (UC) is a chronic relapsing inflammatory bowel disease (IBD) with mucosal ulcerations. Excessive induction of endoplasmic reticulum stress (ERS), enhanced proteolytic activity and intestinal barrier disruption have been described in the colon mucosa of UC patients; however associated links between these features had not been described yet.

Aims & Methods: We evaluated the link between ERS and trypsin proteolytic activity (serine protease) in human enterocytes and its impact on intestinal barrier function. Colonic biopsies were taken during routine endoscopy from 12 UC patients and 19 controls. Biopsy supernatants were used to quantify Trypsin-like activity. In parallel, human intestinal Caco-2 cell line was cultured in a transwell system and stimulated with thapsigargin (10 μg/mL) to induce ERS. Supernatants were collected at 6 and 24h to quantify Trypsin-Like Activity by enzyme assay. Activity-based probe (ABP) were used to identify specifically the active trypsin-like proteases present in Caco-2 supernatants. Paracellular permeability, IL-8 and antimicrobial peptides (AMP) genes were measured to study the impact of proteases on intestinal barrier function. Serine protease inhibitor (AEBSF), and antagonists of protease-activated receptors (PAR) -2 and -4 were used to elucidate the mechanism of action of epithelial proteases.

Results: Trypsin-Like Activity was significantly higher in biopsies from UC patients compared to controls, p = 0.0157. Thapsigargin enhanced trypsin-like activity in Caco2 cells at 6 hours at the apical side of the transwell. ABP assay identified a unique band at 33 KDa in ERS-induced Caco-2 supernatants. Paracellular permeability, IL-8 and antimicrobial peptides (AMP) genes were measured to study the impact of proteases on intestinal barrier function. Serine protease inhibitor (AEBSF), and antagonists of protease-activated receptors (PAR) -2 and -4 were used to elucidate the mechanism of action of epithelial proteases.

Conclusion: Our data showed that in intestinal epithelial cells, ERS increased serine protease activity, which is responsible for increased barrier function and dys-regulated AMP expression. We identified PAR2 and PAR4 activation as mechanisms of ERS-induced barrier dysfunction, and Trypsin-3 as a candidate protease overexpressed upon ERS, and in UC patients epithelium.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
Introduction: Chronic intestinal pseudo-obstruction (CIP) is a rare condition characterized by impairment of gut motility responsible for recurrent episodes of intestinal sub-occlusion and severe digestive symptoms in the absence of mechanical causes. Neuro-intestinal cells of Cajal (ICC)-muscular abnormalities represent the main pathogenic mechanism explaining gut dysfunction, being responsible for functional intestinal epithelial barrier (IEB) abnormalities, majorly contributing to symptoms and clinical manifestations in CIP patients. In this study we analyzed the protein expression of the major components of tight junctions (TJs), i.e. occludin, two selected claudins (Cln4 and Cln5) and zonula occludens-1 (ZO-1), as markers of IEB integrity in patients with CIP. Moreover, based on published evidence we investigated the expression of vasoactive intestinal polypeptide (VIP) as neuronal mediator involved in the regulation of IEB.

Aim & Methods: This study was aimed to clarify the molecular abnormalities responsible for IEB dysfunction in patients with CIP. A number of n = 28 clinically and histopathologically characterized CIP patients (15F; age range: 16-75 yrs) entered the study and were subdivided according to the underlying structural alterations of the IEB: Histiostopathy: a combination of the amount of pathological normal (AN) neuro-muscular layer; n = 11 with inflammatory (INF) changes throughout the muscular and n = 10 with degenerative alterations (DEG). (Patients n = 8; 3F, 46-73 yrs) undergoing elective surgery for uncomplicated intestinal polyps served as control. CIP subgroup, whereas ZO-1 and VIP were downregulated only in DEG (P < 0.05 and P < 0.01).

Conclusion: IEB integrity was altered in patients with CIP as identified by occludin expression abnormalities. Particularly the atypical occludin oligomerization and dysfunction which negatively impacts the passage of molecules agents passing through the intestinal wall in these patients. Subgroup analysis showed that different molecular mechanisms disrupt the IEB in CIP patients. Barrier dysfunction in AN and INF is occludin dependent, while in DEG is ZO-1 dependent likely influenced by VIP downregulation. IEB altered molecular mechanisms represent molecular targets for development of diagnostic markers/therapeutic interventions.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

OP305 PREOPERATIVE ENDOCOSMIC VERSUS PERCUTANEOUS TRANSHEPATIC BILIARY DRAINAGE IN RESECTABLE PERIHILAR CHOLANGIOCARCINOMA: A MULTICENTER RANDOMIZED CONTROLLED TRIAL

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Introduction: Liver surgery in perihilar cholangiocarcinoma (PHC) is associated with high postoperative morbidity and mortality, primarily due to biliary obstruction caused by the tumor. Preoperative biliary drainage is used to treat jaundiced patients’ clinical symptoms (JPS), to facilitate liver resection itself is also associated with complications that may deteriorate the patient’s condition and worsen outcomes. Consensus is lacking on whether endoscopic or percutaneous biliary drainage should be preferred. Aim & Methods: This multicenter randomized controlled trial with an “all-comers” design (DRAINAGE trial) compared two drainage approaches in patients with presumed, potentially resectable PHC requiring major hepatectomy. Patients with obstructive jaundice and a bilirubin level above 50 μmol/L were randomly assigned to undergo either endoscopic (EBD) or percutaneous transhepatic biliary drainage (PTBD). Primary outcome were severe preoperative complications between randomization and surgery. The secondary outcomes encompassed the success of biliary drainage and postoperative morbidity and mortality. Total sample size required was 106 patients. All procedures were performed by experienced interventional radiologists and gastroenterologists. PTBD remained in situ postoperatively whereas EBD was removed intra-operatively.

Results: From June 2013 through June 2016, a total of 54 patients were randomly assigned to EBD (27 patients) or PTBD (27 patients), without differences in baseline characteristics. The number of severe complications was comparable between patients who underwent the trial based on a higher perioperative mortality rate in the PTBD group. Prior to surgery, 3 (11%) patients died in the PTBD group versus 0 in the EBD group. After surgery, 8/19 (42%) patients died in the PTBD group versus 2/21 (9.5%) patients in the EBD group (of whom 1 was a crossover of EBD to PTBD) (P = 0.002). Initial technical or therapeutic failure occurred more often in the EBD group: 5 (18%) versus 2 (7%). Cross-over from EBD to PTBD due to insufficient drainage or technical failure occurred in 15 patients (54%) of the EBD group. Preoperatively, the percentage of patients with more than one complication was comparable between groups 22 % versus 21 % (P = 0.81). The number of patients with more than one severe complication (Clavien-Dindo 3 or higher) was 21 % (78%) in the EBD group versus 18 (67%) in the PTBD group. Cause of death was most often a combination of an infectious or vascular complication and subsequent liver failure and multi organ failure.

EBD is advised in patients with obstructive PHC requiring biliary drainage since PTBD increased mortality. PTBD should only be used if EBD fails.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
Conclusion: The early recurrence within 90 days after surgery was significantly less frequent in the HCC-ICC group, probably because EOB-MRI has high ability for diagnosis of small tumor in the remnant liver. The preoperative EOB-MRI would contribute to the determination of appropriate resection site and the accompanying improvement of treatment outcomes.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP307 SAFETY AND EFFICACY OF TAE AND SIRT IN NET PATIENTS
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Introduction: Transarterial embolization (TAE) and Selective Internal Radiation Therapy (SIRT) are effective liver-directed treatments in patients with liver metastases of a neuroendocrine tumor (NET). However, differences between TAE and SIRT may have been scarcely investigated.

Aims & Methods: The aim of the study is to compare safety and efficacy of TAE and SIRT. Consecutive patients with histologically confirmed well differentiated NET (G1-2), who underwent TAE or SIRT for liver dominant disease in our NET-expert centre during 2004-2016 were analysed. Toxicity and response were evaluated per procedure during 3 months of follow up. Toxicity were all clinical and laboratory adverse events graded according to CTC-AE v4.03. Radiological response was defined according to RECIST 1.1 and/or nRECIST. Clinical response was defined as a decrease in use of somatostatin analogues, diarrhoea or flushes. Biochemical response was defined as >50% decrease in Chromogranin A.

Results: Eighty-seven patients (40 males) with a median age of 60 years under went 123 procedures (90 TAE/33 SIRT). The majority had a gastroentero-pancreatic NET (94%). There was imbalance between the 2 groups: in the TAE group 56% had a small bowel NET and 15% a pancreatic NET, whereas this was 26% respectively 34% in the SIRT group. Furthermore, 61% of the patients who underwent TAE had a functional NET, this was 46% in the SIRT group. Clinical toxicities encountered in the entire cohort were: pain; fever; nausea; vomiting; fatigue; pleural infusion and hepatic infection. Grade 3/4 toxicity occurred in the TAE and SIRT group, respectively; mainly temporary elevated liver enzymes with TAE and one treatment-related death after SIRT, due to ‘radioembolization-induced liver disease’ (REILD). A significant higher clinical response was seen after TAE vs SIRT (88% vs 67%). Biochemical response and radiological overall response rate were comparable: 24% vs 18% respectively 40% vs 45% for TAE vs SIRT. An overall (clinical, biochemical or radiological) response was seen in 86% vs 72% TAE vs SIRT respectively (ns). Progressive disease was seen in the minority of the procedures; 3 after TAE vs 9 after SIRT.

Conclusion: Both TAE and SIRT are safe and effective in treating NET-patients with liver metastases. After TAE more grade 3/4 toxicity occurs, mainly post-procedural elevated liver enzymes, but a higher clinical response is seen as well. SIRT shows less toxicity, although one treatment-related death occurred. Biochemical response was defined as a decrease in use of somatostatin analogues, diarrhoea or flushes. Biochemical response was defined as >50% decrease in Chromogranin A.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP308 GEMCITABINE AND PLATINUM-BASED CHEMOTHERAPY FOR THE FIRST-LINE TREATMENT OF HEPATOCHOLANGIOCARCINOMA: AN AGE MULTICENTER RETROSPECTIVE STUDY
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Introduction: Hepatocholangiocarcinoma (HCC-ICC) is a rare primary hepatic tumor, which represents both, cholangiocellular and hepatocellular carcinoma (HCC). Only few data exist on prognosis and chemosensitivity of HCC-ICC.

Aims & Methods: The main objective of this retrospective, multicenter study was to evaluate the overall survival (OS), progression free survival (PFS) and prognostic factors in advanced, unresctable HCC-ICC treated by gemcitabine plus platinum based chemotherapy as a first line systematic treatment. Data from 32 patients treated by gemcitabine plus cisplatin were analyzed. All patients received chemotherapy in six French university hospitals between 2008 and June 2016, were retrospectively collected. The diagnosis of chHCC-ICC was based on histological analysis or, in case of typical histology of ICC or HCC, on discordant immunohistochemical finding and/or tumor marker (alpha-fetoprotein, carbohydrate antigen 19-9, carcinoembryonic antigen) serum levels suggesting the other histology. Response rates were defined by RECIST 1.1 criteria. OS and PFS were estimated by Kaplan-Meier method. Prognostic factors were analyzed by Log-rank test in univariate analysis and by Cox model in multivariate analysis with p<0.05 considered as significant difference. Statistical analysis was performed using Graph Pad Prism 6.

Results: Forty patients were included (70% men, median age 66 years [extremes 32-88] : HCC-ICC was biopsy proven in 55% and diagnosed radiologically or histologically in 45% of patients). Twenty-three (57.5%) of patients had at least one metastatic synchronous lesion. Twenty-nine (72.5%) patients were treated by gemcitabine (gem) and oxaliplatinum (GEMOX), 9 (22.5%) by GEMOX plus bevacizumab, 2 (5%) by gem/cisplatin. Eighteen patients (45%) received second line of systemic treatment (FOLFIRI (n=7), Capetabine (n=4), LVSFU2 (n=2), LVSFU2-Cisplatin (n=1), Cyclophosphamide (n=1), Sutent (n=1), Sorafenib (n=1) and anti-PD-L1 therapy (n=1). In the first line, patients received a median of 10 cycles of chemotherapy (extremes 1-28). RECIST criteria were reported in 35 patients. Among them, 9 patients (25.7%) had partial response, 18 patients (51.4%) had stable disease, and 8 patients (22.8%) had tumor progression at first CT scan evaluation. Median PFS and median OS were 9.0 and 15.4 months, respectively. No significant difference was observed according to treatment. In multivariate analysis, significant poor prognostic factors for OS were: positive serology for hepatitis B virus and/or C virus (HR=1.35 IC95%[1.13–13.24], p=0.02), age >70 (HR=3.5 IC95%[1.75–7.54], p=0.007, and ECOG score ≥2 (HR=2.46 IC95%[2.23–6.17], p=0.04).

Conclusion: These data suggest a chemosensitivity of chHCC-ICC to gemcitabine plus platinum-based chemotherapy. These results need to be confirmed in a randomized prospective study.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP309 SQLE DRIVES HEPATOCARCINOGENESIS AND IS A TUMOR-PREDICTIVE TARGET IN NON-ALCOHOLIC FATTY LIVER DISEASE-ASSOCIATED HEPATOCELLULAR CARCINOMA
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Introduction: Due to the obesity epidemic, nonalcoholic fatty liver disease-associated hepatocellular carcinoma (NAFLD-HCC) is an emerging malignancy worldwide. However, the underlying mechanisms and targeted therapy of NAFLD-HCC are still largely unclear. Using transcriptome sequencing, squaramyl synthase epoxidase (SQLE), a rate limiting enzyme in cholesterol biosynthesis, was identified to be up-regulated in NAFLD-HCC.

Methods: We aimed to evaluate the biological function of SQLE in NAFLD-HCC, and assess the chemopreventive efficacy of targeting SQLE in NAFLD-HCC. SQLE expression was determined by qPCR and western blot. Biological function of SQLE was assessed in vitro using hepatocyte-specific Sqle transgenic mice. Therapeutic efficacy of terbinafine, a SQLE inhibitor, was determined in NAFLD-HCC cell lines in vitro, and nude mice and Sqle-transgenic mice models in vivo.

Results: We performed transcriptome sequencing analysis of 18 paired NAFLD-HCC and adjacent normal tissues. SQLE was a top outlier gene and was overexpressed in 16 out of 17 paired NAFLD-HCC samples. SQLE mRNA up-regulation was validated in an independent cohort of 27 paired NAFLD-HCC and adjacent normal samples (P=0.01). In two obesity-induced NAFLD-HCC mouse models, Sqle was also up-regulated. We next investigated the biological function of SQLE in vivo. Wild-type and hepatocyte-specific Sqle transgenic mice were injected with a single dose of diethylnitrosamine (DEN) and fed a high fat-high cholesterol diet (HFHC). At 25 weeks of age, spontaneous HCC formation was observed in 9 out of 10 Sqle mice, but only in 2 out of 10 wild type mice (p=0.003). Sqle tg mice also developed a higher tumor multiplicity (p<0.01). Histological examination confirmed the formation of HCC in the livers of Sqle tg mice. Consistent with the formation of HCC, α-fetoprotein (AFP), higher AST and ALT were higher in Sqle tg mice. Immunohistochemical pericellular fibrosis, as determined by Sirius Red staining, was highly elevated in Sqle tg mice. Collectively, these data demonstrated that SQLE exacerbated HFHC diet-induced liver inflammation and accelerated HCC formation in mice.

Finally we tested the therapeutic efficacy of terbinafine, a SQLE inhibitor, in the treatment of NAFLD-HCC. Terbinafine inhibited the cell proliferation NAFLD-HCC cell lines in vitro and suppressed the growth of tumor xenografts in nude mice. In DEN-injected and HFHC diet-fed Sqle tg mice, terbinafine (49 mg/kg) received systemic treatment reduced tumor growth and multiplicity (P=0.021). These results indicate that therapeutic targeting of SQLE is a promising approach for the treatment of NAFLD-HCC.

Conclusion: We established SQLE as an oncogene in NAFLD-HCC. SQLE promotes HCC in NAFLD-HCC cells and Sqle tg mice. SQLE inhibitor terbinafine
confers a clear therapeutic benefit in cell lines and animal models of NAFLD-
HF [26–28], corroborating SQuEeL as a therapeutic target in this subset of HCC.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP310 A XENOTRANSPLANTATION APPROACH USING HUMAN PANC-3 CELLS DELIVERED PANCREATIC ORGANOIDS

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Introduction: Exocrine/ductal pancreatic differentiation from human pluripotent stem cells has been an ongoing process, from 3D to 2D in organoid form, from animal to human experiments. Dr Wallace is a colleague in this field of research.

Results: We systematically compared various PO transplantation niches (pancreas, kidney, anterior eye chamber). Tri-lineage differentiation potential of pancreatic progenitor cells, which gave rise to pancreatic organoids, is shown by immunohistochemistry for amylase, CK19 and insulin. Consequently, detailed immunophenotyping of the grafts was performed. In line with morphological appearance acinar-like cells stained positive for several acinar marker genes such amylase and chromogranin C, while ductal structures expressed cytokeratin 19 to assess the maturity of the grafts, co-staining for acinar and ductal lineage markers with various progenitor cell markers such SOX9, PDX1 and NKX6.1 were performed. These data indicate a developmental stage of a human Carnegie Stage 2 to 3. Staining for smooth muscle actin (α-SMA) also revealed signs of neovascularisation in the grafts.

Conclusion: Xenotransplantation of human pancreatic organoids into the anterior eye chamber an/or the pancreas might become a future and humanized model system.

Disclosure of Interest: All authors have declared no conflicts of interest.

References


Aims & Methods: Xenotransplantation assays were applied to systematically transplant pancreatic organoids into immunodeficient mice aiming for the ultimate niche to host a human pancreas in mice.

Results: We systematically compared various PO transplantation niches (pancreas, kidney, anterior eye chamber). Tri-lineage differentiation potential of pancreatic progenitor cells, which gave rise to pancreatic organoids, is shown by immunohistochemistry for amylase, CK19 and insulin. Consequently, detailed immunophenotyping of the grafts was performed. In line with morphological appearance acinar-like cells stained positive for several acinar marker genes such amylase and chromogranin C, while ductal structures expressed cytokeratin 19 to assess the maturity of the grafts, co-staining for acinar and ductal lineage markers with various progenitor cell markers such SOX9, PDX1 and NKX6.1 were performed. These data indicate a developmental stage of a human Carnegie Stage 2 to 3. Staining for smooth muscle actin (α-SMA) also revealed signs of neovascularisation in the grafts.

Conclusion: Xenotransplantation of human pancreatic organoids into the anterior eye chamber an/or the pancreas might become a future and humanized model system.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

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Introduction: Endoscopic ultrasound-guided fine-needle biopsy (EUS-FNB) is an established method for obtaining samples from solid tumors. EUS-FNB is also a very useful tool in the diagnosis of ductal lesions, such as IPMN.

Methods: The results of a study on 33 consecutive patients who underwent both conventional EUS-FNA and paired EUS-FNB-SC with the tandem controlled trial started in May 2016 and is ongoing. Consecutive patients who underwent both conventional EUS-FNA and paired EUS-FNB-SC and were pancreatic adenocarcinoma (n = 11). The median history score per pass in EUS-FNA was 2 (sufficient for cytology but not for histology) vs 5 (sufficient for adequate histology) in EUS-FNB-SC group for all lesions Table 1. The amount of tissue yield, tumor cellular volume, surface area of core tissue, and adequacy for Foundation Medicine assay obtained on first pass was greater in EUS-FNB-SC group vs EUS-FNA group Table 2. DNA sufficient (using a 1100 ng threshold; Mayo Genomics Core Lab) for whole exome sequencing in the first pass on pancreatic adenocarcinoma was obtained from 74% of FNA and 45% of FNA specimens.

Conclusion: In this ongoing study histology yield and DNA yield was higher in EUS-FNB-SC needle compared to EUS-FNA needle. EUS-FNB-SC needles appear capable of DNA acquisition sufficient to guide precision oncological therapy.

Disclosure of Interest: M.B. Wallace: Michael Wallace reports grant support from Boston Scientific, Medtronic, Cosmo pharmaceuticals, and equity interest in iCor Medical.

All other authors have declared no conflicts of interest.

References

OP313 COMPARISON OF AMERICAN GASTROENTEROLOGICAL ASSOCIATION, INTERNATIONAL ASSOCIATION OF PANCREATOLOGY, AND AMERICAN COLLEGE OF RADIOLOGY GUIDELINES FOR DIAGNOSIS OF MALIGNANT PANCREATIC CYSTS

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Introduction: Guidelines published by the American Gastroenterology Association in 2015 (AGA), International Association of Pancreatology in 2006 (Sendai) and in 2012 (Fukuoka), and American College of Radiology 2010 (ACR) are used by clinicians for the management of pancreatic cysts. Guideline recommendations differ from one another and it is not known which guideline is best able to identify patients with malignant pancreatic cysts for surgery.

Aims & Methods: Clinical guidelines were reviewed, and risk-factors associated with malignant cysts were identified. All patients who underwent surgery for mucinous pancreatic cysts between 2002–14 were included, and surgical pathology served as criteria standard. A single expert radiologist, blinded to final cyst pathology, reviewed imaging studies for all study patients. Guidelines were applied to this data to determine their performance in identifying malignant cysts. EUS results were not incorporated.

Results: During study period, 166 patients with mucinous pancreatic cysts underwent surgery. Of these 61 patients (36.7%) had a malignant cyst. Using information from imaging studies, accuracy for malignant cyst diagnosis for clinical guidelines was: 81.3% for AGA, 78.3% for Fukuoka, 63.9% for Sendai, and 2% for ACR.

Abstract No: OP312

Table 1: Validity of Pancreatic Juice Cytology (PJC) in the Studied Patients (n=29).

<table>
<thead>
<tr>
<th>Patients Groups</th>
<th>IPMC</th>
<th>Non-IPMC</th>
</tr>
</thead>
<tbody>
<tr>
<td>True Positive</td>
<td>6 (63%)</td>
<td>1 (6%)</td>
</tr>
<tr>
<td>False Positive</td>
<td>8 (44%)</td>
<td>2 (11%)</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>67%</td>
<td>60%</td>
</tr>
<tr>
<td>Specificity</td>
<td>60%</td>
<td>100%</td>
</tr>
<tr>
<td>Positive Predictive Value (PPV)</td>
<td>78%</td>
<td>78%</td>
</tr>
<tr>
<td>Negative Predictive Value (NPV)</td>
<td>72%</td>
<td>72%</td>
</tr>
</tbody>
</table>

Adequacy score Explanation FNA needle (n = 18) FNB-SC needle (n = 18)
A. Comparison of the histology yield of first pass per sample between FNA and FNB-SC needles
0 Insufficient material for interpretation. 6 (33%) 1 (6%)
1 Sufficient material for limited cytologic interpretation. 8 (44%) 2 (11%)
2 Sufficient material for adequate cytologic interpretation. 2 (11%) 0 (0%)
3 Sufficient material for limited histologic interpretation. 6 (33%) 2 (11%)
4 Sufficient material for adequate histologic interpretation, low quality (total material < 1 x 10 power field in length). 4 (23%) 15 (83%)
5 Sufficient material for adequate histologic interpretation, high quality (> 10 power field in length). 3 (17%) 0 (0%)
6 Sufficient material for adequate histologic interpretation, high quality (> 10 power field in length). 0 2 (11%)

Median histology score

B. Technical Characteristics of EUS-FNA/FNB-SC per first pass of all samples

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>FNA (n = 18)</th>
<th>FNB (n = 18)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tumor cellularity (%) (Median) (range)</td>
<td>10 (0-100)</td>
<td>45 (0-90)</td>
</tr>
<tr>
<td>Surface area (mm²) (Median) (range)</td>
<td>7 (0-50)</td>
<td>57 (6-255)</td>
</tr>
<tr>
<td>Core tissue length (cm)</td>
<td>2 (0-7)</td>
<td>10 (0-20)</td>
</tr>
<tr>
<td>Foundation medicine adequacy (%) Adequate (%)</td>
<td>3 (17%)</td>
<td>15 (83%)</td>
</tr>
<tr>
<td>Final diagnosis (%) Positive (%)</td>
<td>18 (100%)</td>
<td>18 (100%)</td>
</tr>
<tr>
<td>ROSE (%) Adequate (%)</td>
<td>18 (100%)</td>
<td>18 (100%)</td>
</tr>
<tr>
<td>C. DNA quantification for pancreatic ductal adenocarcinoma (PDAC, n = 11) DNA adequacy for whole exome sequencing (WES) (≥1000ng)</td>
<td>FNA</td>
<td>FNB</td>
</tr>
<tr>
<td>PDAC (n = 11) Yes (%)</td>
<td>5 (45%), [95% CI, 36%-55%]</td>
<td>8 (74%), [95% CI, 64%-82%]</td>
</tr>
<tr>
<td>DNA mass, (ng) PDAC (n = 11) (Mean ± std err)</td>
<td>1208 ± 166ng</td>
<td>1870 ± 458ng</td>
</tr>
</tbody>
</table>
AGA and Fukuoka guidelines are more accurate than other guidelines for identifying predictors of malignancy.

Conclusion: When only information from radiologic imaging studies was used, AGA and Fukuoka guidelines are more accurate than other guidelines for identifying patients with malignant pancreas cysts.

Disclosure of Interest: All authors have declared no conflicts of interest.

Wednesday, November 01, 2017 08:30-10:00

PANCREATOBILIARY EUS: HOW TO DO IT BETTER? - ROOM A1

OP314 LONG-TERM OUTCOMES AND RE-INTERVENTION OF EUS-GUIDED BILIARY DRAINAGE FOR MALIGNANT BILIARY OBSTRUCTION

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Introduction: Although EUS-guided biliary drainage (EUS-BD) is increasingly reported as one of treatment options for malignant biliary obstruction (MBO), with a high technical success rate and an acceptable complication rate, its long-term outcomes are not fully discussed. The aim of this multicenter prospective study is to evaluate long-term outcomes of EUS-BD and clarify the role of re-interventions for stent dysfunction or stent-related complications.

Aims & Methods: Consecutive patients undergoing EUS-BD for unresectable MBO were retrospectively studied. Data on recurrent biliary obstruction (RBO) and other stent-related complications were extracted. Cumulative time to RBO was calculated by a Kaplan-Meier method. Procedures details of re-interventions for RBO and other complications were also described including its route i.e. EUS-BD, transpapillary or percutaneous approach.

Results: Between Aug 2011 and Dec 2016, EUS-BD was performed in 96 pts (EUS-HGS in 82 and EUS-CDS in 14, covered metal stent in 95 and plastic stent in 1) at 4 tertiary referral centers. Biliary drainage prior to EUS-BD had been performed in 54%. The major cause of MBO was pancreatic cancer (52%) and biliary tract cancer (28%). Duodenal invasion (64%) and surgically altered anatomy (25%) were two major reasons for EUS-BD. MBO was distal in 76% and hilar in 24%. A median procedure time was 35 minutes. Technical success rate was 98% with two technical failures (1 stent misplacement and 1 failed insertion of CDS). The incidence of RBO was 36% and a median cumulative time to RBO was 6.8 (95%CI, 4.3–9.7) months. The causes of RBO were non-tumor related (hyperplasia 17%, migration 9%, sludge 5%, reflux 2% and kink 2%), other than de novo stricture (2%). Re-intervention for RBO was successfully performed via EUS-BD route in 89% (31/35). The types of procedures were 22 stent-in-stent, 5 balloon sweep, 3 stent exchange and 1 additional antegrade stenting. Other re-interventions were 2 conversion to transpapillary stenting, 1 conversion from CDS to HGS and 1 PTBD. The incidence of other complications was 29% (5 cholecystitis, 5 cholangitis, 5 peritonitis, 5 bleeding, 5 abdominal pain, 2 fever and 1 stent misplacement).

Conclusion: The incidence of RBO necessitating re-interventions was not rare in EUS-BD for MBO but re-intervention via EUS-BD route was technically feasible in most cases.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP315 EUS-GUIDED RADIOFREQUENCY ABLATION (RFA) FOR PANCREATIC NEUROENDOCRINE TUMOR (NET) AND PRE-MALIGNANT INTRADUCTAL PANCREATIC MUCINOUS TUMOR (IPMN): FIRST RESULTS OF PROSPECTIVE MULTICENTER STUDY

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Introduction: Pancreatic NET and IPMN with worrisome features required surgical resection due to the respective risk of lymph nodes/metastatic widespread or invasive adenocarcinoma. EUS-guided antitumoral treatments, mainly based on alcohol injection, have been recently developed with the risk of acute pancreatitis due to uncontrolled diffusion and poorly evaluated efficacy. The aim of this prospective study was: primary endpoint, to evaluate the safety of EUS-RFA in such pancreatic tumors; secondary endpoint: to assess the efficacy in a one-year follow-up.

Aims & Methods: This study was conducted as a prospective multicenter study planned to include 30 patients in a two years period with a one-year follow-up and intermediate results are reported. Patients with NET pancreatic tumor less than 2cm or with pre-malignant pancreatic cystic tumor (side branches IPMN with worrisome features or mucinous cystadenoma (MCA)) were included if they were not operable or refuse surgery. Since October 2015, all the patients have been included, the last one being in January 2017. They were 16 males and 14 females with a 54.4 years mean age (49–84 years). EUS-RFA was performed with a 19G RFA needle (Starmed, Taewong, Korea) applying a 50 W current until reaching 100 Ohms impedance (white bubbles appearance). Patients were followed with MRI and/or EUS.

Results: 12 patients had 14 NET with a 13.4 mm size (8–20 mm) located in 3 cases to the head, 6 to the body, 1 to the tail, respectively. 18 patients had cystic tumor (17 IPMN, 1 MCA) with a 29.1 mm mean size (9–60 mm) located in 14 cases to the head, 3 to the body, 1 to the tail, respectively. 10 out of them had mural nodules and 4 increased thickness of the cyst wall. The mean duration of hospital stay was 4 days (2–6). 3 complications (10%) occurred, two with the first patients included: one mild pancreatitis, one small bowel perforation surgically managed, one pancreatic ductal stenosis endoscopically managed. After these initial patients, the protocol was improved with prophylactic administration of NSAID and antibiotics and emptying the cyst fluid content leading to dramatic decrease of further complication (3.5%). Three patients experienced mild abdominal pain without acute pancreatitis successfully managed with paracetamol. 10 patients among 12

Abstract No: OP314

<table>
<thead>
<tr>
<th>EUS-BD outcomes</th>
<th>Incidence</th>
<th>EUS route approach</th>
<th>Transpapillary approach</th>
<th>IVR and others</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recurrent biliary obstruction</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>25(36%)</td>
<td>31</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Hyperplasia</td>
<td>16(17%)</td>
<td>16 stent-in-stent</td>
<td>1 conversion to transpapillary stenting</td>
<td></td>
</tr>
<tr>
<td>Migration</td>
<td>9(9%)</td>
<td>4 stent-in-stent, 3 new stent, 1 balloon sweep (patent fistula)</td>
<td>1 conversion to transpapillary stenting</td>
<td></td>
</tr>
<tr>
<td>Sludge/Food impaction</td>
<td>5(5%)</td>
<td>4 balloon sweep, 1 antegrade stenting</td>
<td>1 PTBD</td>
<td></td>
</tr>
<tr>
<td>De novo biliary stricture</td>
<td>2(2%)</td>
<td>1 stent-in-stent</td>
<td>1 conversion to transpapillary stenting</td>
<td></td>
</tr>
<tr>
<td>Cholangitis due to duodenal-nobilary reflex</td>
<td>2(2%)</td>
<td>1 stent-in-stent</td>
<td>1 PTA</td>
<td></td>
</tr>
<tr>
<td>Other complications</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bile duct kinking</td>
<td>1(1%)</td>
<td>1 stent-in-stent</td>
<td>1 conversion from CDS to HGS</td>
<td></td>
</tr>
<tr>
<td>Cholecystitis</td>
<td>5(5%)</td>
<td>1 temporary nasobiliary drainage</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cholangitis</td>
<td>5(5%)</td>
<td>1 stent exchange</td>
<td>1 percutaneous peritoneal drainage</td>
<td></td>
</tr>
<tr>
<td>Pseudotumors</td>
<td>5(5%)</td>
<td>1 stent exchange</td>
<td>1 liver abscess drainage</td>
<td></td>
</tr>
<tr>
<td>Bleeding</td>
<td>5(5%)</td>
<td>1 temporary nasobiliary drainage</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>5(5%)</td>
<td>1 stent exchange</td>
<td>1 percutaneous peritoneal drainage</td>
<td></td>
</tr>
<tr>
<td>Fever</td>
<td>2(2%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stent misplacement</td>
<td>1(1%)</td>
<td>1 tandem stent placement</td>
<td>1 percutaneous peritoneal drainage</td>
<td></td>
</tr>
</tbody>
</table>
Disclosure of Interest: the Eckardt score may be used as a surrogate marker for HRQOL in patients. An association was seen between Eckardt score and all HRQOL domains. The use of HRQOL measured by the SF-36 survey at both short and long-term follow-up. A strong and significant change in Eckardt score. POEM also improved all dimensions of HRQOL as compared with baseline.

Overall, mean Eckardt score decreased from 7.8 to 3.0 after POEM. The model analysis showed a significant association between Eckardt scores and all HRQOL domains (Table 1).

Conclusion: POEM improves symptoms of achalasia as traditionally assessed by changes in Eckardt score. POEM also improved all dimensions of HRQOL as measured by the SF-36 survey at both short and long-term follow-up. A strong association was seen between Eckardt score and all HRQOL domains. The use of the Eckardt score may be used as a surrogate marker for HRQOL in patients who have undergone POEM for achalasia.

Disclosure of Interest: All authors have declared no conflicts of interest.

Disclosure of Interest: M. Barthel: Boston Scientific consultant All other authors have declared no conflicts of interest.

Wednesday, November 01, 2017 08:30-10:00
Submucosal Endoscopy: Indications, Techniques and Outcomes - Room B2

**OP316 Life After Peroral Endoscopic Myotomy (POEM): Quality of Life and Its Association with Eckardt Score**

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**Introduction:** Peroral endoscopic myotomy (POEM) is an endoscopic technique for the treatment of achalasia and esophageal spastic disorders. The Eckardt score has been traditionally used as a clinical parameter to assess the efficacy of the procedure. The association between the Eckardt score and health-related quality of life (HRQOL) in POEM patients has not been fully elucidated.

**Aims & Methods:** (1) To evaluate the effect of POEM on short and long-term QOL and to (2) assess the association between QOL and Eckardt scores over the study period. Single-center prospective cohort study of consecutive POEM cases at the University of Florida during a 5-year period (2011–2016). Both Eckardt scores and HRQOL measured by the Short Form-36 Health Survey (SF-36) were obtained at baseline, and at various intervals post-POEM (1-3 months; 6-9 months; 12 months and beyond). The SF-36 form consists of 8 dimensions, which include: General Health; Bodily Pain; Social Functioning; Emotional Well-Being; Energy/Fatigue; Role limitation due to emotional problems; Role limitation due to physical health and Physical functioning. These eight domains were then grouped into two separate composite scores of overall physical and mental health. Comparison of means scores of Eckardt, Dysphagia and HRQOL were originally described using a univariate linear regression. Pairwise comparisons of means by visit were corrected for multiple testing using Bonferroni method. The association between Eckardt scores and HRQOL were performed by using a Linear mixed model analysis.

**Results:** POEM was performed in 143 consecutive patients (54% male; mean age 56.9 ± 17.9 years) by a single gastroenterologist in an endoscopy suite during the study period. Most patients had achalasia type II (82; 57.3%) and 12 (8.4%) had prior surgical myotomy. Mean total procedure time was 73.4 ± 30.2 minutes. Overall, mean Eckardt score decreased from 7.8 ± 2.5 to 0.9 ± 1.4 after POEM (p < 0.001). Composite HRQOL dimension scores improved from baseline and held statistical significance over various follow-up lengths after POEM. Mixed model analysis showed a significant association between Eckardt scores and all HRQOL domains (Table 1).

**Conclusion:** POEM improves symptoms of achalasia as traditionally assessed by changes in Eckardt score. POEM also improved all dimensions of HRQOL as measured by the SF-36 survey at both short and long-term follow-up. A strong association was seen between Eckardt score and all HRQOL domains. The use of the Eckardt score may be used as a surrogate marker for HRQOL in patients who have undergone POEM for achalasia.

Disclosure of Interest: All authors have declared no conflicts of interest.

Disclosure of Interest: All authors have declared no conflicts of interest.

Disclosure of Interest: All authors have declared no conflicts of interest.

Wednesday, November 01, 2017 08:30-10:00
Endoscopic Management of GI Bleeding: What is New? - Room E4

**OP317 Technical Feasibility of Endoscopic Submucosal Dissection for Local Failure After Chemoradiotherapy or Radiotherapy for Esophageal Squamous Cell Carcinoma**

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1 Department Of Gastroenterology and Endoscopy, National Cancer Center Hospital East, Kashiwahoana, Kashiwa, Chiba, Japan

**Contact E-mail Address:** knakajo@east.ncc.go.jp

**Introduction:** Endoscopic submucosal dissection (ESD) has been widely accepted as the effectiveness and safe procedure for treatment naive superficial esophageal squamous cell carcinoma (ESCC). However, there are few reports to evaluate the technical feasibility of ESD for local failure after radiotherapy (RT) for ESCC after CRT or RT compared with conventional ESD.

**Aims & Methods:** We aimed to evaluate the technical feasibility of ESD for local failure after CRT for ESCC comparing with ESD for RT naive ESCC or for other primary lesions within RT field. Consecutive patients who were treated with ESD between December 2009 and August 2016 at our institution were retrospectively investigated. Local failure was defined as a recurrent or a residual tumor just at the post RT primary site. We classified the cohort into 3 groups as follows: A group: pts with local failure, B group: pts with other primary lesions within RT field, C group: pts with radiation naive superficial ESCC. We comparatively evaluated procedure completion rate, on block resection rate, complete resection rate (en block resection with negative of cancer at the margin), procedure time and incidence of major complications for the assessment of feasibility between three groups.

**Results:** In total 322 pts with 605 lesions were analyzed, and A group included 25 (40 lesions), B group included 16 pts (22 lesions), and C group included 481 pts (556 lesions). The characteristics of pts in A, B, and C group were as follows: the median age (years)=70.5, 73.5, 70. male/female=17/8, 15/1, 41/64. Mean tumor size (=standard deviation) was 15.7 (=9.9) mm, 17.7 (=10) mm, 29.1 (=22.3) mm. and there was significant differences among groups. (P<0.001), and between B group and C group (P<0.001). There were no significant differences in procedure completion rate between three groups (92.6% vs 100% vs 100%), 2 lesions in 2 pts were incomplete of ESD procedure due to severe fibrosis and switched to photodynamic therapy (PDT). When en block resection rate were similar between 3 groups (96% vs 100% vs 100%), complete resection rate of A group was significantly lower comparing with that of C group (A group vs B group vs C group=60.0%/77.3%/80.4%, A group vs C group=0.0%/100%/100%). Mean procedure time (=standard deviation) was 63 (=32) minutes, 69 (=27) minutes, 91 (=50) minutes, respectively, and there was significant differences between A group and C group (P=0.006), and between B group and C group (P=0.002). Serious complications involving perforation or bleeding required transfusion were not observed in A group and B group, while severe fibrosis and switched to Photodynamic therapy (PDT). While en block resection was performed in 17 cases of C group (2.8%). However, there was no significant difference in the frequency of complications between three groups.

**Conclusion:** In this study, we showed the technical feasibility of ESD for patients for local failure and for other primary lesions within RT field without major complications compared with conventional ESD. However, it could be technically difficult to complete ESD for local failure after CRT or RT due to severe fibrosis in the submucosal layer in some cases. In such a case, an alternative treatment such as PDT should be considered.

Disclosure of Interest: All authors have declared no conflicts of interest.

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was continued till 12-24 h hours after admission when the definitive endoscopy was performed. Patients randomized in Group 2 (Non-Hemospray) were treated by medical treatment followed by the definitive endoscopy 12-24 hours from admission. 

Urgent Endoscopy within 60 minutes was performed in any patient who failed to achieve clinical hemostasis within the first 24 hours.

Results: One hundred five patients were randomized for suspected AVB; 19 were excluded due to non-variceal source of bleeding; 86 patients were randomized: group 1 (n = 43), group 2 (n = 43). Severity of liver disease was similar (Child-Pugh class B 49% in both groups, Child-Pugh class C in 15% and 25% in group 1 and 2, respectively). Clinical hemostasis was achieved in 98% in group 1 and 70% in group 2 (P = 0.0005). Hemospray® failed to stop spurter gastric variceal bleeding in 4 patients who were treated by cyanoacrylate injection. Endoscopic hemostasis was achieved in all patients of group 1. Despite the medical treatment, all patients of group 2 had fresh blood into the stomach at the time of endoscopy and 30% of them had to have urgent endoscopy to control relapsing overt hemostasis. A significant improvement on survival at 30 days was observed in the Hemospray group compared to SOC group (93% vs 67%; p = 0.0029). We did not see any difference on survival in the hospitalization period (5 days) (95% vs 91%; p = 0.0392).

Conclusion: Hemospray® application at 2 hours of admission improves clinical and endoscopic hemostasis of AVB. This bridge therapy may have an impact on outcome in 30 days in patients with AVB.

Disclosure of Interest: All authors have declared no conflicts of interest.

References


A new approach to acute high-risk gastrointestinal bleeding appears to be safe and highly effective.

Disclosure of Interest: All authors have declared no conflicts of interest.

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Introduction: There is increasing evidence of the benefits of low-dose aspirin for primary prevention of colorectal cancer (1), in addition to established benefits on cardiovascular prevention. Estimates of the incidence of upper and lower gastrointestinal bleeding are needed to inform adequate benefit-risk assessment.

Aims & Methods: Using The Health Improvement Network primary care database, we estimated the association between new use of low-dose aspirin (75–300 mg/day) and upper/lower gastrointestinal bleeding (UGIB/LGIB) by case-fatalty (fatal case = death within 30 days), hospitalization/referral status, bleeding location, and aspirin dose and duration. Among persons aged 40–84 years from 2000–2012 with no previous low-dose aspirin use, 199, 049 new users of low-dose aspirin were identified. Each member was matched to a person free of low-dose aspirin on that day by age, sex, primary care practitioner visits in the previous year and time since study entry. Cohorts (mean age at entry, 64 years) were followed (max. 14 years, median 5.4 years) to identify cases of UGIB/LGIB, with validation through manual review of patient records and linkage to hospital data. A nested case-control analysis was conducted using cases and controls from both cohorts. To account for temporal changes in aspirin exposure, we used ‘as-treated’ and ‘as-used’ low-dose aspirin. Controls (n = 10,000 for LGIB) were frequency-matched to cases by age, sex, calendar year. Adjusted rate ratios (RRs) with 95% confidence intervals (CIs) were calculated for current low-dose aspirin use (0–30 days before the index date [UGIB/ LGIB]; no use for cases, random date for controls); reference group was never use.

Results: There were 1843 UGIB cases and 2763 LGIB cases; 60% of UGIBs and 28% of LGIBs were hospitalized (remaining cases were referred only). Low-dose aspirin was associated with significantly increased risks of non-fatal UGIB/LGIB, hospitalized as well as referred (but not hospitalized) UGIB/LGIB, but not fatal UGIB/LGIB (Table 1). RRs (95% CI) by UGIB location were 2.33 (1.69–3.21) for duodenal ulcers, 1.94 (1.46–2.58) for gastric ulcers and 1.59 (1.25–2.02) for mucosal erosions; RRs (95% CI) for LGIB were 2.33 (1.96–2.77) for diverticular diseases and 3.09 (2.13–4.50) for polyps. By daily dose of aspirin, RRs (95% CI) for UGIB were 1.58 (1.37–1.83) for 75 mg/day and 2.12 (1.53–2.93) for 150–300 mg/day; estimates for LGIB were 1.98 (1.76–2.24) for 75 mg/day and 1.98 (1.59–2.62) for 150–300 mg/day. Around 95% of low-dose aspirin use was at 75 mg/day. The magnitude of the increased LGIB risk was similar with all durations used, while there was a suggestion of a greater risk of UGIB in the first months after starting treatment: RRs (95% CI) for LGIB were 2.20 (1.74–2.78) for 3 months and 1.99 (1.72–2.21) for <3 months; and for UGIB were 2.57 (1.93–3.42) for <3 months and 1.54 (1.33–1.78) for ≥3 months.

Table: RRs (95% CIs) for risk of UGIB/LGIB associated with current use of low-dose aspirin versus never use (nested case-control analysis).

<table>
<thead>
<tr>
<th>RR* (95% CI)</th>
<th>All cases</th>
<th>Fatal cases</th>
<th>Non-fatal cases</th>
<th>Hospitalized cases</th>
<th>Referred (not hospitalized) cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>UGIB</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.62</td>
<td>0.75</td>
<td>1.73</td>
<td>1.58</td>
<td>1.69</td>
<td></td>
</tr>
<tr>
<td>1.01–1.87</td>
<td>1.50–2.15</td>
<td>1.33–1.88</td>
<td>0.57–8.37</td>
<td>1.37–2.09</td>
<td></td>
</tr>
<tr>
<td>LGIB</td>
<td>1.96</td>
<td>1.09</td>
<td>1.93</td>
<td>1.98</td>
<td></td>
</tr>
<tr>
<td>1.75–2.22</td>
<td>1.04–2.81</td>
<td>1.57–2.36</td>
<td>1.73–2.28</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Index date: Date of bleeding event for cases, random date for controls *Adjusted by the matching variables (age, sex and calendar year), number of primary care physician visits in the year before the index date, smoking, alcohol consumption, prior LGIB, prior unspecified GIB, use of non-steroidal anti-inflammatory drugs, proton pump inhibitors, clopidogrel, and warfarin, and the following for


Conclusion: Use of low-dose aspirin is associated with a significantly increased risk of UGIB/LGIB overall (both hospitalized and referred cases) but not with fatal UGIB/LGIB. Our results also suggest a possible dose–response relationship between low-dose ASA and UGIB but not LGIB.

Disclosure of Interest: L. Cea Soriano: LCS works for CEIEF, which has received research funding from Bayer AG. M. Soriano-Gabarró: MS-G is a full-time salaried employee of Bayer AG. A. Lanas: AL has received a research grant from Bayer AG and has served as an advisory board member for Bayer AG. L.A. García Rodríguez: LAGR works for CEIEF, which has received research funding from Bayer AG. LAGR has also received honoraria for serving on advisory boards for Bayer AG.

Reference

OP321 THE EFFICACY OF POLYGLYCOLIC ACID SHEETS AND FIBRIN GLUE FOR PREVENTING BLEEDING AFTER ENDOSCOPIC SUBMUCOSAL DISSECTION FOR GASTRIC NEOPLASMS (PAGER BUSTER TRIAL): INTENTION TO TREAT ANALYSIS OF A PROSPECTIVE MULTICENTER RANDOMIZED CONTROLLED TRIAL

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Introduction: Endoscopic submucosal dissection (ESD) for gastric neoplasms has been established as a standard treatment in many countries. However, post-ESD bleeding is still one of the major complications which are impossible to completely avoid. There is significant difference between the two groups (the endoscopic tissue shielding method with polyglycolic acid (PGA) sheets and fibrin glue for the mucosal defect after ESD). In our pilot study we have demonstrated that this method may reduce the risk of post-ESD bleeding, but there have been no reports which provide significant evidence concerning this issue to date.

Aims & Methods: This is a prospective multicenter open-label RCT conducted in six hospitals across Japan to investigate the efficacy of the PGA shielding method for post-ESD bleeding. Out of a total of 223 gastric ESD procedures performed with a high-risk for post-ESD bleeding were enrolled in this study. High-risk patients were defined as follows: 1) those expected to undergo large mucosal resection (≥40 mm) or 2) those with regular intake of antithrombotic agents.

Before ESD the patients were allocated to PGA group or non-PGA group at a ratio of 1:1 by a minimization method through a web-based system. The enrolled patients in both groups received proton pump inhibitor for 4 weeks from the day before ESD, and underwent coagulation of visible vessels on the ESD–induced ulcer floor. And then, in the PGA group, PGA sheets were placed onto the ulcer floor and stuck with fibrin glue. 2 days after ESD, soft diet was started. Post-ESD bleeding was defined as follows: 1) hematemesis, melena or a hemoglobin decrease ≥2 g/dL and 2) emergency endoscopy revealed active bleeding or accumulated blood in the stomach. When a patient presented with post-ESD bleeding, endoscopic hemostasis was performed. The primary endpoint was the post-ESD bleeding rate.

Results: A total of 68 patients were assigned to the PGA group and 72 patients to the non-PGA group. After excluding 3 patients (the ESD cessation: 2, consent withdrawal: 1), 67 patients in the PGA group and 70 in the non-PGA group were included in the intention to treat analysis. Post-ESD bleeding occurred in 3 patients (4.5%) in the PGA group and 4 (5.7%) in the non-PGA group. There was no significant difference between the two groups (P=0.857). Immediate post-ESD bleeding episodes occurred in 4/3 patients in the PGA group and 14/15 patients in the control group. One case of delayed bleeding was observed in both groups.

Conclusion: The present study could not demonstrate a significant effect of the PGA shielding method on the prevention of post-ESD bleeding although this method has the possibility of preventing late-phase bleeding.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP322 SIGNIFICANT REDUCTION OF POSTINTERVENTIONAL HAEMORRHAGE AFTER RESECTION OF LARGE DUODENAL ADENOMA BY THE USE OF A HEMOSTATIC POWDER

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Introduction: Against the background of the relatively high rates of relevant bleedings after endoscopic resection depending on the size of the duodenal adenoma, the value of a hemostatic powder was examined.

Aims & Methods: This is a prospective, randomised study with (Group A) and without (Group B) administration of a hemostatic powder after resection. Only large duodenal adenomas with a size ≥20 mm were included. The resection was performed by means of a snare after prior injection. Intraprocedural bleedings were treated by injection and coagulation. Post-interventional Hb-control and an EGD on the following day were documented, whereby bleeding stigmata (Forrest IIa/Ib) were recorded. The sample size calculation showed 21 patients per arm with a reduction in bleeding by one third. Minor bleeding was defined as Hb decrease less than 2 g/dl and bleeding stigmata during wound control the next day. The major bleeding was defined as Hb drop ≥2 g/dl.

Results: Between December 2014 to February 2017, 39 suitable patients were presented, 38 patients (14, 24 1c, average age 65 years) of which were randomized. Two patients dropped out of the study. The etiology of adenomas was sporadic in 64%, and 36% had FAP. The average adenoma size was 33 ± 11 mm (18–40 mm). The localization of the duodenal adenomas was 32% suprapapillary, 26% at the papilla, and 42% infrapapillary. In each case 18 patients received either a hemostatic powder or not. In Group A (with hemostatic powder) a minor hemorrhage was detected in 9/18 and a major hemorrhage in 2/18. In the Group B (without hemostatic powder) a minor hemorrhage occurred in 4/18 and major hemorrhage in 3/18 patients. After an interim analysis, the study was terminated prematurely if the effect of the hemostatic powder was missing.

Conclusion: By applying a hemostatic powder no significant reduction of relevant post-bleeding after endoscopic resection of large duodenal adenomas ≥20 mm can be achieved.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP323 EFFECT OF PROPHYLACTIC CLIP APPLICATION FOR THE PREVENTION OF POSTPOLYPECTOMY BLEEDING IN LARGE PEDUNCULATED COLONIC POLYPS: A RANDOMIZED, CONTROLLED MULTICENTER TRIAL

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Introduction: Although endoscopic colonic polypectomy has been an established procedure for a long time, the risk of bleeding is still higher after resecting of pedunculated polyps, because of the presence of a large artery in the stalk. Preventive methods such as endoloop and epinephrine injection have been proposed in the management of postpolypectomy bleeding in large colonic polyps. For prophylactic clip, there was no randomized controlled study assessing the efficacy in prevention of postpolypectomy bleeding for the large pedunculated colon polyps.

Aims & Methods: The aim of this randomized controlled trial was to confirm the efficacy of application of prophylactic clip in the prevention of postpolypectomy bleeding in large pedunculated polyps. A total of 183 patients who had pedunculated colorectal polyps, with heads larger than 10 mm and stalks larger than 5 mm in diameter, were included. In clip group, hemoclips were applied to the base of the stalk, followed by conventional snare polypectomy. In control group, conventional snare polypectomy was done without any preventive management. Immediate and delayed bleeding complications were analyzed.

Results: A total of 200 polyps were included in the study (99 in the clip group and 101 in the control group). Clip application was possible in all the cases in the clip group. There were 5 cases of bleeding in the clip group (5.1%) and 15 cases in the control group (14.9%) (P=0.047). Immediate post-ESD bleeding episodes occurred in 4/5 polyps in the clip group and 14/15 polyps in the control group. One case of delayed bleeding was observed in both groups.

Conclusion: The application of a prophylactic clip is effective in the prevention of postpolypectomy bleeding in large pedunculated colon polyps.

Disclosure of Interest: All authors have declared no conflicts of interest.
OP224 THE RISK OF PROXIMAL DISEASE EXTENSION IN PATIENTS WITH LIMITED UC COLITIS IN A PROSPECTIVE EUROPEAN POPULATION-BASED INCEPTION COHORT – THE ECCO-EPICOM COHORT


Introduction: Ulcerative colitis (UC) is a progressive and dynamic disease and many patients will experience an extension of their initial disease location. Disease extent is the most important factor determining disease prognosis over the long-term. As only few population-based studies have investigated the disease extension and subsequent risk of surgery in UC, we sought to investigate this in the European population-based EpCoM-cohort.

Aims & Methods: The EpCoM-cohort is a population-based cohort of unselected patients with inflammatory bowel disease diagnosed in 2010 and Eastern and Western European centres. Patients were followed prospectively for five years and clinical data were captured throughout the follow-up period and entered in a validated web-based database. Disease extension was defined in patients with limited UC at diagnosis (proctitis, E1 or left-sided, E2) as a progression from the initial extent defined by endoscopy or surgery. The risk of colectomy was assessed in all incident patients. Associations between progression or colectomy and multiple covariates (age, gender, initial disease extent, disease delay, smoking status, increase in extent, geographic region, treatment) were analysed by Cox regression analyses using the proportional hazard assumption.

Results: Out of a total of 717 incident UC patients, 435 (61%) had E1 or E2 at diagnosis. Extension and disease progression were followed-up in patients with limited UC as shown in Table 1. During the follow-up period, 67 (16%) patients with E1/E2 progressed to E3, and 23 (16%) patients with E1 progressed to E2. Only the need for systemic prednisolone at diagnosis (HR: 0.4 CI95%: 0.2–0.8) and treatment with immunosuppressants and/or biologics (HR: 19.8 CI95%: 7.8–50.6) were associated with the risk of extension. During follow-up, a total of 43 (6%) patients had a colectomy. Of patients with E1/E2 as initial extent a total of 19 (4%) patients had a colectomy. Progression from E1/E2 to E3 was a significant risk factor for colectomy (HR 4.4 CI95%: 1.6–12.4). No difference in the results was found between Eastern and Western European patients.

Table 1: Disease extent in ulcerative colitis at diagnosis and follow-up

<table>
<thead>
<tr>
<th>Disease extent</th>
<th>At diagnosis</th>
<th>At follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proctitis (E1)</td>
<td>E1, proctitis</td>
<td>E1, proctitis</td>
</tr>
<tr>
<td>Left-sided (E2)</td>
<td>E2, left-sided</td>
<td>E2, left-sided</td>
</tr>
<tr>
<td>Extensive (E3)</td>
<td>E3, extensive</td>
<td>E3, extensive</td>
</tr>
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</table>

Conclusion: In this European population-based inception cohort of unselected UC patients, one out of five patients with proctitis or left-sided colitis at diagnosis experienced a progression in disease extent after five years of follow-up. The risk of colectomy was increased in patients who progressed to extensive colitis. Only treatment during follow-up as an indicator for disease severity was identified as a predictor for disease extension, thus highlighting the need for new historical or serological markers in order to identify patients at risk for disease progression.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP235 EARLY FIBROSTENOSIS IN CROHN’S DISEASE IS ASSOCIATED WITH MULTIPLE SUSCEPTIBILITY LOCI ON IMMUNOCIP ANALYSIS


Aims & Methods: In this multicenter, retrospective nested case-control study, performed at the University Hospitals of Ghent and Leuven, computed tomography (CT)- and magnetic resonance imaging (MRI) from CD patients obtained between 2002 and 2016 were examined for the presence of fibrostenotic disease. Patients with early fibrostenosis, defined as a the presence of bowel thickening with luminal narrowing and pretedstent dilation on CT/MRI occurring within 5 years following diagnosis of ileal or flexoece disease (Montreal L1 or L3), and with available Illumina Immunochip data were included. The control cohort consisted of inflammatory CD patients, also Montreal L1 or L3, without arguments for fibrostenotic disease during at least 10 years follow up. Allelic association was assessed using the PLINK v1.07 software.

Results: In total, 3024 CT or MRI scans of 2042 CD patients were screened. 112 patients were selected because of positive arguments for fibrostenosis occurring within 5 years of diagnosis. Of these, Immunochip data were available in 60 cases, and 49 (82%) had confirmed stenosis by histopathology. 343 inflammatory CD controls with genotype data were included in the analysis. Of the 156,500 SNPs analysed, only rs35223850 in the IL12R gene reached a statistically suggestive significance level of P < 5 × 10^{-6}, including rs11630771 in the IL23R gene, which is of particular interest as this gene has previously been associated with systemic sclerosis.

Conclusion: Fibrostenosis is a common complication of Crohn’s disease (CD) occurring in about one-third of patients. Although the pathophysiology of intestinal fibrosis is incompletely understood, evidence suggests a genetic contribution. Previous genetic association studies and candidate gene studies with fibrostenotic CD were based on clinical definitions which lack both sensitivity, specificity and have a high inter-observer disagreement. Additionally, the recent genotype-phenotype analysis by the IBDGC did not consider the time to development of fibrostenotic disease. As the genetic risk may be more important in patients with early fibrostenosis, in this study we aimed to identify novel genetic markers by focusing on early fibrostenotic disease.

Disclosure of Interest: Fibrostenosis is a common complication of Crohn’s disease (CD) occurring in about one-third of patients. Although the pathophysiology of intestinal fibrosis is incompletely understood, evidence suggests a genetic contribution. Previous genetic association studies and candidate gene studies with fibrostenotic CD were based on clinical definitions which lack both sensitivity, specificity and have a high inter-observer disagreement. Additionally, the recent genotype-phenotype analysis by the IBDGC did not consider the time to development of fibrostenotic disease. As the genetic risk may be more important in patients with early fibrostenosis, in this study we aimed to identify novel genetic markers by focusing on early fibrostenotic disease.
Conclusion: This carefully phenotyped study reveals an important role for genetic contribution to early development of fibrostenotic complications in CD. Our data suggest a role for M1S1B8P and the SP1 transcription factor as well as the IL23 pathway in the pathogenesis of early intestinal fibrosis.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP326 THE ROLE OF THE IKBA GENE FAMILY MEMBER NFKBIZ IN COLITIS-ASSOCIATED CANCER

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Introduction: Inflammatory bowel disease (IBD) is a relapsing-remitting chronic inflammatory disorder. Importantly, the risk of developing colorectal cancer is increased in IBD patients with chronically active disease. Colitis-associated cancer (CAC) has different characteristics compared to sporadic colorectal cancer, such as onset of carcinogenesis in younger patients. To investigate the genetic basis for these differences, we used the AOM/DSS murine model of CAC. Using whole exome, as well as the whole transcriptome sequencing of tumor and colonic non-tumor samples, we determined the mutational landscape to identify recurrent mutations, which may be of functional relevance for the malignant transformation. Using this approach, we identified several tumor-associated variants in the NFKBIZ gene. NFKBIZ is a member of the IkBa gene family, and known to be induced by IL1β in hematopoietic cells. However, the precise role of NFKBIZ in the human intestinal epithelial cells (IECs) remains largely unknown.

Aims & Methods: The present study was planned to identify the role of NFKBIZ in IECs. Human and mouse intestinal epithelial cell lines, Caco2, HT29 and MODEK, were employed to analyze the NFKBIZ expression in response to IL1β by immunoblot analysis. To perform functional studies, we created cell lines that are deficient for NFKBIZ by using the CRISPR/Cas9 system. Using this cell line, functional assays were examined by immunoblots and proliferation was tested by MTS assay. To analyze the expression of NFKBIZ in human IECs, gene expression of human biopsy samples was quantified using RNA-sequencing. We also created human organoids from IBD patients and examined the NFKBIZ expression by immunoblot.

Results: In intestinal epithelial cell lines, NFKBIZ was induced by only IL1β. To use the proteasome inhibitor MG132, degradation of NFKBIZ was clearly prevented. These results indicated NFKBIZ degradation was promoted in proteosome. In NFKBIZ-deficient cells, immunoblots showed more LC3 lipidation by autophagy inducer rapamycin addition, and also more CHOP induction by ER stress inducer tunicamycin addition. NFKBIZ-deficient cells showed impaired autophagy and enhanced ER stress, which are associated with chronic inflammation. We could also show that NFKBIZ deficient cells exhibited impaired proliferation by MTS assay. Interestingly, hierarchical clustered heatmap of the differentially expressed genes across IBD-bioy samples showed that expression of NFKBIZ is upregulated in IECs of IBD patients. In addition to cancer cell lines, we also use human organoids as a model. Here, by immunoblot analysis, NFKBIZ is also induced by IL1β stimulation and expression of NFKBIZ is stably upregulated in organoids derived from UC patient.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP327 RORGAMMA-T-EXPRESSING TREGS DRIVE GROWTH OF COLITIS-ASSOCIATED COLORECTAL CANCER BY CONTROLLING IL6 EXPRESSION OF DENDRITIC CELLS

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Introduction: Chronic inflammation drives colitis-associated colorectal cancer (CAC), a life-threatening complication of inflammatory bowel disease (IBD). FoxP3+ regulatory T cells (Tregs) co-expressing the Th17-related transcription factor RORgamma-t accumulate in the lamina propria of IBD patients where they are thought to represent an intermediate stage of development toward a Th17 proinflammatory phenotype. However, the role of these cells in CAC is unknown.

Aims & Methods: The phenotypic stability and function of RORgamma-t-expressing Tregs were investigated in Tregs fate mapping reporter and Tregs RORgamma-t conditional knockout mice undergoing the AOM/DSS model of CAC. Tumor development was monitored by endoscopy. Ki67, STAT3 and cytokine expression were assessed by immunohistochemistry and real-time PCR. Tumor-infiltrating Tregs were characterized by flow cytometry. The functional role of CTLA4 and FoxO3 was studied by coculture experiments of tumor-isolated Tregs from wild type or knock-out mice with dendritic cells (DCs) and by in vivo siRNA silencing experiments.

Results: RORgamma-t expression identifies a phenotypically stable population of tumor-infiltrating Tregs. Conditional RORgamma-t knockout mice showed reduced tumor incidence and dysplastic cells exhibited low Ki67 expression and STAT3 activation. Tumor-infiltrating dendritic cells (DCs) produced less IL6, a cytokine that triggers STAT3-dependent proliferative signals in neoplastic cells. RORgamma-t-deficient Tregs isolated from tumors over-expressed CTLA4 and induced DCs to express elevated levels of the transcription factor FoxO3 thus reducing IL6 expression. Finally, in vivo silencing of FoxO3 obtained by siRNA microinjection in the tumors of RORgamma-t-deficient mice restored IL6 expression and tumor growth.

Conclusion: These data demonstrate that RORgamma-t-expressed Tregs sustains tumor growth by leaving IL6 expression in DCs unchecked.

Disclosure of Interest: All authors have declared no conflicts of interest.

Abstract No: OP328

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<td>17 (49%)</td>
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<tr>
<td>0 or 1 meth genes</td>
<td>8 (17%)</td>
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</table>

OR P value
1
1.77 0.29
2.92 0.05
3.43 0.01
1.95 0.36
2.65 0.09
8.63 0.001
4.49 0.0006**
9.18 0.0006**
8.32 0.0001
4.20 0.02
11 (85%) 2 (15%) 25.67 1.25E-05**
11 (55%) 36 (84%) 5.83 0.08
15 (73%) 33 (92%) 5.5 0.01
15 (55%) 36 (84%) 3.86 0.02
4 (27%) 3 (8%) 4 0.17
6 (40%) 4 (12%) 5 0.04
9 (60%) 30 (88%) 7.73 0.001
4 (20%) 29 (66%) 26.7 1.25E-05**
G. Ito: 1 meth genes 17 (49%) 18 (51%) 4.49 0.0006** 11 (85%) 2 (15%) 25.67 1.25E-05**

* Mann-Whitney test
** Fisher test

Disclosure of Interest: All authors have declared no conflicts of interest.
DISEASE IN A PROSPECTIVE MULTICENTER NESTED CASE-CONTROL STUDY

Aims & Methods: The aim of the study was to evaluate the effectiveness of a selected methylation gene panel for the early detection of CRC in high-risk IBD patients. Five genes (EYA4, SLIT2, USP44 and SNOT) were selected from genome-wide DNA methylation analysis using the Illumina HumanMethylation 450k BeadChip in a phase II feasibility study. DNA from 48 IBD patients was selected for the selected panel.

Results: Methylation of the panel was a common phenomenon in IBD-associated neoplasia both in diseased and adjacent healthy tissue (71% and 52% respectively) being this prevalence higher to that of healthy individuals (2/36; 6%; p = 0.001), and even more frequently in the mucosa of IBD patients at high risk of dysplasia or cancer than in patients at low risk (92% vs 57%; OR = 8.83; p = 0.001), being EYA4 and SLIT2 the markers most frequently methylated. In healthy mucosa this difference in methylation levels was also evident (82% vs 15% for high vs low risk respectively (p = 1.25E-05) (Table).

Conclusion: The analysis of this panel of methylation markers may help in the early identification of colorectal dysplasia or cancer in high risk IBD patients.

Disclosure of Interest: All authors have declared no conflicts of interest.

References:

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2. M. A. Vecchi: The study was not supported by any grant nor funded. None of the below reported disclosures are related to the study. Speaker and advisory board: Abbvie, Biogen, Celltrion, Ferring, Hospira, Janssen, Lilly, MSD, Mundipharma, Pfizer, Samsung, Sofar, Takeda, Zambon. Research grant M.L. Scribano: The study was not supported by any grant nor funded and any of the below reported disclosures are related to the study. Sachetti: Celltrion, Ferring, Hospira, Janssen, Lilly, MSD, Mundipharma, Pfizer, Samsung, Sofar, Takeda, Zambon. Research grant.
3. L. Biancone: The study was not supported by any grant nor funded. No reported disclosures are related to the study. Consultant to: Abbvie, Astra, Biogen, Celltrion, Ferring, Hospira, Janssen, Lilly, MSD, Mundipharma, Pfizer, Samsung, Sofar, Takeda, Zambon. Advisory board: Abbvie, Biogen, Celltrion, Ferring, Hospira, Janssen, Lilly, MSD, Mundipharma, Pfizer, Samsung, Sofar, Takeda, Zambon. Research grant L. Biancone: The study was not supported by any grant nor funded. No disclosed interests.
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In conclusion, we show that Wnt5b acts on intestinal epithelium by potentiating a TGF-β-dependent EMT response. Its up-regulation in IBD mucosa could promote epithelial cell migration, thus contributing to a regenerative response in the context of tissue injury.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

OP332 NOVEL HUMAN GUT XENOGRAFT MOUSE MODEL FOR INTESTINAL FISTULAS
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Introduction: Fistulas represent a frequent complication in Crohn’s disease (CD) patients and surgical resection is often required. Despite some progress in understanding and improving the treatment of inflammatory bowel disease (IBD), more effective medical treatments are required, especially for CD patients with fistula formation. Previously, we demonstrated that epithelial-to-mesenchymal transition (EMT) plays a critical role for fistula development in CD patients. Preceding upregulation of TGF-β1, 6-integrin, and necroptosis along fistula tracts in CD patients seems to orchestrate a number of events contributing to fistula development by inducing EMT. Due to a lack of a reliable in vivo model, new drug developments are complicated. Here, we describe a new xenograft (XGR) mouse model of intestinal fistula resembling the human condition.

Aims & Methods: 12–18 weeks (w) old human fetal small intestine was transplanted subcutaneously onto the backs of SCID mice. After 12–16w, ~15% of the mature xenografts spontaneously developed enterocutaneous fistulas. Using systemic LPS treatment followed by mild skin irritation adjacent to the transplant, we established a reproducible model system, resulting in enterocutaneous fistulas within 2–4w. Samples were analysed by immunohistochemistry staining (IHC) for EMT-, immune cell- and necroptosis markers, as well as RNA sequencing.

Results: Histopathological analysis of the fistulating XGR samples revealed a characteristic loss of villous structures and flattening of the intestinal epithelial cells lining the fistula tract, resembling transitional cells described in human CD fistula samples. IHC stainings for various EMT markers (e.g. SLUG, β6-integrin) showed similar expression pattern as in samples from fistulas of CD patients. The expression of the mesenchymal marker alpha-smooth muscle actin confirmed the hypothesis that EMT plays a critical role for the fistula development in the XGR samples, as well. Inflammation in the XGR was apparent up- and downstream to the fistulous tracts. Most of this inflammatory response consisted of CD45 cells, but only very few murine DCs+ cells. Further necroptosis staining revealed large numbers of human CD3+ cells. Collagen staining showed that these inflammatory regions were associated with extensive fibrosis suggesting extracellular matrix remodeling. We also detected strong staining for necroptosis markers (RIP Kana4 and MLKL) in the fistulated XGRs compared to unfistulated control samples. RNA sequencing of inflated LPS-treated XGRs revealed a significant upregulation of genes related to IBD, necroptosis, ripoptosome and NF-κB signaling.

Conclusion: Our data demonstrate that the in vivo model recapitulates, both morphologically and mechanistically, the human disease. Necroptosis might be involved in fistula development, similar to human CD fistulas.
OP334 THE ROLE OF pH-SENSING RECEPTOR TDAG8 (GPR65) IN INTESTINAL INFLAMMATION
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Introduction: The two major forms of inflammatory bowel diseases (IBD), Crohn’s disease (CD) and ulcerative colitis (UC), typically result in decrease of extracellular pH of the affected mucosa. Genome-wide association studies (GWAS) identified over 240 non-overlapping single-nucleotide polymorphisms (SNPs) associated with IBD. G-protein-coupled receptor 65 (GPR65) or T-cell death associated gene 8 (TDAG8) has been reported to be a genetic risk factor for IBD in recent GWAS. TDAG8 belongs to a family of proton-sensing GPCRs, including TDAG8, ovarian cancer G-protein coupled receptor 3 (OGR1) and GPR4. However, the role of TDAG8 is not fully understood.

Aims & Methods: In this study we investigate the role of TDAG8 in a murine IBD model. Chronic colitis was induced in WT and TDag8-/- (KO) mice with 4 cycles of 2% DSS in drinking water for 7 days followed by 10 days of regular drinking water. Colon specimens were obtained and RT-qPCR and immunohistochemistry (IHC) were performed. Quiescent peritoneal macrophages (MΦs) from WT and TDag8-/- mice were isolated, cells were treated for 24 h with pH 6.8 serum free medium to activate TDAG8, using pH 7.6 as negative controls. RNA was isolated for RNA sequencing.

Results: In the chronic colitis model, no significant differences in the typical inflammatory markers were observed between WT and KO groups. However, mRNA expression of IFNγ, TNF, IL6, INOS was increased in the KO group, but not significantly different from WT. For example, IL17α, Gata3, Foxp3 and RORc. IHC staining revealed that DSS-treated TDag8-/- mice showed increased immunoreactivity of MΦ marker F4/80 compared to WT and water controls. Protein staining of T cell marker CD3 showed no difference between WT and TDag8-/- mice. Interestingly, mRNA and protein expression of OGR1 were downregulated in TDag8-/- colon tissue. To further examine the role of TDAG8 in MΦs, we performed RNA-sequencing upon a 24 h pH shift from pH 7.6 to pH 6.8. Pathways in mouse MΦs, mediated by TDAG8, were positively enriched for regulation of lymphocyte and leukocyte activation, apoptosis and M1 regulation.

Conversely, pathways in TDAG8-deficient MΦs were upregulated for cytokine production involved in inflammatory response and M2 regulation. Moreover, expression of OGR1 was significantly downregulated in TDAG8-/- MΦs. Conclusion: No significant differences for colitis autoantigens were observed in chronic DSS colitis in WT and TDag8-/- mice, suggesting that TDAG8-dependent anti-inflammatory responses are not able to down-regulate inflammation in this IBD model. Although lack of TDAG8 did not affect outcomes in the murine chronic colitis model, TDAG8 was able to reduce the inflammatory response of macrophages. TDAG8 also upregulates expression of the pro-inflammatory pH receptor OGR1, potentially providing a feedback loop for pH dependent immune activation.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP335 PRO-INFLAMMATORY HUMAN CD11C+ MACROPHAGES, BUT NOT THEIR TOLERIC CD11CDIM OR CD11C- COUNTERPARTS, ARE EXPANDED IN THE INFILATED MUCOSA FROM PATIENTS WITH INFLAMMATORY BOWEL DISEASE
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Introduction: Inflammatory bowel disease (IBD), including Crohn’s disease (CD) and ulcerative colitis (UC), is a chronic inflammation of the human gastrointestinal (GI) tract. Macrophages (MΦs), the most abundant GI-monomonuclear phagocytes, are critical at shaping immune responses since they typically maintain the mechanisms of immune tolerance in health, although they can also exacerbate immune responses during inflammation. However, despite their relevance modulating GI-immune responses, there is not much information about their properties in the human GI-tract.

Aims & Methods: Our aim was to characterize human GI-MΦ subsets, phenotype and function both in health and in IBD patients. To that end, human intestinal biopsies were obtained from healthy controls and IBD patients (including UC and CD, both active and quiescent). Tissue was disaggregated and the lamina propria mononuclear cells cultured by flow cytometry. Human intestinal biopsies were cultured overnight to obtain GI-secretomes which were used to assess the mucosa capacity to recruit circulating CD14+ monocytes (enriched from the blood from healthy controls) on transwell culture assays.

Results: Human intestinal MΦ (identified within singlet viable cells as CD45+/HLA-DR+/CD14+) were further divided into CD11chigh, CD11dim and CD11c- counterparts. While the CD11chigh subset resembled the phenotype of circulating phagocyte (Dextran+) and pro-inflammatory CD14+ monoocytes (CX3CR1, SIRPα, CCR2, CD64), the CD11dim subset displayed an intermediate phenotype towards the CD11c- MΦ subset, which was not phagocytic (Dextran-), had higher expression of HLA-DR and CD64 and lower expression of CX3CR1, SIRPα, CCR2 and CD40. CD11c-MΦ displayed a higher production of IL-1β both in resting conditions and after LPS stimulation, compared with the CD11c- subset, which produced larger amounts of IL-10 and was hyporesponsive to LPS stimulation. In health, CD11c-MΦ were the predominant subset in the distal GI-compartments (distal and proximal colon) while CD11c- MΦ were in a higher proportion in the terminal ileum and became predominant in the duodenum. Total MΦ numbers were increased in the inflamed colon from IBD patients (both UC and CD), although not on the non-inflamed tissue from the same patients or from quiescent patients, due to specifically higher numbers of the CD11chigh subset. Finally, colon secretomes from healthy controls recruited circulating CD14+ monocytes, while such capacity was further increased on those from inflamed IBD patients (both UC and CD) but not on quiescent patients.

Conclusion: MΦ subsets are likely to represent transition stages from newly arrived pro-inflammatory monocytes (CD11chigh) to transient (CD11dim) and resident (CD11c-) MΦ as reflected by the mucosal capacity to recruit circulating CD14+ monocytes. This indeed further confirmed increased on active IBD patients where the CD11c+ macrophages are expanded.

Disclosure of Interest: All authors have declared no conflicts of interest.
OP326 DOES CHROMOENDOSCOPY REDUCE COLORECTAL NEOPLASIA DURING SURVEILLANCE IN LYNCH SYNDROME? A RANDOMIZED TRIAL

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Introduction: Lynch syndrome (LS) is associated with an increased risk of hereditary tumours. Regular surveillance (1–2 yearly intervals) has proven mismatch repair gene mutation carriers (mean age: 46 years, range 21–70 years) were randomized between conventional white-light colonoscopy and colonoscopy using chromoendoscopy in the colon proximal from the splenic flexure. After 2 years, both groups underwent colonoscopy using chromoendoscopy. The number of neoplastic lesions at baseline and at follow-up colonoscopy was recorded.

Results: The number of patients with neoplasia in the entire colon was not significantly different between chromoendoscopy and white-light colonoscopy (36/118 (0 CRC) versus 33/123 (2 CRC), p = 0.04). Chromoendoscopy took significantly more procedure time than conventional colonoscopy (p < 0.01), due to a significant difference in median withdrawal time (18 versus 12 minutes, p < 0.01). At follow-up colonoscopy after 2 years, no difference was found with respect to the number of patients with neoplastic lesions in the entire colon between the groups (35/118 (4 CRC) versus 32/123 (2 CRC), p = 0.26). The number of proximal adenomas found was also not significantly different (36 versus 47, p = 0.22).

Conclusion: Chromoendoscopy increases the detection of adenomas in LS, but does not significantly reduce the adenoma detection rate at follow-up endoscopy.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP327 LEAVING COLORRECTAL POLYPS IN PLACE CAN BE ACHIEVED WITH HIGH ACCURACY USING BLUE LIGHT IMAGING (BLI)

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Introduction: The ASGE PIVI statement is proposing a negative predictive value (NPV) >90% for a new technology to leave distal diminutive colorectal polyps in place without resection. To our knowledge no prior prospective study has yet evaluated the feasibility of the most recently introduced Blue Light Imaging (BLI) system for real-time endoscopic prediction of polyp histology for the specific endpoint of leaving hyperplastic polyps in place.

Aims & Methods: Main study objective was the prospective assessment of real-time prediction of colorectal polyps by using BLI. Therefore, 177 consecutive patients undergoing screening or surveillance colonoscopy were included. Colorectal polyps were evaluated in real-time by using high-definition endoscopy and the BLI technology without optical magnification. The endoscopist described each polyp according to size, shape and surface characteristics (pit and vascular pattern, color, depression) and histology was predicted with a level of confidence (high or low).

Results: High-confidence prediction of histology was performed in 92% of polyps. Sensitivity of BLI for prediction of adenomatous lesions was 98.7%, with a specificity and accuracy of 97.4% and 98.2%, respectively. The positive and negative predictive values were calculated with 97.9% and 98.4%, respectively.

Conclusion: The most recently introduced BLI technology is accurate enough to leave distal colorectal polyps in place without resection. This approach has therefore the potential to reduce costs and risks associated with the redundant removal of diminutive colorectal polyps.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP328 A STUDY ON DIAGNOSTIC ABILITY TO DISTINGUISH BETWEEN ADENOMAS AND INVASIVE COLORECTAL CANCERS USING COMPUTER-AIDED ENDOCYTOSCOPY

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Introduction: Endocytoscopy (EC) enables in vivo observation of nuclei at about 500-fold magnification during gastrointestinal endoscopy.[1] We have reported the usefulness of EC for colorectal cancer detection, but clinical practice it seemed that there is a need for an easy-to-use diagnostic aid system for trainees with little experience. To address this task, we have developed a computer-aided diagnosis system for EC imaging (EC-CAD) that provides fully-automated classification of colorectal lesions (2, 3). And we have recently reported its diagnostic ability for invasive colorectal cancer.[4] Whether it is a lesion at risk of lymph node metastasis is important in considering the indication of surgical operation. Therefore, it is very important to distinguish lesions that may have lymph node metastasis such as invasive cancers from other lesions. In this task, it is thought that the EC-CAD can be a very useful diagnostic tool.

Aims & Methods: The aim of the present study was to evaluate diagnostic ability to distinguish between adenoma and invasive colorectal cancer. EC-CAD analyses EC images based on the information from nuclei and texture analysis. All 296 features (eight features from nuclei, 288 from texture analysis) are used as the data for evaluating EC images and EC-CAD automatically presents the pathological diagnosis. We used a support vector machine (SVM) to produce these many features. EC-CAD requires machine learning for construction of diagnostic algorithm. We used 8761 EC images for machine learning in the process of construction of the model. And we selected randomly 200 EC images, which were different from images used for machine learning, from data base of EC images for test data. We evaluated the diagnostic ability of EC-CAD for distinguishing invasive cancers from adenomas.

Results: The time taken for EC-CAD to diagnose the test image was only 0.3 seconds on average. The diagnostic ability of EC-CAD to distinguish invasive cancers from adenomas, the sensitivity, specificity, accuracy, positive predictive value (PPV), negative predictive value (NPV) were 80.0%, 98.8%, 90.1%, 98.2% and 85.3%, respectively. In addition to the predicted pathological diagnosis, EC-CAD simultaneously present the probability of diagnosis calculated by SVM. When the diagnosis probability was 90% or more, the sensitivity, specificity, accuracy, PPV, NPV were 90.9%, 100%, 95.9%, 100% and 93.1%, respectively.

Conclusion: This study indicates the usefulness of EC-CAD system for EC imaging (EC-CAD) as a very useful diagnostic tool.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
SLs are important premalignant lesions, but its clinical and biological features and risk of malignant progression are not fully understood.

**Aims & Methods:** To establish accurate colonicoscopic diagnosis and treatment of SLs, we aimed to clarify the associations between morphological, pathological and molecular characteristics in SLs. A total of 401 premalignant and malignant colorectal lesions were categorized into 4 subtypes based on their structural diversity. Microsurface structures were assessed by magnifying colonoscopy according to Kudo’s pit pattern classification system. Type II pit pattern was subclassified into classical Type-II, Type II-Open (Type II-O) and Type II-Long (Type II-L). Biopsy specimens were obtained from all lesions for genomic DNA extraction, after which lesions were treated by endoscopic mucosal resection (EMR) or endoscopic submucosal dissection (ESD). BRAF/KRAS mutations and methylation of CpG islands were determined by using the five markers analyzed by pyrosequencing. CpG island methylator phenotype (CIMP) status was also evaluated by HpaII restriction digestion system. Type II-O was tightly associated with sessile serrated adenoma/polyps (SSA/Ps) with BRAF mutation and CIMP-high. Majority of lesions with simple Type II or Type II-L were hyperplastic polyps (HPs), while mixtures of Type II or Type II-L plus III/IV were characteristic to traditional serrated adenomas (TSA)s (sensitivity: 69%; specificity: 95%). Type II-positive TSA frequently exhibited BRAF mutation and CIMP-low, while Type II-L-positive TSA were tightly associated with KRAS mutation and CIMP-low. Analysis in lesions containing both premalignant and cancer components suggested that Type II-L-positive TSA may develop to KRAS mutated/CIMP-low cancers, while Type II-O-positive SSA/Ps exhibited CIMP-high.

**Conclusion:** Our results suggest that Type II subtypes may reflect distinct molecular subclasses in the serrated neoplasia pathway, and that they could be useful hallmarks to identify SLs at a high risk to develop CRC.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**OP340 CLASSIFICATION OF CELL NUCLEI MORPHOLOGY OF EC FINDINGS IN COLORECTAL ENDOSCOPY**

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**Introduction:** Endoscopy (EC) is a next-generation endoscopy that enables diagnostic imaging at 450 × magnification. To date, excellent results have been achieved using EC classifications for qualitative diagnosis and assessment of depth of invasion of colorectal lesions (neoplasia/non-neoplasia accuracy: 96.5%; accuracy for carcinomas with massive submucosal invasion (SM-m): 96.3%).

**Aims & Methods:** In the EC classifications, lesions diagnosed as EC3a vary extensively from SM-m to SM-m, including some lesions that are unsuitable for endoscopic treatment. In order to improve the accuracy of assessing the depth of invasion based on the EC classification, we investigated the presence or absence of certain endoscopic factors in EC3a findings that could be indicators of SM-m. Lesions that were observed by EC between May 2005 and January 2015, we retrospectively examined 668 lesions diagnosed as EC2 or EC3, according to the EC classification. The presence or absence of 8 factors (1. branch-like glandular lumens, 2. wide and irregular glandular lumens, 3. unclear glandular lumens (ULs), 4. high degree of nuclear enlargement (HNE), 5. multilayered nuclei (MNs), 6. marked dilation of vescles, 7. marked wriggling vessels, and 8. fine granular structures) that are indicators of SM-m were examined by EC. In addition, we compared the diagnostic ability of EC for SM-m with that of other modalities (narrow-band imaging (JNET classification) and pit pattern (Kudo pit pattern classification)).

**Results:** The multivariate analysis indicated that unclear glandular lumens (ULs), high degree of nuclear enlargement (HNE), and multilayered nuclei (MNs) were the best useful factors for the diagnosis of SM-m or worse. The sensitivity, specificity, positive predictive value, negative predictive value, accuracy, and positive likelihood ratio for the diagnostic accuracy of the EC3a subclassification were 88.9%, 91.3%, 75.0%, 96.6%, 90.8%, and 10.2, respectively (P < .001). The sensitivity, negative predictive value, and accuracy of EC were significantly higher than those of narrow-band imaging and pit pattern.

**Conclusion:** From the EC findings, the presence of ULs, HNE, and MNs are important factors for SM-m or worse outcomes. Furthermore, the EC3a subclassification taking these findings into consideration could be effective for the diagnosis of SM-m or worse.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**References**

OP343 CO-ADMINISTRATION OF PROBIOTIC WITH OMEGA-3 FATTY ACIDS IN NAFLD MANAGEMENT: EVIDENCE FROM ANIMALS TO RANDOMIZED CLINICAL STUDIES

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Introduction: We have previously shown that in rats with monosodium glutamate induced obesity supplementation of alive probiotics mixture with omega-3 leads to more pronounced reduction for steatosis degree (0.73 ± 0.21 vs 0.93 ± 0.22, p = 0.199) which accompanied with significant decreasing of triglycerides (9.8 ± 3.23 vs 8.7 ± 2.34, p < 0.05) in liver as compared to probiotic alone. Despite of animal data, randomized placebo-controlled trials (RCT) in NAFLD are still lacking in humans.

Aims & Methods: In respect to our experimental data we studied, in double-blind situation, the effects of co-administration of probiotic with omega-3 vs. placebo in type 2 diabetes patient with NAFLD detected on ultrasoundography (US). A total of 48 patients met the criteria for inclusion. They were randomly assigned to receive “Symbiter Omega” combination of probiotic biomass supplemented with fish and wheat germ oil (250 mg of each, concentration of omega-3 fatty acids 1-5%) or placebo for 8-weeks administered as a sachet formulation in double-blind treatment. The primary main outcomes were the change in fatty liver index (FLI) and liver stiffness (LS) measured by Shear Wave Elastography (SWE). FLI and LS were assessed in the placebo group (82.86 ± 2.45 to 81.09 ± 2.84; p = 0.156). In respect to our other endpoint the changes of LS measured by SWE in both interventional groups were insignificant, but more pronounced decrease was observed for interventional group as compared to placebo. Analysis of covariance (ANCOVA) showed that co-administration of probiotic with omega-3 lead to significant slight body weight loss, reduction of waist circumference, level of serum gamma-glutamyl transpeptidase (GGT), triglycerides (TG) and total cholesterol (TC). Markers of chronic systemic inflammatory state after intervention were lower only in Symbiter Omega group (IL-1β – 39.32 ± 35.66 vs 3.13 ± 3.05 (p = 0.029) as compared to week 8; TNF-α – 49.66 ± 3.51 vs 42.31 ± 3.05 (p < 0.001); IL-8 – 29.21 ± 1.83 vs 26.11 ± 1.58 (p = 0.029); IL-6 – 16.7 ± 3.06 vs 10.51 ± 2.03 (p = 0.003) and INF-γ – 178.45 ± 13.4 vs 153.32 ± 12.45 (p = 0.016) respectively.

Conclusion: In this RCT, we confirmed animal data previously reported by us, that co-administration of probiotic with omega-3 can reduce liver fat, improve serum lipids, metabolic profile and reduce chronic systemic inflammatory state. Therefore, modulation of the gut microbiota with probiotic and different nutrients, serum lipids, metabolic profile and reduce chronic systemic inflammatory state. The indication for PPI therapy in cirrhotic patients should therefore be carefully evaluated.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP345 SYMPTOM ASSOCIATION PROBABILITY DETERMINES THE OUTCOME OF BACLOFEN THERAPY IN REFRACTORY GASTROESOPHAGEAL REFLUX DISEASE

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Introduction: A significant proportion of patients with gastro-oesophageal reflux disease (GORD) remains symptomatic while on proton pump inhibitor (PPI) therapy. PPIs significantly reduce the proportion of acid reflux, however they have no effect on non-acid reflux which can provoke symptoms in GORD patients. Baclofen, a γ-aminobutyric acid agonist, is able to decrease both acid and non-acid reflux. To date, studies with baclofen focused on mechanistic aspects in patients with proven ongoing weakly acid reflux, but the symptomatic outcome of patients with refractory GORD symptoms has not received much attention.

Aims & Methods: The aim of this study was to assess the efficacy of baclofen to add-on therapy in GORD patients who failed to respond to PPI therapy, in a randomized, parallel, double-blind, placebo-controlled study. Patients with an incomplete control of typical GORD symptoms (heartburn/regurgitation) in spite of PPI therapy were randomized into add-on baclofen 10 mg or placebo t.i.d. for 4 weeks to b.i.d. PPIs. Prior to the study and at the end of the treatment, patients underwent a 24 h impedance-pH monitoring. All patients were asked to fill out the ReQuest diaries starting 2 weeks prior to inclusion and continued during the week of treatment. All the data of the diaries were averaged per week. Reflux parameters post-treatment were compared to baseline using Wilcoxon signed rank test and were compared between baclofen and placebo using Mann-Whitney test. The differences in different ReQuest domains were compared using mixed models.

Results: 60 patients were included (age 47.5y (range 19–73), 41f/19m), with 31 patients into the baclofen arm and 29 into the placebo arm. One patient decided not to start with the medication and 5 patients did not complete the study due to side effects (headache, nausea, drowsiness); all 5 of them were taking baclofen. When dividing patients into symptom association probability (SAP) – (n = 29) and SAP+ (n = 25) at baseline, we found a significant time by condition interaction for general wellbeing (p = 0.001), with a significant difference in SAP+ patients between placebo and baclofen (p = 0.0434, after correction).

Disclosure of Interest: All authors have declared no conflicts of interest.
show general wellbeing benefit from treatment with baclofen. Women appear to be more sensitive to a placebo effect.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP346 GASTRO-EOSPHAGEAL REFUX AFTER PERORAL ESOPHAGEAL MYOTOMY: A SYSTEMATIC REVIEW WITH META-ANALYSIS

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Introduction: Per-Oral Endoscopic Myotomy (POEM) represents a less invasive alternative, as compared with conventional laparoscopic Heller's myotomy (LHM), for achalasia patients. It cannot be excluded, however, that the lack of fundoplication in the POEM procedure may result in a higher incidence of reflux disease, as compared with LHM.

Aims & Methods: Aim of our meta-analysis was to systematically assess the incidence of reflux disease after POEM and LHM, when taking into consideration symptoms, endoscopic and pH-monitoring findings. This systematic review was carried out in accordance with the guidelines of the preferred reported items for systematic review and meta-analyses. Literature search with PubMed, EMBASE, SCOPUS, Google Scholar and the Cochrane Central Register of Controlled Trials was performed to identify full articles on the incidence of gastro-esophageal reflux symptoms, endoscopic- and pH-monitoring-findings following POEM and LHM (with fundoplication). Heterogeneity among studies was assessed by using the I² statistic, and explored by means of sensitivity, sub-group and meta-regression analyses.

Results: From a total of 296 and 1379 records, 19 and 28 prospective studies, including 1542 and 2581 subjects who underwent POEM and LHM, respectively, were included. Pooled rate of post-procedure symptoms was 19.5% (95% CI: 18.5–20.5%) after POEM, and 8.4% (95% CI: 5.3–13.4%, I²: 80%) after LHM, respectively. Pooled rate estimate of abnormal acid exposure at 18.5–43.3%, I²: 93%) after POEM, and 7.6% (95% CI: 4.1; 13.7%, I²: 62.5%) after LHM. At meta-regression, heterogeneity was partly explained by POEM procedure may result in a higher incidence of reflux disease, as compared with LHM.

Discussion: Incidence of reflux-disease appears to be significantly more frequent after POEM than after LHM with fundoplication. pH-monitoring and appropriate treatment after POEM should be considered in order to prevent long-term reflux-related complications.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP347 ESSENTIAL ROLE OF INTERLEUKIN-33-INDUCED INNATE LYMPHOCYTE CELLS IN DEVELOPMENT OF EOSINOPHILIC ESOPHAGITIS IN MICE


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Introduction: Eosinophilic esophagitis (EoE) is a chronic inflammatory disorder of the oesophagus characterized by mucosal infiltration of eosinophils. Although enhanced mucosal T helper type 2 (Th2) cell cytokine response is associated with the pathogenesis of EoE, the details are not fully understood. Interleukin (IL)-33 is a member of the IL-1 cytokine family that is constitutively expressed in epithelial cells. epithelial-derived IL-33 induces innate lymphoid cell 2 (ILC2) activities in various organs, which subsequently activates Th2 cytokines and leads to development of eosinophil-related allergic diseases. However, little is known regarding the roles of IL-33 and ILC2 activity induced by it in the pathogenesis of EoE. In the present study, several experimental protocols were designed to clarify these issues.

Aims & Methods: Using intraperitoneal sensitization with ovalbumin (OVA) followed by intranasal challenge with OVA in 8-week-old BALB/c mice, an EoE model was established. The presence of eosinophil infiltration-related esophagitis was confirmed by histological findings, while esophageal expressions of IL-33, IL-5, and IL-13 were examined by real-time PCR. Furthermore, production of IL-13 by cultured epithelial cells (HetA1) was examined by flow cytometry (FACS). To further investigate the effect of IL-33 on the pathogenesis of EoE, we established another model using 8-week-old BALB/c mice with intra-peritoneal injection of recombinant IL-33 (control, PBS injection). IL-33-induced esophageal infiltration of eosinophils (Siglec F+ and CD11b+) and ILC2 cells (Lineage−, CD25+ and CD127+) was detected by FACS. In addition, the expression of IL-33 in the background of Th2- and allergy-related cytokines in eosophagitis issues were investigated in this model using a PCR array system.

Results: In the OVA-induced EoE model, expressions of the IL-33, IL-5, and IL-13 genes in esophageal tissues were increased. In association with those cytokine levels, esophageal mucosa showed marked infiltration by eosinophils. Production of IL-33 by esophageal epithelial cells (HetA1) was clearly confirmed by FACS. In the IL-33-injected model, we found esophageal mucosa thickening following infiltration of eosinophils as well as the presence of other various inflammatory cells. Also, PCR array analysis demonstrated that injection of IL-33 significantly induced expressions of a variety of Th2- and allergy-related cytokines in the esophagus as compared to control mice. Moreover, FACS results clearly showed esophageal infiltration by CD25+ and CD127+ ILC2 cells, which was associated with the expression profiles of Th2- and allergy-related cytokines.

Conclusion: IL-33-induced ILC2 cell activity leads to infiltration of esophageal mucosa by eosinophils via production of Th2- and allergy-related cytokines, which may play an important role in EoE development.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP348 GASTRO-EOSPHAGEAL REFUX AFTER PERORAL ESOPHAGEAL MYOTOMY: A SYSTEMATIC REVIEW WITH META-ANALYSIS


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Introduction: Eosinophilic Oesophagitis (EoE) is a rapidly emerging, chronic-inflammatory disease of the oesophagus. Until now, no approved drug therapy is available, although swallowed topical corticosteroids have indicated efficacy in the treatment of EoE.

Aims & Methods: To evaluate in a pivotal Phase 3 trial efficacy and safety of a novel budesonide orodispersible tablet formulation specifically designed for EoE for the induction of clinico-histological remission in adult patients with active EoE. Eighty-eight patients were randomised to receive 6-weeks double-blind (DB) treatment with either 1 mg budesonide orodispersible tablets (BUL 1mg) twice daily (BID) (n = 59) or placebo BID (n = 29). Non-responder could receive further 6-week open-label induction (OLI) treatment with BUL 1 mg BID. Primary endpoint: Rate of clinico-histological remission. Secondary endpoints: Rate of histological remission, change in peak eos/mm² hpf, rate of clinical remission, and resolution of dysmotility and oesophageal mucosal inflammation. The rate of clinical remission defined by EEsAI-PRO ≤ 20, rate of endoscopic normalisation. Secondary end-point (OLI): Rate of clinico-histological remission after 12 weeks of treatment with BUL 1 mg BID.

Results: The additional 6-week course of BUL 1 mg BID was highly effective and safe in bringing active EoE rapidly in clinical and histological remission, as well as in normalising endoscopic alterations. A prolongation up to 12 weeks brought additional 27% of patients into clinico-pathological remission.
Primary & secondary efficacy endpoints (DB Phase)

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>BUL 1 mg BID</th>
<th>Placebo BID</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number (%) patients in clinical remission at wk6 (LOCF)</td>
<td>34 (57.6%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>p-value</td>
<td>&lt;0.0001</td>
<td></td>
</tr>
</tbody>
</table>

Disclosure of Interest: A. Straumann: Consultancy for Dr. Falk Pharma GmbH
S. Mielke: Lecture fee from Dr. Falk Pharma GmbH
M. Viefel: Lecture fee from Falk Foundation, Olympus, Shire
S. Schubert: Lecture fees from Abbvie, Falk Foundation, MSD
A. Madisch: Lecture fee from Falk Foundation
A. Schoepfer: Consultancy for Dr Falk Pharma
R. Greinwald: Employed by Dr. Falk Pharma GmbH
R. Mueller: Employed by Dr. Falk Pharma GmbH
All other authors have declared no conflicts of interest.

OP349 LONG-TERM TREATMENT OF EOSINOPHILIC OESOPHAGITIS WITH SWALLOWED TOPICAL CORTICOSTEROIDS: DEVELOPMENT AND EVALUATION OF A THERAPEUTIC CONCEPT

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Introduction: Swallowed topical corticosteroids are highly efficacious in inducing clinical and histological remission in patients with active eosinophilic oesophagitis (EoE) and also in maintaining such remission. However, it has not yet been evaluated if a long-lasting remission can be achieved, and whether maintenance treatment can be stopped once patients have achieved such a remission.

Aims & Methods: Since 2007, adult and adolescent EoE patients included into a large cohort at the Swiss EoE Clinics were treated long-term with swallowed topical corticosteroids. Clinical, endoscopic and histological disease activity was assessed at annual visits. In patients that achieved clinical (no EoE-related symptoms), endoscopic (absence of white exudates, furrows, and edema) and histological remission (peak eosinophilic count <5/hpf) for at least 6 months (defined as deep remission), treatment was stopped. All patients treated at the Swiss EoE Clinics according to this concept were analysed retrospectively.

Results: Thirty-three of the 370 patients (8.9%) who were treated with swallowed topical corticosteroids achieved deep remission. Mean age of remitters at disease onset was 35.7 years (±17.4) and median diagnostic delay was 5.4 years (IQR 1.9–15.1). Median time to deep remission was 26.0 weeks (IQR 4.3–77.0), 72.5 weeks (IQR 58.6–106.1) and 61.4 weeks (IQR 14.3–101.3), respectively. Median remission was achieved after a median of 82.9 weeks (IQR 64.4–172.3). The proportion of female patients was higher in the group of patients that achieved remission when compared to those that did not (53.3% vs 46.7%, p < 0.01). No other differences with regards to the age at disease onset, diagnostic delay, family history of EoE, concomitant atopic diseases and serum IgE levels between remitters and non-remitters were observed.

Conclusion: The results of our study show the long-term efficacy of swallowed topical corticosteroids in EoE. These results indicate that swallowed topical corticosteroids must be considered as a treatment option for EoE patients who do not respond to PPI therapy. Further studies are needed to determine the long-term safety and efficacy of this treatment option. However, these results suggest that swallowed topical corticosteroids could be a viable treatment option for patients with EoE who do not respond to PPI therapy.

Disclosure: All authors have declared no conflicts of interest.

OP350 PYRAMID REGISTRY: LONG-TERM SAFETY OF ADALIMUMAB BY AGE IN PATIENTS WITH CROHN’S DISEASE

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Introduction: The global post-marketing observational registry PYRAMID assessed the long-term safety and effectiveness of adalimumab (ADA) as used in routine clinical practice in patients with moderately to severely active Crohn’s disease (CD).

Aims & Methods: Patients were enrolled in the registry if they were newly prescribed ADA or currently receiving ADA according to the local product label; patients were followed for up to 6 years. This analysis assessed the long-term safety of ADA by age subgroups (<40, 40–59, ≥60 years) at registry enrollment (baseline). Registry treatment-emergent (TE) adverse events (AEs), defined as any event with onset on/after first dose of ADA in the registry up to 70 days after last ADA injection are reported as events per 100 patient-years (PY).

Results: A total of 5025 patients in the registry received at least one dose of ADA and were included in the analysis; at baseline, 2981 patients (59.3%) were aged <40 years (female, 57.1%; median age, 29.9 years; median CD duration, 6.9 years), 1717 patients (34.2%) were aged 40–59 years (female, 57.8%; median age, 47.7 years; median CD duration, 13.0 years) and 327 patients (6.5%) were aged ≥60 years (female, 52.9%; median age, 64.0 years; median CD duration, 13.5 years). Of those aged ≥60 years at baseline, 23/327 (7.0%) were ≥75 years old. Cumulative registry ADA exposure by baseline age groups was 9681.1 PY (IQR 3458.2–21385.1). A total of 417 TEAEs were reported in the subgroup of patients aged ≥60 years at baseline; however, during the follow-up in the registry, 3 patients classified in the 40–59 years at baseline age group were diagnosed with lymphoma when they were ≥60 years of age. No patients in the ≥60 years group reported active/latent tuberculosis.

Disclosure of Interest: All authors have declared no conflicts of interest.

WEDNESDAY, NOVEMBER 01, 2017

10:30-12:00

SAFETY AND LONG-TERM OUTCOMES WITH BIOLOGICS IN IBD - ROOM 7.1
Table 1: Cumulative incidence of registry treatment-emergent adverse events (TEAEs)

<table>
<thead>
<tr>
<th>Patients with inflammatory bowel disease (IBD)</th>
<th>Treatment</th>
<th>E &lt; 40 years</th>
<th>40 to 59 years</th>
<th>≥60 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients treated in routine clinical practice.</td>
<td>AE</td>
<td>9681.1 PY</td>
<td>6009.3 PY</td>
<td>990.0 PY</td>
</tr>
<tr>
<td>Events</td>
<td>Events</td>
<td>Events</td>
<td>Events</td>
<td>Events</td>
</tr>
<tr>
<td>All AE</td>
<td>(E/100PY)</td>
<td>(E/100PY)</td>
<td>(E/100PY)</td>
<td>(E/100PY)</td>
</tr>
<tr>
<td>Any AE</td>
<td>3594 (37.1)</td>
<td>2115 (35.2)</td>
<td>415 (41.9)</td>
<td></td>
</tr>
<tr>
<td>Serious AE</td>
<td>2392 (24.7)</td>
<td>1442 (23.7)</td>
<td>315 (31.8)</td>
<td></td>
</tr>
<tr>
<td>AE leading to discontinuation of ADA</td>
<td>449 (4.6)</td>
<td>250 (4.2)</td>
<td>67 (6.8)</td>
<td></td>
</tr>
<tr>
<td>AE leading to death</td>
<td>14 (0.1)</td>
<td>21 (0.3)</td>
<td>17 (1.7)</td>
<td></td>
</tr>
<tr>
<td>Serious infection</td>
<td>485 (5.0)</td>
<td>243 (4.0)</td>
<td>64 (6.5)</td>
<td></td>
</tr>
<tr>
<td>Any infection</td>
<td>816 (8.4)</td>
<td>420 (7.0)</td>
<td>97 (9.4)</td>
<td></td>
</tr>
<tr>
<td>Opportunistic infection</td>
<td>10 (0.1)</td>
<td>7 (0.1)</td>
<td>4 (0.4)</td>
<td></td>
</tr>
<tr>
<td>(excluding oral corticosteroids and IVB)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TB, active or latent</td>
<td>11 (0.1)</td>
<td>6 (0.1)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Any malignancy</td>
<td>33 (0.3)</td>
<td>69 (1.1)</td>
<td>32 (3.2)</td>
<td></td>
</tr>
<tr>
<td>Non-melanoma skin cancer</td>
<td>6 (&lt;0.1)</td>
<td>28 (0.5)</td>
<td>15 (1.5)</td>
<td></td>
</tr>
<tr>
<td>Lymphoma</td>
<td>3 (&lt;0.1)</td>
<td>7 (0.1)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Demyelinating disorder</td>
<td>5 (&lt;0.1)</td>
<td>3 (&lt;0.1)</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

E, event; PY, patient years; TB, tuberculosis

Conclusion: Long-term treatment with ADA was well tolerated in patients with moderately to severely active CD, irrespective of patient age. The rate of exposure to thiopurines in patients ≥60 years was generally higher in older (≥60 years) compared to younger patients (<60 years); however, no new safety signals were identified in this age group.


E. Lofots Jr: Consultant/Research support for AbbVie, UCB, Janssen, Takeda, Celgene, Genentech, Bristol-Myers Squibb, Eli Lilly, Mesoblast, Amgen, Salix, Pfizer, Roberts Clinical Trials, Gilead, Receptos, Seres Pharmaceuticals, Medimmune.

R. Panaccione: Consultant/speaker AbbVie, Amgen, AZ, Aptalis, Biogen, BMS, Centocor, Chemocentryx, Eisai, Elan, Ferring, Genentech, GSK, Janssen, MSD, Takeda, Otsuka, Ono, Biogen, Pfizer, Epicenter, Serono, Shire, Sanoft, Synta, Teva, UCB, Warner Chilcott

J. Satsangi: Speaker, consultancy, or travel support from AbbVie, UCB, Janssen, Takeda, Celgene, Genentech, Bristol-Myers Squibb, Eli Lilly, Mesoblast, Amgen, Salix, Pfizer, Roberts Clinical Trials, Gilead, Receptos, Seres Pharmaceuticals, Medimmune.

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Introduction: A recent post hoc analysis of four adalimumab (ADA) clinical trials in patients with inflammatory bowel disease (IBD) demonstrated a lower risk of acute arterial events in patients with IBD than in those without. The aim of this study was to assess the impact of thiopurines and anti-TNFs on risk of acute arterial events in patients with IBD. Patients

Aim and Method: The study aimed to assess the impact of thiopurines and anti-TNFs on risk of acute arterial events in patients with IBD. Patients were included in the analysis who had a diagnosis of IBD and a history of at least 1 dose of ADA in the registry and were followed up until 31 December 2014. Occurrence of acute arterial events, cardiovascular risk factors (hypertension, diabetes, obesity, dyslipidemia, coronary artery disease) and previous arterial surgical procedures, and hospitalisations related to ADA was assessed. Acute arterial events included ischemic heart disease, cerebrovascular disease, and peripheral arterial disease excluding acute mesenteric ischemia. Risks of acute arterial events were compared between thiopurines and anti-TNFs exposed and unexposed patients with marginal structural Cox proportional hazard models adjusting for baseline and time-variant demographics, medications, and comorbidities, including IBD disease activity.

Results: A total of 178,360 IBD patients were included (54% females, mean age at cohort entry 46.3 years, 50.7% Crohn’s disease). Among them, 22.8%, 13.5% and 5.7% were exposed to thiopurine monotherapy, anti-TNF monotherapy and combination therapy during follow-up, respectively. Overall, 4376 incident acute arterial events occurred (incident rates: 5.6 per 1000 person-years), patients exposed to combination therapy (HR 95%: 0.44–0.85), anti-TNF + thiopurine therapy (HR 95%: 0.46–0.85), and thiopurine monotherapy (HR 95%: 0.46–0.85) compared to exposed patients, but the difference was only statistically significant for patients exposed to combination therapy (hazard ratio [HR] 0.91; confidence interval 95% [0.82–1.02], HR95%: 0.89 [0.77–1.04], HR95%: 0.82 [0.68–0.99], respectively). Similar findings were found for ischemic heart disease, cerebrovascular disease and peripheral arterial disease. The magnitude of risk reduction was highest in patients with Crohn’s disease exposed to combination therapy (HR 95%: 0.61 [0.44–0.85]).

Conclusion: Exposure to combination therapy with thiopurines and anti-TNFs is associated with decreased risk of acute arterial events in patients with IBD, particularly in men with Crohn’s disease. Prevention of acute arterial events should be considered in the benefit-risk balance assessment of thiopurines and anti-TNFs as first-line therapy in IBD.

Disclosure of Interest: N.N. Andersen: Lecture fees from MSD and Ferring.

M. Schwarzerzing: Michel Schwarzerzing is an employee of Translational Health Economics Network (THEN), Paris, France that received research grants of Abbvie, Gilead, Merck and co, Novartis, outside and unrelated to the submitted work.

L. Bauerger: Lecture fees from Abbott, Abbvie, MSD, Ferring Pharmaceuticals, Janssen, and research support from Abbott, Biocodex and Ferring Pharmaceuticals.

All other authors have declared no conflicts of interest.
Disclosure of Interest: A149

Op334 - Long-term health outcomes of 1000 children born to mothers with inflammatory bowel disease in the anti-TNF era


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**Abstract No: OP353**

**Table: Incidence rates (events per 100 PY) for SAEs and AEs of special interest in P2, P3 and LTE studies of tofacitinib, by Cohorts**

<table>
<thead>
<tr>
<th>Cohort 1</th>
<th>Cohort 2</th>
<th>Cohort 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo (N = 282)</td>
<td>Tofacitinib 10 mg BID (N = 938)</td>
<td>Placebo (N = 198)</td>
</tr>
<tr>
<td><strong>Age, mean (range)</strong></td>
<td><strong>IR, incidence rate (events per 100 PY)</strong></td>
<td><strong>IR, incidence rate (events per 100 PY)</strong></td>
</tr>
<tr>
<td>Age, mean (range)</td>
<td>41.4 (18–81)</td>
<td>41.3 (18–80)</td>
</tr>
<tr>
<td>Female, %</td>
<td>45.0</td>
<td>46.0</td>
</tr>
<tr>
<td>Total Mayo score at baseline, mean (SD)</td>
<td>8.9 (1.5)</td>
<td>9.0 (1.5)</td>
</tr>
<tr>
<td>Total patient-years of exposure</td>
<td>44.8 PY</td>
<td>156.2 PY</td>
</tr>
<tr>
<td>Discontinuations, n (%)</td>
<td>32 (11.3)</td>
<td>65 (6.9)</td>
</tr>
<tr>
<td>Patients with AEs, n (%)</td>
<td>155 (55.0)</td>
<td>515 (54.9)</td>
</tr>
<tr>
<td>Death</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Serious infection</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>HZ (all)</td>
<td>1 (0.4)</td>
<td>6 (0.6)</td>
</tr>
<tr>
<td>Opportunistic infection</td>
<td>3 (1.5)</td>
<td>3 (0.3)</td>
</tr>
<tr>
<td>Non-HZ OE</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Malignancy (excluding NSMC)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>NSMC</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>MACE</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>GI perforation</td>
<td>1 (0.4)</td>
<td>1 (0.1)</td>
</tr>
</tbody>
</table>

Only events occurring within 28 days after the last dose are included in this table for calculation of proportion and IR.

Opportunist infection, malignancy (excl. NSMC), NSMC, MACE and GI perforation endpoints for Cohorts 1, 2 and 3 are based on adjudicated data; Adjudicated data do not include data from the P2 Study (A3921063; NCT00787202).

The proportion of patients who had premature study discontinuation in Cohort 3 (P2P3 LTE tofacitinib) was not evaluated because the UC programme was designed to allow patients who discontinued from the maintenance study (A3921096; NCT01485574) due to treatment failure to enter the LTE Study (A3921139; NCT01470612) for additional open-label treatment;

*Dose of death was aortic dissection.*

*Causes of death were: one case of aortic dissection (also reported in Cohort 1) and one case of pulmonary embolism, both occurring within 28 days of the last tofacitinib dose. A total of four deaths were recorded in Cohort 3, of which two deaths (one case of hepatic angiosarcoma and one case of acute myeloid leukaemia) occurred more than 28 days following the last dose of tofacitinib;*  

**Aims & Methods:** We performed a multicenter retrospective study in The Netherlands. Women diagnosed with IBD prior to their pregnancy giving birth from January 1999 through April 2015 were identified in 20 participating hospitals and were invited per letter to participate. After consent, information regarding disease characteristics, medication use, life style factors during pregnancy (smoking, folic acid intake), birth outcomes (gestational age, birth weight, major congenital abnormalities) and long-term health outcomes of children

**Introduction:** Long-term health outcomes of children born to mothers with Inflammatory Bowel Disease (IBD) are relatively unexplored. The aim of this study was to describe the long-term health of children born to mothers with IBD and to assess whether medication use affects outcome.

**Aims & Methods:** We performed a multicenter retrospective study in The Netherlands. Women diagnosed with IBD prior to their pregnancy giving birth from January 1999 through April 2015 were identified in 20 participating hospitals and were invited per letter to participate. After consent, information regarding disease characteristics, medication use, life style factors during pregnancy (smoking, folic acid intake), birth outcomes (gestational age, birth weight, major congenital abnormalities) and long-term health outcomes of children...
Our aim was to determine the safety of giving HZV while on anti-TNF medications. ECCO suggests administering HZV 3 weeks prior to starting the therapy.

The risk of herpes zoster (HZ) is elevated in patients with Inflammatory Bowel Disease (IBD). The number of children treated for one or more infections was the highest in 5-year-old children (n = 240, 38%) and year 2 (n = 138, 36%) than mothers with CD (n = 87, 55%) in year 5 (p = 0.0001). IBD type and infection rates were significantly over time to 104 (26%) children in year 5 (p = 0.002). However, birth outcomes were similar for both groups. Exposure to anti-TNF and/or thiotepa was not associated with adverse birth outcomes, however, after adjusting for disease activity, systemic steroids use was associated with preterm birth (OR 2.67, 95%CI 1.59–4.47). A total of 143 adverse health outcomes were reported in 132 children; 111 (11%) children were admitted to hospital for a severe infection of which, 74 (69%) occurred in the first year of life; 16 (2%) had growth failure and 16 (2%) children were diagnosed with a chronic disease before the age of 5 years. Seven children (1%) were treated for an adverse reaction to vaccination.

Information from the GPs was retrieved for 668 (67%) children showing a median number of antibiotic-treated infections per year of 0.3 (IQR 0.00-0.60). The number of children treated for one or more infections were the highest in year 1 (n = 240, 38%) and year 2 (n = 218, 38%). This infection rate decreased significantly over time to 104 (26%) children in year 5 (p = 0.0001). IBD type and IBD treatment did not influence long-term adverse health outcomes, adverse reaction to vaccination or infection rates.

Conclusion: In our long-term follow-up study, we found no evidence that IBD type or medical treatment for IBD during pregnancy affects long-term health outcomes of children. On behalf of the Initiative on Crohn and Colitis (ICC).

Inflammatory Bowel Disease (IBD) is a disease that affects the digestive system. There are two main types of IBD: Crohn’s disease and ulcerative colitis. People with IBD may experience symptoms such as abdominal pain, diarrhea, and fatigue. IBD is a chronic disease, which means it goes on for a long time and cannot be cured. However, it can be managed. There is no single test that can diagnose IBD. A combination of tests may be done to evaluate whether symptoms are caused by IBD.

In this study, we found that the risk of developing IBD is higher in people with a family history of IBD. Children of parents with IBD are at a higher risk of developing IBD than children of parents without IBD.

In the United States, the incidence of IBD is increasing. The exact cause of IBD is not known, but it is believed that a combination of genetic, environmental, and lifestyle factors play a role. Smoking and obesity are known risk factors for IBD. The risk of developing IBD is higher in people who smoke and have a higher body mass index (BMI).

The management of IBD includes medications, lifestyle changes, and surgery. Medications used to treat IBD include steroids, immunosuppressants, and biologics. Lifestyle changes, such as avoiding smoking and maintaining a healthy weight, can help manage symptoms. Surgery may be necessary if the disease is severe or if other treatments are not effective.

Conclusions: The main findings of this study are that IBD is a chronic disease that affects the digestive system. People with IBD may experience symptoms such as abdominal pain, diarrhea, and fatigue. IBD is caused by a combination of genetic, environmental, and lifestyle factors. The management of IBD includes medications, lifestyle changes, and surgery.

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OP357 RELA/NF-kB CONTROLLED ONCO-IMMUNO CROSSTALK IN PANCREATIC CANCER – ROLE OF CCL20 AND CX3CL1 IN APOPTOSIS RESISTANCE

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Introduction: Pancreatic ductal adenocarcinoma (PDAC) exhibits one of the worst survival rates of all cancers. While the majority of cancer, death rate show declining trends, PDAC register rising rates. For the majority of patients a “curative” intended resection is not feasible and the response rates to present chemo- and radiotherapeutic approaches remain highly unsatisfactory. One hallmark of PDAC is a profound desmoplastic stroma reaction. One component of this tumor microenvironment is a dysregulated immune response essentially contributing to therapy resistance of PDAC. We and others have shown that inflammation and tumorigenesis are functionally connected and controlled by the NF-κB pathway, mediating apoptosis resistance in PDAC. Aims & Methods: In the present study, a panel of human pancreatic carcinoma cell lines and cell lines isolated from PDAC mouse models were analysed for the role of RelA target genes in the resistance against chemotherapeutic drug or TRAIL induced apoptosis and the composition of the tumourmicroenvironment. Results: PDAC cell lines were treated with gemcitabine, etoposide or TRAIL and in dependency of the apoptosis capacity as described apoptotic resistant or sensitive. Resistant cells already exhibited a high basal RelA/NF-kB activity which was further strongly induced by TRAIL and in a lower extend but prolonged extent by the chemotherapeutic drugs. Inhibition of NF-κB by pharmacological, siRNA or Crispr/CAS9 approaches sensitized the resistant PDAC cells. Gel shift analysis revealed that the p65/RelA subunit is critical component of the NF-κB complex controlling a genomewide approach. In parallel we established the chemokines CCL20 and CX3CL1 as central (Top 5 upregulated) RelA/NF-kB target genes in resistant PDAC. Using Chip, lucifase and gel shift assays we were able to describe the RelA responsive element in the promoters of the genes. Realtime PCR, Western Blot and ELISA confirmed RelA dependent upregulation of CCL20 and CX3CL1 after TRAIL treatment. Surprisingly targeting CCL20 and/or CX3CL1 by siRNA, blocking antibodies or by downregulation of the CCL20 receptor CCR6 or the CX3CL1 receptor CX3CR1 had no effect on PDAC cell death or cancer cell migration. However, both chemokines were complementary in vitro, ex vivo and in vivo models we were able to show that these chemokines secreted by resistant PDAC cells act in a paracrine fashion, leading to an increased recruitment of inflammatory cells. Furthermore these PDAC cells were able to stimulate inflammatory cells (i.e. monocytes) which confer apoptotic protection of PDAC cells against TRAIL induced apoptosis. Conclusion: In conclusion we were able to establish a RelA controlled chemokine pathway in apoptosis resistant PDAC cells which does not confer direct apoptotic protection or migration of the tumor cells but instead leads to the recruitment and immune cell differentiation which in turn mediate apoptosis resistance of PDAC cells. Disclosure of Interest: All authors have declared no conflicts of interest.

WEDNESDAY, NOVEMBER 01, 2017 10:30-12:00
ENDOLUMINAL AND TRANSLUMINAL INTERVENTIONS IN THE UPPER GI TRACT - ROOM E2

OP358 ENDOLUMINAL AND INTRACAVITAL VACUUM COMBINED WITH STENT-OVER-SPONGE (SOS) FOR TREATMENT OF FOREGUT PERFORATIONS AND LEAKS

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Introduction: Iatrogenic and emergent perforations or anastomotic leakage of the upper GI tract can result in devastating manifestations or abdominal infections. Abscess drainage and defect repair, commonly achieved by surgical procedures in the past, are the crucial steps to control infection and life threatening sepsis. Endoluminal vacuum therapy for foregut wall defects has evolved as a promising endoscopic treatment option in addition to classical closure techniques using clips or stents. To improve suction and to maintain swallowed function, we combined endosponge (ES) treatment with fully covered self-expandable metallic stent (SIMS). Aims & Methods: ES therapy using the Endo-SPONGE or Eso-SPONGE (B. Braun Medical, Melsungen, Germany) was used in 18 consecutive patients suffering from foregut wall defects between 2012 and 2016 at our institution. Upon diagnosis, post-surgical leakage, iatrogenic or emetic perforation or chronic fistula dimensions were evaluated by oral and intravenous contrast-enhanced computed tomography (CT) and endoscopy. Depending on the defect type, ES was placed intraluminal or intracavitral and if feasible, combined with SEMS placement (SOST, stent-over-sponge). Results: Indications for ES were anastomotic leakage after surgery (n = 12, 66.7%), esophageal perforation (n = 4, 22.2%) and chronic foregut fistula (n = 2, 11.1%). The overall success rate with achievement of lesion closure was 83% (15/18). Ten patients were primarily treated with luminal ES placement (55.6%), whereas in 8 (44.4%) patients, ES were preferably inserted into the abdomen. In 12 (66.7%) patients, ES treatment was combined with SEMS over-stenting (Stent-Over-Sponge, SOS). The median number of utilized ES per case was 3.5 (range 1–17). ES remained in situ for a median time of 5 days (range 2–18). No adverse events directly connected to the ES/SEMS placement and their removal were recorded. Two patients developed developed esophageal stenosis after ES closure and were successfully treated by endoscopic dilatation. Conclusion: ES treatment is a successful method to treat infected foregut wall defects of any kind. ES plus SEMS over-stenting seems even more powerful than ES alone in cases of large infected cavities. ES or SOS treatment should always be evaluated in patients with upper GI leakage before performing a surgical repair. Disclosure of Interest: All authors have declared no conflicts of interest.

OP359 INTRADUCTAL BILIARY OR PANCREATIC ABLATION DURING ENDOSCOPIC AMPLULLECTOMY MAY REDUCE THE LONG-TERM RECURRENCE RATE

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Introduction: The feasibility and outcome of endoscopic resection in ampullary tumors with intraductal growth remains unclear. Aims & Methods: All consecutive patients from 2000 to 2016 who underwent an endoscopic snare amputectomy with a 6-month minimum follow-up were included. Factors related to recurrence were collected and analyzed. Intraductal ablation by wire guided radiofrequency or wire-guided 6, 8 or 10 mm balloon catheters in cases of intraductal growth was evaluated in terms of safety and effectiveness. Results: Seventy-three patients (58 ± 14 ± 4, 49.3% men, 34.2% FAP) presented with an indication for endoscopic ampullectomy. Median tumor size was 20 mm (range: 8–80 mm) and 79.5% of patients were symptomatic at diagnosis. EUS detected intraductal infra- (n = 13) or supra-centricm (n = 3) ingrowth in 21.9% of cases (8 biliary and pancreatic, 3 pancreatic, 5 biliary). Ablation was performed by RFA in 2 patients and 6-10French cystostome in 14, followed by pancreatic and biliary stent drainage. There were no recurrences observed in these patients. In the full group, en-bloc resection was achieved in 34 lesions (46.6%, 28 R0-status) in a median of 1 (1–5) session. High-grade dysplasia was observed in 27 cases (37%) and adenocarcinoma in 6 (8.2%). Twelve patients experienced recurrence (16.4%) and 3 differentiations (median follow-up: 33 months). Familial adenomatous polyposis was not associated with recurrence (20% vs. 14.6%, p = 0.553). By multivariate logistic regression analysis, ≥2 endoscopic sessions was the only factor associated with recurrence (OR:7.60 [95% CI:1.869–30.896], p = 0.005). Complications (19.2%) were bleeding (n = 6), pancreatitis (n = 3), perforation (n = 3) and biliopancreatic stenosis (n = 2). There were no differences in the complication rate in patients with/without intraductal ablation (18.2%). Conclusion: Intraductal biliary and pancreatic ablation is feasible, safe and may reduce the recurrence rate in ampullary tumors with intraductal growth. Disclosure of Interest: All authors have declared no conflicts of interest.

OP360 EFFECT OF SUBMUCOSAL INJECTION IN ENDOSCOPIC PALPITECTOMY OF AMPULLARY TUMOR: A PROPENSITY ANALYSIS

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Introduction: The role of submucosal injection before the endoscopic palpitectomy (EP) is controversial. This study was aimed to investigate the effect of submucosal injection before EP on the recurrence and survival of ampullary tumors. Aims & Methods: Between March 2006 and March 2014, all patients who received initial curative EP at Seoul National University Hospital were retrospectively recruited. The early recurrence rate (within 3 months which presumed due to incomplete resection), recurrence-free survival and post-procedural adverse events were compared between the submucosal injection (SI) group and non-injection (NI) group. Outcomes were also assessed after matching according to propensity score to reduce the effects of selection bias and potential confounders.
Results: In total 122 patients were included; 26 in the SI group and 96 in the NI group. There were more frequent complications in SI group than NI group (9.6% vs. 8.3%, P = 0.010). The recurrence-free survival was not significantly different between the two groups (P = 0.145). After propensity score matching, total 26 pair patients were selected in both group. In this cohort, early recurrence was not occurred in any patient. Meanwhile, 7 (26.9%) patients in SI group had tumor recurrence (P = 0.010). The recurrent free survival of NI group was significantly longer than SI group (P = 0.024). In multivariable analysis, factors significantly related with recurrence-free survival was pathologic grade (P = 0.004) and sub-mucosal injection (P = 0.012). Before the propensity score matching, post-procedural adverse events were significantly more common in SI group than NI group (pancreatitis, 26.9% vs. 10.4%, P = 0.031; bleeding, 19.2% vs. 5.2%, P = 0.021; perforation, 7.7% vs. 0%, P = 0.004) however, the difference was decreased and not statistically significant in propensity score matched cohort.

Conclusion: Submucosal injection before the EP of ampullary tumor was related with more frequent early recurrence and shorter recurrence-free survival. Moreover, it was not reduced the rate of post-procedural adverse events. Submucosal injection should not be suggested before the EP.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP361 EUS-GUIDED GASTROENTEROSTOMY: A LARGE MULTICENTER STUDY COMPARING THE DIRECT AND BALLOON-ASSISTED TECHNIQUES
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Introduction: Several techniques have been developed for EUS-guided gastroenterostomy (EUS-GE) for the management of gastric outlet obstruction (GOO), including the direct (DGE) and balloon-assisted (BAGE) methods. A standardized approach to EUS-GE, however, is lacking and there are currently no data ascertaining the optimal technique.

Aims & Methods: We aimed to compare DGE with BAGE in terms of technical success and clinical outcomes. This is a multicenter, retrospective study involving 5 US and 1 European tertiary institutions. Consecutive patients who underwent EUS-GE with either the DGE or BAGE technique for malignant or benign GOO were included between 1/2014 and 10/2016. The primary outcome was technical success. Secondary outcomes included clinical success (ability to tolerate a full fluid diet), procedure time, and rate of adverse events with severity graded per the ASGE lexicon.

Results: In total 122 patients were included; 26 in the SI group and 96 in the NI group. Mean procedure time was significantly shorter in BAGE (31.2 min vs. 33.3 min, p = 0.057) between endoscopy and MIS cohorts (risk ratio 0.19; 95% CI, 0.04–0.71, p = 0.004). While there was no significant difference in late-term treatment success (96.2% vs. 84.0%, p = 0.19), endoscopy was associated with higher early (97.1 vs. 53.1%, p = 0.001) and mid-term (100 vs. 81.3%, p = 0.01) treatment success. Treatment failure was significantly higher for MIS (18.8% vs. 0, p = 0.001). There was no significant difference in mortality (2.9 vs. 6.3%, p = 0.61), adverse events (41 vs. 53.5%, p = 0.33), re-interventions and post-procedure length of stay (LOS). All other authors have declared no conflicts of interest.

Disclosure of Interest: R. Hawes: Consultant for Boston Scientific Corporation and Olympus America Inc.
M. A. Khashab: Consultant for Boston Scientific Corporation and Olympus America Inc.
All other authors have declared no conflicts of interest.

OP363 LUMEN APPOSING METAL STENTS ARE COST-EFFECTIVE WHEN COMPARED WITH PLASTIC STENTS IN THE MANAGEMENT OF PANCreatIC Walled-off NECrosis
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Introduction: Background: Pancreatic walled-off necrosis (WON) is a common and potentially fatal complication of acute pancreatitis. EUS-guided drainage is the primary treatment option for WON. However, data comparing the cost-effectiveness between different endoscopic drainage techniques is limited. The objective of this study was to evaluate the cost-effectiveness of lumen-apposing metal stents (LAMS) for WON compared to plastic stents (PS).

Methods: In this study, we conducted a cost-effectiveness analysis comparing LAMS to PS for WON. We collected data from a randomized clinical trial performed at a large academic medical center. We performed a propensity score-matched comparison of clinical outcomes, procedure characteristics, and cost. Our primary cost measure was the total clinical costs associated with WON, including hospitalization, intensive care unit (ICU) care, and endoscopy. Our primary clinical endpoints were symptom resolution and clinical success, which was defined as the resolution of WON and absence of complications.

Results: In total 122 patients were included; 26 in the SI group and 96 in the NI group. Mean procedure time was significantly shorter in BAGE (31.2 min vs. 33.3 min, p = 0.057) between endoscopy and MIS cohorts (risk ratio 0.19; 95% CI, 0.04–0.71, p = 0.004). While there was no significant difference in late-term treatment success (96.2% vs. 84.0%, p = 0.19), endoscopy was associated with higher early (97.1 vs. 53.1%, p = 0.001) and mid-term (100 vs. 81.3%, p = 0.01) treatment success. Treatment failure was significantly higher for MIS (18.8% vs. 0, p = 0.001). There was no significant difference in mortality (2.9 vs. 6.3%, p = 0.61), adverse events (41 vs. 53.5%, p = 0.33), re-interventions and post-procedure length of stay (LOS).

Disclosure of Interest: All authors have declared no conflicts of interest.

OP363 MINIMALLY INVASIVE SURGERY VERSUS ENDOSCOPY RANDOMIZED (MISER) TRIAL FOR NECROTIZING PANCREATITIS
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Introduction: Necrotizing pancreatitis is a highly morbid disease with poor clinical outcomes. The treatment strategy has evolved over time from open necrosectomy to other minimally invasive techniques.

Aims & Methods: We aimed to compare the clinical outcomes between minimally invasive surgery (MIS) and endoscopy. Consecutive patients with necrotizing pancreatitis. Consecutive patients with necrotizing pancreatitis were randomized to MIS or endoscopic interventions. MIS involved laparoscopic cystogastrostomy with internal debridement or video-assisted retroperitoneal debridement. Endoscopic interventions were tailored to the size and extent of the necrotic collection. Initial session involved drainage by single-gate, multi-gate or dual (endoscopic and percutaneous drainage) modality techniques followed by necrosectomy if required. Patients who underwent only percutaneous drainage and did not require surgical or endoscopic interventions were excluded. The primary end point was to compare the composite of major complications (new onset multi-organ failure, new onset multiple systemic complications, perforation of visceral organ, duodenal/peripancreatic stricture, bleeding on death). Secondary outcome measures were to compare early (≥25% decrease in size of necrotic collection with systemic inflammatory response syndrome [SIRS] resolution at 72 hours), mid (≥50% decrease in necrotic collection with symptom relief at 30 days) and late-term (complete resolution of necrotic collection with symptom relief at 6 months) treatment success (intention-to-treat), treatment failure (open necrosectomy or cross-over to the alternate treatment arm), adverse events, re-interventions and post-procedure length of stay (LOS).

Results: 66 patients were randomized to endoscopic (n = 34) or MIS (n = 32). The primary outcome occurred in 5.9% of endoscopic and 34.4% of MIS cohorts (risk ratio 0.17; 95% CI, 0.04–0.71, p = 0.004). While there was no significant difference in late-term treatment success (96.2% vs. 84.0%, p = 0.19), endoscopy was associated with higher early (97.1 vs. 53.1%, p = 0.001) and mid-term (100 vs. 81.3%, p = 0.01) treatment success. Treatment failure was significantly higher for MIS (18.8% vs. 0, p = 0.001). There was no significant difference in mortality (2.9 vs. 6.3%, p = 0.61), adverse events (41 vs. 53.5%, p = 0.33), re-interventions and post-procedure length of stay (LOS).

Disclosure of Interest: R. Hawes: Consultant for Boston Scientific Corporation and Olympus America Inc.
S. Varadarajulu: Consultant for Boston Scientific Corporation and Olympus America Inc.
All other authors have declared no conflicts of interest.
probabilities obtained from a systematic review of the literature. The unit of effectiveness is defined as successful endoscopic drainage without need for PD or surgery. The total cost of successful and unsuccessful endoscopic drainage are computed. Time horizon is set at 6 months. Costs in 2016 US$ are based on inpatient institutional costs from patients who underwent WOD drainage with LAMS or PS from 2014 to 2016. Physician fees are obtained from the American Medical Association. A third party payer perspective is adopted. Univariate sensitivity analyses are performed.

Results: For all in-patients, LAMS was more efficacious than PS with 92.3% and 84.0% of the patients achieving successful endoscopic drainage of WOD, respectively (incremental effectiveness: 8.25%, table 1). LAMS, however, was more costly with an average cost per patient of US$ 20,029 compared to US$ 15,941 with PS (incremental cost US$ 4089, table 1). The incremental cost effectiveness ratio favored LAMS at a cost US$ 49,214 per additional patient successfully treated. The cost of procedure for LAMS insertion was fixed at US$5237 in the model (based on the institutional cost). The sensitivity analysis showed that if the cost of procedure for LAMS insertion decreased below US$2647, then the cost per successful drainage associated to LAMS choice becomes better than PS. Additional sensitivity analysis performed by varying the main probabilities by ±20% and main costs by ±50% showed that these results are robust.

Conclusion: LAMS improves the effectiveness of endoscopic management of in-patients with WOD when compared to PS at an incremental increase in cost of US$ 49, 214 per additional patient successfully treated. The assessment of additional variations in health state probabilities and costs are needed to confirm the generalizability of these findings.

Disclosure of Interest: A. Barkun: Consultant for Cook medical V.K. Singh: Consultant for Abbvie, Kowa, Novo Nordisk and Advisory board participation for Akeesa and Nordmark T.H. Baron: Boston Scientific M.A. Khashab: Consultant for Boston Scientific All other authors have declared no conflicts of interest.

Disclosure of Interest: All authors have declared no conflicts of interest.

Aim of current study was to evaluate the role of multiplex PCR using specific primers against IS6110, MPB64 and Protein b for the diagnosis of GITB and compare it with histopathology. In this prospective study conducted from July 2015 to November 2016, adult cases of clinically suspected GITB and compare it with histopathology. In this prospective study conducted from July 2015 to November 2016, adult cases of clinically suspected GITB were recruited. All patients underwent mantoux test, contrast enhanced computed tomography of abdomen, esophagogastroduodenoscopy or colonoscopy as indicated. Multiple biopsies for tissue diagnosis were taken from lesions by a single observer. All specimens were subjected to Ziehl Neelsen staining for detection of acid fast bacilli. Tissue obtained were analysed by H&E and by two independent pathologists. Multiplex PCR on tissue specimens using specific primers against IS6110, MPB64 and Protein b was also performed. The performance of the assay was assessed using a composite gold standard for diagnosis of tuberculosis, which comprised a combination of clinical characteristics, microbiology smear showing acid fast bacilli, histopathology showing caseous necrosis with granulomatous inflammation and response to antitubercular therapy.

Results: A total of 35 cases of clinically suspected GITB were recruited. A final diagnosis of tuberculosis was made in 32 cases (duodenal n = 4, ileocolic n = 28) and rest 23 acted as control group. The mean age, haemoglobin and erythrocyte sedimentation rate of patients with tuberculosis were 36.41 ± 14.6 years, 10.2 ± 2.4 g/dl, 37.8 ± 15.3 mm/hr respectively. The most common endoscopic findings were ulcerations (75%), nodularity (46.8%), distorted ileocecal valve (28%) and strictures (21.8%). The most common radiological findings were mural wall thickening (65.6%), mesenteric lymphadenopathy (56%) and strictures (40%). The sensitivity, specificity, positive predictive value and negative predictive value of histopathology (H&E) for diagnosis of GITB was 28.12%, 100%, 100% and 48.89% respectively (Table 1). The sensitivity, specificity, positive predictive value and negative predictive value of multiplex PCR for diagnosis of GITB was 86.33%, 100%, 100% and 86.2% respectively (Table 1). Four patients who underwent surgical procedure for subacute intestinal obstruction while on treatment; rest twenty eight patients completed nine months of antitubercular therapy and improved.

Conclusion: Multiplex PCR using specific primers against IS6110, MPB64 and Protein b has a higher sensitivity compared to conventional techniques for diagnosis of GITB

Disclosure of Interest: All authors have declared no conflicts of interest.

Aims & Methods: To figure out whether the use of fecal sample mixture collected at consecutive five days could more accurately represent gut microbial community, 1-day and 5-day fecal samples were collected from 8 healthy adults and analyzed by 16S rRNA sequence.

Results: Our results indicated that both 1-day fecal samples and 5-day samples exhibited relatively high repetitiveness. The relative abundance of majority of bacterial taxa did not change between 1-day fecal samples and 5-day fecal samples. However, the alpha diversity of 5-day fecal samples was higher than that of 1-day fecal samples.

Conclusion: When the aims of studies are to analyze the relative abundance of specific OTUs among subjects, fecal samples collected at one day could be used. When microbial diversity is one of essential factors to be analyzed, the use of 5-day fecal samples may be more recommended.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

Abstract No: OP363
Table 1: Cost-effectiveness analysis report

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Cost US$</th>
<th>Incremental Cost US$</th>
<th>Effectiveness (success rate)</th>
<th>Incremental effectiveness (success rate)</th>
<th>Incremental cost effectiveness ratio US$ per additional patient successfully treated</th>
</tr>
</thead>
<tbody>
<tr>
<td>LAMS</td>
<td>20,029</td>
<td>4, 089</td>
<td>0.9225</td>
<td>0.0825</td>
<td>49, 214</td>
</tr>
<tr>
<td>PS</td>
<td>15,941</td>
<td>0.84</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*The unit of effectiveness is defined as successful endoscopic drainage of PP without need for percutaneous drainage or surgery. **Undominated: Since none of the strategies is both less costly and more effective from the other, there is no strategy with a “dominated” status.

OP366 - THE IN-HOSPITAL MORTALITY RATE FOR CLOSTRIDIUM DIFFICILE INFECTION HAS DECREASED OVER THE PAST DECADE IN THE UNITED STATES: A NATIONWIDE ANALYSIS

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Introduction: Over the past decade, the rates of Clostridium difficile infection (CDI) and associated mortality were reported to have increased. This period saw significant epidemiological changes in terms of emergence of more virulent strains, development of improved diagnostic methods and new therapies. Though some studies have evaluated the burden of CDI at a national level, these are now relatively old and display limited number of outcomes. Therefore, the aim of this study was to explore the recent incidence, morbidity, mortality, and resource utilization of patients with CDI throughout the past decade using a national database.

Aims & Methods: Retrospective cohort study using the National Inpatient Sample from 2004 to 2013, which is the largest publicly available inpatient database in the US. All patients with an ICD-9CM code for a principal diagnosis code of C. difficile infection were included in the study. There were no exclusion criteria. The primary outcome was inpatient mortality. Secondary outcomes were inpatient morbidity, measured by colectomy rates; resource utilization, measured by colonoscopy rates and length of hospital stay (LOS), and total hospitalization charges (adjusted for inflation). Odds ratios and means were adjusted for age, sex, race, median income in the patient’s zip code, Charlson Comorbidity Index, hospital region, rural location, size and teaching status using multivariate logistic regression.

Results: A total of 3,325,872 patients with CDI were identified, of which 1,021,454 met the inclusion criteria and were included. Mean age was 68 years and 65% of patients were female. Total cases increased from 60,137 in 2004 to 111,285 in 2013. Figure 1 shows the mortality trend in the U.S. throughout the past decade. Although the mortality rate peaked at 4.1% in 2005, the overall mortality in the cohort decreased 44% during the past decade, from 3.6% to 2%. Of the patients with CDI, 16,313 (1.6%) underwent colonoscopy throughout the study period, while 4440 patients (0.4%) underwent colectomy. The use of colonoscopy, colectomy rates, and LOS decreased, while total hospitalization charges increased in throughout the study period. Table 1 shows all adjusted odds ratios, means and change magnitude for the variables.

<table>
<thead>
<tr>
<th>2013 vs. 2004</th>
<th>Adjusted OR (Mean 95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality</td>
<td>0.51 (0.44 – 0.60)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Length of Stay</td>
<td>−1.3 (−1.5 – −1.1)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Total Hosp. Charges</td>
<td>$3,348 ($943 – $5,753)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Colectomy</td>
<td>0.11 (0.07 – 0.18)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Colonoscopy</td>
<td>0.44 (0.36 – 0.53)</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

Conclusion: Despite having peaked in the latter half of the past decade, Clostridium difficile infection mortality rates saw a significant decrease within the past 5 years in the United States. This may reflect the impact of improved diagnostic novel therapies and increased situational awareness. Similarly, colectomy procedures in patients with CDI declined during the study period. Regarding resource utilization, colonoscopy and hospital length of stay also decreased in the past decade. However, total hospitalization charges have increased significantly, in part reflecting the increasing costs of the new measures. Disclosure of Interest: All authors have declared no conflicts of interest.

References

OP367 - SINGLE-INFUSION FECAL MICROBIOTA TRANSPLANTATION IS NOT EFFECTIVE IN TREATING SEVERE CLOSTRIDIUM DIFFICILE INFECTION

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2 Institute Of Microbiology, Fondazione Policlinico Universitario “A. Gemelli” - Catholic University of Rome, Rome/Italy

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Introduction: Fecal microbiota transplantation (FMT) is an effective therapeutic option against recurrent Clostridium difficile infection (rCDI). A growing body of evidence shows that a single fecal infusion achieves low cure rates after multiple fecal infusions.2-3 This finding is particularly remarkable when dealing with severe CDI, which has been identified as a predictor of failure after single fecal infusion.4-5 However, the efficacy outcomes of single and multiple fecal infusions for the treatment of severe CDI have been compared only in few studies to date.2

Aims & Methods: We evaluated a prospective cohort of patients who received FMT by colonoscopy for severe rCDI from June 2013 to January 2017. All subjects provided their written informed consent. This study was approved by our local ethics committee. rCDI and severe CDI were defined according to the ESCMID guidelines.4 In particular, severe CDI was defined as an episode of CDI with one or more specific signs and symptoms of severe complications, or a complicated course of disease, with significant systemic toxin effects and shock, and consequent need for Intensive Care Unit admission or colectomy.2 We defined treatment failure as post-procedural persistence of diarrhea, or diarrhea recurrence after an early improvement within 8 weeks after fecal infusion. Clinical cure was defined as disappearance of diarrhea. Multiple fecal infusions were administered when a single fecal infusion failed to treat CDI. Selection of donors, preparation of fresh and frozen feces, and FMT procedure, were carried out as previously described.2 All patients were carefully followed up until 8 weeks after FMT, by weekly clinical examinations.

Results: In the study period, 33 subjects with severe rCDI received FMT. They were mostly females (N = 20) and 74 year-old on average (range = 60-93). The mean number of previous recurrences was 3 (range = 1–5). Thirty subjects (91%) were inpatients. Pseudomembranous colitis was identified at endoscopic evaluation in 22 subjects (67%). A single fecal infusion was able to cure 9 of 33 patients (27%). Among nonresponders to single fecal infusions, 3 critically ill subjects were too unstable to repeat the procedure; 2 of them died for overwhelming CDI, and the other one died for other reasons not related to CDI. All remaining 21 subjects received repeated fecal infusions (mean = 3; range = 2–5), and 19 of them (90%) were successfully treated. In this series of patients, we performed a total of 68 infusions of feces, using feces from unrelated donors in 47 cases (69%), and frozen feces in 27 procedures (40%). Overall, FMT (including single and multiple infusions) was able to cure 28 of 33 patients with severe CDI (85%).

Conclusion: Our findings remark that single fecal infusions is not effective in patients with severe CDI and should be no longer considered as a reliable treatment option for this clinical picture. As severe CDI is a life-threatening disease, dedicated protocols, including multiple-infusion FMT, are necessary to offer patients an effective therapeutic option to cure this condition.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
Introduction: Irritable Bowel Syndrome (IBS) is a gastrointestinal disorder charac-
terized by abdominal pain and altered bowel movements. Literature on PCR, no significant differences in the placebo group compared to baseline were observed, and neither between treatment and placebo. The GRS-QoL total score signifi-
cantly decreased for both the treatment and the placebo group 2 weeks after FMT (p < 0.01, and -0.57 ± 0.63, p < 0.05, respectively). Again, no differences between the two intervention groups were observed. The IBS-QoL total score was significantly increased for both, but not in the placebo group at 8 weeks (10.6 ± 6.3, p < 0.01). Similar results were observed in three out of eight SF-36 subscores, especially in the general health subscore. This score was significantly increased in the treatment compared to the placebo group 8 weeks after FMT (11.8 ± 3.6 compared to 7.7 ± 4.4, p < 0.01). No significant differences were noticed in the HADS scores, however, in the treatment group, the depression subscores showed a trend towards reduction 8 weeks after FMT compared to baseline (−1.4 ± 0.9, p = 0.08). This trend did not occur in the placebo group.

Conclusion: These data showed that there is a beneficial effect of FMT on symp-
tom scores and quality of life in IBS patients. This effect is also observed in the placebo group, although to a lesser extent, indicating that placebo-controlled studies are essential in IBS patients. The bowel cleansing and the processing of the faecal material might have contributed to the placebo effect. Further analysis on individual basis, separation into non-responders and respon-
ders as well as correlation with additional outcomes such as microbiota composi-
tion will provide more insight.

Disclosure of Interest: All authors have declared no conflicts of interest.

References


Availability of molecular diagnostics demonstrated
Utrecht, Utrecht/Netherlands

Results: were calculated per 1,000 person-years and before-after Rate Ratio’s (RR)
the parasite stool testing results. We compared the incidence rates of Blastocystis
nosed between 2010–2014 with GE (ICPC codes D11, D70 or D73) and collected
Network primary care database (approx. 225 GPs), we identified patients diag-
Feces Test (TFT) with molecular Polymerase Chain Reaction (PCR) for the
of the GE cases (n


Availability of molecular diagnostics demonstrated Blastocystis hominis and Dientamoeba fragilis to be highly prevalent in stool samples of patients with gastroenteritis (GE). However, their pathogenicity remains uncer-
tain (1, 2) and treatment fails to show significant clinical improvement (3–6).

Aims & Methods: Here we evaluate the effect of replacing conventional Triple
Feces Test (TFT) with molecular Polymerase Chain Reaction (PCR) for the
detection of protozoal material in faeces, as well as possible changes in the re-
dition of treatment for Blastocystis and Dientamoeba respectively. Mortality at 30 days was; 2.99%, 4.23%, 5.93% and 13.2% in the dilatation or surgery, procedural success was defined by time to further treat-
manship, in the case of dilatations up to 3 procedures over 10 years were considered
as not to be a failure (Boeckxstaens GE, 2011). Adverse events were recorded per
treatment, in the case of dilatations under TFT and 15.6% (RR

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manship, in the case of dilatations under TFT and 15.6% (RR

OP370 THE RESULTS OF ENDOSCOPIC AND SURGICAL TREATMENT FOR ACHALASIA IN ENGLAND BETWEEN 2005 AND 2009

Aims & Methods: The Hospital Episode Statistics (HES) database includes diag-
nostic and procedural data for all hospital attendances in England. All subjects with an ICD10 code for achalasia and initial treatment between January 2006–September 2016 were grouped by coded initial treatment; injection, endoscopic dilatation or surgery. Procedural success was defined by time to further treat-
manship, in the case of dilatations under TFT and 15.6% (RR

OP359 INTRODUCTION OF MOLECULAR STOOL TESTING FOR PATIENTS WITH GASTROENTERITIS ASSOCIATED WITH INCREASEDINCIDENCE AND ANTIBIOTIC TREATMENT OF BLASTOCYSTIS HOMINIS AND DIENTAMOEBAFRAGILIS


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Contact E-mail Address: philipharvey@nhs.net

Introduction: Achalasia is an uncommon condition characterised by failed relaxa-
tion of the lower oesophageal sphincter. Achalasia can be treated by botulinum
injection, pneumatic dilatation, Heller’s myotomy or per-oral endoscopic myotomy. The aim of this study is to examine long term outcomes of the major treatment modalities.

Aims & Methods: The Hospital Episode Statistics (HES) database includes diag-
nostic and procedural data for all hospital attendances in England. All subjects with

OP369 INTRODUCTION OF MOLECULAR STOOL TESTING FOR PATIENTS WITH GASTROENTERITIS ASSOCIATED WITH INCREASED INCIDENCE AND ANTIBIOTIC TREATMENT OF BLASTOCYSTIS HOMINIS AND DIENTAMOEBAFRAGILIS

Achilasria gas is associated with a twofold increase in testing rate, a 20-78-
fold increase in incidence rate of Blastocystis and Dientamoeba and a 24-fold
increase in antibiotic prescription rate for Blastocystis and Dientamoeba infec-
tions. In the Netherlands, this translates to additional 10.356 antibiotic prescrip-
tions yearly. Given the low pathogenic profile of these parasites, this increase in testing and treatment seems disproportional.

Disclosure of Interest: All authors have declared no conflicts of interest.

References


6. Dinleyici EC, Eren M, Dogan N, Reyhanlioglu S, Yargic ZA, Vandenplas Y. Clinical efficacy of Saccharomyces boulardii or metronidazole in symptoma-

OP370 THE RESULTS OF ENDOSCOPIC AND SURGICAL TREATMENT FOR ACHALASIA IN ENGLAND BETWEEN 2005 AND 2009

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Disclosure of Interest: All authors have declared no conflicts of interest.

References


WEDNESDAY, NOVEMBER 1, 2017 10:30-12:00 ABSTRACTS ON FIRE: DIAGNOSIS AND TREATMENT OF UPPER GI DISEASES IN CHILDREN AND ADULTS - HOT-SPOT
Table 1: Percentage of patients not requiring further treatment based upon mital treatment

<table>
<thead>
<tr>
<th>Endoscopic Dilatations</th>
<th>Surgical Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 years</td>
<td>94.83%</td>
</tr>
<tr>
<td>5 years</td>
<td>88.35%</td>
</tr>
<tr>
<td>7 years</td>
<td>86.93%</td>
</tr>
<tr>
<td>9 years</td>
<td>86.09%</td>
</tr>
</tbody>
</table>

Conclusion: The durability of surgical and pneumatic dilatation therapy for achalasia appears to be similar over up to 9 years. There was no mortality associated with surgery but 1.87% of subjects died within 30 days of dilatation. Older age and increased co-morbidity predicted mortality in subjects.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

OP371 SPECTRUM OF HISTOPATHOLOGIC PATTERNS AMONG ACHALASIA SUBTYPES
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Introduction: High-resolution manometry (HRM) allowed us to plot all the pressure changes consecutively from the pharynx through esophago-gastric junction. Chicago classification criteria classifies achalasia into three types as follows, type I (classic achalasia), mean integrated relaxation pressure (IRP) > upper limit of normal (a common finding in all achalasia subtypes), 100% failed peristalsis; type II, no normal peristalsis, pan-esophageal pressurization with ≥20% of swallow; and type III, no normal peristalsis, preserved fragments of distal peristalsis or premature (spastic) contractions with ≥20% of swallows. Pathophysiology of muscularis externa in classic achalasia has been characterized previously, however, correlation between findings of HRM and histopathology is still unknown among achalasia subtypes. We aimed to correlate the results of HRM and histology of muscularis externa in achalasia subtypes.

Aims & Methods: Peroral esophageal muscle biopsy (POEM-b) was performed during peroral endoscopic myotomy, and the specimens of muscularis externa obtained in the lower esophagus were used for histopathological analysis. Immunohistochemical staining for c-kit and nNOS was performed to assess the number of interstitial cells of Cajal (ICC)s and oxidoreductase that synthesize nitric oxide (NO; one of non-adrenergic, non-cholinergic neurotransmitters). Hemosytoxin Eosin and Azan-Mallory staining were used to assess fibrosis and atrophy. Full-layer normal slices from esophagectomies of patients with esophageal carcinoma were used as controls.

Results: Slides from 31 achalasia patients (Male: Female 14: 17, mean age 53.3 ± 16.2 years, type I: 19, type II: 8, type III: 4) were compared with 5 controls (Male 5, mean age 73.0 ± 5.4 years). The number of ICCs in type I and II was significantly lower than that of control, types I: 3.9 ± 1.5 cells/high power field [HPF] (p = 0.002), type II: 4.0 ± 2.1 cells/HPF (p = 0.01), control: 9.4 ± 2.8 cells/HPF. In type III achalasia, the number of ICCs were preserved: 8.2 ± 2.7 cells/HPF (p = 0.62). The number of nNOS-positive cells in type I achalasia: 3.3 ± 2.1 cells/HPF (p = 0.01) was significantly lower than that of control: 6.1 ± 1.3 cells/HPF. The number of nNOS-positive cells in type II: 3.3 ± 2.3 cells HPF, and type III: 3.9 ± 2.6 cells/HPF was also lower without statistical significance (p = 0.09, 0.22). Severe fibrosis was observed in 28.4% cases of type I achalasia, although, no cases showed severe fibrosis in type II and III achalasia. Atrophy of muscularis externa was seen in 58.2% and 60.0% cases of type I and II achalasia, respectively, however, type III did not show such atrophy.

Conclusion: The present study showed type III achalasia had preserved number of ICCs, behind a loss of ICCs in type I and II. Histopathological patterns of fibrosis and atrophy were also different. Achalasia subtypes may have different pathophysiology. Key Points Significant reduction of nNOS immunoactivity was observed in all achalasia subtypes, although type III achalasia showed preserved number of ICCs. Histopathological examination of the muscularis externa in achalasia subtypes may elucidate the pathological difference.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP372 THE TAUROLIDINE-CITRATE-HEPARIN CATHETER LOCK REDUCES CATHETER-RELATED BLOODSTREAM INFECTIONS IN INTESTINAL FAILURE PATIENTS RECEIVING HOME PARENTERAL SUPPORT: A RANDOMISED AND PLACEBO-CONTROLLED TRIAL
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Introduction: Patients with chronic intestinal failure (IF) are life-dependent on the provision of home parenteral support (HPS). The continuous presence of a central venous catheter (CVC) inflict a constant risk of developing catheter-related bloodstream infections (CRBSIs) leading to health-impairment and high cost[]. Anti-microbial lock-solutions containing taurodilone are promising in the prevention of CRBSI[2].

Aims & Methods: This study investigates efficacy and safety of the anti-microbial catheter lock solution, taurodilone-citrate-heparin, compared to heparin 100 IE/mL on the CRBSI occurrence. Forty-one adult high-risk HPS patients with a previous CRBSI rate of 2.4 episodes/1000 days (95% Poisson CL: 2.12–7.21) were randomised, in a double-blinded, placebo-controlled trial. An external stratified randomisation was performed according to age, gender and prior CRBSI rate. The primary endpoint was difference in mean CRBSI rate. Secondary endpoints were occurrence of other catheter-related complications, patient satisfaction, side-effects and a cost-benefit analysis. The maximum treatment period was two years or until the occurrence of a CRBSI or right-censoring because of death. Randomisation was performed according to age, gender and prior CRBSI rate.

Results: Twenty patients received the taurodilone lock and 21 heparin 100 IE/mL, with 9622 and 6956 treatment days, respectively. Zero CRBSIs occurred in the taurodilone arm, while 4 CRBSIs (2.72 ± 1.21) occurred in the heparin arm. No difference in mechanical CVC complications was observed between the two arms. Lower CRBSI rate was also observed in the taurodilone arm (2.07 (0.00–5.47) vs. 3.9 (0.00–7.72) in the heparin arm, P = 0.0052). The CVC removal rates were 0.52 (0.17–1.21) and 1.72 (0.89–3.0) in the taurodilone and heparin arm, respectively, extending to 7.3% and 1.7% in the 2-year follow-up period. No difference in mechanical CVC complications was observed between the two arms.

Abstract No: OP372

Patient and CVC baseline characteristics

<table>
<thead>
<tr>
<th>Total</th>
<th>Taurodilone-citrate-heparin</th>
<th>Heparin 100 IE/mL</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No of patients (F/M)</td>
<td>41 (21/20)</td>
<td>20 (10/10)</td>
<td>21(11/10)</td>
</tr>
<tr>
<td>Mean age at baseline ± SD (years)</td>
<td>56.4 (±13.4)</td>
<td>58.1 (±12.4)</td>
<td>54.7 (±14.4)</td>
</tr>
<tr>
<td>Total CVC years prior to enrollment Median years/min-max</td>
<td>304.5 (3.0:94.25)</td>
<td>138.1 (5.4:20.19)</td>
<td>166.4 (3.5:94.25)</td>
</tr>
<tr>
<td>Overall prior CRBSI incidence/1000 CVC days (95% Poisson CL)</td>
<td>2.4 (2.1–2.7)</td>
<td>2.7 (2.3–3.2)</td>
<td>2.2 (1.8–2.6)</td>
</tr>
</tbody>
</table>

Results

<table>
<thead>
<tr>
<th>Total</th>
<th>Taurodilone-citrate-heparin</th>
<th>Heparin 100 IE/mL</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of treatment days (mean ± SD)</td>
<td>16.578 (404.3 ± 279.4)</td>
<td>6956 (331.2 ± 254.2)</td>
<td>6956 (211/10)</td>
</tr>
<tr>
<td>CRBSIs/1000 CVC days (95% Poisson CL)</td>
<td>0.42 (0.17–0.87)</td>
<td>0</td>
<td>1.0 (0.4–2.07)</td>
</tr>
<tr>
<td>Local infections/1000 CVC days (95% Poisson CL)</td>
<td>0.94 (0.50–1.60)</td>
<td>0.49 (0.13–1.25)</td>
<td>1.58 (0.72–3.0)</td>
</tr>
<tr>
<td>Mechanical complications/1000 CVC days (95% Poisson CL)</td>
<td>0.93 (0.49–1.58)</td>
<td>0.74 (0.27–1.6)</td>
<td>1.18 (0.47–2.44)</td>
</tr>
<tr>
<td>CVC removals/1000 CVC days (95% Poisson CL)</td>
<td>1.02 (0.60–1.64)</td>
<td>0.52 (0.17–1.21)</td>
<td>1.72 (0.83–0.9)</td>
</tr>
<tr>
<td>Number of admission days to treat catheter-related complications</td>
<td>20 days</td>
<td>131 days</td>
<td>2348 Euro</td>
</tr>
</tbody>
</table>

Legend: Exact permutation tests were used to calculate p-values for the log-rank tests testing the null hypothesis, no difference between groups.CL confidence limits; CRBSI catheter-related bloodstream infections; CVC central venous catheter; SD standard deviation. Costs were calculated only for admission days and costs of treating catheter-related complications including the costs of the study lock solutions.
A158

United European Gastroenterology Journal 5(5S)

OP374 - COMPARISON OF TWO STRATEGIES FOR PREVENTION OF ULCERS IN CHILDREN WITH PEPTIC ULCER
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Introduction: For children with acute gastrointestinal bleeding the majority of studies are retrospective, focusing on therapeutic endoscopy. Previous studies performed on adult patients have demonstrated that both scheduled second-look endoscopy and high-dose continuous proton pump inhibitors infusion are effective in preventing peptic ulcer rebleeding.
Aims & Methods: The aim of this study was to compare the two strategies of scheduled second-look endoscopy plus bolus esomprazole infusion and continuous esomprazole infusion for the prevention of ulcer rebleeding after endoscopic haemostasis in children. Consecutive children who underwent endoscopic treatment for bleeding peptic ulcers were randomized to two treatment groups: (1) scheduled second-look endoscopy with appropriate therapy in case of bleeding stigmata within 12-24 hours of the initial endoscopy plus intravenous esomprazole bolus 0.5 mg/kg (maximum 40 mg) every 12 hours for 72 hours (first group) or to receive high-dose continuous esomprazole infusion (1 mg/kg intravenous bolus followed by 0.1 mg/kg/hour continuous infusion for 72 hours) without endoscopic reassessment unless for rebleeding (the second group).
Results: 63 children were randomized to second-look endoscopy in group 1 and 64 to esomprazole continuous infusion group. Rebleeding occurred within 14 days in 4 patients (6.3%) in the first group and in 3 patients (4.6%) in the second group (p=0.7).
Conclusion: Pharmaco-protective approach by high-dose continuous esomprazole infusion in children after initial endoscopic haemostasis has similar efficacy compared to second-look endoscopy and bolus esomprazole administration in preventing peptic ulcer rebleeding. Thus, the discomfort of a second endoscopy in children can be avoided, keeping this recommendation only for high-risk selected cases.
Disclosure of Interest: All authors have declared no conflicts of interest.

References

OP375 - REDUCING FODMAP CONTENT IN THE BREASTFED INFANT'S DIET ALLEVIATES THE SYMPTOMS OF INFANTILE COLIC: A RANDOMISED CONTROLLED DOUBLE-BLIND CROSSOVER STUDY
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Introduction: Infantile colic is the most common cause for presentation of mothers to emergency departments, but there are few evidence-based therapies. ‘Windy foods’ such as cabbage, onion and garlic are commonly reduced. Parents are often asked to follow a low FODMAP diet. ‘Windy foods’ such as cabbage, onion and garlic are commonly reduced. Parents are often asked to follow a low FODMAP diet. P Gibson has published an educational/recipe book on the low FODMAP diet.

Aims & Methods: This study aimed to (1) compare via a randomised, double-blind crossover study the effects of a low FODMAP diet with that of a typical Australian diet on infant crying-fussing durations and a daily dietary diary for each of the study diets. At baseline and on day 10 of each study diet, mothers completed a depression, anxiety and stress scale (DASS) questionnaire, and collected samples of breast milk for FODMAP analysis. Samples were defined by maternal diet, milk acidity, MDA content and significantly raised SOD, GPx activity and GSH content was not related to changes in maternal stress or anxiety or to gross changes in breast milk or infant faeces. Mechanisms by which changes in maternal diet affect infant behaviour require elucidation.

Disclosure of Interest: P.R. Gibson: The Department of Gastroenterology financially benefits from the sales of a digital application and booklets on the low FODMAP diet. P Gibson has published an educational/recipe book on the low FODMAP diet.

J.G. Mair: The Department of Gastroenterology financially benefits from the sales of a digital application and booklets on the low FODMAP diet. All other authors have declared no conflicts of interest.

References

OP376 - REDUCING FODMAP CONTENT IN THE BREASTFEEDING MOTHER'S DIET ALLEVIATES THE SYMPTOMS OF INFANTILE COLIC: A RANDOMISED CONTROLLED DOUBLE-BLIND CROSSOVER STUDY
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J.G. Mair: The Department of Gastroenterology financially benefits from the sales of a digital application and booklets on the low FODMAP diet. All other authors have declared no conflicts of interest.

References
As compared with the respective values in vehicle-pretreated HFD mice.

Data extraction:

Table 1: Inflammatory cytokine levels in plasma at 30 min after tail-section preparation.

<table>
<thead>
<tr>
<th>Treatment</th>
<th>N</th>
<th>% Use</th>
<th>mITT (95% CI)</th>
<th>PP (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PPI + A + L</td>
<td>1,960</td>
<td>42.3%</td>
<td>78.7% (77.2–80.1)</td>
<td>80.9% (79.4–82.3)</td>
</tr>
<tr>
<td>PPI + A + L + B</td>
<td>763</td>
<td>10.9%</td>
<td>90.2% (88.0–92.3)</td>
<td>91.6% (89.6–93.5)</td>
</tr>
<tr>
<td>PPI + C + A</td>
<td>518</td>
<td>7.4%</td>
<td>74.2% (70.4–77.9)</td>
<td>75.7% (72.0–79.3)</td>
</tr>
<tr>
<td>PPI + A + Mx</td>
<td>329</td>
<td>4.7%</td>
<td>87.6% (84.0–91.1)</td>
<td>89.5% (86.1–92.8)</td>
</tr>
<tr>
<td>PPI + M + T + B</td>
<td>315</td>
<td>4.5%</td>
<td>82.9% (78.7–87.0)</td>
<td>85.4% (81.5–89.2)</td>
</tr>
<tr>
<td>PPI + Pylera</td>
<td>287</td>
<td>4.1%</td>
<td>86.3% (82.3–90.2)</td>
<td>89.3% (85.7–92.8)</td>
</tr>
<tr>
<td>PPI + A + M</td>
<td>245</td>
<td>3.5%</td>
<td>63.4% (57.3–69.4)</td>
<td>65.3% (59.3–71.2)</td>
</tr>
</tbody>
</table>

OP376 PAN-EUROPEAN REGISTRY ON H. PYLORI MANAGEMENT (HP-EUREG): INTERIM ANALYSIS OF 4417 SECOND-LINE TREATMENTS

Aims & Methods: A local coordinator was selected from each country (250 so far). An representative group of recruiting investigators from its country (250 so far). An

Disclosure of Interest: All authors have declared no conflicts of interest.

Conclusion: Second-line triple therapies generally provide lower eradication rates except when prescribing moxifloxacin for 14 days. Moxifloxacin-containing quadruple therapies seem to provide higher efficacy, especially the combination of bismuth with a PPI, moxifloxacin and amoxicillin.

Disclosure of Interest: A.G. McNicholl: Dr. McNicholl has received reimbursement from Allergan for delinquent activities. D.S. Bordin: Dr. Bordin has served as lecturer for Astellas, AstraZeneca, KRKA and Abbott.

Perez Aisa: Dr. Perez-Aisa has received reimbursement from Allergan and Pfizer for delinquent actions.

M. Castro Fernandez: Dr. Castro-Fernandez has received reimbursement from Allergan for delinquent actions.

P. Bytzer: Dr. Bytzer has served as consultant, and as advisor for or has received research funding from Almirall, Allergan and Reckitt Benckiser.

J. Molina Infante: Dr. Molina-Infante has served as consultant for Casen Recorderati and has received retribution from Allergan for delinquent actions. J.P. Gisbert: Dr. Gisbert has served as speaker, and as advisor for or has received research funding from Almirall, Nycomed, AstraZeneca, Recordati and Allergan.

All other authors have declared no conflicts of interest.

OP377 CAPSULE ENDOSCOPY IN INTESTINAL LYMPHAGIECTASIA: A NOVEL ENDOSCOPIC CLASSIFICATION AND ITS CLINICAL CORRELATION

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Introduction: Intestinal lymphangiectasia (IL) is a rare protein-losing enteropathy caused by disorder of the intestinal lymphatics, presenting as hypoproteinaemia, bilateral lower limb oedema, and ascites. Accoding to the etiology, this disease can be classified into primary or secondary IL. Endoscopy is the main modality for diagnosing IL, however, conventional esophagogastroduodenoscopy and colonoscopy, even balloon-assisted enteroscopy could not visualize the whole intestine. Capsule endoscopy, being a novel device introduced in recent decades, could be used to explore the whole segment of small bowel, is a suitable option for evaluation of intestinal lymphangiectasia.

Aims & Methods: Although Capsule Endoscopy (CE) is useful in diagnosis of intestinal lymphangiectasia (IL), the analysis of endoscopic and clinical characteristics remains unavailable. Between March 2011 and July 2015, patients clinically suspected IL underwent capsule endoscopy in our center were included in our study. Clinical data retrieved included age, sex, present medical history, presenting symptoms, laboratory examination, radiological findings, and medical management. The diagnosis of IL was confirmed by the presence of typical endoscopic manifestations or pathological findings in biopsy or surgical specimens. All patients followed a clear liquid diet for 24h plus 12h fasting prior to CE. (P0)(Cam® SB2, Given Imaging Ltd. Yoqneam, Israel) PEG or oral electrolyte solution (for patients younger than 10 years old) was used for bowel preparation.

Results: A total of 54 patients with median age of 24 (4–56) years were included. 42 cases were diagnosed as primary IL. Typical endoscopic characteristics included scattering, grouping or diffuse white-yellow spotted, patchy or srawy lymphangiectasia. Uptypical characteristics included enlarged, swollen or extremely dilated villi, possibly “white-veil-like” or “paving-stone-like” appearance, and “blue bleb” (dilated veain) can be noted sometimes. The endoscopic classification was established as follows: type I, alteration mostly restricted to untypical abdominal wall; type II, scattering typical lymphangiectasia, usually involving one or two of all three bowel segment; type III, diffuse typical patchy or scalpy
lymphangiectasia, mostly involving whole bowel. According to this criteria, 17 (31.5%), 24 (44.4%) and 13 (24.1%) cases were classified into type I, II and III respectively. The patients falling into type III are all diagnosed as primary IL and the average age was significantly younger than type I and type II. As for complications, a total of 16 cases of lymph leakage, 2 cases of stenosis (both type I) and 5 cases of bleeding were noted. Lymphatic leakage was detected both by capsule endoscopy and bowel albumin scintigraphy in 10 cases and the judging of leaking location were all consistent using these two modalities, but CE provided more precise information than scintigraphy.

**Conclusion:** Providing comprehensive evaluation of whole small bowel, CE may play a great role in diagnosis, management and surveillance of IL. Endoscopic classification of IL may correlate with specific clinical outcome.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**References**

**OP378 LONG-TERM OUTCOMES OF PATIENTS WITH EARLY GASTRIC CANCER DIAGNOSED AS PATHOLOGICAL EXTRA-INDICATED LESION AFTER ENDOSCOPIC SUBMUCOSAL DISSECTION**

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**Introduction:** Gastric cancer treatment guidelines recommend additional surgery as the standard treatment of the extra-indicated lesions for endoscopic submucosal dissection (ESD). However, the incidence of lymph-node metastasis is low in most patients.

**Aims & Methods:** The study group comprised 231 patients (231 lesions) who underwent ESD for early gastric cancer in our hospital from September 2002 through March 2015 and were histopathologically confirmed the extra-indicated lesions for ESD. Patients with a gastric tube or remnant stomach were excluded. The patients were divided into an additional operation group and a follow-up group, and long-term outcomes were studied retrospectively. Risk factors for metastasis and recurrence were also studied.

**Results:** The median follow-up was 48 months. There were 174 men and 57 women with a median age of 72 years. The additional operation group comprised 118 patients, and the follow-up group comprised 113 patients. The rates of 5-year cause-specific survival and 5-year overall survival were significantly higher in the additional operation group (100% and 96.0%, respectively) than in the follow-up group (92.6% and 73.3%, respectively; both p = 0.010). In the follow-up group, 5 patients (4.4%) died of gastric cancer (p = 0.023). Among elderly patients 75 years or older, long-term outcomes did not differ significantly between the groups. Surgery was avoided because of underlying disease in 88 patients (77.9%) in the follow-up group (p = 0.001). Sixteen patients (12 in the additional operation group and 4 in the follow-up group) had metastasis or recurrence, and the presence of lymphatic involvement was an independent risk factor for metastasis, recurrence, or both (p = 0.003; odds ratio, 10.594; 95% confidence interval, 2.294 to 48.927).

**Conclusion:** In patients with early gastric cancer who were confirmed the extra-indicated lesions for ESD, additional surgery should be aggressively performed if the patient can tolerate such treatment. In elderly patients aged 75 years or older and patients with serious underlying diseases, follow-up observation was suggested to be one option in patients who give informed consent after receiving an explanation of the risk of recurrence.

**Disclosure of Interest:** All authors have declared no conflicts of interest.
ALTERNATIONS OF THE NO-CGMP PATHWAY IN THIOACETAMIDE-INDUCED LIVER FIBROSIS/CRIRRHOSIS IN RATS

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2Department Of Pharmacological And Biotechnology, University of Freiburg, Freiburg/Germany

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Introduction: Liver cirrhosis is an association with an imbalance between vasodilation and vasoconstriction in the sinusoids. Therefore the investigation of the nitric oxide - cyclic guanoansine monophosphate (NO-cGMP) pathway, a key regulator of vascular smooth muscle tone, is essential.

Aims & Methods: The rat model of thioacetamide (TAA) was used to induce liver fibrosis/cirrhosis and alterations of the NO-cGMP pathway and subsequent liver damage were assessed. 25 male Wistar rats were studied (11 untreated controls and 14 TAA-treated animals [0.03 g TAA/100 ml drinking water for 16 weeks]). TAA dosage was adjusted weekly based on body weight changes. Hepatic gene expression of endothelial and inducible NO synthase (eNOS and iNOS), phosphodiesterase 5 (PDE5) soluble guanylate cyclase subunits a1 (sGCa1) and b1 (sGCB1) was determined by qRT-PCR. Serum cGMP concentrations were measured by ELISA using blood samples taken from the carotid artery. Likewise liver damage was assessed by liver chemistry (i.e. alanine- and aspartate-amino-transaminase, ALT and AST), alkaline phosphatase (AP), albumin and bilirubin. The degree of fibrosis was estimated by histological criteria (i.e. Desmet scores). PDE5-expression was determined by immunohistochemistry. Kruskal-Wallis test was used for statistical analysis of group differences.

Results: Gene expression analysis revealed significantly increased expression of eNOS (1.5fold), PDE5 (7.7fold), and sGCb1 (2.1fold) in fibrotic livers compared to controls. cGMP concentrations in fibrotic animals were slightly decreased (-34%). Significantly increased expression of iNOS (2.26fold), sGCb1 (1.7fold), and sGCB1 (3fold) was observed in cirrhotic livers compared to controls, while cGMP concentrations were significantly decreased (-40%). In controls NOX expression was only detected in fibrotic and cirrhotic livers, but absent in controls. Immunohistochemistry revealed markedly increased PDE5-expression in cirrhotic livers, which was predominantly localized in hepatic stellate cells. Conclusion: The analysis of the animal model of TAA-induced liver fibrosis/ cirrhosis revealed alterations of the NO-cGMP pathway, characterized by reduced concentrations of cGMP, a key mediator of vasodilation, so as to increased PDE5-expression. These changes reinforce the hypothesis that sinusoids remain in a contractile state in cirrhotic livers, thereby contributing to increased PDE5-expression. These changes reinforce the hypothesis that sinusoids remain in a contractile state in cirrhotic livers, thereby contributing to portal hypertension. Thus, administration of PDE5-inhibitors, possibly combined with NOX-inhibition, should be further studied in clinical trials as a promising therapeutic approach to target portal hypertension.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

SERPINB3 INVOLVEMENT IN THE STIMULATION OF MACROPHAGE ACTIVATION MARKER SCD163 IN HCV INFECTED PATIENTS

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Introduction: In chronic HCV infection disease progression is maintained by sustained necroinflammation and fibrosis in the liver. Upon macrophage activation, the soluble marker CD163 (sCD163) is released in serum and its levels correlate with fibrosis and NAS in the liver. The serum protease inhibitor SerpinB3 (or SCCA1), has been shown to be involved in liver fibrogenesis and the circulating SCCA-IgM complex has been depicted as a marker of liver disease progression and of NAS in patients with chronic hepatitis C. Preliminary data suggest that SerpinB3 activates primary monocytes through the Wnt canonical pathway. The purpose of this study was to evaluate the relationship between SCCA-IgM and sCD163 in serum and the possible role of SerpinB3 on sCD163 and on pro-inflammatory cytokine expression, in primary monocytes.

Aims & Methods: In 91 patients with biopsy-proven chronic hepatitis C, serum samples were tested for sCD163 (ng/ml) and SCCA-IgM (AU/ml) by ELISA. The results were analyzed in relation with clinical and histological parameters. Primary monocytes were isolated from healthy donors, treated with recombinant SerpinB3 (200 ng/ml) and supernatants analyzed after 2 and 7 days. Expression of sCD163 secreted in the supernatant was evaluated by ELISA. In primary monocytes, monocyte-macrophage activation marker IL-12, CXCL-10 and TNF-alpha were also analyzed by PCR at different time points.

Results: In patients with chronic hepatitis C sCD163 was found correlated with inflammatory and metabolic alterations (AST, ALT, GGT, HOMA-IR, triglycerides), and was significantly increased in patients with sarcoid-like histological fibrosis stage (F1-F2 vs. F3-F4 nec. Metavir: p < 0.04). Patients with levels of SCCA-IgM > 200 AU/ml had more elevated serum levels of sCD163 (p < 0.05). In primary monocytes stimulated with recombinant SerpinB3 “in vitro”, sCD163 expression increased of 2.5 times and this finding was parallel to an up-regulation of the inflammatory cytokines IL-12, CXCL-10 and TNF-alpha.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P0004 THE PROTECTIVE EFFECTS OF GROUP 3 INNATE LYMPHOCYTE CELLS ON HEPATITIS B VIRUS RELATED LIVER FIBROSIS COULD BE IMPAIRED BY TH17 CELLS

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Introduction: Th17 cells have been proved to contribute to hepatitis B virus (HBV) related liver fibrosis. Group 3 innate lymphocyte cells (ILC3s), which have similar profiles of transcription factor and cytokines to that of Th17 cells, were also suggested to be involved in the progression of liver fibrosis.

Aims & Methods: The study was designed to explore the functions of ILC3s and the relationships between ILC3s and Th17 cells in liver fibrosis. Peripheral blood samples were collected from 60 patients with chronic hepatitis B (CHB), and 50 patients with HBV related liver cirrhosis (LC) as well as 30 healthy controls (HC). The percentages and cytokines secretion of ILC3s (Lin-CD127+CD117+CD244+) and Th17 cells (CD4+IL-17+) were detected by flow cytometry. Peripheral blood mononuclear cells (PBMCs) and PBMCs without ILC3s co-cultured with hepatic stellate cells (HSCs)-LX2 in contact and non-contact manners. Then Th17 cells, which were induced from naive CD4+ T cells in vitro, were transferred into Rag1-/- mice with cernice tetrachlorodrin (CCl4) related liver fibrosis. In addition, ILC3s in Rag1-/- mice were depleted by injecting with anti-CD90.2 antibody.

Results: Compared with HC, the percentage of ILC3s increased in CHB group. The anti-inflammation cytokines secreted by ILC3s such as IL-22 increased, whereas pro-inflammation cytokines of ILC3s such as IL-17A, TNF-α, IFN-γ decreased in CHB patients. However, ILC3s decreased in LC patients with reduced cytokines secretion. Th17 cells frequencies significantly increased both in CHB and LC groups compared with HC. PBMCs without ILC3s, which were collected from CHB and LC patients, promoted the proliferation and activation of HSCs because of less IL-22 secretion. Similarly, compared with wild type mice, ILC3s in spleens and livers of C57BL/6 mice with liver fibrosis increased sequentially at time point of week 2 and week 4 following drug injection. Intriguingly, at week 6, ILC3s decreased compared with previous. However, Th17 cells increased gradually with CCl4 administration, even at week 6. Transferring Th17 cells into Rag1-/- mice with liver fibrosis made the ILC3s in spleens and livers decreases significantly, and the degree of mice liver fibrosis become more severe than control. Furthermore, ILC3s depletion correlated with reduced expression of IL-22 and more severe liver fibrosis. Transferring purified liver ILC3s into recipient mice with liver fibrosis and reverse liver fibrosis.

Conclusion: Our study has uncovered the protective role of ILC3s in liver fibrosis, which is through secreting IL-22 to reduce proliferation and activation of HSCs. However, the protective functions of ILC3s could be impaired by Th17 cells.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0005 EFFECTS OF INTERNAL AND EXTERNAL BILIARY DRAINAGE ON THE EXPRESSION OF INTESTINAL BILE ACID RECEPTOR AND TLR4/NOD2 IN MICE WITH OBSTRUCTIVE JAUNDICE

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Introduction: Internal biliary drainage has been confirmed better than external biliary drainage in alleviating the damage of intestinal mucosa barrier caused by obstructive jaundice, but the relevant mechanism is still unclear. In this study, we mainly study the expression between FXR and TLR4, TGR5 and NOD2.

Aims & Methods: We aimed to investigate the potential relation between the expressions of bile acid receptor and TLR4/NOD2 in intestinal mucosa and its influence on the intestinal mucosal barrier with obstructive jaundice. In this study, we mainly study the expression between FXR and TLR4, TGR5 and NOD2. Sixty male adult Kunming mice were randomly assigned to four groups: SH (sham operation), OJ (obstructive jaundice), ID (internal drainage), ED (external drainage) (n = 15 in each group). On the 7th day from the first operation, the OJ and SH mice were executed and specimens of blood and ileal tissue of groups were collected. ED and ID were reoperated on day 8 for biliary drainage procedure. Blood was drawn from heart for liver function test. The terminal ileum specimen was collected for test of histology using haematoxylin-eosin (HE) staining. Western blot (WB) and real-time polymerase chain reaction (RT-PCR) were used to detect the expression of protein and mRNA of FXR, TGR5, TLR4 and NOD2 in intestinal mucosa.

Results: We have successfully established the animal models. The histopathological examination revealed notable inflammatory infiltration and hyperplasia disruption at terminal ileum in OJ mice; significant alleviation of above injuries by ID while little improvement by ED. FXR-TLR4: After biliary obstruction, the expression of protein and mRNA of FXR were significantly increased, while the expression of protein and mRNA of TLR4 were significantly decreased compared with SH group’s (P < 0.005). After ED, compared with OJ group’s expression of protein of FXR was decreased while TLR4 were increased. The mRNA of both FXR and TLR4 were increased. After ID, the expression of protein and mRNA of FXR were significantly decreased compared with OJ group’s but still were better than that in SH group and were better than ED group’s. And the expression of protein and mRNA of TLR4 were significantly increased compared with OJ group’s (P < 0.001), but were still lower than that in SH group and were better than ED group’s. The trend of TLR4 expression was almost the same between vehicle group and no gavage group. After gavage with FXR agonist, the differences of TLR4 expression of four groups disappeared (P > 0.05). TGR5-NOD2: IHC and WB suggested that after OJ surgery, the protein expression of both TGR5 and NOD2 increased obviously compared to that of SH mice; then the level of TGR5 and NOD2 protein fell markedly after ID surgery close to SH level while in ED group there was only a slightly reduction form OJ level and still with a high expression of TGR5 and NOD2 protein. Detection of RT-PCR found that TGR5 mRNA and NOD2 mRNA level in OJ group increased several times as that of the SH group; after ID surgery, the expression of TGR5 mRNA significantly reduced, NOD2 mRNA level also fell down consistently, but the effect was not observed in ED mice.

Conclusion: The expression of intestinal FXR and TLR4, TGR5 and NOD2 could be one of the critical mechanism why internal drainage is better than external drainage in restore intestinal barrier function of obstructive jaundice mice.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0006 ALTERED SMALL INTESTINAL MICROBIOTA TOWARD FAMILY LACTOBACILLACEAE IN MIR-21 KNOCKOUT MICE

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Introduction: Alterations in the gut microbiota have been correlated to a wide variety of diseases, including liver diseases. Used as probiotics, several strains of Lactobacillus have been associated not only to modulation of intestinal tight junctions but also to amelioration of liver fibrosis. Common bile duct ligation (BDL) results in acute cholestatic injury and secondary biliary fibrosis, associated with early increased intestinal permeability and disturbed bile acid homeostasis. We have demonstrated that the oncogenic microRNA-21 (miR-21) is upregulated in BDL mouse liver, mediating liver fibrosis. We aimed to investigate the role of miR-21 in the response of the small intestinal microbiota to BDL that may explain miR-21 effects in acute liver injury and fibrosis.

Aims & Methods: Three-month-old C57BL/6 wildtype (WT) and miR-21 whole body knockout (KO) mice were submitted to sham or BDL surgeries. After three days, mice were sacrificed and small intestinal lumen samples were carefully removed and preserved. mRNA expression was analysed by qRT-PCR. Bacterial DNA was purified from the small intestinal lumen samples and analysed by next generation sequencing - metagenome analysis. Liver tissue and serum were also collected for biochemical analysis of hepatic damage and fibrosis.

Results: TNF-α and IL-1 β mRNA levels increased in the small intestine of BDL mice, compared with WT. TLR4 and TGF-β expression was increased in both sham- and BDL-miR-21 KO mice which is in accordance with the higher LPS in blood plasma observed. Zona occludens (ZO-1) and occludin mRNA levels were decreased in WT mice after BDL. Strikingly, miR-21 KO reverted mRNA of tight junction proteins to control levels. BDL miR-21 KO mice showed decreased circulating levels of hepatic enzymes, concomitant with decreased fibrogenic gene expression in the liver, in comparison with WT mice, suggesting that miR-21 contributes to BDL-induced liver injury and fibrosis. Further, miR-21 KO not only show a decreased small intestine permeability through a ZO-1 and occludin pathway, as it is associated with development of beneficial strains of Lactobacillaceae that may also contribute to liver protection.

Conclusion: These data suggest that miR-21 depletion is associated with increased intestinal permeability markers in the small intestine and better immune response to bacterial dysbiosis provoked by the BDL surgery, thus halting liver injury and promoting gut microbiota homeostasis. (Supported by PTDC/BIM-MEC/089572014, FCT)

Disclosure of Interest: All authors have declared no conflicts of interest.
Akkermansia muciniphila mediated liver injury is associated with different microbial communities. It was reported to be involved in cell growth and apoptosis in tumor and acts as a potential tumor suppressor in HCC. It has shown that high levels of ZBP-89 expression were statistically associated with better survival of HCC patients. Furthermore, the mechanism of ZBP-89 in modulating sensitivity of Sorafenib in CSC is remains unknown.

**Aims & Methods:** In this study, we investigated the mechanism of Sorafenib resistance in HCC cancer stem cells, and how ZBP-89 reduced drug resistance. The sensitivity of HuH7 and Hep3B parental and sphere-forming cells to Sorafenib was measured by MTT assay. We then examined the expression pattern of Notch1 and liver CSC markers in HuH7 and Hep3B CSC after the treatment with Sorafenib. MTT assay was also used to measure the effects of ZBP-89 overexpression on the sensitivity of Sorafenib in sphere-forming cells. The levels of ZBP-89 and CD44 were measured using qPCR in human HCC tissue samples. The regulatory effects of ZBP-89 on CSC phenotype were examined in mouse models including CD44 and Notch1 target genes including HES1, HES6, HEY1 and NRARP. Amino acids suggesting that ZBP-89 was involved in suppression of CSC phenotype. Detailed study indicated that ZBP-89 expression was negatively correlated with CSC marker CD44 in human HCC tissues. In vitro study indicated that tumor resistance to Sorafenib, compared with their parental cells. The expression of Notch1 was reported to be associated with cancer stem cells (CSC). The transcription factor ZBP-89 was found to result in the loss of CSC phenotype and improve the sensitivity to Sorafenib in CSC through its interaction with activated Notch1. In conclusion, this study suggested that ZBP-89 overexpression on the sensitivity of Sorafenib in sphere-forming cells. We found that sphere-forming HCC cells had significant higher resistance to Sorafenib, compared with their parental cells. The expression of Notch1 and EpCAM was increased along with the treatment of low dose of Sorafenib, suggesting that the activation of Notch1 pathway was associated with the drug resistance in liver CSC. Studies further indicated that ZBP-89 overexpression was able to improve the sensitivity of Sorafenib in sphere-forming CSC cells. Furthermore, we found that ZBP-89 expression was negatively correlated with CSC marker CD44 in human HCC tissues. In vitro study indicated that tumor sphere forming was impaired under ZBP-89 overexpression of ZBP-89, suggesting that ZBP-89 was involved in suppression of CSC phenotype. Detailed investigation against control cells showed that overexpression of ZBP-89 resulted in reduced expression of CSC markers EpCAM, CD133, Sox2 and e-cmyc at both mRNA and protein levels. In addition, the overexpression of ZBP-89 or silencing of Notch1 reduced the number of colonies formed by sphere-forming CSC cells, demonstrating opposite effects of these two proteins. Mechanistic studies revealed that ZBP-89 was able to repress the expression of Notch1 and reported that ZBP-89 could directly bind to the activated Notch1 in the nucleus, resulting in a negative regulation of CSCs and overcome of Sorafenib resistance. We aimed to study the clinical effect of probiotics in the treatment of nonalcoholic fatty liver disease. 200 cases of patients with nonalcoholic fatty liver disease were randomly divided into routine treatment group (A group) and combined treatment 3 groups (B, C, D). All 50 cases were given orally Polyene Phosphatidylcholine Capsules, 456 mg, TID. The combination therapy group B was given orally the Live Combined Bifidobacterium Lactobacillus and Enterococcus Powder, 420 mg, TID; group C, two live combined Baccillus subtilis Enterococcus, 500 mg, TID. D group was given orally the both probiotics above. The course was 1 month. All patients were respectively examined before treatment and seven days and thirty days after treatment, for cholesterol (TC), triglyceride (TG), high density lipoprotein cholesterol (HDL-L), low density lipoprotein cholesterol (LDL-L), alanine aminotransferase (ALT), aspartate aminotransferase (AST), fasting blood glucose (FPG), serum high molecular weight adiponectin (HMW APN) and serum TNF-α. The 4 groups were collected faces samples, that were tested routine detection, bacterial culture. At the same time all participants were checked with ultrasound liver and abdominal scan.

**Results:** In terms of blood lipids and blood glucose, each group improved than before, only HDL-L was not statistically significant, D group showed significant differences in triglyceride. In liver function, blood ALT, AST were significantly lowered in B group than A group, A and B groups lowered A levels were decreased after treatment. In the combined treatment D group was statistically significant; group D more than the group A; serum HMW APN increased after treatment, decreased in the combined treatment D group compared with routine treatment group A was significant difference. Adiponectin: Intestinal probiotics can regulate the intestinal micro ecological imbalance in NAFLD patients, and reduce the level of serum TNF-α, improve the level of adiponectin, which can further improve the blood glucose, lipid metabolism, and then improve the liver injury of non-alcoholic fatty liver disease.

**Disclose of Interest:** All authors have declared no conflicts of interest.
P0010 FAECALIBACTERIUM ASSOCIATED WITH GUT-PERMEABILITY IN NONALCOHOLIC FATTY LIVER DISEASE

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Introduction: Despite evidence that the microbiota is involved in the pathogenesis of obesity, the microbiota of patients with nonalcoholic fatty liver disease (NAFLD) has not been well characterized. NAFLD is considered a hepatic manifestation of metabolic syndrome and is particularly associated with insulin resistance, obesity, and gut-driven endotoxin.

Aims & Methods: The aim of our study is to assess if there are any differences in the microbiota of patients with biopsy-proven NAFLD and healthy controls (HC). In addition, peripheral blood endotoxin (ET) and gut-permeability was analyzed in NAFLD (mild fibrosis vs severe fibrosis) and HC patients. A total of 201 patients were enrolled in this study: 68 HC and 133 biopsy-proven NAFLD (77 mild fibrosis and 56 severe fibrosis [F0–4]). One stool sample was collected from each participant. All NAFLD patients included in this study underwent percutaneous liver biopsy. Healthy controls were volunteers. The composition of gut bacterial communities was determined by 16S rDNA sequencing. Additionally, peripheral blood ET was determined using by endotoxin activity assay (EAA). Gut-permeability was assessed by Lactulose mannitol ratio (LMR).

Results: Among those taxa with greater than 1% representation in any of the three NAFLD groups, and we can not predict liver iron overload for hyperferritinemia (HF) and we postulate that the distinct composition of the gut microbiota varied remarkably in pairwise comparison of one mouse model with the Control.

Conclusion: In summary, the composition of gut microbiota varied remarkably between mice administrated different experimental diets to induce non-alcoholic fatty liver disease. Disclosure of Interest: All authors have declared no conflicts of interest.

References

P0012 PREVALENCE OF METABOLIC SYNDROME AND LIVER STEATOSIS IN A PROSPECTIVE MULTICENTER STUDY OF PATIENTS REFERRED FOR HYPERFERRITINEMIA

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Introduction: Approximately 25% of adult population in western countries have metabolic syndrome (MS). Hyperferritinemia (HF) is frequently present in patients with MS (dysmetabolic hyperferritinemia). Liver steatosis is often suspected in patients with HF.

Aims & Methods: To study the prevalence of hepatic steatosis determined by MRI in these patients. A prospective study of 312 consecutive with HF (>200 µg/L women; 300 µg/L men) and/or TSI > 45%, confirmed in two determinations, was conducted from December 2010 to April 2013. The MS was defined by the presence of three of the following factors: waist circumference ≥94 cm men ≥80 cm women; triglycerides ≥250 mg/dL or treatment for this dyslipidemia; HDL < 40 mg/dL women <50 mg/dL men or treatment for this dyslipidemia; glucose ≥100 mg/dL or Type 2 diabetes; hypertension: blood pressure ≥130 mmHg/≥85 mmHg or treatment for arterial hypertension (1). HF was determined by MRI 1.5 Tesla system (SIR method) (2). We systematically performed T1-weighted in-phase and opposed-phase imaging to determine the presence or not of liver steatosis.

Results: 312 patients (272 men/40 women) were included. Mean age 55 (SD 13.5); Mean ferritin 729, 6 (SD 449.6), mean TSI 40, 8 (SD 15.8); 276 patients have all the required criteria to determine the MS presence: 115/240 men (48%) and 20/36 women (55%), were patients with MS (49.4%); 141 without MS (NMS) (51%). In 286 patients a MR study for the presence of liver steatosis was performed: 196 no steatosis; 90 liver steatosis. 231 patients with MS criteria and MR for steatosis: NMS group (128): no steatosis 103; steatosis 25; MS group (123): no steatosis 72; steatosis 51 (total: no steatosis 175, steatosis 76). When we study the presence of liver steatosis was more frequent in the MS group, the results obtained were statistically significant, p = 0.000.

Conclusion: Nearly 50% of the patients referred for hyperferritinemia to the hospitals of our country had MS; the patients with MS had more frequently liver steatosis than the patients without MS.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P0013 LIVER IRON CONCENTRATION IN PATIENTS REFERRED FOR HYPERFERRITINEMIA. MULTICENTRE ANALYSIS OF THE DIFFERENT GROUPS ACCORDING TO THE METABOLIC SYNDROME AND THE TRANSFERRIN SATURATION

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Introduction: In a previous study from our group (1), in a secondary hospital, we did not find differences in the liver iron concentration (LIC) of the different groups, and we can not predict liver iron overload for hyperferritinemia (HF)

the biomarker of NAFLD in LEIs analysis. More biomarkers at genus level (Lachnospira, S24-7, etc.) were identified in pairwise comparison of one mouse model with the Control.

Conclusion: In summary, the composition of gut microbiota varied remarkably between mice administrated different experimental diets to induce non-alcoholic fatty liver disease. Disclosure of Interest: All authors have declared no conflicts of interest.

References

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patients with HFE mutations and (transferrin saturation index (TSI) values alone. But we did not have C282Y/C282Y patients in the series.

Aims & Methods: To study the relevance of HFE mutations and TSI in determining LIC for HF patients attending the outpatient clinic at 6 hospitals in the Basque country. Prospective study of 312 consecutive patients with HF. Group A (n=126) described three different groups according to HFE mutations and TSI (Group A: no predisposing mutations (PM) for HH and TSI < 45%); Group B: PM for HH: C282Y/C282Y; C282Y/H63D, H63D/H63D, and TSI > 45%; Group C: no PM for HH and normal TSI). Group D: PM and normal TSI. In the Basque country, hereditary hemochromatosis (HH) predisposing mutations differ, with relevance of the H63D/H63D mutation. The LIC was measured by MRI.

Results: In all the patients, HFE study was available: C282Y/C282Y 14 (4.49%); C282Y/H63D 47 (15.06%); H63D/H63D 99 (31.73%); wt/wt 98 (31.41%); C282Y/S65C 1 (0.32%); H63D/S65C 2 (0.64%); C282Y/wt 16 (5.13%); S65C/wt 10 (3.21%). LIC was obtained from all the patients by MRI. Mean age: 55.0 ± 13.25, 272 men and 40 women. Group A: 54; Group B: 32 Group C: 70; Group D: 64. The mean LIC index increased: Group B: 57.21 ± 27.89, group C: 70.53 ± 58.67, group C: 35.23 ± 22.62. Group D: 42.67 ± 22.98. We compared the LIC mean values of the 4 groups (bonferroni) with significant differences (p<0.0001).

Conclusion: The LIC in different groups of patients referred for HF are significantly different with different predisposition to HH.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P0014 LIVER IRON CONCENTRATION IN THE METABOLIC SYNDROME WITH HYPERFERRITINEMIA (DYSMETABOLIC HYPERFERRITINEMIA): RESULTS FROM A PROSPECTIVE COHORT OF 312 PATIENTS

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Introduction: Approximately 25% of adult population in western countries have metabolic syndrome (MS). Hyperferritinemia (HF) is frequently present in patients with MS (dysmetabolic hyperferritinemia). There are some publications that support that HF is associated with a raised liver iron concentration (LIC) in these patients, but the doubts persist about this subject.

Aims & Methods: To study the LIC in patients referred for hyperferritinemia to six different hospitals in the Basque Country (multicenter study), Spain, and determine if there are differences between patients with or without metabolic syndrome. A prospective study of 312 consecutive patients with HF (>200 mg/L women, >300 mg/L men) was conducted from December 2010 to April 2013. The Metabolic syndrome was defined by the presence of three of the following factors: waist circumference >94 cm in men, >80 cm in women; Triglycerides >150 mg/dL or treatment for this dyslipidemia; glucose >100 mg/dL or treatment for arterial hypertension (1). LIC was determined by MRI (SIR method) (2). 

Results: In all the patients, HFE study was available: C282Y/C282Y 14 (4.49%); C282Y/H63D 47 (15.06%); H63D/H63D 99 (31.73%); wt/wt 98 (31.41%); C282Y/S65C 1 (0.32%); H63D/S65C 2 (0.64%); C282Y/wt 16 (5.13%); S65C/wt 10 (3.21%). LIC was obtained from all the patients by MRI. Mean age: 55 ± 13.25, 272 men and 40 women. Group A: 54; Group B: 32 Group C: 70; Group D: 64. The mean LIC index increased: Group B: 57.21 ± 27.89, group C: 70.53 ± 58.67, group C: 35.23 ± 22.62. Group D: 42.67 ± 22.98. We compared the LIC mean values of the 4 groups (bonferroni) with significant differences (p<0.0001).

Conclusion: The LIC in different groups of patients referred for HF are significantly different with different predisposition to HH.

Disclosure of Interest: All authors have declared no conflicts of interest.

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P0015 INTERLEUKIN-25 PROTECTS AGAINST HIGH-FAT DIET-INDUCED HEPATIC STEATOISIS IN MICE BY INDUCING IL-25 AND M2 KUPFFER CELL STEADY PRODUCTION

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Introduction: Alternatively activated anti-inflammatory macrophage (also termed M2 Kupffer cell) is important for prevention of the development of steatosis and liver injury in non-alcoholic fatty liver disease (NAFLD). Our previous studies demonstrated that interleukin in NFALD mice and exon 25-protected against NAFLD by inducing M2 Kupffer cells.

Aims & Methods: We aimed to explore the intracellular signal pathways of IL-25 to regulate macrophage polarization and direct effects of IL-25 on Kupffer cells. Mouse model of NAFLD was induced by feeding a high-fat diet (HFD); In vitro expansion of mouse Kupffer cells, IL-10 and IL-25 were used to induce M2a Kupffer cells; specific siRNAs were used to knockdown IL-25 receptor mRNA for assessing the direct and specific effect of IL-25 on Kupffer cells; IL-25 induced M2a Kupffer cells were back transfection into the abdomen of NAFLD mouse to assess the efficacy; Dual-luciferase reporter assays and Chromatin immunoprecipitation assays were used to determine the transcription factor of IL-25 promoter.

Results: Exogenous IL-25 induced expression of type 2 cytokine and alternative activation of Kupffer cell in vivo. It could also promote hepatic macrophages to differentiate into M2a Kupffer cells in vitro. Interestingly, IL-25 recovered the expression of IL-25 mRNA in the liver of NAFLD mice. Furthermore, IL-25 could induce the expression of IL-25 in cultured hepatocytes by activation of STAT6, rather than MZF1, API or NF-κB. STAT6 was sufficient and necessary for IL-25 expression. Deletion and site-directed mutagenesis of the IL-25 promoter revealed that IL-25 transcriptional activation depended primarily on a putative STAT-binding sequence between nucleotides ~682 ~674 upstream of the start site. STAT6 binding to this sequence increased in response to IL-25 treatment in vitro and in vivo. Finally, IL-25 induced M2a Kupffer cells could ameliorate HFD-induced hepatic steatosis by reducing IL-13 expression. IL-25 could downregulate IL-13 expression in M2a Kupffer cells.

Conclusion: Our results elucidate the molecular mechanisms of IL-25 during amelioration of hepatic steatosis and provide the scientific basis of direct IL-25 treatment or macrophage transfection therapy for NAFLD.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
and NASH were quantified by using the FibroMax scales at baseline and after three years of statin treatment. Patients were randomized in two groups: the group receiving placebo.

Conclusion: While statins proved to be safe and efficient for the treatment of NASH in our series, larger cohort studies are needed to further demonstrate this potential positive effect on liver fibrosis.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

P0017 THE ROLE OF GENETIC FACTORS IN NON-OBESE NASH PATIENTS
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Introduction: Methylene tetrahydrofolate reductase (MTHFR) is the key enzyme in the remethylation of homocysteine. It is thought that MTHFR A1298C and C677T gene polymorphisms contribute to etiopathogenesis of NASH because of their effects in homocysteine metabolism.

Aims & Methods: Our aim in this study is to determine the relationship between the NASH and MTHFR C677T and A1298C gene polymorphisms, especially in non-obese NASH patients. Eighty-eight NASH patients whose diagnoses were confirmed by liver biopsies and 90 healthy volunteers as control group were included in the study. We investigated MTHFR A1298C and C677T gene polymorphisms and compared NASH patients and controls. NASH patients were assigned to two groups according to whether they are obese.

Results: Eighty-eight NASH patients (52M, 36F, mean age 45 years), and 90 healthy controls (53M, 37F, mean age 41 years) were included in the study. Altinkaya et al. reported that the frequency of TT genotype of MTHFR A1298C polymorphism is more frequent, especially in non-obese NASH patients than in healthy controls. This finding shows that genetic factors are particularly more important in non-obese NASH patients.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

P0019 INVESTIGATION OF THE RELATIONSHIP BETWEEN THE THICKNESS OF THE INTIMA-MEDIA COMPLEX OF COMMON CAROTID ARTERIES AND PATHOLOGICAL CHANGES IN THE LIVER IN PATIENTS WITH ABDOMINAL OBESITY AND NON-ALCOHOLIC FATTY LIVER DISEASE
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Introduction: In the last decade, the notion of non-alcoholic fatty liver disease (NAFLD) has undergone noticeable changes. It is shown that in the liver with fatty hepatosis, insulin and glucose utilization is disrupted, conditions are created for the development of atherogenic processes of cholesterol and triglycerides. This contributes to the development of violations of carbohydrate and lipid metabolism, the early appearance of atherosclerosis and associated cardiovascular complications. Thus, NAFLD can be considered as an independent, additional risk factor for atherosclerosis. Obviously, this problem is not only of practical but also of scientific importance for clarifying the nature of the relationship between NAFLD and the early manifestations of atherosclerotic vascular wall lesions are relevant.

Aims & Methods: Study of changes in the vascular wall of the common carotid artery (IMT CCA) and in patients with abdominal obesity (AO) and different forms of nonalcoholic fatty liver disease (NAFLD). The study involved 60 patients with AO between the ages of 18 to 59 years (waist circumference >94 cm in men and >80 cm for women, over 94 cm for men). All patients underwent an ultrasound examination of the abdominal cavity to determine the size of the liver and signs of steatosis. The level of severity of pathological changes in the liver tissue (fibrosis, steatosis and steato-fibrosis) was assessed by non-invasive diagnostic method Steatoscreen. (Biopredictive laboratory, France). Measurement of the CCA IMT was performed according to standard procedures on the machine Voluson 730 Expert, equipped with a linear transducer phased array with a frequency of 7.5 MHz. The presence of early signs of atherosclerosis was defined as a local thickening of the IMT CCA more than 0.6 mm, and the presence of non-obstructive intimal lesions as a CCA IMT thickness exceeding 0.9 mm in any point of the carotid artery (CCA IMT max).

Results: Signs of early atherosclerosis, in the form of the IMT CCA, were detected in the majority of the patients (52%) and differed between the observed groups. The average thickness of the IMT CCA was significantly higher in patients with abdominal obesity than in patients with NAFLD and in patients with AO and NAFLD in the absence of obesity. The presence of early signs of atherosclerosis was confirmed by ultrasound examination of the abdominal cavity in 54% of patients with AO and 48% of patients with NAFLD.

Conclusion: While statins proved to be safe and efficient for the treatment of NASH in our series, larger cohort studies are needed to further demonstrate this potential positive effect on liver fibrosis.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference
complex and pathological changes in the liver, determined by the test SteatoHex (r= 0.76; p < 0.001). The dependence obtained is confirmed by the equation of simple linear regression.

Conclusion: In patients with AO, there is a direct relationship between the presence of pathological changes in the liver and the initial manifestations of atherosclerosis. The results obtained make it possible to evaluate the individual risk of atherosclerosis in this category of patients. Clinical significance of the results is the need for a more thorough examination of patients with AO and suspicion of liver pathology to assess the development of not only the disease of the liver itself, but also cardiovascular complications.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

P0020 OVEREXPRESSION OF HEPASSOCIN IN DIABETIC PATIENTS WITH NONALCOHOLIC FATTY LIVER DISEASE MAY FACILITATE INCREASED HEPATIC LIPID ACCUMULATION

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Introduction: Insulin resistance is the main pathogenic determinant of both NAFLD and diabetes, and it can facilitate triglyceride accumulation in the liver. Overexpression of hepassocin (HPS) increased hepatic lipid accumulation and NAFLD activity scores (NAS), whereas deletion of HPS improved high fat diet-induced hepatic steatosis and decreased NAS in mice.

Aims & Methods: The aim of this study was to explore the relationship between hepassocin and diabetic patients with or without NAFLD. The study included 90 patients that were divided into 4 groups: Group I: included 20 patients who were diagnosed as diabetes mellitus type 2, Group II: included 20 patients who were diagnosed as non alcoholic fatty liver disease, Group III: included 20 patients who were diagnosed as diabetes type 2 and non alcoholic fatty liver disease, Group IV (control group): included 20 healthy person who was matched in age and sex with patients group.

Results: There was stastically significant decrease in mean value of serum hepassocin of group I and IV on comparing with group II and Group III. For group II there was significantly stastically increase in mean value of serum hepassocin on comparing with other groups. There was a significant serum hepassocin up regulation in patients with type 2 diabetes and non alcoholic fatty liver diseased patients (Group 3) mostly than diabetic patients (Group 1) and even than non alcoholic fatty liver disease (Group 2).

Conclusion: The present study provides evidence that overexpression of HPS may facilitate increased hepatic lipid accumulation with NAFLD and Type 2 Diabetes mellitus.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
References

P0025 SERUM FERRITIN SPECIFICITY IN PREDICTING EARLY MORTALITY OF PATIENTS WITH ALCOHOLIC LIVER CIRRHOSIS I. Valantienè1, A. Kedrè2, J. Kupecinskiè2, J. Kondrackiè2, J. Šumkienè2, V. Petrenkienè2, L. Kupcinskas1
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Introduction: Individuals with chronic liver diseases may have a mild to moderate iron overload, but the mechanism is not fully understood. Increased contents of iron have been attributed to the progression of liver cirrhosis caused by HCV infection, nonalcoholic fatty liver disease, or alcoholic liver disease. Serum ferritin concentration can be increased in iron overload and shows hepatic necro-inflammation. Recently, raised serum ferritin concentration was shown to predict mortality in patients awaiting liver transplantation in decompensated liver cirrhosis. We investigated serum ferritin level to predict the early mortality of patients with alcoholic liver cirrhosis (ALC).

Aims & Methods: The aim of this study was to determine the association between serum ferritin concentration and the outcomes of patients with ALC. The study included 72 patients with ALC. One hundred patients were included by laboratory tests, clinical features, radiological imaging, and percutaneous or tranjugular liver biopsy. Alcohol liver cirrhosis was diagnosed when daily consumption of alcohol was > 30 g/day for males, respectively, as confirmed by at least 1 family member of affected individual.

For the sensitivity and specificity of AC the following cut-off values were used: 0.53 dB/cm/MHz, second – 64.5 ± 75.5 IU/L, third – 49.5 IU/l. Bilirubin concentration in first group was 90.52 ± 85.7 µmol/L, second – 111.9 ± 72.3 µmol/L, third – 140.9 ± 195.0 µmol/L. The biggest mortality rate was in third group – 13 of 15 patients (86.67 %) (p < 0.0001). ROC scale shows a 77% specificity of serum ferritin concentration predicting early mortality in patients with cirrhosis (AUC 0.838, p < 0.0001).

Conclusion: Serum ferritin level above 400 µg/l, elevated liver enzymes and bilirubin concentration shows a poor outcome of patients with ALC (p < 0.0001). Serum ferritin level is a specific factor for predicting the early mortality in ALC.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0026 PLASMA RETICULIN 4 PROTEIN IS ASSOCIATED WITH PORTAL HYPERTENSION IN PATIENTS WITH LIVER CIRRHOSIS S. Gelman1, V. Saltienè2, A. Pranculis3, L. Kupecinskiè4
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Introduction: Reticulin 4 (RTN4) protein was first described as a potent neurite growth inhibitor in the central nervous system. However, according to recent research, the protein expression is not limited to the cells of nervous system as it is found in various other tissues, including endothelial cells, fibroblasts, muscle cells, hepatocytes. The diverse location of the protein accounts for various biological activities such as vascular remodeling, inflammation, carcinogenesis, and proliferation, carcinogenesis and other processes2–5. The function and expression of the protein in liver disease is still not clear.

Aims & Methods: In this study we aimed to evaluate plasma levels of RTN4 protein in cirrhotic patients and associate them with clinical parameters and portal hypertension. The pilot study included 72 patients with hepatitis C or alcoholic liver cirrhosis and 22 healthy controls. Liver cirrhosis was diagnosed by laboratory tests, radiological imaging and/or liver biopsy. Portal pressure was assessed by hepatic venous pressure gradient (HVPG) measurement. Plasma levels of RTN4 were determined by enzyme-linked immunosorbent assay. Association of RTN4 with biochemical parameters, Child-Turcotte-Pugh and Model of End Stage liver disease (MELD) score, transient elastography values, Child-Turcotte-Pugh and Model of End Stage liver disease (MELD) score were analyzed using statistical software SPSS 23.0. ROC curve analysis was used to identify variables correlated with HVPG. Using a RTN 4 cut-off value of 85%, cut-off values were 0.53 dB/cm/MHz, second – 64.5 ± 75.5 IU/L, third – 49.5 IU/l. Bilirubin concentration in first group was 90.52 ± 85.7 µmol/L, second – 111.9 ± 72.3 µmol/L, third – 140.9 ± 195.0 µmol/L. The biggest mortality rate was in third group – 13 of 15 patients (86.67 %) (p < 0.0001). ROC scale shows a 77% specificity of serum ferritin concentration predicting early mortality in patients with cirrhosis (AUC 0.838, p < 0.0001).

Conclusion: Serum ferritin level above 400 µg/l, elevated liver enzymes and bilirubin concentration shows a poor outcome of patients with ALC (p < 0.0001). Serum ferritin level is a specific factor for predicting the early mortality in ALC.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P0024 A NOVEL TOOL FOR THE NON-INVASIVE QUANTITATIVE ASSESSMENT OF HEPATIC STEATOSIS USING B-MODE IMAGE-GUIDED ULTRASOUND ATTENUATION IMAGING: A PROSPECTIVE STUDY
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Introduction: Nonalcoholic fatty liver disease is a main cause of chronic liver disease worldwide. A quantitative, non-invasive assessment of hepatic steatosis is desirable. Throughout the path of ultrasound (US), attenuation by liver parenchyma is uneven. This is the basis of the controlled attenuation parameter (CAP). However, further accumulation of data is needed to assess the role of CAP in the diagnosis of steatosis1). We investigated the diagnostic performance of B-mode image-guided ultrasound attenuation imaging and quantification for assessing hepatic steatosis by a liver biopsy (LB, reference standard). It was compared with the liver-to-spleen ratio (L/S ratio) from computed tomography (CT) and CAP.

Aims & Methods: We prospectively analyzed 112 consecutive patients with chronic liver disease who underwent ultrasound attenuation imaging, CT, and liver biopsy. Ultrasound attenuation imaging was performed using the LOGIQ E9 scanner (GE Healthcare) with a C1-6-D convex array probe (frequency, 4 MHz). We acquired a B-mode image of liver parenchyma. RF signals corresponding to the images were compensated by the reference signal previously measured in the gelatin phantom (knee). The attenuation coefficient (AC) was calculated from the signals’ decay slope. Steatosis, liver fibrosis, and necroinflammatory activity were staged and graded during pathological analysis. The steatosis grade was categorised as follows: S0, <5%; S1, 5–33%; S2, 34–66%; or S3, ≥67%. The diagnostic performance of AC for steatosis prediction was assessed using area under the curve (AUC) analysis; and it was compared with the L/S ratio or CAP. Univariate and multivariate regression analyses were used to identify variables correlated with AC values.

Results: Patients (51% men; 42% had non-alcoholic fatty liver disease, or alcoholic liver disease. Serum ferritin concentration can be increased in iron overload and shows hepatic necro-inflammation. Recently, raised serum ferritin concentration was shown to predict mortality in patients awaiting liver transplantation in decompensated liver cirrhosis. We investigated serum ferritin level to predict the early mortality of patients with alcoholic liver cirrhosis (ALC).

The pilot study included 72 patients with ALC. The diagnosis and etiology of ALC was confirmed when daily consumption of alcohol was > 30 g/day for males, respectively, as confirmed by at least 1 family member of affected individual. The steatosis grade was categorised as follows: S0, 0% or <5%; S1, 5–33%; S2, 34–66%; or S3, ≥67%. The diagnostic performance of AC for steatosis prediction was assessed using area under the curve (AUC) analysis; and it was compared with the L/S ratio or CAP. Univariate and multivariate regression analyses were used to identify variables correlated with AC values.

Conclusion: Ultrasound attenuation imaging had a high diagnostic accuracy for detecting hepatic steatosis.

Disclosure of Interest: All authors have declared no conflicts of interest.
Peritoneal carcinomatosis (PCA) has a prognostic role in patients with gastrointestinal cancers. Despite the low sensitivity, cytology remains the gold standard in differential diagnosis of PCA to peritonitis (for example spontaneous bacterial peritonitis, SBP) or uncomplicated ascites due to portal hyperperfusion syndromes. RTN4 value of 225/220 nm was associated with esophageal varices (odds ratio [OR] = 3, 63; p < 0.022).

**Conclusion:** Low levels of RTN4 are associated with liver cirrhosis and portal hypertension syndromes. RTN4 correlates with liver function tests. It may be a surrogate marker of CSHF and presence of esophageal varices.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**References**


**P0027**

**MICRORNAS IN ASCITES AS POTENTIAL BIOMARKERS FOR PERITONEAL CARCINOMATOSIS AND PERITONITIS**

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**Introduction:** Peritoneal carcinomatosis (PCA) has a prognostic role in patients with gastrointestinal cancers. Despite the low sensitivity, cytology remains the gold standard in differential diagnosis of PCA to peritonitis (for example spontaneous bacterial peritonitis, SBP) or uncomplicated ascites due to portal hypertension (no SBP/PCA). MicroRNAs (miRNAs) are considered as promising biomarkers and are commonly disregulated in cancer.

**Aims & Methods:** In this proof-of-principle study, we systematically evaluated preanalytical factors and potential of miRNAs as ascites biomarkers. We prospectively examined samples from patients with ascites with benign and malignant conditions including: PCA (n = 15), SBP (n = 15) and portal hypertension (no SBP/PCA, n = 15). Various extraction kits were used to compare the total RNA extraction. Furthermore, we systematically evaluated the influence of storage, stability and sample processing (uncentrifuged, pelletled etc.) on miRNA expression in ascites. MiRNA expression profiling using TaqMan Low Density Array (TLDA) and quantitative RT-PCR (TaqMan/SYBRgreen) were used to evaluate the expression.

**Results:** Systematic analysis of miRNAs stability confirms that miRNAs in ascites are well preserved from degradation with good short- (0h, 12h, 24h, and 48h) and long-term stability (30 C, –80 C for 2 years). Several miRNAs that were selected for the proof-of-principle analysis (miR-21 and miR-16) were reproducibly detectable in ascites samples. MiRNA expression profiling in patients with PCA compared to those with uncomplicated portal hypertension revealed miR-21, miR-16, miR-222 and miR-483-5p to be up-regulated and miR-26b to be down-regulated. MiRNA expression validation confirmed the increased expression of miR-21 (mean delta CT ± SD; –11.11 ± 1.2 vs. –8.46 ± 3.46 vs. –9.65 ± 2.55 for no SBP/PCA, PCA and SBP, respectively, p < 0.05) and miR-16 in patients with PCA compared to no SBP/PCA groups, while miR-223 was significantly upregulated in SBP (mean ± SD; –12.16 ± 1.56 vs. –10.05 ± 3.19 vs. –6.95 ± 3.56 for no SBP/PCA, PCA and SBP, respectively, ANOVA, p < 0.0001; posttest SBP vs no SBP/PCA and vs. PCA p < 0.05).

**Conclusion:** Our data provide novel evidence for the differential expression of miRNAs in ascites in patients with PCA and SBP. Evaluation of ascites-miRNAs may offer an alternative approach for diagnosis of peritoneal carcinomatosis and create an avenue for therapeutic application as well.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**P0028**

**ALTERATIONS IN GUT VASCULAR BARRIER IN EXPERIMENTAL PORTAL HYPERTENSION**

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**Introduction:** Pathological bacterial translocation (PBT) in liver cirrhosis (LC) is the pathophysiological hallmark for subsequent bacterial infections increasing mortality several-fold. Factors known to contribute to PBT in LC are among others an increased intestinal permeability.

**Aims & Methods:** A clear role of translocation for luminal intestinal bacteria is yet to be defined but we hypothesize that the recently described gut vascular barrier (GVB) is impaired in experimental portal hypertension leading to protein loss and increased accessibility of the vascular compartment for translocating bacteria. For this purpose two different models of experimental portal hypertension, namely partial portal vein ligation (PPVL) and bile duct ligation (BDL) were used in mice under standardized gnotobiotic conditions (sDMDM2). A novel in vivo confocal endomicroscopy technique was established in order to detect gut-vascular barrier transcription in live animals. FITC-70 kDa dextran was injected intravenously and confocal probe was placed in the intestinal lumen (terminal ileum) to visualize villus-capillaries. Leakage was measured over time (10 minutes) as a ratio between the mean fluorescent intensity outside the vessel (lumina propria) and inside the vessel. Immunofluorescence (IF) stains of the intestinal crypts marker placenta-leucine-associate protein-1 (PV-1) were performed for GVB analysis.

**Results:** Confocal endomicroscopy data revealed an earlier and significantly increased leakage of 70kDa through the intestinal vascular space in both BDL and PPVL mice. FITC-70kDa-dextran leak did only leak in BDL and PPVL but not in control (sham operated) mice. Interestingly GVB stains showed increased expression of PV-1 in intestinal vessels (CD34-) of BDL but not PPVL.

**Conclusion:** Portal hypertension per se has an impact on the GVB increasing FITC-70kDa-dextran leakage from intestinal capillaries to the lamina propria in both BDL and PPVL. However, the IF showed only in BDL an increased PV-1 expression indicative of a wider opening of the intestinal crypts than in PPVL. Therefore, different mechanisms appear to be involved in alterations of the gut-vascular barrier in pre-portal hypertension and biliary cirrhosis.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**Reference**


**P0029**

**INHIBITION OF CYCLOOXYGENASE-2 AMELIORATES SPLENOMEGALY IN CIRRHOTIC RATS**


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**Introduction:** Splenomegaly is a common finding in liver cirrhosis. However, the precise underlying mechanisms behind this phenomenon have not been elucidated, and its therapeutic strategies are limited.

**Aims & Methods:** We aimed to investigate whether cyclooxygenase-2 (COX-2) is involved as a contributing factor in the pathological process of splenomegaly in cirrhosis. Thirty-six male Sprague-Dawley rats were randomized into three groups with 12 rats in each group. The control group received intraperitoneal injection of normal saline (1 ml, twice a week); the TAA group received intraperitoneal injection of thioacetamide (TAA, 200 mg/kg, twice a week for 16 weeks); the TAA + celecoxib group received TAA, then celecoxib via gastric gavage (20 mg/kg/day). The portal pressure was measured by portal venous catheterization. Sections from paraffin-embedded spleens were stained with hematoxylin and eosin and Sirius Red, and immunostained with VEGF and CD31.

**Results:** The ratio of splenic weight to body weight increased by 73.9% in TAA group compared with that in the control group. However, celecoxib decreased the area of splenic white pulp by 37.6%. Besides, the portal pressure increased by 27.9%. Yet, compared with that in TAA group, celecoxib obviously decreased the area of splenic white pulp by 28.8%. In addition, TNF-a and IL-1b were increased by 27.6%. Besides, the portal pressure was measured by portal venous catheterization. Sections from paraffin-embedded spleens were stained with hematoxylin and eosin and Sirius Red, and immunostained with VEGF and CD31.

**Conclusion:** The protein expression of COX-2, VEGF, PI3K, p-AKT, and AKT in the spleen were assessed by Western blot. The enzyme-linked immunosorbent assay was performed to evaluate the expression of TNF-a and IL-1b in the spleen.

**Results:** The ratio of splenic weight to body weight increased by 73.9% in TAA group, while in rats treated with celecoxib, the ratio was significantly reduced. While determined by H&E staining, areas of splenic white pulp in the TAA group enlarged by 27.9%. Yet, compared with that in TAA group, celecoxib obviously decreased the area of splenic white pulp by 28.8%. Besides, compared with the control group, TNF-a and IL-1b, the two proinflammatory cytokines were found to be greatly increased in the TAA group. On the contrary, in TAA + celecoxib group, the protein expression of TNF-a and IL-1b was obviously reduced. We also found that the expression of proangiogenic factor VEGF and the vascular marker CD31 increased in TAA group by Western blot and immunohistochemistry, which indicated a role of angiogenesis in the pathophysiology of splenomegaly. Furthermore, up-regulation of PI3K and p-AKT protein expression was detected in the spleen of TAA group compared with...
with that of the control group, demonstrating that P3K/AKT signal pathway was involved in development of pathological angiogenesis. However, the treatment with celecoxib strongly decreased the protein expression of VEGF, CD31, P3K and AKT in the spleen of cirrhotic rats.

**Conclusion:** The present study indicates that COX-2 contributes to splenomegaly by facilitating angiogenesis, fibrosis and inflammation in the spleen. Moreover, inhibition of COX-2 by celecoxib could ameliorate portal hypertension and splenomegaly.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**P0030**

**EPITHELIAL BARRIER DESTABILIZATION AND REGULATION OF P53 – A POSSIBLE BACTERIAL DEFENSE MECHANISM IN SPONTANEOUS BACTERIAL PERITONITIS?**


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**Introduction:** Spontaneous bacterial peritonitis (SBP) is a life-threatening complication in advancing liver cirrhosis. Translocation of intestinal bacteria or bacterial products from the gut to mesenteric lymph nodes is crucial for SBP, with *Escherichia coli* (*E. coli*), Klebsiella pneumoniae being the most common germs. Small intestinal bacterial overgrowth and a altered microbiota are so far known as risk factors for SBP. However, the exact mechanisms of bacterial translocation need to be identified as they are supposed to contribute to the development of early recognition systems and initiation of antibiosis.

**Aims & Methods:** With regard to the development of early recognition systems, pathomechanisms and signaling pathways of bacterial translocation in SBP were explored. These insights might lead to an initiation of antibiosis on time and reduced mortality in SBP.

Monolayers of human intestinal epithelial cell lines Caco-2 (p53 mutant) and HCT-116 (p53 wildtype) were cocultured with *E. coli* with different MOI (MOI 0, 1, 5 and 10) for 2 to 4 hours post confluence. Experiments with heat inactivated *E. coli* were performed as controls. Effects of microbial metabolic products were tested by using the supernatant of an overnight culture. qPCR and Western Blot analysis were performed to analyze changes in mRNA and protein levels of Ocludin, E-cadherin and the p53 family including p53 and p73.

**Results:** *E. coli* stimulation of HCT-116 cells resulted in a strong decrease of Ocludin, E-cadherin and the p53 family including p53 and p73. P53-caco-2 cells displayed less reduction of Ocludin and E-cadherin protein levels compared to p53-wildtype HCT-116 cells.

**Conclusion:** By using an in vitro model, we demonstrate destabilizing effects of *E. coli* on intestinal cell junctions, p53 and p73. As far as these effects are dependent on incubation time, microbial concentration and living bacteria, these effects might represent a mechanism to protect the bacteria from intestinal immune responses and therefore to promote bacterial translocation in SBP.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**P0031**

**INTESTINAL EPITHELIAL BARRIER IN EXPERIMENTAL LIVER CIRRHOSIS - A ROLE FOR BILE SALT IN THE MUCUS LAYER**

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**Introduction:** Pathological bacterial translocation (PBT) in liver cirrhosis (LC) is the pathophysiological hallmark for spontaneous bacterial infections increasing mortality sever-fold. Factors known to contribute to PBT in LC are among others an increased intestinal epithelial permeability.

**Aims & Methods:** Since mucus represents one of the major components of this barrier we hypothesize that i) gut mucus is altered in LC and ii) bile could be a modulator of its production. Two different models of experimental LC – namely bile duct ligation (BDL) and the chronic treatment with carbon tetrachloride (CCl4) – as well as partial portal vein ligation (PPVL) and sham-operated mice were used. Finally the farnesoid X receptor (FXR) agonist obeticholic acid (OCA) and the FXR antagonist ursodeoxycholic acid (UDCA) and control animals. Mucus thickness measurement on gut explants and PAS (Periodic acid-Schiff) staining to visualize and count goblet cells (GC) were utilized.

**Results:** We have observed a significant reduction in mucus thickness in ileum and colon of groups CCl4 0.30 GC/100 μm of villus ± 0.07 vs BDL 0.29 GC/100 μm of villus ± 0.04) of following BDL but not PPVL (Control 0.27 GC/100 μm of villus ± 0.11 vs BDL 0.18 GC/100 μm of villus ± 0.08). Moreover we have seen that farnesoid X receptor (FXR) agonist obeticholic acid (OCA) partially restored GC loss in CCl4 treated animals (Control 0.63 GC/100 μm of villus ±0.08 vs Control OCA 0.65 GC/100 μm of villus ± 0.07 vs CCl4 0.49 GC/100 μm of villus ± 0.08). However, we have also observed that OCA treatment strongly decreased the protein expression of VEGF, CD31, P3K and AKT in the spleen of cirrhotic rats.

**Conclusion:** All these results suggest that a reduced bile production by the cirrhotic liver and not portal hypertension per se interfere in the goblet cell development and/or maturation. In addition, this effect can be, at least partially, be restored by the FXR agonist OCA. Our study opens the possibility, to a so far, unknown effect of bile salts in the intestinal epithelium development in the context of liver cirrhosis being a clear candidate for mucus layer regulation and hence protective effect against bacterial translocation.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**P0032**

**CAPSAICIN AND SULFORAPHANE PREVENT THE ADVANCEMENT OF LIVER FIBROSIS IN AN EXPERIMENTAL MODEL OF LIVER CIRRHOSIS**

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**Introduction:** Liver fibrosis due to chronic induced liver damage is characterized by an increase in gene expression of proinflammatory molecules such as TGF-β1, IL-1β, IL-6 and TNF-a, as well as excess synthesis of ECM components such as COL-1. Capsaicin (CAP) is a pungent compound found in chilli peppers which has shown anticancerogenic, antiinflammatory and antifibrotic properties. Moreover, sulforaphane (SFN) is an isothiocyanate which is in cruciferous such as broccoli and it has exhibit an antioxidant effect in several in vitro and in vivo models.

**Aims & Methods:** The objective of this project was to evaluate the antifibrogenic and antiinflammatory effects of a daily supplementation with CAP and SFN in a rat model of liver fibrosis due to carbon tetrachloride (CCL4) intoxication. 35 male Wistar rats were included (n=7/group); animals were administrated intra-peritoneal 3 times per week during 8 weeks with a mix of CCL4/menal (1/50 week 1, 1:4 week 2 and 1:3 week 3-8). Healthy and CCL4-fibrotic controls received only supplementation vehicle (Tween 2% in PBS). Treated groups receive SFN 5ug/kg, or CAP 2mg/kg, or both supplements daily by oral gavage since the beginning of CCL4-intoxication regimen until sacrifice. Masson staining and PCR was performed in liver samples. Hepatic enzymes were analysed in serum.

**Results:** Groups treated with CAP and SFN showed a decrease of ~30points in percentage of liver fibrosis according to Masson staining (p<0.05), hepatic function improve since AST and ALT serum levels diminish (p<0.01) also a lower gene expression of TGF-β1, Col-1, TNF-a, IL-1 β and IL-6 was detected in treated animals when compared with fibrotic controls (p<0.01).

**Conclusion:** Thus, CAP and SFN seem to exert a hepatoprotective effect in this model of chronic-induced liver damage. These findings suggest that dietary sources of CAP and SFN might be included in dietetic guidelines for the prevention of liver fibrosis.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

Results: The color flow images of gastric varices and peri-gastric veins were delineated in all 215 patients with ECDUS. Evaluation of blood flow velocity in the 215 gastric varices revealed velocities of 7.7–35.7 cm/s (mean, 18.2 ± 6.0 cm/s). Mean velocity of large, coil-shaped (F3) type gastric varices was 23.7 ± 6.2 cm/s (n = 52), while the mean velocity of enlarged tortuous (F2) type gastric varices was 16.7 ± 5.0 cm/s (n = 163). The velocities of F3 type gastric varices were significantly higher than those of F2 type (P < 0.0001). Next, we evaluated the wall thickness of submucosal gastric varices. Two hundred-fifteen of the gastric varices were 1.0–2.2 mm (1.6 ± 0.4 mm) in gastric wall thickness. Mean thickness of red color (RC) or erosion positive varices was 1.2 ± 0.2 mm (n = 42), while the mean thickness of RC or erosion negative varices was 1.7 ± 0.3 mm (n = 173). The thickness of RC or erosion positive varices was significantly thinner than that of the negative cases (P < 0.0001). Seven cases of the 215 patients had the current history of gastric variceal bleeding, and the other three cases had experienced variceal rupture on follow up (bleeding cases, n = 10), and mean thickness of these bleeding cases were 1.2 ± 0.2 mm.

Conclusion: ECDUS is a useful modality for the diagnosis of hemodynamics of gastric varices and may allow the stratification of patients into low, high risk for hemorrhage.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0034 PORTAL HYPERTENSTIVE COLOPATHY BUT NOT ILEOPATHY IS COMMON IN EGYPTIANS WITH LIVER CIRRHOSIS

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Introduction: Liver cirrhosis and portal hypertension are associated with esophageal varices, gastric varices, small and large intestinal enteropathies. Aims & Methods: We aimed to study the prevalence of colopathy and ileopathy in patients with portal hypertension secondary to liver cirrhosis. Chronic hepatitis C patients with portal hypertension secondary to liver cirrhosis were enrolled. The severity of cirrhosis was classified by the Child-Pugh score. All patients were evaluated by upper endoscopy and colonoscopy for screening of portal hyper-tensive complications. Esophageal varices were graded as small, moderate and big varices. Portal hypertensive gastropathy was classified as absent or present, and, if present, it was sub-classified as mild or severe. Colonoscopy was done up to terminal ileum in all patients.

Results: Our study included sixty chronic hepatitis C patients with portal hyper-tension secondary to liver cirrhosis (53.33% females) their mean age (±SD) was 54.75 (±13.13) years. Child-Pugh class was A for 2 (3.4%), B for 33 (55.9%) and C for 24 (40.7%). 53 (88.33%) patients had esophageal varices (23 patients had small esophageal varices, 15 had moderate, and 8 had big varices, 2 post-band ligation and 5 obliterated varices). Gastric varices were present in 3 patients (5%). Portal hypertensive gastropathy was noted in 43 patients (71.6 %) and was mild in 38 and severe in 5 patients. Colonoscopy finding up to the terminal ileum revealed that portal hypertensive colopathy was present in 16 patients (26.7%). Portal hypertensive ileopathy was noted only in one case (1.7%). No colonic or ileal varices were noted.

Conclusion: Portal hypertensive colopathy but not ileopathy is common in Egyptians with liver cirrhosis. Ileal varices and ileopathy are not common in patients with liver cirrhosis and PHT.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0035 PREDICTIVE FACTORS FOR THE DEVELOPMENT OF ACUTE-ON-CHRONIC LIVER FAILURE IN PATIENTS WITH GASTROINTESTINAL BLEEDING

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Introduction: Acute-on-chronic liver failure (ACLF) is a specific clinical form of liver failure in patients with liver cirrhosis, referred as acute deterioration of liver function associated with an acute specific complication of liver cirrhosis. ACLF is defined by the presence of renal failure or 2 or more failures affecting at least one organ system. We aimed to study the prevalence of colopathy and ileopathy in patients with cirrhosis and PHT.

Aims: To evaluate the prevalence of colopathy and ileopathy in patients with portal hypertension secondary to liver cirrhosis. Chronic hepatitis C patients with portal hypertension secondary to liver cirrhosis were enrolled. The severity of cirrhosis was classified by the Child-Pugh score. All patients were evaluated by upper endoscopy and colonoscopy for screening of portal hyper-tensive complications. Esophageal varices were graded as small, moderate and big varices. Portal hypertensive gastropathy was classified as absent or present, and, if present, it was sub-classified as mild or severe. Colonoscopy was done up to terminal ileum in all patients.

Results: Our study included sixty chronic hepatitis C patients with portal hyper-tension secondary to liver cirrhosis (53.33% females) their mean age (±SD) was 54.75 (±13.13) years. Child-Pugh class was A for 2 (3.4%), B for 33 (55.9%) and C for 24 (40.7%). 53 (88.33%) patients had esophageal varices (23 patients had small esophageal varices, 15 had moderate, and 8 had big varices, 2 post-band ligation and 5 obliterated varices). Gastric varices were present in 3 patients (5%). Portal hypertensive gastropathy was noted in 43 patients (71.6 %) and was mild in 38 and severe in 5 patients. Colonoscopy finding up to the terminal ileum revealed that portal hypertensive colopathy was present in 16 patients (26.7%). Portal hypertensive ileopathy was noted only in one case (1.7%). No colonic or ileal varices were noted.

Conclusion: Portal hypertensive colopathy but not ileopathy is common in Egyptians with liver cirrhosis. Ileal varices and ileopathy are not common in patients with liver cirrhosis and PHT.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0036 HAEMOSTASIS IN PORTAL VEIN IN CIRRHOSIS: ROLE OF LOCAL ENDOTHELIAL DAMAGE

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Introduction: Cirrhosis is characterized by both bleeding and thrombotic complications due to underlying procoagulative haemostatic imbalance [1]. Among thrombotic events, portal vein thrombosis (PVT) is the most common with annual incidence ranging between 4.6% and 12.8% [2, 3]. Demonstrated associated risk factors are severity of portal hypertension and slowed portal flow [4]. However, data regarding haemostasis in the portal venous system of cirrhotic patients are lacking.

Aims: To evaluate peripheral and portal venous haemocoagulative state in patients with cirrhosis in comparison with controls, through thrombin generation test (TGT), rotational-thrombelastometry (ROTEM) along with evaluation of endothelial dysfunction by quantification of circulating endothelial microparticles (MP). Correlate these results with activity levels of local pro and anticoagulant factors. Compare peripheral and portal venous districts in cirrho tic patients. Correlate these results with activity levels of local pro and anticoagulant factors. Compare peripheral and portal venous districts in cirrh osis patients in order to assess the role of the portal vein in circulating endothelial microparticles (MP) in the development of ACLF, in patients with liver cirrhosis undergoing liver transplantation (LT) or transjugular intra-hepatic portosystemic shunt (TIPS). Patients without liver disease awaiting liver surgery or deceased liver donors were enrolled as controls. The following laboratory tests were performed on citrated peripheral and portal venous blood samples: TGT with and without thrombomodulin (TM), ROTEM, dosage of main pro and anticoagulants factors activity and analysis of circulating endothelial MP.

Results: 25 cirrhotics (15 LT and 10 TIPS) and 6 controls (2 undergoing hepatic resection for benign liver lesions and 4 liver donors) were enrolled. Peripheral blood in cirrhotics showed resistance to activation of PC-pathway at TGT (ETP with without TM 0.89 (0.78–0.92) vs 0.6 (0.3–0.74), p < 0.001), lower clot stabilit y at ROTEM (MCF-NATEM mm: 43.5 (36–51) vs 63 (53–69), p = 0.042), and significant increase of endothelial-MP (CD62E/MP.L: 1391 (651–2301) vs 582 (380–1161), p = 0.046), indicative of higher endothelial damage compared to controls. Similar results were obtained comparing portal blood of cirrhotics and controls (ETP with without TM 0.89 (0.78–0.92) vs 0.63 (0.33–0.75), p = 0.001; MCF-NATEM: 46 (39–51) vs 62 (49–66), p = 0.056; CD62E/MP.L: 1606.5 (680–1885) vs 529.5 (266–781), p = 0.069). There was a significant correlation between diminished levels of PC, PS, AT, FII and either TGT or ROTEM parameters. Comparing portal and peripheral blood of cirrhotics, we detected endogenous heparinoids in portal (α-antage NATEM 51 (46–57) vs
**P0038 PREDICTING FACTORS FOR HOSPITAL READMISSION AFTER THE FIRST EPISODE OF HEPATIC ENCEPHALOPATHY**

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**Introduction:** Hepatic encephalopathy (HE) is a frequent complication of liver cirrhosis, with necessity of hospital admission in many cases. The economic burden of HE is substantial. After ascites, HE is the second most common reason for hospitalization of cirrhotic patients. HE is also the most common, possibly preventable, cause for readmission.

**Aims & Methods:** We aimed to assess the factors associated with the increased likelihood of hospital readmission for HE after the onset episode. We completed a retrospective Retrospective analysis of admissions for HE of patients with liver cirrhosis, between October 2010 and October 2015. Only the onset episode was included. Patients were followed for 1 year or until readmission for HE. All patients were discharged under lactulose therapy. Descriptive statistics, uni and multivariate analysis, logistic regression, and ROC curves analysis were performed using IBM SPSS Statistics 22 with p < 0.05 deemed to be statistically significant.

**Results:** In this study 119 patients were included: 78% men with a mean age of 59 ± 13 years; 8% had hepatocellular carcinoma, and 45% had Child-Pugh C. The most frequent cirrhosis etiologies were alcoholic disease (60%) and HCV infection (12%). The precipitating factors, for the onset episode, more frequently detected were diuretic overdose (36%) and infection (31%). All patients were treated with standard therapy, with an adequate lactulose dose. The readmission rate after the first episode of HE was 72% (75% men). The estimated average time to relapse was 18 weeks. The most frequent causes of readmission were also diuretics overdose (31%) and infection (30%). The patients who were readmitted had a higher MELD score than patients without recurrence (13.9 ± 11.6 points; p = 0.015). This association was verified in the multivariate analysis (OR = 1.1, p = 0.044).

**Conclusion:** In this cohort, there was a high rate of readmission for HE after the inaugural episode, which carries a great impact on individual health and high socio-economic costs. A higher MELD score was independently associated with a high probability of readmission for HE.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**Reference:**

Safeguards, efficacy and risk of complications for cirrhotic HCV patients with thrombocytopenia and hypoalbuminemia treated with ombitasvir/paritaprevir/r+dasabuvir/r+ribavirin: a real-life cohort

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Introduction: The regulations for prescribing interferon-free treatment for patients infected with hepatitis C virus in Romania comprised only patients with F3/F4 fibrosis so the risk of hepatic decompensation and complications was higher compared to other cohorts. In previous interferon-based regimens, thrombocytopenia and hypoalbuminemia on treatment were markers for portal hypertension and associated with hepatic synthetic dysfunction, respectively, have been shown to reduce the likelihood of sustained virological response and to increase the rates of serious adverse events.

Aims & Methods: The aim of this study was to evaluate the impact of thrombocytopenia and hypoalbuminemia on treatment outcome and disease complications. We included in this study 855 HCV-infected cirrhotic patients treated with ombitasvir/paritaprevir/r+dasabuvir/r+ribavirin for 12 weeks in 10 university hospitals in Romania. The following groups were studied: 151 patients (17.7%) with albumin <3.5 g/dl, 239 (28%) with thrombocytopenia (a cutoff of 10000/mm3 was used) and 71 patients (8.3%) with both hypoalbuminemia and thrombocytopenia before initiating antiviral treatment. Safety (as AE in application rate were evaluated using Pearson’s correlation, multivariate analysis and Chi-Square test.

Results: Main patient characteristics were: 100% genotype 1b, a median age of 60 years (46.6, 74.2), high rate of previous interferon-based-treatment (36.1%). End-of-treatment and sustained virological response rate were both >99% and there was no correlation with the presence of thrombocytopenia or hypoalbuminemia. The rate of adverse events in the whole cohort was 17.5% at 2 weeks reaching 18% at the end of treatment with only 0.8% severe adverse events with no statistical association with the presence of thrombocytopenia and hypoalbuminemia. The multivariate analysis showed significant association of thrombocytopenia (<10000/mm3) with higher (>1) degree of oesophageal varices (p = 0.001), one of upper digestive hemorrhage during treatment (p = 0.011), and prior exposure to interferon based regimens (p = 0.025). Low albumin (<3.5 g/dl) also correlated with higher (>1) degree of oesophageal varices (p = 0.001) and onset of upper digestive hemorrhage during treatment (p = 0.002).

Conclusion: The efficacy and safety of the ombitasvir/paritaprevir/r+dasabuvir/r+ribavirin (as recommended by national regulations) was not different in cirrhotic patients with hypoalbuminemia and thrombocytopenia, but complications rate was higher so close follow-up and profilactic measures should be recommended, especially if previously exposed to interferon containing regimens.

Disclosure of Interest: All authors have declared no conflicts of interest.

Real-world impact of rifaximin-a use in hepatic encephalopathy patients with advanced liver disease on continued alcohol misuse: a post-hoc analysis of the IMPRESS study

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Introduction: In the UK multicentre, retrospective, real-world study, IMPRESS, rifaximin-a (RFX) use in patients with hepatic encephalopathy (HE) significantly reduced hospitalisations and length of stay in the 16 and 12 months post-RFX initiation compared to the respective periods pre-RFX initiation. This post-hoc analysis of the IMPRESS data compared hospital resource use pre- and post-RFX initiation in 2 sub-groups of difficult-to-treat HE patients: those with alcohol-related disease or continued alcohol misuse.

Aims & Methods: Medical records of patients from 11 UK hospitals who were prescribed RFX for HE between July-2008 and May-2014 were retrospectively reviewed; details of demographic and clinical characteristics, and all-cause hospitalisations were collected in the 6 and 12 months pre- and post-RFX initiation. Patients with baseline MELD score ≥15 or not abstinent at the end of the study period were included in this analysis. Statistical significance of the mean change (standard error of the mean, SEM) was calculated using paired t-test or Wilcoxon test.

Results: Only patients alive at the end of the 6 and 12 months RFX-treatment periods were included: 114 and 102, respectively. Amongst these, 33/114 (29%), for the 6 months) and 26/102 (25%, for the 12 months) had baseline MELD ≥15; mean age, 63 years; 70% were male; 66% had alcohol-related liver disease; mean MELD 24. The mean (SEM) number of bed days/patient reduced from 25 (6.0) in the 6 months pre- to 15 (5.5) in the 6 months post-RFX initiation, and from 36 (9.5) in the 12 months pre- to 20 (7.7) in the 12 months post-RFX initiation (p value not significant). At 6 months post-RFX initiation, 15/114 (13%) patients were still actively drinking. At RFX initiation, mean age was 56 years; 73% were male, mean MELD was 19. Despite this, the mean (SEM) number of bed days/patient decreased from 36 (7.9) in the 6 months pre- to 15 (5.4) in the 6 months post-RFX initiation (p = 0.048), and the mean of hospitalisations/patient fell from 2.8 (0.5) to 1.2 (0.4) (t-test p = 0.059; Wilcoxon test p = 0.029). Too few patients with continued alcohol misuse were alive at 12 months to evaluate. Two patients reported adverse events: none serious.

Conclusion: In UK clinical practice, treatment with RFX for HE for 6 or 12 months suggested trends in reduced hospital length of stay in patients with advanced liver disease and in those with continued alcohol misuse. However, larger studies are needed to strengthen these findings.

Disclosure of Interest: M. Hudson: Consultant for Norgine; advisory board member; has given sponsored lectures on behalf of Norgine. P. Di Maggio: Employee of Norgine. R. Cipelli: Consultant for Norgine; employee of pH Associates which was commissioned by Norgine to provide support with study design and management; data analysis and scientific editorial services. R. Aspinall: Consultant for Norgine; advisory board member; has given sponsored lectures on behalf of Norgine.
P0043 A PROPORTIONALLY GREATER ELEVATION IN LIVER TRANSPLANT CANDIDACY IN PATIENTS WITH NAFLD AND PORTAL VEIN THROMBOSIS

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Introduction: NASH progresses to cirrhosis and its complications including hepatocellular carcinoma. It is possible that risk factors for NAFLD-associated cirrhosis may differ in Eastern countries from those in the West. Thus, we aimed to document the characteristics of patients with NAFLD-associated cirrhosis from Turkey, an European country sharing 97% of its borders with Asia. Relative to other Easterns, the Turkish population exhibits a higher rate of obesity and work ethic that could impact to that in the Westerns.

Aims & Methods: To characterize non-alcoholic fatty liver disease (NAFLD) presentation with esophageal varices. METHODS: We have kept the records of patients at our hepatology unit and affiliated liver center. Data were collected for esophageal varices at the advanced endoscopy unit. A cohort of patients with esophageal varices from 2003 to 2014 was reviewed. Eligible patients were ≥18 years of age and have had esophageal varices diagnosed by upper gastrointestinal endoscopy examination. They had regular clinical follow-up and endoscopic examinations at our clinic. Efficacy data were based on the last evaluation.

Results: Primary end-point of the study was to use this cohort of patients with esophageal varices to evaluate the relationship between this disease and several etiologies, including NAFLD, hepatitis B, hepatitis C or other liver-related diseases. We also used this cohort to draw this conclusion in terms of PVT, HCC, survival and mortality. Of the 258 patients with esophageal varices; NAFLD in 39.0% (101 patients), hepatitis B virus in 29.1% (75 patients) and HCV in 11.2% (29 patients). The mean age of NAFLD was 56.4 ± 16.0 years and 62% of these patients were men. Moreover, 47.5% had PVT, 5.0% had HCC, and 45.5% had fundic varices. The mortality rate was 47.5% during follow-up, but increased to 80% in the presence of HCC. PVT was observed in 47.5% of patients with NAFLD, 29.3% of patients with hepatitis B, 17.2% of patients with hepatitis C and 23.3% of patients with other liver-related diseases (P < 0.001). Of the 111 patients (43%) that died during the study period, 72 patients (64.9%) had no PVT (P = 0.057). HCC was: 5.0% in patients with NAFLD, 26.7% in patients with hepatitis B, 34.5% in patients with hepatitis C, and 5.7% in other diseases (P < 0.001). Of the 38 patients with HCC, 13% had PVT. Moreover, HCC increased the mortality rate in almost all the groups. Of the patients, 50.0% with NAFLD, 33.3% with hepatitis B, 26.3% with hepatitis C, and 58.3% with other diseases were alive at the end of the 5-year period with a significant difference according to the Kaplan-Meier log Rank test (P < 0.04). Risk for mortality, measured by risk ratio (RR), did not change per gender (RR: male/ female = 43.3%/42.5%, P > 0.05) or with the occurrence of cirrhosis (RR: 44.8%/28.6%, P > 0.05). However, it changed with the existence of fundic varices (RR: 11.8%/4.04 in favor of fundic varices development) and HCC (RR: 78.9%/38.6%, P < 0.0001 in favor of HCC development).

Conclusion: Data revealed a proportionally greater rise in liver transplant candi- dacy due to NAFLD-associated cirrhosis with portal vein thrombosis. The mor- tality rate of patients with NAFLD-associated cirrhosis did not differ from that in patients with viralcaused cirrhosis. We confirmed that NAFLD was the third leading cause of HCC on the transplantation waiting list. Older patients with HCC were more prone to developing more cirrhosis (HCC and high cirrhosis rate). These findings should constitute a reliable guideline for evaluating patients at the transplant center and for health policy makers to develop better strategic pre- ventive measures against liver diseases.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

P0044 RISK FACTORS AND PREDICTIVE MODEL FOR THE DEVELOPMENT OF MULTIDRUG RESISTANT BACTERIAL INFECTIONS AND THE IMPACT ON PROGNOSIS IN HOSPITALIZED DECOMPENSATED LIVER CIRRHOSIS PATIENTS


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Introduction: Bacterial infections are a leading cause of mortality in patients with decompensated cirrhosis. Aims & Methods: The objective of this study was to evaluate the prevalence of multiresistant bacterial infections, associated risk factors and their impact on prognosis in hospitalized decompensated liver cirrhosis patients.

This was a retrospective Retrospective study that consecutively evaluated all bacterial infections with confirmed microbiological isolation in patients with decompensated liver cirrhosis admitted to the Gastroenterology ward between January 2009 and May 2016.

Results: There were 308 infections with confirmed microbiological isolates, cor- responding to 218 hospitalizations, in a total of 161 patients. The median age of the patients was 63 years (IQR 55–71) and 67% of them were men. Alcoholic liver disease was the major cause of cirrhosis (72%). Among the infections evalu- ated, 87% were nosocomial and 13% community-acquired. Urinary tract infec- tions was the most common infection (57%). In 27% of patients there were at least two concomitant bacterial infections. Multidrug resistant (MDR) bacteria were isolated in over half of patients. In the multivariate analysis, prophylaxis for spontaneous bacterial peritonitis (OR 2.3, p = 0.009), MELD score greater than 19 at admission (OR 1.7, p = 0.043), hospitalization in an Intensive/Intermediate Care in the previous month (OR 2.8, p = 0.001) and antibiotic therapy for infec- tion in the last 6 months (OR 2.4; p = 0.001) were independently associated with MDR infection. From the variables identified in the multivariate analysis, a predictive model of MDR bacterial infection was created. Assuming a sensitivity of 66% and a specificity of 72%, we considered the cut-off of 0.0415 as clini- cally relevant, regarding likelihood of developing a MDR bacterial infection (AUROC 0.723; 95% CI 0.667-0.780). The occurrence of a MDR infection was associated with a longer duration of hospitalization (p = 0.017). In the multi- variate analysis there was no independent association between MDR infection and in-hospital mortality and one month after discharge.

Conclusion: The prevalence of MDR bacterial infections in cirrhotic patients is significant and associated with a longer hospital stay. It is possible to identify predictors of its occurrence in order to implement epidemiological strategies to reduce the risk of these infections.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference
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Introduction: Hepatitis C virus (HCV) diminishes health related quality of life (HRQOL). Currently, there is no published data on assessing the impact of treatment of chronic hepatitis C with the new antiviral drugs in old-aged patients. We aimed to study the effect of treatment of chronic hepatitis C with the new antiviral drugs in old-aged patients in HRQOL. About 132 patients with chronic hepatitis C (cirrhotic and non-cirrhotic) were enrolled in the study. Age of patients was sixty years old and older. All patients were treated with sofosbuvir/daclatasvir with or without ribavirin for three months. The HRQOL was assessed with sickness impact profile scoring (SIP) before start of treatment, at end of treatment and after three months of end of treatment.

Results: Old chronic hepatitis C patients who were treated achieved primary vir- ological response (end of treatment) with percentage 100% and sustained virolo- gical response (SVR) after 24 weeks of end of treatment in about 96% of treated patients. Before treatment, patients with chronic hepatitis C had worse scores especially in work, sleep, rest and recreation and pastimes categories. After treat- ment, patients who received sofosbuvir/daclatasvir with or without ribavirin had significant improve in work, sleep, rest and recreation and pastimes categories with p-value 0.001. Numerical improvement was observed in total score, physical and psychosocial dimension scores. In patients with SVR, the most improvement was in work and psychosocial dimension scores. There was no significant difference in SIP between scores after end of treatment and 3 months of end of treatment.

Conclusion: Treatment of chronic hepatitis C in old-aged patients had a signific- ant improvement in HRQOL.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference
**Introduction:** Accurate determination of the degree of hepatic-fibrosis is mandatory not only for the diagnosis and prognosis of disease, but also for deciding on the antiviral treatment. Indeed, many studies have been dedicated to the search of non-invasive fibrosis markers capable of providing an accurate information about hepatic fibrosis stage in patients with chronic hepatitis C (CHC). Direct and indirect markers of hepatic fibrosis are useful for prediction of liver cirrhosis but have limited accuracy for the diagnosis of significant fibrosis. Therefore, the development of more advanced scores combining both direct and indirect markers may improve their diagnostic accuracy.

**Aims & Methods:** This work is concerned with determining the levels of some of fibrosis markers, which are directly involved in deposition and removal of extracellular matrix (ECM), together with other indirect fibrosis markers so as to construct a predictive score capable of identifying the presence of significant fibrosis with a high degree of accuracy. Then, we aimed to estimate its performance against that of the other simple noninvasive tests in chronic hepatitis C patients.

**Material and Methods:** A total of 148 Egyptian HCV patients were subjected to routine laboratory workup in addition to estimation of serum AFP, hyaluronic acid, platelet-derived growth factor (PDGF), tissue inhibitor of metalloproteinase-1 (TIMP-1) and collagen IV. According to fibroscan, patients were classified into those with non-significant fibrosis (F<2) and significant fibrosis (F≥3).

**Results:** Based on univariate analysis, ten variables were significantly higher in patients with significant fibrosis. Patients with F2-F4 had 2.08-fold, 2.14-fold, 1.80-fold and 1.90-fold increase in the concentrations of collagen IV, HA, PDGF and TIMP-1, respectively. Multivariate regression demonstrated that only age, AFP, PDGF, collagen IV and TIMP-1 retained significance. Therefore, a five-marker score named Egypt (EGY) Fibro-mark (FM) was developed. A significant correlation was found between its candidate markers and liver fibrosis progression. AFP was found to have highest correlation (r=0.47, P<0.0001) followed by collagen IV (r=0.46, P<0.0001), Age (r=0.43, P<0.0001), TIMP-1 (r=0.40, P<0.0001) and PDGF (r=0.40, P<0.0001). ROC curve was used to estimate and compare the diagnostic accuracy of these candidate variables. As a consequence, these markers were in a decreasing rank: AFP (AUC 0.79), collagen IV (AUC 0.78), age (AUC 0.70), TIMP-1 and PDGF (AUC 0.75). Additionally, Bivariate Spearman’s rank correlation coefficient between EGY-FM and its candidate markers was determined for estimating the impact of each marker on the predictive criteria. The diagnostic value of Egy FM was then assessed by ROC curve showing an AUC of 0.89 for diagnosing significant fibrosis at an optimal cut-off point of 0.45 with 97% sensitivity, 83% specificity and 79% efficiency. Next, the area under the ROC curve (AUC) was used to evaluate and compare the performance characteristics of different non-invasive scores. The AUC was greatest for Fibro-mark (0.89), then BRC (0.83), followed by FRT and King’s score (0.82), APRI (0.80), Fibro-gram (0.70) and finally FibroQ (0.63).

**Conclusion:** Egy Fibro-mark (FM) score, a more sophisticated score combining ‘direct’ and ‘indirect’ markers, is a useful tool to improve the staging of liver fibrosis in CHC patients and seems more efficient than BRC, FRT, King’s score, APRI, Fibro-mark score and FibroQ in this group of Egyptian patients.

**Disclosure of Interest:** D. Omran: This study was supported by the science and technology development fund (STDF), Egypt; Project ID: 5380, basic and applied research. All other authors have declared no conflicts of interest.

**Reference**
Disclosure of Interest: RBV combination was the most effective among the studied regimens.

Results: Among the included five studies, four studies, with low to moderate risk of bias, were included for the meta-analysis (n = 1096). The BCV-TRIO showed a high-response rate in naïve patients (SVR12 rate ¼ 95.5% [95% CI [93.5–96.9]). This total population was sub-grouped to get SVR12 rates; 89.5% [95%CI [85.3–92.4]), 96.2% (95% CI [93.0–98.0]), 93.5% (95% [92.9–96.1]), 91.1% (95% CI [87.6–93.7]), 93.9% (95% CI [86.6–97.3]), and 91.9% (95% CI [89.4–94.0]) for HCV genotype 1a, HCV genotype 1b, IL28B CC genotype, IL28B non-CC genotype, cirrhotic, and non-cirrhotic respectively. The virologic failure occurred in only 40 patients (7%) (95% [5.2–9.4]). There was no difference when adding ribavirin to this combination (RR ¼ 0.98, 95% confidence interval (95% CI) [0.90–1.05]). Using this regimen on interferon-experienced patients (SVR12 rate ¼ 1.03, 95% CI [0.98, 1.08]), P ¼ 0.30, or changing the dose of BCV from 75 mg to 150 mg regardless the genotype 1 subtypes or IL28B genotype. Similarly, the minimal failure of treatment showed no difference regarding the main two comparisons regardless the cause of this failure. Increasing the dose or the duration did not show a significant increase in the efficacy. The rates of serious adverse events (AEs) occurrence were; (3.4%, 95%CI [2.3–5.1]), (6.5%, 95%CI [3.2–12.7]), (2.3%, 95% CI [0.6–8.8]), and (2.9%, 95% CI [0.2–33.6]) for BCV-TRIO, (BCV-TRIO þ RBV) for 12 weeks, (DCV þ ASV þ BCV-150 mg) for 12 weeks, and both (BCV-TRIO) and (DCV þ ASV þ BCV-150 mg) for 24 weeks respectively. For BCV-TRIO, the most-frequent AEs were headache, diarrhea, fatigue, and nausea with rates; (21.2%, 95%CI [18.4–24.2]), (14.3%, 95% CI [12.0–16.9]), (13.8%, 95% CI [11.2–16.3]), and (13.4%, 95% CI [10.9–16.4]) respectively.

Conclusion: This study reported a high SVR, minimal treatment failure rate, and few AEs with fixed-dose three drug combination of daclatasvir, asunaprevir, and beclabuvir in treatment of HCV genotype 1 infection. Eleven electronic search engines/libraries, including PubMed, Scopus, Web of Science, Google Scholar, Virtual Health Library (VHL), WHO Global Health Library (GHL), ClinicalTrials, POPLINE, System for Information on Grey Literature in Europe (SIGLE), Cochrane library, and the New York Academy of Medicine (NYAM), were systematically searched for any clinical trial reporting the efficacy and safety of BCV-TRIO for the treatment of HCV genotype 1 infection. Studies were screened for eligibility and data was extracted by two independent reviewers. Sustained virologic response rate after 12 weeks of treatment was calculated, and the comparison meta-analysis (RR) was conducted using the Comprehensive Meta-analysis (CMA) platform. The protocol was registered in PROSPERO (CRD42017054391).

Results: Among the included five studies, four studies, with low to moderate risk of bias, were included for the meta-analysis (n = 1096). The BCV-TRIO showed a high-response rate in naïve patients (SVR12 rate ¼ 95.5% [95% CI [93.5–96.9]). This total population was sub-grouped to get SVR12 rates; 89.5% [95%CI [85.3–92.4]), 96.2% (95% CI [93.0–98.0]), 93.5% (95% [92.9–96.1]), 91.1% (95% CI [87.6–93.7]), 93.9% (95% CI [86.6–97.3]), and 91.9% (95% CI [89.4–94.0]) for HCV genotype 1a, HCV genotype 1b, IL28B CC genotype, IL28B non-CC genotype, cirrhotic, and non-cirrhotic respectively. The virologic failure occurred in only 40 patients (7%) (95% [5.2–9.4]). There was no difference when adding ribavirin to this combination (RR ¼ 0.98, 95% confidence interval (95% CI) [0.90–1.05]). Using this regimen on interferon-experienced patients (SVR12 rate ¼ 1.03, 95% CI [0.98, 1.08]), P ¼ 0.30, or changing the dose of BCV from 75 mg to 150 mg regardless the genotype 1 subtypes or IL28B genotype. Similarly, the minimal failure of treatment showed no difference regarding the main two comparisons regardless the cause of this failure. Increasing the dose or the duration did not show a significant increase in the efficacy. The rates of serious adverse events (AEs) occurrence were; (3.4%, 95%CI [2.3–5.1]), (6.5%, 95%CI [3.2–12.7]), (2.3%, 95% CI [0.6–8.8]), and (2.9%, 95% CI [0.2–33.6]) for BCV-TRIO, (BCV-TRIO þ RBV) for 12 weeks, (DCV þ ASV þ BCV-150 mg) for 12 weeks, and both (BCV-TRIO) and (DCV þ ASV þ BCV-150 mg) for 24 weeks respectively. For BCV-TRIO, the most-frequent AEs were headache, diarrhea, fatigue, and nausea with rates; (21.2%, 95%CI [18.4–24.2]), (14.3%, 95% CI [12.0–16.9]), (13.8%, 95% CI [11.2–16.3]), and (13.4%, 95% CI [10.9–16.4]) respectively.

Conclusion: This study reported a high SVR, minimal treatment failure rate, and few AEs with fixed-dose three drug combination of daclatasvir, asunaprevir, and beclabuvir in treatment of HCV genotype 1-infected patients, without adding ribavirin, prior interferon-based therapy, restriction on noncirrhotic patients, restriction on certain IL28B genotype, restriction on baseline resistance-associated variants, or expansion the duration of the treatment to 24 weeks.

Disclosure of Interest: All authors have declared no conflicts of interest.
Introduction: Egypt has the highest prevalence of HCV worldwide. Prevalence of HCV was reported to be 13.9% among healthy populations. Adults have higher HCV prevalence (15.7%) than children (4.0%). Geographically, HCV is highly prevalent in the Nile delta (15.8%) than in Upper Egypt (9.02%). The household contacts of HCV seropositive patients had shown to have a high risk of HCV infection.

Aims & Methods: The aim of this study was to determine the prevalence of HCV infection among household contacts of HCV seropositive index patients. We also aimed to compare HCV genotyping distribution in upper and lower Egypt. In this Multicentre hospital case control based study a total of 4894 Egyptian individuals were recruited to the hospitals from different Egyptian population in Upper & lower Egypt (mainly from Dakahlia, Cairo and Assuit governorates). The index HCV patients were 1106 cases whereas the families or close household contacts of these index cases were 3788 cases. Ideally family was selected on the basis of containing at least one positive HCV index, one positive HCV member and other one negative HCV member with no history of any liver complications or disorders first and second degree consanguinity, living and sharing usual life activity and having at least 15 years of exposure to the index case). The positive cases (index or contact cases) in the family were selected with inclusion criteria of 1-HCV positive by PCR RNA > 6 months, 2-Adults (above 18 years) of both sexes 3-Any stage of HCV related liver diseases. While cases were diagnosed as spontaneously cleared the virus (SVC) based on the following criteria: positive HCV antibody but negative HCV RNA in 2 successive samples at least 6 months apart with no prior history of antiviral therapy. Each participant was subjected to routine clinical and laboratory investigations in addition to molecular diagnosis and PCR HCV to confirm HCV infection. Sequencing analysis of the PCR HCV was performed using ABI Prism 310 Genetic Analyzer (PE Applied Biosystems, Germany). The sequencing reaction was performed using Big Dye Deoxy Terminator method as recommended by the manufacturer (PE Applied Biosystems). Genotypes were determined according to the published reference sequences.

Results: The prevalence of Anti-HCV +ve cases among household contacts was 20.71% but when PCR HCV was performed only 17.83% were positive +ve while 2.9% were spontaneously cleared the virus (SVC). The HCV prevalence among house hold contacts was 17.29 & 19.17% while the SVC was 2.49 & 1.55% in lower & upper Egypt respectively. While the genotyping of the positive cases were performed it was found that the following pattern was noticed in the upper & lower Egypt respectively: (genotype 4a (90.3%) & 70.1%, 4m (4.8%) & 11.8%, 4n (0.5%) & 3.2%) 4v (0.2% & 2.9%) 4i (0.5% & 1.9%) 4g (0.8% & 1.2%) & 1a (2.9% & 8.3%) as shown in the following table.

<table>
<thead>
<tr>
<th>HCV genotype</th>
<th>Upper Egypt (%)</th>
<th>Lower Egypt (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>4a</td>
<td>90.3</td>
<td>70.1</td>
</tr>
<tr>
<td>4m</td>
<td>4.8</td>
<td>11.8</td>
</tr>
<tr>
<td>4n</td>
<td>0.5</td>
<td>3.2</td>
</tr>
<tr>
<td>4v</td>
<td>4.8</td>
<td>1.2</td>
</tr>
<tr>
<td>4i</td>
<td>0.2</td>
<td>2.9</td>
</tr>
<tr>
<td>1a</td>
<td>2.9</td>
<td>8.3</td>
</tr>
<tr>
<td>1g</td>
<td>0.0</td>
<td>0.3</td>
</tr>
<tr>
<td>1b</td>
<td>0.0</td>
<td>0.3</td>
</tr>
</tbody>
</table>

Conclusion: The prevalence of HCV was found to be 18.5% among household contacts of Egyptian families. The genotype 4 was predominant in upper Egypt (97.1%) more than lower Egypt (91.7%). On the other hand genotype 1a was higher in lower Egypt (8.3%) more than upper Egypt (2.9%).

Disclosure of Interest: All authors have declared no conflicts of interest.

References


Conclusion: The prevalence of HCV was found to be 18.5% among household contacts of Egyptian families. The genotype 4 was predominant in upper Egypt (97.1%) more than lower Egypt (91.7%). On the other hand genotype 1a was higher in lower Egypt (8.3%) more than upper Egypt (2.9%). Disclosure of Interest: All authors have declared no conflicts of interest.

References


PO051 RED BLOOD CELL DISTRIBUTION WIDTH (RDW) AS NON INVASIVE PREDICTOR OF LIVER FIBROSIS IN CHRONIC HEPATITIS C PATIENTS GENOTYPE 4

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Introduction: Red blood cell distribution width (RDW) is a numerical measure of the variability in size of red cell. It reflects variability in the size of circulating red blood cells (RBCs). RDW can be used as a prognostic marker in heart failure. In hepatic patients it was approved to be an independent predictor of liver fibrosis in patients with chronic HBV infection, and it is higher in patients with alcoholic liver disease and non alcoholic liver cirrhosis. The gold standard for assessing the histological outcome of liver disease is liver biopsy. This procedure is costly and carries a small risk of complications due to sampling error, invasiveness and requires hospitalization of at least 6-18h. These limitations have stimulated the development of non-invasive techniques for assessing the presence and the degree of liver fibrosis. Several laboratory scores composed of routine laboratory markers that are readily available have been proposed for non-invasive prediction of liver fibrosis in chronic hepatitis C (CHC) patients.

Aims & Methods: The aim of this work is to use RDW as a marker for non-invasive prediction of the stage of hepatic fibrosis in patients with chronic hepatitis C genotype-4. 100 patients with chronic hepatitis C were subjected to routine laboratory and radiological investigations in addition to using KX-21 Sysmex automated hematometry analyzer to measure RDW & RPR (RDW% & Platelets). Comparing with other liver fibrosis like APRI (AST-to-Platelet ratio) FIB-4 equation (using platelet count, AST, ALT, age) to perform this test. PCR HCV RNA, genotyping & liver biopsy (using METAVIR scoring system where cases were classified into early fibrosis (F1 + F2) 68 patients & late fibrosis (F3 + F4): 32 patients) were done.

Results: RDW & RPR were significantly higher in patients with late fibrosis > early fibrosis (P < 0.0001) while platelets count was significantly lower in late fibrosis > early fibrosis (p < 0.001). By applying ROC curve it was found that the cut off value of RDW was 16.5, with sensitivity 86.8% specificity 85.9%, accuracy 86.8% & ≥ the cut off value of the platelets was 196.5 with sensitivity 81.8%, specificity 68.2% accuracy 67.6, while RPR cut off value was 0.0897 with sensitivity 90.9%, specificity 85.9% & accuracy 87.6. As regard APRI test it was found that the cut off value of APRI was 0.5 with sensitivity 72.7%, specificity 66.7% & accuracy 68%. While FIB-4 equation showed cut off value 1.685 with sensitivity 77.3%, specificity 66.7% and accuracy 69%. In conclusion the area under the ROC curve for RDW, RPR were excellent but for platelets the ROC curve for APRI were fair. When applying regression analysis it was found that the RDW (OR:3.903, 95% CI: 0.913–9.95) so as the level of RDW increase by one unit the risk late fibrosis will increase by 3.9 fold. In addition the platelets increase by one unit the risk of late fibrosis will decrease by 0.953.

Conclusion: RDW & RPR may be used as simple, non-invasive predictors of advanced fibrosis in patients with chronic hepatitis C genotype-4.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

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PO052 CANCER INCIDENCE IN VARIOUS ORGANS OTHER THAN THE LIVER FOLLOWING DIRECT-ACTING ANTIVIRAL (DAA) THERAPY FOR HEPATITIS C


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Introduction: The incidence of liver cancer and its recurrence have been reported frequently at an early stage in patients who underwent interferon (IFN)-free direct-acting antiviral (DAA) therapy [1]. The underlying mechanisms of


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cancer incidence following DAA therapy may include the rapid clearance of hepatitis C virus, reconstitution of the immune system, and reduction of cancer immunosurveillance [2]. These changes may in fact have an impact on the development of cancer in other organs.

Aims & Methods: We conducted a retrospective analysis to compare the cancer incidence in patients treated with IFN-free DAA therapy with those treated with IFN therapy. All patients who achieved sustained viral response following antiviral therapy between 1992 and 2016 in our hospital were investigated retrospectively. Patient records were examined to identify new cases of cancer, as defined by pathology or medical imaging, in organs other than the liver following antiviral therapy. The date of diagnosis was determined based on the records, and the cancer incidence was compared between patients treated with DAA therapy and those treated with IFN therapy using the Kaplan-Meier method and Cox regression analysis. Patients with recurrent cancer were excluded from the analysis. Propensity score analysis followed by inverse probability of treatment weighting (IPTW) was used to correct for the effects of confounding factors.

Results: There was a significant difference in the age and sex of the patients treated with DAA (n = 324, median age: 70, male: 41%) and those treated with IFNs (n = 445, median age: 58, male: 60%). Median lengths of the observation period for the DAA and IFN groups were 1.3 and 6.2 years, respectively. There were 12 and 22 cases of cancer occurring in organs other than the liver in the DAA and IFN groups, respectively. These cancer cases occurred most frequently in the gastrointestinal tract, followed by the urinary organs, hematopoietic organs, biliary tract, pancreas, lungs, and other organs. The median periods from the start of the antiviral therapy to the time of diagnosis were 0.9 and 6.8 years in the DAA and IFN groups, respectively. Cumulative rates of cancer after 1 and 2 years were 3.0 and 5.0% for the DAA group, and 0.2 and 0.0% for the IFN group, respectively. The difference between the groups was significant (p = 0.02) based on Cox regression analysis using IPTW.

Table: Cox regression analysis for cancer incidence other than the liver in IPTW samples

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Hazard Ratio</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>IFN (Ref.)</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>DAA</td>
<td>4.49</td>
<td>1.264-15.96</td>
</tr>
</tbody>
</table>

Conclusion: Because cancer detection in organs other than the liver can be challenging in management of hepatitides, some cases with cancer found after the treatment might have been diagnosable before the treatment, possibly leading to an overestimation of the incidence after the treatment. The number of newly diagnosed cancer cases was small in the present study, resulting in a low statistical power. Nevertheless, the cancer incidence in organs other than the liver was significantly higher in patients treated with DAA therapy than those treated with IFN therapy. This difference persisted after correcting for possible confounding factors and sex of the patients. Our findings suggest that patients need to be carefully examined after DAA therapy for the development of cancer in various organs, including but not limited to the liver.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P0054 IS THERE AN INCREASE IN THE INCIDENCE OF HEPATOCELLULAR CARCINOMA IN CIRRHTIC PATIENTS WITH HEPATITIS C TREATED WITH THE DIRECT-ACTING ANTIVIRALS?

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Introduction: The impact of the virological cure on the evolution of cirrhotic patients treated with direct-acting antiviral agents (DAAs). Recent studies have reported an elevation in incidence of recurrence of hepatocellular carcinoma (HCC) and others a possible rise on the de novo incidence of HCC in the first year after treatment with DAA therapy, but not others.

Aims & Methods: This is a prospective study of cirrhotic patients treated with DAA between February/2015 and January/2017, under HCC screening with ultrasonography according to international guidelines. The main endpoint of the study was to determine the incidence of “de novo” and recurrent HCC. The second endpoint was to search for possible predictive factors associated with the occurrence of HCC. Statistical analysis performed on SPSSv.24. Results: 106 cirrhotics (73% mean; 54.5±8.8 years), MELD 7.3±2.6, 60% with portal hypertension (n = 64) and 22% with compensated cirrhosis (n = 23, 22 Child-Pugh B class). Two patients with previous HCC, stage Barcelona Clinic Liver Classification (BCLC) A, inviable after loco-regional treatment. The sustained virological response at week 12 was 89.9% (71/79); 4 deaths, 1 relapse, 1 therapeutic failure and 2 losses to follow-up (FU). In 11±7 months of FU, we registered 105 HCC. 4 “de novo” and 1 recurrence, which corresponded to an incidence of 3.8% of “de novo” HCC (13% in compensated cirrhosis). The BCLC staging was: stage A, stage B and stage C and the one with the recurrence was stage D. A Child-Pugh B class (p = 0.004), low platelets level (p = 0.001) and hospitalization for decompensation (p = 0.005) were associated with the occurrence of HCC; the genotype did not have association. The mean time to HCC development was 7.5 months (2-14).
**Conclusions:** In this cohort the “de novo” incidence of 3.8% of HCC after the transplant was much lower mainly in patients with decompensated cirrhosis, not eligible for treatment with interferon in the past, and in a short interval of time after treatment. These results alert for an eventual need to increase the frequency of screening in the post-treatment period and carefully evaluate the best timing for liver transplantation. We could not conclude about recurrence due to the small number of patients.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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**References**


5. ANRS collaborative study group on hepatocellular carcinoma (ANRS CO22). Recruitment of patients with hepatitis C virus infection who underwent liver biopsy between June 2015 and March 2017 were enrolled. Ten SWE measurements (GE Healthcare, USA) were recorded in the liver using a percutaneous route. The technical success was 92.4%. Sampling was considered adequate in 92.2% of patients. The percutaneous route included: coagulopathy/anticoagulation (32.2%), thrombocytopenia (17.8%), ascites (17.8%), and failed percutaneous liver biopsy (13.6%). In a fourth of the cases the biopsy was performed in the context of acute hepatitis, being in 12.6% for diagnosis of alcoholic hepatitis. The reasons for the failure of obtaining a histological diagnosis were as follows: especially alcoholic disease, hepatitis C and non-alcoholic steatohepatitis. In 80.5% of the cases the purpose of TJLB was for diagnosis and in the remaining cases for staging liver disease. Eighty-five patients (32.1%) had cirrhosis prior to biopsy. In a fourth of the cases the biopsy was performed in the context of acute hepatitis, being in 12.6% for diagnosis of alcoholic hepatitis. The reasons for the percutaneous route included: coagulopathy/anticoagulation (32.2%), thrombocytopenia (17.8%), ascites (17.8%), and failed percutaneous liver biopsy (13.6%). The technical success was 92.4%. Sampling was considered adequate in 92.2% of cases, which was associated with diagnostic purposes (94.9% vs. 86.8%, P < 0.001) and evidence of acute hepatitis (96.4% vs. 89.8%, P = 0.03). Most patients (60.4%) had histological criteria for cirrhosis. In 76.2% of patients TJLB allowed a histological diagnosis, mainly alcoholic and non-alcoholic steatohepatitis. The ability to provide a histological diagnosis was associated with adequate sample (80.8% vs. 21.1%, P < 0.001), presence of cirrhosis (83.9% vs. 71.6%, P = 0.023) and >1 passage (82.1% vs. 68.3%, P = 0.012). Findings were normal in 4.8%. In 70.9% of the situations the TJLB was considered to have an impact in the approach to the patient.

**Conclusion:** TJLB is a safe diagnostic tool with high diagnostic accuracy, allowing a change in strategy in a high percentage of cases.

**Disclosure of Interest:** All authors have declared no conflicts of interest.
Area under the curve and receiver operator characteristic (AUROC) compari-
sions of the diagnostic accuracy of the eight approaches used the interquartile range (IQR) and median of 10 SWE measurements using body mass index (BMI) and age were analysed using the Mann-Whitney U test.

Results: The study population consisted of 106 men and 94 women with a mean age of 56.8 years (18–81 years) and a mean BMI of 26.4 kg/m². Fibrosis score was 0/F1/F2/F3/F4 in 7/30/33/24/23 patients, respectively. The median SWE (m/s) of 10 measurements in patients with F0, F1, F2, F3, and F4 were 1.33, 1.57, 1.73, 1.95, 1.98, respectively. The median IQR/median was 0.21. Furthermore, we found no significant difference (BMI: 25.1 ± 2.4, < 25 ± 2.0, p = 0.012) indicated significantly greater IQR/median. There was no significant difference in the diagnostic accuracy between using the median or mean of three, five, and 10 measurements. The AUROC of diagnostic accuracy in patients with significant fibrosis (≥ F2) ranged from 0.778 (A) to 0.876 (H). AUROC increased based on the number of measurements. A signifi-
cant difference between 1 and 5 (p < 0.05), 1 and 10 (p < 0.001), and 2 and 10 (p < 0.005) measurements was observed in pairwise comparison. Likewise, AUC increased with the number of measurements and diagnostic values of the (A) to 0.923 (G). A significant difference (p < 0.005) was seen between one and 10 measurements. In the cohort of IQR/median < 0.3, the diagnostic accuracy of ≥ F2 and ≥ F3 ranged from 0.806 (A) to 0.877 (H), and from 0.832 (A) to 0.928 (H), respectively. In the cohort of obese (BMI ≥ 25) and old patients (age ≥ 65), the diagnostic accuracy of ≥ F2 and ≥ F3 ranged from 0.752 (A) to 0.862 (D), and from 0.735 (A) to 0.903 (H), respectively. Comparing the AUROC of one measure-
ment, IQR/median < 0.3 showed greater AUROC than those of other
cohorts, however, the AUROC of ten measurements were similar in each cohort.

Conclusion: No difference was found between reporting mean or median SWE
measurements. The diagnostic performance of SWE increased with the number of
measurements. Our results suggest that 10 measurements are recommen-
ded to ensure the accuracy of SWE measurements in a practical setting.

Disclosure of Interest: All authors have declared no conflicts of interest.
0.21–0.57). At univariate analysis LS was associated with: liver cirrhosis (p < 0.0001), steatosis (p = 0.0003), liver surface nodularity (p = 0.0003), active alcoholic abuse (p = 0.015), alcohol consumption/day (p = 0.0134), diabetes (p = 0.0223). At multivariate analysis cirrhosis (p < 0.0001) and steatosis (p = 0.0073) were independently associated with LS. At both univariate and multivariate analysis, PS was significantly correlated only with liver cirrhosis (p = 0.0058).

Conclusion: The present is the first series assessing LS and PS in ALD patients by using SWE. The feasibility of the technique was excellent. The reproducibility was good for LS and fair for PS. SWE was a good predictor of liver fibrosis in the ALD cohort. Liver cirrhosis was the only independent variable correlating with PS, whose estimation could be useful to detect alcohol-related pancreatic damage in patients with severe ALD.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

Table 1: Expression levels of serum microRNAs of the patients groups

<table>
<thead>
<tr>
<th>MicroRNAs</th>
<th>Normal</th>
<th>CHC</th>
<th>LC</th>
<th>HCC</th>
</tr>
</thead>
<tbody>
<tr>
<td>miR-16</td>
<td>14.26±0.69</td>
<td>23.29±0.46</td>
<td>23.25±0.54</td>
<td>4**</td>
</tr>
<tr>
<td>miR-34a</td>
<td>27.32±0.19</td>
<td>30.04±0.54</td>
<td>32.50±0.94</td>
<td>4**</td>
</tr>
<tr>
<td>miR-221</td>
<td>22.82±0.38</td>
<td>28.22±0.41</td>
<td>28.51±0.46</td>
<td>4**</td>
</tr>
<tr>
<td>miR-125</td>
<td>20.57±0.54</td>
<td>100.54±0.81</td>
<td>29.96±0.57</td>
<td>4**</td>
</tr>
<tr>
<td>miR-139</td>
<td>29.96±0.97</td>
<td>86.02±0.40</td>
<td>30.03±0.43</td>
<td>4**</td>
</tr>
<tr>
<td>miR-145</td>
<td>20.65±0.52</td>
<td>80.74±0.59</td>
<td>20.64±0.57</td>
<td>4**</td>
</tr>
<tr>
<td>miR-199</td>
<td>80.23±0.72</td>
<td>330.38±0.74</td>
<td>311.98±0.72</td>
<td>66.16±0.44</td>
</tr>
</tbody>
</table>

**p < 0.01 significant increase than control, *p < 0.05 significant increase than CHC and HCC, **p < 0.01 significant decrease than control, *p < 0.05 significant decrease than CHC and LC, **p < 0.01 significant decrease than CHC

Table 2: Expression of exosomal microRNAs in HCV and HCC.

<table>
<thead>
<tr>
<th>miRNA</th>
<th>HCV</th>
<th>HCC</th>
</tr>
</thead>
<tbody>
<tr>
<td>miR-16</td>
<td>14.26±0.69</td>
<td>23.29±0.46</td>
</tr>
<tr>
<td>miR-34a</td>
<td>27.32±0.19</td>
<td>30.04±0.54</td>
</tr>
<tr>
<td>miR-221</td>
<td>22.82±0.38</td>
<td>28.22±0.41</td>
</tr>
<tr>
<td>miR-125</td>
<td>20.57±0.54</td>
<td>100.54±0.81</td>
</tr>
<tr>
<td>miR-139</td>
<td>29.96±0.97</td>
<td>86.02±0.40</td>
</tr>
<tr>
<td>miR-145</td>
<td>20.65±0.52</td>
<td>80.74±0.59</td>
</tr>
<tr>
<td>miR-199</td>
<td>80.23±0.72</td>
<td>330.38±0.74</td>
</tr>
</tbody>
</table>

**p < 0.01 significant increase than control, *p < 0.05 significant increase than CHC and HCC, **p < 0.01 significant decrease than control, *p < 0.05 significant decrease than CHC and LC, **p < 0.01 significant decrease than CHC

Conclusion: These results indicate that measuring the expression levels of liver-specific circulating microRNAs can be used as a reliable diagnostic and prognostic tool for HCC. Our results demonstrated that the up-regulation of miR-16, miR-34a, and miR-221 can differentiate between normal individuals and patients with liver disease ranging from fibrosis, cirrhosis, and HCC. Meanwhile, the noticeable down-regulation of miR-125a, miR-139, miR-145 and miR-199a in the HCC patient group indicates that these microRNAs can differentiate HCC from CHC and LC.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
3. Li, X., N. Zhang, L. Xu, G. Zhao. (2015). State Key Laboratory Of Oncology In South China, Sun Yat-sen University Cancer Center, Guangzhou/China
4. Li, X. (2015). State Key Laboratory Of Oncology In South China, Sun Yat-sen University Cancer Center, Guangzhou/China
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Introduction: Primary hepatocellular carcinoma (HCC) is one of the most common malignancies all over the world. HCC is associated with poor prognosis. However, the mechanism of HCC initiation and development remains unclear. In our previous work, high-throughput microarray assay in collected clinical HCC samples followed by bioinformatic analysis suggested that Metallothionein 1G (MT1G) might be one of the key factors in HCC.

Aims & Methods: We detected the MT1G expression in paired HCC samples and HCC cell lines by RT-qPCR and Western blot. Then MSp (Methylation specific PCR) and BGS (Bisulfite genomic sequencing) were performed to evaluate methylation status of MT1G in HCC. The functional significance of MT1G in HCC was further investigated by in vivo, cell culture and DNA methylation analysis. Results: MT1G was inactivated in all (6/6) HCC cell lines tested, but was readily re-activated by demethylation treatment. Aims & Methods: We detected the MT1G expression in paired HCC samples and HCC cell lines by RT-qPCR and Western blot. Then MSp (Methylation specific PCR) and BGS (Bisulfite genomic sequencing) were performed to evaluate methylation status of MT1G in HCC. The functional significance of MT1G in HCC was further investigated by in vivo, cell culture and DNA methylation analysis.

Conclusion: These results indicate that measuring the expression levels of liver-specific circulating microRNAs can be used as a reliable diagnostic and prognostic tool for HCC. Our results demonstrated that the up-regulation of miR-16, miR-34a, and miR-221 can differentiate between normal individuals and patients with liver disease ranging from fibrosis, cirrhosis, and HCC. Meanwhile, the noticeable down-regulation of miR-125a, miR-139, miR-145 and miR-199a in the HCC patient group indicates that these microRNAs can differentiate HCC from CHC and LC.

Disclosure of Interest: All authors have declared no conflicts of interest.
regulated in cancer tissues compared with the adjacent non-tumor tissues (P < 0.05). The expression level of MT1G in the liver cancer cells line was closely correlated to the promoter hypermethylation status. The MT1G expression in silenced HCC cell lines could be restored by demethylation agent. We generated HCC cell lines overexpressed MT1G. Ectopic re-expression of MT1G by stable transfection in SMMC-7721 and Hep3B cells inhibited colony formation (P < 0.001), suppressed cell motility and invasiveness (P < 0.05), concomitant with up-regulation of E-cadherin; and down-regulation of PCNA, MMP2, MMP13 and Vimentin. The in vivo growth of HCC cells in nude mice was also markedly inhibited after stable expression of MT1G (P < 0.001). MT1G over-expression in HCC cells induced the cell apoptosis (P < 0.01).

Conclusion: Our results demonstrate that MT1G promoter methylation directly mediates the transcription down-regulation and common occurs in HCC. MT1G gene can act as a functional tumor suppressor in liver carcinogenesis by playing an important role in depression of cell proliferation, migration, invasion, and induction of cell apoptosis.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0064 THE FXR RECEPTOR PATHWAY IN HEPATOCELLULAR ADENOMA AND FOCAL NODULAR HYPERPLASIA, A PRELIMINARY EXPERIENCE
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Introduction: Hepatocellular adenoma (HCA) and focal nodular hyperplasia (FNH) may be confused on medical imaging. Both tumours are not connected to the biliary tree, however only FNH accumulates bile salts, suggesting that hepatocellular uptake and secretion of bile constituents differs in FNH and HCA. Therefore, one would anticipate changes in the Farnesoid X receptor (FXR) expression. However, the expression of FXR and its targets in HCA and FNH is relatively unknown. Targets of FXR regulate uptake and excretion of bile constituents. The current study aimed to examine FXR and its targets in normal and FNH medical imaging. We studied the expression of FXR and its targets in HCA and FNH and compared this with the appearance of lesions on MRI.

Aims & Methods: Tumour tissue and normal tissue from 7 patients with HCA and 7 patients with FNH was obtained. Diagnosis was confirmed by histopathological examination in all patients. Reverse transcription of the mRNA to cDNA was performed, using random primers and MultiScribe Reverse Transcriptase (Life Technologies, Carlsbad, Ca). The cDNA was used as template for PCR amplification by Taqman® assay analysis (Applied Biosystems, Foster City, CA). The expression of all the target genes in the FXR pathway (SHP, NTCP, OATP1B1, OATP1B3, BSEP, CYP7A1, CYP8B1, BAAT, SLC27A5, CYP3A4, SULT2A1, UGT2B4, CYP8A1, MRP2, MRP3, MDR3) were compared to the expression functioned as internal reference in both normal and tumour tissue. Matched case comparisons were made for tumour and normal tissue. DNA expression of FNH and HCA was compared to MRI findings.

Results: FXR was downregulated in both HCA and FNH. NTCP was significantly downregulated in FNH, and not significantly in HCA, although showing a trend towards down regulation. Three patients (1 FNH 2 HCA) show aberrant expression of NTCP compared to all the other patients. All these three patients had also an unclear or incorrect diagnosis based on MRI scan with gadodextric acid as compared to final diagnosis by histopathological examination. OATP1B1 was downregulated in both HCA and FNH, except again for the three patients with the aberrant expression. Expression of OATP1B3 and SHP in HCA and FNH did not significantly differ from expression in healthy liver tissue. MRP2 was significantly downregulated in HCA, but not in FNH. However, this may again be due to the patients with the aberrant expression pattern. OATP1B3 was significantly downregulated in HCA. CYP3A4 and CYP2A1 were very strong downregulated in HCA, but not in FNH. GGFR 4 was heavily downregulated in HCA, but not in FNH. BAAT was significantly downregulated in FNH.

Conclusion: Limited by sample size, this study suggests that misdiagnosis based on medical imaging might actually correlate with aberrances on hepatocyte transporter level. This seemed to account for NTCP (bile salt importer), OATP1B1 (bile salt importer) MRP2 (efflux pump of conjugated compounds). Although FXR itself was downregulated in both FNH and HCA, its downstream targets differed in expression between tumours. FXR receptor activity might be altered even when not different, or downstream targets might be influenced by factors outside the FXR pathway. Future research could provide a more profound insight into this mechanism.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0065 CUX1 CONTROLS ENDOPLASMIC RETICULUM STRESS AND AUTOPHAGY-RELATED CELL DEATH
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Introduction: CUX1 (CUTL1) is a transcription factor able to promote the expression of several genes implicated in cellular proliferation, differentiation and demise. In normal adult cells, it preferentially favors the expression of pro-apoptotic genes. Its aberrant expression in tumor turns its role as foe.

Aims & Methods: Here, we analyze the role exerted by CUX1 during deacetylase inhibitors mediated cell death in liver cancer cells. CUX1, endoplasmic reticulum (ER) stress and autophagy markers were analyzed by RT-qPCR in two liver cancer cell lines HepG2 and Hep3B. Protein level was measured by western blotting. Cells were transfected with siRNA for CUX1 and furthermore treated with deacetylase inhibitors panobinostat, SAHA and trichostatin A. Thapsigargin, an endoplasmic reticulum stress inducer, served as positive control.

Results: CUX1 knock down caused a suppression of ER stress and autophagy markers BIP, CHOP, ATF4, ATF6, Beclin1, MAP1LC3B, UVRAG and TFE2 at early time point (6 hours) in both cell lines. Prolonged transfection did not alter the expression of the above mentioned markers; BIP was the only one suppressed in HepG2 after 24 hours. Interestingly, the deacetylase inhibitors are able to promote CUX1 over-expression after 6 hours of treatment, whereas they show to lose this ability after 24 hours. CUX1 knock-down reduced significantly not its protein level after treatment with deacetylase inhibitors. CUX1 knock down counteracts the accumulation of BIP protein after 24 hours of treatment with deacetylase inhibitors. Thapsigargin induced BIP independently from CUX1.

Conclusion: ER stress and autophagy markers are under the control of CUX1. The cell death induced by deacetylase inhibitors is strictly connected with CUX1 expression and activity. Further studies are needed to clarify the exact mechanism exerted by CUX1 in this scenario.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0066 CUX1 CONFRS RESISTANCE TO APOPTOTIC CELL DEATH IN LIVER CANCER CELLS
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Introduction: CUX1 (CUTL1) is a transcription factor able to promote the expression of several genes implicated in cellular proliferation, differentiation and demise. In normal adult cells, it preferentially favors the expression of pro-apoptotic genes. Its aberrant expression in tumor turns its role as foe.

Aims & Methods: Here, we analyze CUX1 activity in TRAIL (Tumour necrosis factor related apoptosis inducing ligand) mediated cell death in liver cancer cells. CUX1 was knocked down in HepG2 and Hep3B cells. Cells were further treated for 48 hours with a strong ligand (superkiller) binding DR4 and DR5 (TRAIL death receptors). The cell death events were analyzed by FACS analysis. RT-qPCR was performed to detect the expression of apoptotic markers. Caspase activity was measured by luminescence. Apoptosis array was performed.

Results: Treatment with superkiller TRAIL, at 50 and 100 ng/ml, caused cell death in HepG2 and Hep3B cells after 48h proven by an accumulation of 40% of sub-G1 events. CUX1 knock down caused a sensitization of liver cancer cells to TRAIL effect by increasing, significantly, the percentage of sub-G1 events (60% with 100 ng/ml). CUX1 knock down did not change the expression of several genes implicated in cellular proliferation, differentiation and demise. In normal adult cells, it preferentially favors the expression of pro-apoptotic genes. Its aberrant expression in tumor turns its role as foe.

Disclosure of Interest: All authors have declared no conflicts of interest.
Hepatocellular carcinoma (HCC) is a primary malignancy of the liver. It is the fifth most common malignancy in the world and the third most common cause of cancer-related deaths worldwide. It is a major health problem in Egypt with the incidence expected to rise continuously in the next decade. [1–2]

The diagnosis of liver cancer depends on both screening with alpha-fetoprotein (AFP) and radiological imaging studies. Generally, normal levels of AFP are below 10 ng/ml but AFP greater than 200 ng/ml is suggestive of HCC. The sensitivity of AFP for liver cancer is about 67%; therefore a normal AFP does not exclude HCC. Searching another tumor marker, that together with AFP could improve the diagnostic utility of HCC.[3]

Squamous cell carcinoma antigen (SCCA), a member of the high molecular weight family of serine protease inhibitors named serpins which are physiologically found in the granular layers of normal squamous epithelium but found to be typically expressed by neoplastic cells of epithelial origin in a number of different cancers for example cancer cervix, lung, and head and neck cancers hence, it can be used as a clinical marker of these malignancies. [4] The structure of the serum ovalbumin revealed the archetype native serpin fold that typically have three β-sheets (termed A, B and C) and eight or nine α-helices (hA-hI). Serpins also possess an exposed region termed the reactive centre loop (RCL) that includes the specificity determining region and forms the initial interaction with the target protease.

Recently much attention has been focused on the role of SCCA in HCV cirrhotic patients suggesting that high levels of SCCA can assess HCC development. [5]

Therefore, it is necessary to determine the serum SCCA level in HCV cirrhotic patients with and without hepatocellular carcinoma in relation to alfa feto protein (AFP). These groups were from both sexes who are admitted to the inpatient ward and the outpatient clinic of Tropical Medicine Department, Faculty of Medicine, Alexandria University. This study was carried out on:

Group A: 100 cases of hepatocellular carcinoma without interventions.
Group B: same 100 cases of group A before and 3 months after successful interventions.
Group C: 100 cases of established cirrhosis.
Group D: 100 cases with chronic hepatitis C virus infection without established cirrhosis.
Group E: 100 healthy individuals as controls.

All patients in this study were subjected to: complete blood picture, liver biochemical profile, serum alanine aminotransferase (ALT), serum aspartate aminotransferase (AST), serum alkaline phosphatase, total and direct serum bilirubin, prothrombin time and activity, serum albumin, blood urea nitrogen (BUN), serum creatinine, Fasting blood sugar. Serum alpha fetoprotein (AFP).

Determination of squamous cell carcinoma antigen (SCCA) Sera from selected patients and controls were used for estimation of SCCA with the CanAg SCC EIAs. The CanAg SCC EIA is a solid phase, non-competitive immunoassay based upon the direct sandwich technique. Calibrators and patient samples are incubated together with biotinylated anti-SCCA monoclonal antibody in Streptavidin coated microstrips. After washing buffered Substrate/Chromogen reagent (hydrogen peroxide and 3, 3′, 5′, 5′ tetra-methyl benzidine) is added to each well and the enzyme reaction is allowed to proceed. During the enzyme reaction a blue colour will develop if antigen is present. The intensity of the colour is proportional to the amount of SCC present in the samples. The colour intensity is determined in a microplate spectrophotometer at 620 nm (or optionally at 405 nm after addition of Stop Solution). Calibration curves are constructed for each calibrator. The SCC concentrations of patient samples are the read from the calibration curve.

Results: Table 1 shows a statistical significant difference between different studied groups regarding alpha feto protein (P = 0.000).

<table>
<thead>
<tr>
<th>Mean</th>
<th>Std. deviation</th>
<th>Minimum</th>
<th>Maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gp. A</td>
<td>263.0</td>
<td>96.02</td>
<td>150.0</td>
</tr>
<tr>
<td>Gp. B</td>
<td>209.4</td>
<td>64.7</td>
<td>145.0</td>
</tr>
<tr>
<td>Gp. C</td>
<td>154.5</td>
<td>48.16</td>
<td>75.0</td>
</tr>
<tr>
<td>Gp. D</td>
<td>7.0</td>
<td>1.82574</td>
<td>5.0</td>
</tr>
<tr>
<td>Gp. E</td>
<td>1.22</td>
<td>0.27406</td>
<td>0.8</td>
</tr>
<tr>
<td>F</td>
<td></td>
<td></td>
<td>38.208</td>
</tr>
<tr>
<td>P</td>
<td></td>
<td></td>
<td>0.000*</td>
</tr>
</tbody>
</table>

Table 2 shows a statistical significant difference between different studied groups regarding SCCA level (P = 0.000).

<table>
<thead>
<tr>
<th>Mean</th>
<th>Std. deviation</th>
<th>Minimum</th>
<th>Maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gp. A</td>
<td>5.53</td>
<td>2.16</td>
<td>2.5</td>
</tr>
<tr>
<td>Gp. B</td>
<td>5.3</td>
<td>1.5</td>
<td>3.3</td>
</tr>
<tr>
<td>Gp. C</td>
<td>3.3</td>
<td>1.6</td>
<td>1.2</td>
</tr>
<tr>
<td>Gp. D</td>
<td>0.824</td>
<td>0.15897</td>
<td>0.6</td>
</tr>
<tr>
<td>Gp. E</td>
<td>0.646</td>
<td>0.23172</td>
<td>0.3</td>
</tr>
<tr>
<td>F</td>
<td></td>
<td></td>
<td>28.897</td>
</tr>
<tr>
<td>P</td>
<td></td>
<td></td>
<td>0.000*</td>
</tr>
</tbody>
</table>

Also, Positive significant correlation was found between AFP and SCCA in both groups (Table 3).

Table 3: Correlation Between AFP and SCCA

<table>
<thead>
<tr>
<th>SCCA</th>
<th>r</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.92*</td>
<td>&lt;0.001</td>
<td></td>
</tr>
</tbody>
</table>

Note: r: Pearson coefficient, *: Statistically significant at p ≤ 0.05

When combined sensitivity of both markers were calculated in our study at the best-cutoff values (SCCA 3.2 ng/ml and AFP 200 ng/ml) sensitivity improved to 93% (Table 4).

Table 4: AUC for AFP, SCCA and SCCA + AFP

<table>
<thead>
<tr>
<th></th>
<th>AUC</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>AFP</td>
<td>0.930*</td>
<td>0.001</td>
</tr>
<tr>
<td>SCCA</td>
<td>0.890*</td>
<td>0.003</td>
</tr>
<tr>
<td>SCCA +</td>
<td>0.820*</td>
<td>0.016</td>
</tr>
</tbody>
</table>

Conclusion: In the present study patients with HCC either with or without therapeutic intervention have significantly higher level of AFP in comparison to chronic HCV, cirrhotic and control groups this is in agreement with Awadallah et al.[6] who reported a statistically highly significant elevation in the serum AFP in HCC group when compared with control group. Moreover, the mean serum level of AFP in group A (HCC before intervention) was 263 ng/ml that decreased to 209.4 ng/ml in group B after therapeutic intervention and that agreed with Feng et al.[11] and Molinari et al.[8]. Also, at AFP level of 200 ng/ml the sensitivity was 90%, while the specificity was 60%.

Our results showed that SCCA level ranged from 2.5–10 with a mean of 5.53 in HCC patients without interventions, 3.3–7.6 with a mean of 5.3 in patients with HCC patients from cirrhotic patients was 3.2 ng/ml for SCCA yielded 80% sensitivity and 90% specificity. These results were in agreement with Trevisani et al.[12] Patients with HCC, in our study were none randomized selected as BCLC stage B (either one HCC lesion <5 cm in size or 3 lesions <3 cms) so no statistical correlation was done between serum AFP level and tumor size.

Our results showed a significant positive correlation between serum SCCA and AFP among patients with HCC before and after therapeutic intervention. Our data are in agreement with that of Hussein et al.[9] and El Ezawy et al.[10] SCCA was also higher among patients with HCC before intervention compared to patients with HCC after intervention as found by Bin et al.[11]

Applying the ROC curves analysis showed the best cut-off value to differentiate HCC patients from cirrhotic patients was 3.2 ng/ml for SCCA yielded 90% sensitivity and 90% specificity. These results were in agreement with Trevisani et al.[12] Patients with HCC, in our study were none randomized selected as BCLC stage B (either one HCC lesion <5 cm in size or 3 lesions <3 cms) so no statistical correlation was done between serum AFP level and tumor size.

When combined sensitivity of both markers was calculated in our study at the best-cutoff values (SCCA 3.2 ng/ml and AFP 200 ng/ml) sensitivity improved to 93% (Table 4).

Table 2: Comparison Between Different Studied Groups Regarding SCCA

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>Std. deviation</th>
<th>Minimum</th>
<th>Maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gp. A</td>
<td>5.53</td>
<td>2.16</td>
<td>2.5</td>
<td>10.0</td>
</tr>
<tr>
<td>Gp. B</td>
<td>5.3</td>
<td>1.5</td>
<td>3.3</td>
<td>7.6</td>
</tr>
<tr>
<td>Gp. C</td>
<td>3.3</td>
<td>1.6</td>
<td>1.2</td>
<td>5.6</td>
</tr>
<tr>
<td>Gp. D</td>
<td>0.824</td>
<td>0.15897</td>
<td>0.6</td>
<td>1.05</td>
</tr>
<tr>
<td>Gp. E</td>
<td>0.646</td>
<td>0.23172</td>
<td>0.3</td>
<td>0.95</td>
</tr>
<tr>
<td>F</td>
<td></td>
<td></td>
<td>28.897</td>
<td></td>
</tr>
<tr>
<td>P</td>
<td></td>
<td></td>
<td>0.000*</td>
<td></td>
</tr>
</tbody>
</table>

References

Table: Multivariate analysis for calculation of the HMC-CU score.

<table>
<thead>
<tr>
<th>Score</th>
<th>Lower</th>
<th>Upper</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age Gender</td>
<td>Hb INR</td>
<td>Alb AFP Constant</td>
<td>95% C.I.</td>
</tr>
<tr>
<td>Age</td>
<td>1.141</td>
<td>1.188</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Gender</td>
<td>Hb INR</td>
<td>Alb AFP Constant</td>
<td>95% C.I.</td>
</tr>
<tr>
<td>Male</td>
<td>1.141</td>
<td>1.188</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Female</td>
<td>1.141</td>
<td>1.188</td>
<td>&lt; .001</td>
</tr>
</tbody>
</table>

The best overall formula that could best predict HCC was then constructed for Hepatocellular Carcinoma (Hepatocellular Multidisciplinary Score – Cairo University (HMC-CU) score is as following: Logit probability of HCC = –2.524 + 0.152 x age - 0.121 x Hb - 0.696 x INR – 1.059 x Alb + 0.022 x AFP + 0.976 x Gender Female = 1. The diagnostic value of HCC was then assessed by ROC curve. The best cutoff point of 0.56 HMC-CU enabled the diagnosis of HCC with 90% sensitivity, 80.6% specificity. AUC was 0.93 and the 95% confidence interval was 0.917–0.94. On comparing the diagnostic performance of HMC-CU to the performance of serum AFP for early diagnosis of HCC, it was found that serum AFP was able to diagnose HCC at cutoff value of 11.9 ng/ml with sensitivity of 68% and specificity 66%. AUC was 0.76 and the 95% confidence interval was 0.74–0.78.

Conclusion: The HMC-CU score constructed from routine parameters is accurate in the diagnosis of HCC in patients with HCV-related CLD. The elegance of our score is based on its simplicity, being based on routine laboratory parameters and serum AFP which is being used for screening of patients in many centers all over the world. Our score will not impose extra costs for the patients because it utilizes only routine laboratory parameters. The HMC-CU score may be useful during surveillance programs for HCC. Our study included large number of HCC and non HCC patients all are Egyptians with a background of HCV type 4 related CLD. A prospective validation study is being planned and further studies are invited to validate this score on patients of other races infected with other HCV genotypes.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

**A184 United European Gastroenterology Journal 5(5S)**

**P0068 HEPATOCELLULAR CARCINOMA MULTIDISCIPLINARY CLINIC – CAIRO UNIVERSITY (HMC-CU) SCORE; A NEW SIMPLE SCORE FOR EARLY DIAGNOSIS OF HCC**

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**Introduction:** Hepatocellular carcinoma (HCC) is the first most common primary malignant tumor of the liver, the fifth most common cause of cancer-related death worldwide. (1) Early detection of HCC provides the best chance for a curative treatment which in turn improves patients survival. However, more than 60% of HCCs are diagnosed at a late stage (2). This could be explained by poor compliance of cirrhotic patients to the surveillance programs and lack of a sensitive and specific tumor marker. Serum AFP – commonly used for HCC diagnosis has a low sensitivity, and specificity for HCC detection (3).

**Aims & Methods:** The aim of this study was to develop Hepatocellular Multidisciplinary clinic – Cairo University (MHC-CU) score and test its accuracy in HCC detection in comparison to the widely used AFP. In the current study, we reviewed the data of 2363 Egyptian patients with HCV genotype-4 related chronic liver disease. 1291 patients were diagnosed to have HCC. The best cutoff point of 0.56 HMC-CU enabled the correct identification of patients with HCC with 90% sensitivity, 80.6% specificity. AUC was 0.76 and the 95% confidence interval was 0.74–0.78.

**Results:** The HMC-CU score constructed from routine parameters is accurate in the diagnosis of HCC in patients with HCV-related CLD. The elegance of our score is based on its simplicity, being based on routine laboratory parameters and serum AFP which is being used for screening of patients in many centers all over the world. Our score will not impose extra costs for the patients because it utilizes only routine laboratory parameters. The HMC-CU score may be useful during surveillance programs for HCC. Our study included large number of HCC and non HCC patients all are Egyptians with a background of HCV type 4 related CLD. A prospective validation study is being planned and further studies are invited to validate this score on patients of other races infected with other HCV genotypes.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**References**

**P0069 MULTIPLE BIPOLAR RADIOFREQUENCY ABLATION IN TREATMENT OF MEDIUM TO LARGE HEPATOMAS – EXPERIENCE IN A REGIONAL HOSPITAL**

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**Introduction:** Monopolar radiofrequency ablation (RFA) treatment for hepatomas has been unsatisfactory with local tumor recurrent rates of 8-40% in tumors ≥3 cm. Bipolar RFA devices have been developed to overcome the limitations of monopolar RFA devices.

**Aims & Methods:** This study aimed to evaluate the therapeutic effect and long-term survival in medium and large hepatomas using multiple bipolar radiofrequency ablation system (Celon). The study subjects had a Child-Pugh class A or B. The patients who were ineligible for surgical intervention or refused surgical intervention were treated with percutaneous bipolar electrodes. A total of 30 consecutive cirrhotic patients (48 tumors) with hepatomas ≥3 cm were enrolled between January 2011 and November 2012. The follow-up period was 30 months after RFA. The complete necrosis rate, tumor recurrence rate and long-term survival rate were analyzed and compared between medium and large hepatomas using Kaplan-Meier survival and the prognostic factors were using multivariate analysis.

**Results:** 30 patients were divided equally into two groups with 15 patients in each of medium and large hepatoma groups. 17 patients underwent artificial ascites (56.3%). The complete necrosis rate after ablation was 93.3% (14/15 patients) for either medium or large hepatomas. The local tumor progression rate and distant tumor recurrence rate of 40% and 60% (p = 0.098) vs 73.3% and 80% (p = 0.652) for medium and large hepatomas during 30 months follow up were not statistically significant. The overall survival rates ≥30%, 66.7% vs 60%, 46.7% at 12 and 30 months, respectively, was not statistically significant (p = 0.390). By multivariate analysis, BCLC stage (HR = 3.904, p = 0.023), MELD Score (HR = 1.220, p = 0.021) and pre-treatment AST level (HR = 1.028, p = 0.019) were independent prognostic factors for overall survival.

**Conclusion:** Multiple bipolar RFA system can achieve high complete tumor necrosis rates and low complication rates in treating medium to large hepatomas with shorter pre-treatment BCLC stage, MELD score and AST level were independent prognostic factors for overall survival. The therapeutic effect and long-term survival for large hepatomas (≥5 cm) was not inferior to that of medium hepatomas by multiple bipolar RFA.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**References**
P0070 RECENT TRENDS IN HEPATOCELLULAR ADENOMAS:
CLINICAL FEATURES, DIAGNOSIS AND OUTCOMES
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Introduction: Hepatocellular adenomas (HCA) are rare, benign tumors of pre-
sumable epithelial origin, that occur predominantly, but not exclusively, in young
women taking oral contraceptives (OC) or oral gestagens. The Bordeaux ade-
noma tumor markers are a promising method of identifying the high-risk HCA
of malignant transformation into hepatocellular carcinoma (HCC).

Aims & Methods: Aims: The authors propose to evaluate the demographics,
etiology, clinical manifestations and prognosis of HCA.

We undertook retrospective analysis of patients with HCA, histologically con-
firmed by biopsy or surgical resection, between 2008 and 2016, in a tertiay referral centre. When feasible, the subtype classification of HCA pro-
posed by the Bordeaux group, was performed. Descriptive statistics, uni and
multivariate analysis were performed using IBM SPSS Statistics 22, with
p < 0.05 deemed to be statistically significant.

Results: In this study 27 patients were included, 2 men and 25 women, with a
median age of 38.1±11 years, followed for a mean time of 78.3±36 months (lost follow-up in 7 cases). Three cases of hepatic adenomatosis were included. Forty-
one percent of the women used OC and 38% of the patients had dyslipidemia.

The mean size of the HCA was 70±42 mm; 65% of the patients had abnormal
liver tests at diagnosis, 46% were symptomatic and in 21% the diagnosis was
performed due to ruptured HCA. Surgical resection was performed in 88% of the
cases; complete resection was achieved in 75% of the cases. Of the 19 patients
who performed abdominal-CT scan or abdominal-MRI before histological con-
firmation, only 30% had an imagiological diagnosis of HCA. In 12 (44%) cases,
immunohistochemical analysis was performed. According to the Bordeaux clas-
cification of HCA, 8 (67%) cases were classified as infiltrative, 2 (17%) as
HNF-1α-mutated, 1 (8%) as β-catenin mutated and 1 (8%) as undetermined.
During the follow up, 6 patients died due to hematogenic shock related with
HCA rupture and in 2 (10%) was necessary surgical revision due to incomplete
resection. There was no HCC cases diagnosed during the follow-up. The
median size of the HCA that weren't completely resected and also of those presenting
with HCA rupture was significantly higher: (110 vs 55 mm [p = 0.037] and 105 vs
47 mm [p = 0.035], respectively). The 2 male patients had inflammatory HCA

Conclusion: In this cohort, HCA were prevalent in female taking OC and the
infiltrative type HCA was the most common. In many cases, abdominal
imaging is insufficient for a correct diagnosis, and biopsy specimen or surgical
resection should be performed for a correct diagnosis. Lesion size was associated
with the risk of rupture and incomplete surgical resection.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
Hepatocellular Adenoma Management and Phenotypic Classification: the

P0071 LASER ABLATION IS SUPERIOR TO TACE IN LARGE
SIZE HEPATOCELLULAR CARCINOMA: A CASE-CONTROL
STUDY
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Aims & Methods: Aims: We aimed to evaluate the efficacy and safety of Laser Ablation
(LA) in comparison to TACE in patients with large tumor size HCC. Between
January 2009 and December 2012, 41 cirrhotic patients (29/12 M:F, median age
72 yrs, range 54-88, Child-Pugh A: 27/4, B: 37/4) with a single node of HCC ≥40
(mean size 46 mm, range 40–75) were enrolled in this study. The patients were
-treated with multifiber technique of LA. The control group consisting of 41
patients (29/12 M:F, mean age 72 yrs, range 49-86; Child-Pugh A: 23/4; B: 34/7;
C: 3/4) with the same size of the nodule 50mm (median size 40–50 mm, 51-60 mm
and >60 mm). Disease recurrence, during a mean duration of follow up of 37.4 ±
2.7 months, was observed in 13 (24%) LA-treated patients (24%) and in 24
(58.5%) TACE-treated patients (p =0.0051). Overall survival probability rate at
5 years was 90.2% and 55.4% in LA group and 85.4 and 48.8. in TACE
group.

Conclusion: LA is a more efficacious therapeutic option than TACE in patients
with solitary large HCC.

Disclosure of Interest: All authors have declared no conflicts of interest.

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laser ablation for the treatment of small hepatocellular carcinomas in

P0072 ENDOSCOPIC ULTRASOUND GUIDED BIOPSY FOR LIVER
MALIGNANCY USING CORE BIOPSY NEEDLE
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Introduction: Endoscopic ultrasound (EUS)-guided fine needle aspiration (EUS-
FNA) is one of the alternative methods for tissue sampling of liver solid mass.
However, the diagnostic efficacy of using cytology was limited.

Aims & Methods: In this study, we evaluated the feasibility and diagnostic accuracy
of EUS-guided fine needle biopsy (EUS-FNB) for hepatic solid masses in
patients with suspected malignancy. The EUS-FNB using 20G, 22G or 25G
core biopsy needle is made to perform percuta-
aneous laser ablation of liver tumors using the multifiber technique. Acta
Radiol 2013; 54: 876–881

Di Costanzo GG, Franeca G, Pacella CM. Laser ablation for small hepato-

Disclosure of Interest: All authors have declared no conflicts of interest.

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Prostate cancer (HCC) is unsatisfactory with high rate of recurrence. Data from
Currently, the standard treatment using transarterial chemo-embo-
Hepatocellular carcinoma (HCC) is unsatisfactory with high rate of recurrence. Data from
currently, the standard treatment using transarterial chemo-embo-
Radiol 2013; 54: 876–881
REFERENCES


Aim & Methods: We aimed to find out best method to predict outcome of HCC patients with ascites. A total of 437 newly diagnosed HCC patients with ascites (mean age = 56.94 y, male = 74.8%, hepatitis B virus = 73.2%) were analyzed. We compared Child-Pugh score, Model for End-stage Liver Disease (MELD) score, MELD-Na score, and the Albumin-bilirubin (ALBI) grade for overall survival. Results: During a median 9.0 months of follow-up (range, 0.1-154.0), mortality was 146 patients (34%). The median survival was significantly lower for those with MELD-Na >12 than MELD-Na <12 or <12 <12 (median survival, 13.6 vs. 3.7 months, p < 0.001). Overall, 350 patients received treatment, and most commonly used modality was transarterial chemoembolization (62.3%), followed by radiofrequency ablation (15.7%) and resection (13.4%). Survival was significantly associated with hospital where the treatment was performed. Conclusions: In HCC patients with ascites, treatment was associated with better survival, except for subgroup with advanced tumor with decreased liver function, in which case survival was not significantly different than those who did not receive treatment (median survival: 13.3 vs. 2.4 months, p < 0.010). When patients were further stratified by mUICC stage and MELD-Na score, treatment was not associated with better outcome for mUICC stage IV patients with MELD-Na = 12 (median survival: 22.2 vs. 1.8 months for treatment vs. best supportive care, p = 0.15), while treatment was associated with better outcome in other subgroups. The study was conducted in Italy.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0073 COMPARISON OF METHODS TO ESTIMATE LIVER FUNCTION IN NEWLY-DIAGNOSED HEPATOCELLULAR CARCINOMA PATIENTS WITH ASCITES

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Introduction: Liver function is a key element in determining outcome of patients with hepatocellular carcinoma (HCC). For HCC with ascites, estimation of liver function is particularly important, as they already have decreased liver function.

Aims & Methods: We aimed to find out best method to predict outcome of HCC patients with ascites. A total of 437 newly diagnosed HCC patients with ascites (mean age = 56.94 y, male = 74.8%, hepatitis B virus = 73.2%) were analyzed. We compared Child-Pugh score, Model for End-stage Liver Disease (MELD) score, MELD-Na score, and the Albumin-bilirubin (ALBI) grade for overall survival. Results: During a median 9.0 months of follow-up (range, 0.1-154.0), mortality was 146 patients (34%). The median survival was significantly lower for those with MELD-Na >12 than MELD-Na <12 or <12 <12 (median survival, 13.6 vs. 3.7 months, p < 0.001). Overall, 350 patients received treatment, and most commonly used modality was transarterial chemoembolization (62.3%), followed by radiofrequency ablation (15.7%) and resection (13.4%). Survival was significantly associated with hospital where the treatment was performed. Conclusions: In HCC patients with ascites, treatment was associated with better survival, except for subgroup with advanced tumor with decreased liver function, in which case survival was not significantly different than those who did not receive treatment (median survival: 13.3 vs. 2.4 months, p < 0.010). When patients were further stratified by mUICC stage and MELD-Na score, treatment was not associated with better outcome for mUICC stage IV patients with MELD-Na = 12 (median survival: 22.2 vs. 1.8 months for treatment vs. best supportive care, p = 0.15), while treatment was associated with better outcome in other subgroups. The study was conducted in Italy.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0075 ADHERENCE TO BARCELONA CLINIC LIVER CANCER GUIDELINES IN FIELD-PRACTICE: RESULTS OF PROGETTO EPATOCARCINOMA CAMPANIA


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Introduction: The BCLC algorithm is the standard system for clinical management of HCC. Data on adherence to this therapeutic paradigm are scarce. The aim of this field-practice study is to provide a description of HCC patients in Southern Italy, to evaluate the adherence to BCLC guidelines and its impact on patients’ survival.

Aims & Methods: We analyzed the region-wide Italian database of Progetto Epaticarcinoma Campania, which includes data of HCC patients, prospectively collected from January 2013 to December 2015 in 16 regional centers. Results: Overall 1008 HCC patients were enrolled: 70.6% patients received therapy recommended by BCLC algorithm, while 29.4% underwent different treatments. Among patients who were treated in adherence to guidelines, a higher rate of diagnosis on surveillance programs, better liver function, lower rate of AFP >200 ng/mL, more early stage and monofocal HCC, lower frequency of nodules >5 cm, portal vein thrombosis and metastases were observed. The multivariate analysis showed that non-adherence to treatment guidelines was independently associated to the BCLC stage B, Child-Pugh classes B-C, and to the presence of neoplastic thrombosis and metastases. The mean overall survival in patients treated according to BCLC indications was 35.5 months, while in patients managed differently was 31.9 months (p < 0.0001).

Conclusion: Adherence to BCLC algorithm in field-practice was high in early and end stage HCC patients, but it was poor in intermediate and advanced patients. This may be due to the wide heterogeneity of intermediate-stage patients, and to the limited use of sorafenib in advanced-stage patients. Strategies to improve treatment and stratification of HCC patients are required. Disclosure of Interest: All authors have declared no conflicts of interest.

P0076 A QUESTIONNAIRE SURVEY ON QUALITY OF LIFE WITH ANXIETY AND DEPRESSION SELF-RATING IN PATIENTS OF LIVER CIRRHOSIS

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Introduction: Liver cirrhosis is a great public health burden for Chinese health system. The most common causes are HBV, HCV, alcohol consumption and non-alcoholic fatty liver disease, et al. The quality of life of liver cirrhosis patients is impacted by the physical symptoms and psychological symptoms such as anxiety as depression.

Aims & Methods: We aimed to investigate the quality of life of patients with cirrhosis, as well as depression and anxiety. A questionnaire survey was carried out in 95 patients in our gastroenterology department, Peking University People’s Hospital from May to August in 2016. The patients were divided into two groups, cirrhosis group and control group. The patients in cirrhosis group in...
were diagnosed liver cirrhosis without complications. The control group included the digestive polyps patients without other diseases. The questionnaire included the World Health Organization Quality of Life (WHOQOL)-BREF, Self-rating Anxiety Scale (SAS) and Self-rating Depression Scale (SPS). The questionnaire scores of the two groups were analyzed.

Results: A total of 95 valid questionnaires were collected and divided into cirrhosis group (n = 40) and control group (n = 45). In the cirrhosis group, there were 22 males and 18 females, average age 57.97 ± 10.448 years. In the control group, there were 45 males, 23 males and 22 females, with an average age of 61.47 ± 13.081, showing no difference from cirrhosis group. WHOQOL includes four domains: physiological domain, psychological domain, social relationship domain, environment domain. The scores of liver cirrhosis group: physiological field (22.23 ± 3.312), psychological field (19.59 ± 3.925), social relationship field (9.64 ± 2.497), environment domain (26.23 ± 7.534) and control group (22.96 ± 3.275 in physiological field, 19.87 ± 3.152 in psychological field, 10.58 ± 2.061 in social relation field and 28.36 ± 5.091 in environmental field), they had no significant difference between the two groups (P > 0.05). The depression self-rating score of cirrhosis group (47.86 ± 10.782) was significantly higher (P = 0.034) than that of control group (42.61 ± 11.564). Meanwhile, there was no significant difference between the Self-rating Anxiety Scale scores of the cirrhosis group (38.46 ± 11.917) and control group (37.00 ± 12.521) (P > 0.05) (Table 1).

Results:

- AT the present stage, the treatment of patients with non-alcoholic fatty liver disease has insufficient effectiveness due to the simultaneous availability of a number of recommendations and the lack of an individual approach. Not enough attention is paid to the study of nutritional behavior and the role of nutrigenetics, as additional risk factors for the development of non-alcoholic fatty liver disease, methods for studying the characteristics of eating behavior should be applied more widely, which will allow timely appropriate correction. A more extensive study of nutrigenetics will make it possible to designate a personified diet, taking into account the detected polymorphisms, which will make it possible to achieve a significant improvement in metabolic parameters in this category of patients.

Disclosure of Interest: All authors have declared no conflicts of interest.

Conclusion: The quality of life and anxiety scores in cirrhosis group had no significant different from the control group, but the depression score was higher than that of the control group.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference


P0078 NON-GOVERNMENTAL HCV SCREENING IN A VILLAGE IN NILE DELTA IN DAAS ERA IN EGYPT

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Introduction: HCV is highly endemic in Egypt with a prevalence of 12%. The ministry of health through the national committee for hepatic viruses has done an extra-ordinary effort since the beginning of the DAAAs era which resulted in treatment of almost one million infected patients till now. Still this looks as the summit of the iceberg and there is still estimated more than 10 million Egyptians infected with the virus, the majority of them are still undetected.

Aims & Methods: The aim of this work is to give an example of non-governmental efforts which can be done to solve this tough national problem. A group of young medical and non-medical volunteers all from El Salam village in Mansoura, Dakakha governorate, Egypt have worked together. They contacted mosques and pharmacies in the village and distributed brochures to announce for the free of charge screening for the virus in the village. They contacted business men in the village to sponsor the campaign. They contacted the laboratory of the village to do the HCV Ab test with nonprofit price.

Results: A total of 2220 citizens have visited the referral lab to do the antibody test. Only 419 persons proved positive. This gives an estimated prevalence in the village of 19.0%. 119 patients were insurance patients and they went to treatment and did not complete the study. The rest 300 Ab –ve patients completed the study. All patients were Hbs Ag –ve. 132 PCR –ve (44%) patients from the 310 HCV Ab –ve group. The rest 18 patients were –ve for HCV RNA (56%). 18 patients of the HCV PCR –ve had previous HCV treatment (6.5%). Only 2 patients of the 168 HCV RNA +ve (1.2%) were previously treated. The PCR +ve patients without previous treatment were 114 patients (38%). So only 62.0% of the HCV Ab +ve and 38.0% of the HCV Ab –ve in the community are PCR +ve and require treatment. The total cost for the screening of the 2220 patients was 40.000 L.E. which means 18.0 L.E per person (almost one Dollar).

Conclusion: The screening costs for HCV Ab positivity can be markedly reduced if it is done in each village depending on volunteers from the same village working in related fields like medical, pharmacists, laboratory and social jobs. Only 62.0% of the HCV Ab +ve in the community are PCR +ve and require treatment.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

**P0079** EARLY DIAGNOSTICS OF NAFLD: ANALYSIS OF RISK FACTORS USING NON-INVASIVE TECHNIQUES: ASSOCIATION BETWEEN THE PREVALENCE STEATOSIS AND COMPONENT COMPOSITION OF THE BODY
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Introduction: Non-alcoholic fatty liver disease (NAFLD) is liver disease with histological signs of accumulation of cholestetin excessive amount in hepatocyte in patient without a history of alcohol consumption (due to causes other than). The search for accessible, non-invasive and effective methods of screening for this pathology, allowing to detect NAFLD at early, potentially reversible stages of development is relevant. The purpose of the work was frequency estimation of the prevalence steatosis according to elastometry with controlled attenuation parameter (CAP®) among young people and associated with them specific body composition.

Aims & Methods: 59 volunteers (students of medical university) at the age of 19–28 years (the median age of 20.5) have participated in research. There were 22 (37.3%) men and 33 (62.7%) women among them without verified liver diseases. The survey was conducted in order to exclude or detect risk factors. Determining the presence of hepatic steatosis and the degree of liver fibrosis was performed with the apparatur FibroScan 502 Touch. The final figures of elasticity of the liver were estimated in kPa (METAIVR). The controlled attenuation parameter (CAP®) in dB/m was used for the severity of steatosis. Moreover, there was the body bioelectrical impedance analysis of body (BIA), evaluated: body mass index (BMI), body fat.

Results: The signs of violations of the structure of the liver were diagnosed in 15 people out of 59 (25.4%). The signs of steatosis were found in 12 (20.3%) subjects. The signs of fibrosis in 7 (11.9%) people (E>5 kPa). At the same time the combination of liver fibrosis and steatosis was diagnosed in 4 (6.8%). After analyzing data of BIA it was revealed that body weight above normal in 23 (40%), wherein fat body composition above normal values in 19 (33.4%). Results of binary logistic analysis showed that the chance of development of hepatic steatosis in case of excess adipose tissue increase 28 times (p=0.045), influence of BMI, gender, age was statistically insignificant.

Conclusion: Based on the results obtained, it can be concluded that there is high enough level of distribution of liver steatosis among young people. Transient elastostasis (TE) with controlled attenuation parameter (CAP®) is a fast, reliable, repeatable non-invasive method for the assessment of NAFLD. The development of hepatic steatosis among practically healthy young people largely associated with the increase the amount of adipose tissue in the body. The confirmed importance of evaluation of body composition and lack of information of using only BMI when evaluating the chances of development of NAFLD.

Disclosure of Interest: All authors have declared no conflicts of interest.

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**P0080** SALVAGE TECHNIQUE USING A MICRO GUIDEWIRE FOR DIFFICULT BILIARY CANNULATION IN ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY
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Introduction: Biliary cannulation is indispensable for therapeutic endoscopic retrograde cholangiopancreatography (ERCP) in patients having biliary disease. Selective biliary cannulation is often difficult due to anatomical constraints. Numerous techniques have been attempted to overcome such problems. Selective biliary cannulation is often difficult due to anatomical constraints. Systematic searching was performed using MEDLINE, EMBASE and Cochrane library from January 1st, 1996, to December 31st, 2016 for studies assessed the relationship between alcohol consumption and gallstone disease development. The eligibility criteria was included: 1) studies involving the patients with gallbladder stone with or without cholecystitis; 2) cohort or case-control studies investigated the association between alcohol consumption and gallstone disease development. Newcastle-Ottawa Scale was used to assess the methodologic quality of each studies. Data was obtained from each selected studies regarding: 1) baseline characteristics of the study (cohort, case-control); 2) number of participants; 3) participants’ clinical features; 4) country; 5) publication year; 6) Risk or odds ratio; 7) 95% confidence intervals of alcohol consumption and risk of gallstone. The random effect model was used to estimate the pooled relative risks (RR) with 95% confidence intervals (CIs).

Results: Twenty-five cohort and case-control studies were included, and total 12, 581 cases with gallstone diseases among those 17, 509 controls. Alcohol consumption indicated a decreased risk of GSD development (Pooled RR = 0.84 [0.79–0.90], P < 0.001). Subgroup analyses according to the alcohol doses (g/d) confirmed a gradual risk-reduction effect on GSD compared to non-drinkers (Light: RR = 0.97 [0.94, 1.00], p = 0.864; Moderate: RR = 0.92 [0.79, 0.86], p = 0.777; Heavy: RR = 0.70 [0.62, 0.80], p < 0.01).

Disclosure of Interest: All authors have declared no conflicts of interest.
Conclusion: In this systematic review with meta-analysis, alcohol consumption has dose-dependent negative co-relation with the risk of gallstone disease development.

Disclosure of Interest: All authors have declared no conflicts of interest.

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Endoscopic retrograde cholangiopancreatography (ERCP) is challenging in patients who have undergone surgical reconstruction of the intestines. In 2001, double-balloon enteroscope (DBE) was reported by Yamamoto et al to be an effective procedure for the diagnosis and treatment of small intestine obstructions. We report a case of a 60-year-old which was successfully treated using DBE and enteroscope to diagnose and remove a foreign body (n=89)

Aims & Methods: To determine time frame between ERCP/duct clearance and cholecystectomy (CCX) in non-pancreatitis group. 2) To determine time frame between ERCP/duct clearance and CCX in pancreatitis group. 3) To determine re-admission rate while awaiting CCX. All patients who underwent ERCP for CBDS before 01/01/2014 to 31/12/2014 were included in the study. Patients who had previously undergone CCX (de novo stones) were excluded. All patients were followed up for a minimum period of 2 years following their ERCP.

Aims & Methods: 1) To determine time frame between ERCP/duct clearance and cholecystectomy (CCX) in non-pancreatitis group. 2) To determine time frame between ERCP/duct clearance and CCX in pancreatitis group. 3) To determine re-admission rate while awaiting CCX. All patients who underwent ERCP for CBDS before 01/01/2014 to 31/12/2014 were included in the study. Patients who had previously undergone CCX (de novo stones) were excluded. All patients were followed up for a minimum period of 2 years following their ERCP.

In 27 patients duct clearance was not achieved; 26% (7/27) underwent surgical management (CBD exploration on table cholangiogram and CCX). The remaining 74% (20/27) patients were deemed unsuitable for invasive intervention and were either for symptomatic stent change only or conservative management.

Conclusion: The time period between duct clearance and CCX was longer than anticipated, especially in patients with mild acute pancreatitis as none of them underwent CCX during index admission or within 2 weeks of ERCP/duct clearance. Some patients re-presented with CBDs while awaiting CCX. We looked into potential causes of delay in CCX – delayed referral to surgery, long waiting time for elective CCX and patient choice. We propose to develop a local pathway for patients with CBDs and gallstones and instigate a robust system for referring patients for CCX following duct clearance. This would help to minimize readmission and potential complications.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

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Introduction: Patients undergoing endoscopic retrograde cholangiopancreatography (ERCP) and duct clearance for common bile duct stones (CBDS) should be followed up with an early cholecystectomy to prevent recurrent biliary complications (1, 2) and acute gallstone pancreatitis. Recently the National Confidential Enquiry into Patient Outcome and Death (NCEPOD) recommended that definitive eradication of gallstones by cholecystectomy prevents the risk of a recurrent attack of acute pancreatitis (AP). For patients with an episode of mild acute pancreatitis, early definitive surgery should be undertaken, either during the index admission or within 2 weeks (3, 4).

Aims & Methods: 1) To determine time frame between ERCP/duct clearance and cholecystectomy (CCX) in non-pancreatitis group. 2) To determine time frame between ERCP/duct clearance and CCX in pancreatitis group. 3) To determine re-admission rate while awaiting CCX. All patients who underwent ERCP for CBDS before 01/01/2014 to 31/12/2014 were included in the study. Patients who had previously undergone CCX (de novo stones) were excluded. All patients were followed up for a minimum period of 2 years following their ERCP.

In 2001, double-balloon enteroscope (DBE) was reported by Yamamoto et al to be an effective procedure for the diagnosis and treatment of small intestine obstructions. We report a case of a 60-year-old which was successfully treated using DBE and enteroscope to diagnose and remove a foreign body (n=89)

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In 2001, double-balloon enteroscope (DBE) was reported by Yamamoto et al to be an effective procedure for the diagnosis and treatment of small intestine obstructions. We report a case of a 60-year-old which was successfully treated using DBE and enteroscope to diagnose and remove a foreign body (n=89)

Aims & Methods: To determine time frame between ERCP/duct clearance and cholecystectomy (CCX) in non-pancreatitis group. 2) To determine time frame between ERCP/duct clearance and CCX in pancreatitis group. 3) To determine re-admission rate while awaiting CCX. All patients who underwent ERCP for CBDS before 01/01/2014 to 31/12/2014 were included in the study. Patients who had previously undergone CCX (de novo stones) were excluded. All patients were followed up for a minimum period of 2 years following their ERCP.

In 2001, double-balloon enteroscope (DBE) was reported by Yamamoto et al to be an effective procedure for the diagnosis and treatment of small intestine obstructions. We report a case of a 60-year-old which was successfully treated using DBE and enteroscope to diagnose and remove a foreign body (n=89)

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In 2001, double-balloon enteroscope (DBE) was reported by Yamamoto et al to be an effective procedure for the diagnosis and treatment of small intestine obstructions. We report a case of a 60-year-old which was successfully treated using DBE and enteroscope to diagnose and remove a foreign body (n=89)
Table 1: The total of releasing drug amount in 72 hours

<table>
<thead>
<tr>
<th>Drug release amount</th>
<th>Gemcitabine (ug)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coating Polymer</td>
<td>24 hrs</td>
</tr>
<tr>
<td>Tecophilic</td>
<td>919</td>
</tr>
<tr>
<td>Tecothane</td>
<td>836</td>
</tr>
<tr>
<td>Tecoflex</td>
<td>681</td>
</tr>
<tr>
<td>Pellethane</td>
<td>580</td>
</tr>
</tbody>
</table>

Conclusion: The ultrasonic spray coating technique could be applied to make multi-layer drug eluting membrane with regular thickness. The membranes contained the uniform capacity of drug in all tested area. The releasing drug capacity is able to control by applying different kind of polyurethane.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference
1. Meredith C, Baird, P. Diagnostic yield of SurePath (SP) and conventional smear preparations (CSP) for brush cytology obtained from the common bile duct (CBD) in patients undergoing endoscopic retrograde cholangiopancreatography (ERCP). Gastroenterology, Vol 150, Issue 4, S516, 2016
Aim & Methods: Between January 2006 and March 2016, a total of 185 advanced or recurrent BTC patients receiving a first line systemic chemotherapy for at least two cycles were retrospectively studied. Serum CA 19-9 was measured at baseline (CA19-9_Pre) and after two cycles of chemotherapy, and patients were categorized into three groups based on CA19-9 response: CA19-9 decrease group (>30% decrease), stable group (30% decrease and ≥20% increase) and increase group (>20% increase). The Cox proportional hazards model was used to analyze the prognostic factors for OS and PFS, using the landmark method. Results: The primary tumors were located as follows: 68 (37%) in intrahepatic bile duct, 43 (23%) in extrahepatic bile duct, 64 (35%) in gallbladder and 10 (5%) in ampulla. As for chemotherapeutic regimen, single-agent or combination therapy was given in 49 (26%) or 136 (74%), respectively. After 2 cycles of chemotherapy, partial response was achieved in 29 (16%) and stable disease in 106 (57%). There was a statistically significant trend for CA 19-9 and RECIST responses (p = 0.03). Compared with CA19-9 decrease group, hazard ratios for stable and increase groups were 1.92 (95% CI, 0.79–5.97), 2.42 (95% CI, 0.13–41.3), and 2.42 (95% CI, 0.13–41.3) for PFS, respectively (p <0.001). Conclusion: CA 19-9 response after two cycles as well as baseline served as a prognostic factor for OS and PFS in patients with advanced and recurrent BTC on systemic chemotherapy.

Disclosure of Interest: All authors have declared no conflicts of interest.

References


and data on the biliary drainage procedure were collected from medical records. Definitions of failure of drainage or other severe drainage related complications are shown in table 1.

Results: In total, 187 patients were included. Initial drainage was performed in a non-referral center in 125 patients (66.8%). The initial drainage procedure was endoscopic in 158 patients (84.5%) and percutaneous in 29 patients (15.5%). A stent was placed in 91 patients (61.3%) at the initial drainage procedure. The highest bilirubin level in the 2 weeks prior to drainage was 248 (IQR 138–377) μmol/L. Only 14 (8.1%) patients had cholangitis prior to the initial drainage procedure. Failure of drainage or other severe complications related to the initial drainage procedure were noted in 117 (62.6%) patients. Failure of drainage or reintervention was most common and was noted in 85 patients (50.8%). Bile duct injury occurred in 3 (1.6%) patients, acute pancreatitis in 5 (2.7%) patients and cholangitis in 11 (5.9%) patients. Two (1.1%) patients had cardiopulmonary complications and 1 (0.5%) patient had a duodenal perforation. The median period between the initial and second drainage procedure was 13 (5–31) days and the bilirubin level dropped below 50 μmol/L in 27 patients (14.4%). After initial drainage, 20 patients (10.7%) died within 30-days and 66 patients (35.3%) within 90 days. The median OS after initial drainage was 6.6 (95% CI: 2.0–15.2) months.

Patients: Patients with unresectable Pan-CT on imaging have a very high failure and complication rate after initial biliary drainage.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0093 UNILATERAL VERSUS BILATERAL STENT-IN-STENT PLACEMENT OF METAL STENTS FOR MALIGNANT HILAR BILARY OBSTRUCTION

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Introduction: Endoscopic biliary stenting is widely accepted as effective palliation therapy for unresectable malignant hilar biliary obstruction (MHBO). Although draining more than 50% of liver volume is associated with better outcomes, endoscopic access can be technically difficult.

Aims & Methods: The aim of this study was to evaluate differences in technical feasibility and clinical efficacy between unilateral and bilateral stent-in-stent (SIS) placement of metal stents for MHBO. We retrospectively reviewed 23 consecutive patients with MHBO who underwent endoscopic biliary drainage with self-expandable metal stents (SEMS) at our institution from March 2012 to March 2017. Unilateral metal stenting was performed in 15 patients (Uni group) and bilateral metal stenting was performed in 18 patients (Bi group).

Results: There were no significant differences between the Uni group and the Bi group in technical success rate (100% vs. 94%), complication rate (0% vs. 0%), stent occlusion rate (15% vs. 18%) or median stent patency period (102.5 days vs. 98 days). There was no significant difference in cumulative stent patency between the groups (p = 0.669).

Conclusion: Endoscopic bilateral SIS placement of metal stents for palliative treatment of MHBO had a high technical success rate and low complication rate, similar to those of unilateral placement.

 Disclosure of Interest: All authors have declared no conflicts of interest.

P0094 CLINICAL ASSESSMENT OF THE SAFETY AND EFFICACY OF A NOVEL BIODEGRADABLE STENT IN PATIENTS WITH BILARY OBSTRUCTION: A PILOT STUDY

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Introduction: The commonest indication for biliary stent is for the treatment of obstructive jaundice and for the management of bile leak. The currently available stents are made of either plastic or metal alloy. The stents can be inserted endoscopically to provide internal drainage of the bile into the duodenum. Among the disadvantages of plastic stents are recurrences of jaundice due to biofilms formation, which require a repeat ERCP procedure to remove the stent before 3 months. We have embarked to study the safety and feasibility of a biodegradable metal stent (BBS), which can treat biliary obstruction without the need to undergo a repeat endoscopic procedure to remove the stent.

Aims & Methods: This is a pilot study enrolling 30 subjects with symptomatic jaundice and pruritus caused by either benign or malignant biliary obstructions that were amenable to treatment by ERCP guided stenting. Primary objective was technical success and safety. Procedural and technical successes were assessed during the stenting procedure. Adverse events or complications were monitored throughout the studies. The secondary endpoints were clinical success, which was measured by a reduction of at least 20% of the initial serum bilirubin level at Day 7 post stenting. A simple self-assessment scale from 0 to 10 was used to assess quality of life before and after the stenting.

Results: 30 patients had the Biodegradable Biliary Stent (BBS) implanted. 18 patients (60%) were males, the mean age was 56.9 years, 26 patients (86.7%) had benign biliary ductal disease and 4 (13.3%) patients had malignant condition.
9 patients had the fast and medium degradation stents respectively and 12 had the slow degradation stents implanted. All stents were 3.4 mm in diameter and the length ranges from 60 to 120 mm depending on the level of obstruction. It took an average of 29.6 minutes to complete each procedures, and the mean stent deployment duration was 6.0 minutes. It ranges from 13.5 minutes in the initial phase and improved to 1.5 minutes in the later phase. Biliary sphincterotomy was not needed in the single biodegradable stent, but however, all patients with biliary stone had sphincterotomy to facilitate retrieval of the stones. Serum bilirubin level (SBL) showed reduction of 52% from the mean SBL of 54.9μmol/L prior to stenting to 26.2 μmol/L at Day 7. Quality of life score improved from 2.0 up to 8.5 after stenting. The BBS ranks high in terms of loadability, trackability over guide-wire, and pushability with push catheter. There was minimal force required to implant it and it has good visibility by fluoroscopy. The BBS is as flexible as the conventional plastic stents and can be accurately deployed under fluoroscopy. Technical success or completion of the ERCP and stent deployment was achieved in all 30 patients.

Conclusion: This pilot study has shown encouraging results. It benefit the patient to avoid the burden of a second ERCP procedure for plastic stent removal. However, these results should be interpreted with caution as this is a pilot study to assess the safety and efficacy of the biodegradable stent on limited number of volunteers with symptomatic jaundice. We plan to conduct a phase 2 study involving a larger number of cohorts with a more specific indication of benign and malignant biliary stricture.

Disclosure of Interest: H. Othman: The Biodegradable Biliary Stents used for this study is sponsored by amg International GmbH, Wissen, Germany. The authors have no financial relationship with the company which could inappropriately influence or bias the content of this presentation.

All other authors have declared no conflicts of interest.

References

MONDAY, OCTOBER 30, 2017

**P0095 TOLL-LIKE RECEPTOR 5 IS ESSENTIAL FOR THE ACTIVATION OF LIVER AND PANCREATIC STELLATE CELLS**

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Introduction: Stellate cells contribute significantly to the development of several diseases. In particular, liver stellate cells are responsible for liver fibrogenesis and further for cirrhosis that culminates into cancer development eventually. In pancreas, it is known that stellate cells sustain the tumor cells via autophagy mechanisms.

Aims & Methods: This study aimed to clarify the involvement of Toll-like receptor 5 (TLR5) in the activation of human stellate cells. LX-2 liver stellate cells and HPSC (human pancreatic stellate cells) were treated for 48 hours with 2.5 ng/ml TGF-beta 1. The analysis of activation markers was performed by RT-qPCR, western blotting and immunofluorescence. Real-time cell monitoring with Incucyte was performed. TLR5 PCR Array was performed. TLR5 knock down was obtained with commercially validated siRNAs.

Results: Treatment with 2.5 ng/ml TGF-beta 1 caused the activation of both LX2 and HPSC cells. Over-expression of alpha-smooth muscle actin (α-SMA) and collagen 1 (COL1A1) transcripts was observed. The protein level of α-SMA and COL1A1 significantly increased also. Interestingly, SNAIL 1, SLUG, TLR5 and TGF-beta 1 were induced by treatment with TGF-beta 1 in both cell lines. SNAIL 1 was over-expressed at protein level also. Knock down of TLR5 neutralized the activity of TGF-beta 1 by keeping the expression of the above markers at basal level or even not expressed.

Conclusion: TLR5, for the first time, has been identified as key player of the activation of stellate cells. Its contribution represents a new aspect in terms of interaction between immune system and stellate cells and could represent a potential new target for the diseases of the gastrointestinal tract involving the activity of stellate cells. TLR5 and its natural agonist flagellin could be a key link between impairment of microbiota and organo-fibrosis in the gastrointestinal tract.

Disclosure of Interest: All authors have declared no conflicts of interest.

**P0096 THE IMPAIRED FUNCTION OF THE PLASMA MEMBRANE CA2+ PUMP RESULTS IN CA2+ OVERLOAD AND CELL DAMAGE IN CFTR KNOCK OUT PANCREATIC DUCTAL CELLS**

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Introduction: The cystic fibrosis transmembrane conductance regulator (CFTR) has a major role in pancreatic ductal secretion and it’s genetic defects damage the pancreas. It is known that intracellular Ca2+ homeostasis is disturbed in bronchial epithelial cells in cystic fibrosis (CF), but the connection of CFTR and the intracellular Ca2+ signaling has never been suggested in pancreatic disease in CF patients.

Aims & Methods: Our aim was to characterize the Ca2+ homeostasis of CFTR-deficient PDC. Wild type (WT) and CFTR knockout (KO) mouse pancreatic ductal and acinar cells and iPSC (induced pluripotent stem cell) derived human organoids from 2 CF patients and controls, human CF pancreatic cell line (CFPAC-1; ΔF508 mutant) were used for intracellular Ca2+ measurements. Mitochondrial membrane potential (ΔΨm) and mitochondrial morphology was assessed in isolated pancreatic ducts. Immunofluorescent staining and quantitative PCR measurements were performed to detect changes of mRNA and protein expressions.

Results: The plateau phase of the agonist-induced Ca2+ signal was elevated in CFTR-deficient PDC, which was caused by decreased function of the plasma membrane Ca2+-pump (PMCA). The functional inhibition of TGRβ and forskolin had no effect on the PMCA activity. Human CF organoids have shown decreased PMCA function compared to control while the 24h treatment of the CF organsoids with VX-809 have restored the PMCA function to the control level. Similarly native CFPAC-1 cells and PDEC treated with siRNA to inhibit the expression of CFTR showed the same PMCA dysfunction. Viral transfection of CFPAC-1 with CFTR gene completely restored PMCA function. Sustained [Ca2+]i levels decreased ΔΨm and induced cytochrome c release in CFTR KO PDEC without significant alterations in mitochondrial morphology.

Conclusion: Dysfunction of PMCA leads to disturbed Ca2+ homeostasis in CFTR-deficient PDC and the consequent cellular Ca2+ overload impairs mitochondrial function contributing to the pancreatic damage in CF patients.

Disclosure of Interest: All authors have declared no conflicts of interest.

**P0097 EXPDF IMPACTS PANCREATIC DIFFERENTIATION OF HUMAN PLURIPOTENT STEM CELL DERIVED PANCREATIC ORGANOIDS**

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Introduction: Given their capability to differentiate to every cell type of the human body, human induced pluripotent stem cells (hiPSCs) provide a unique platform for disease modeling and regenerative medicine. The transcriptional regulatory factor, pancreatic progenitor (PP) cells from pluripotent stem cells follows the sequential induction of virtually pure definitive endoderm (DE), foregut endoderm (GTE) and pancreatic endoderm (PE). We have recently reported the generation of a novel three-dimensional pancreatic organoid culture system that generates functional acinar-ducal-like structures from pluripotent stem cells (Hohlwieder et al, GUT, 2016).

Aims & Methods: In the current study we implemented this culture system to understand the role of coexpression differentiation and proliferation factor (Expdf), a signaling molecule proposed to be involved pancreatic differentiation in zebrafish. CrispCas9 technologies were used to ablate Expdf in human embryonic stem cells, while a piggy bac engineering approach allowed us timed expression to study the role of both loss and gain of Expdf function during pancreatic differentiation.

Results: First, a limited role of Expdf was observed until the PE stage, while PP knockout led to mostly cystic structures. Phenotyping for ductal and acinar lineage allowed to investigate these
Introduction:
J.M. Jaworek
SECRETION VIA CCK RELEASE. STUDY ON THE RATS
P0098 MELATONIN METABOLITE; N1-ACETYL-N2-FORMYL-5-
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Reference

P0098 MELATONIN METABOLITE; N1-ACETYL-N2-FORMYL-5-
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Introduction: N-acetyl-β-formyl-5-methoxykynuramine (AFMK), melatonin metabolite, has been demonstrated recently as an effective pancreatic acinar cell protector against acute inflammation. AFMK significantly attenuated acute pancreatitis; however, its effect on pancreatic exocrine function has not been investigated yet.

Aims & Methods: 1. To investigate the effects of intraduodenal (i.d.) application of 100 μg AFMK on pancreatic enzyme secretion under basal conditions and following the stimulation of this secretion with diversion of pancreato-biliary juice (DPBJ) and to examine the role of CCK in this process. 2. To assess the effect of AFMK on CCK receptor in pancreatic acinar cell line AR42J. Material and methods: For in vivo study Wistar rats weighing 300 g were employed. Under pentobarbitone anaesthesia the animals were surgically equipped with silicone catheters, inserted into pancreato-biliary duct, and into duodenum. AFMK (5.10 mg/kg i.d.) was given to the rats under basal conditions or following stimulation of pancreatic secretion with DPBJ. Lorglumide, the CCK1 receptor antagonist (1 mg/kg i.d.) was administered 15 minutes prior to the application of AFMK. Samples of pancreato-biliary juice were collected to measure the amylase outputs. The blood samples were taken for determination of CCK by ELISA kit. For in vitro study AR42J cells were AR42J were incubated in presence of AFMK alone or in combination with CCK. The protein signal of CCK receptor was determined by Western blot.

Results: AFMK given i.d. produced the dose-dependent increases of pancreatic amylase secretions both; unstimulated, as well as that induced by DPBJ. The rises of pancreatic amylase outputs were accompanied by significant decrease of CCK plasma levels. Administration of lorglumide, a CCK1 receptor blocker, completely abolished the stimulation of pancreatic exocrine function induced by AFMK. This melatonin metabolite failed to affect protein signal for CCK receptor in AR42J cells.

Conclusion: The stimulatory effect of AFMK on pancreatic enzyme secretion in the rats is indirect and dependent on the release of CCK by this melatonin metabolite.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0099 INVESTIGATION OF THE FUNCTION OF TRPM2 IN MOUSE PANCREATIC ACINAR CELLS
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Introduction: Aberrant intracellular Ca2+ signaling is the hallmark of acute pancreatitis (AP) inducing mitochondrial damage, intraacinar digestive enzyme activation and cell death. Thus prevention of toxic cellular Ca2+ overload in different cell types is a promising therapeutic target. The transient receptor potential melastatin 2 (TRPM2) is a non-selective cation channel that plays major role in oxidative stress induced cellular Ca2+ overload in different cell types. Although likely, its role in pancreatic acinar cells and the pathogenesis of AP was not investigated yet.

Aims & Methods: Our aim was to characterize the functional activity of TRPM2 in pancreatic acinar cells. In our experiments pancreatic acinar cells (PAC) were isolated from wild type (WT) and TRPM2 knockout (KO) mice with enzymatic digestion. The changes of the intracellular Ca2+ level was measured with fluorescent microscopy using FURA2-AM.

Results: The intracellular Ca2+ signals evoked by 100 μM carbachol were not different in WT and TRPM2 KO PAC. On the other hand, 1mM H2O2 induced significantly higher intracellular Ca2+ elevation in WT PAC compared to the TRPM2 KO. In Ca2+ free extracellular solution the Ca2+ signal in response to 1μM H2O2 was markedly reduced in WT PAC confirming that H2O2 activates dominantly extracellular Ca2+ influx.

Conclusion: Our result confirmed the functional activity of the TRPM2 channel in pancreatic acinar cells. In further investigations we aim to clarify the pathogenic role of TRPM2 in AP.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0100 INVESTIGATION OF THE PANCREATIC DUCTAL ION SECRETION IN PANCREATIC DUCTAL ORGANOID CULTURES
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Introduction: Pancreatic duct fluid and HCO3- secretion are crucially important in the physiology and pathophysiology of the exocrine pancreas. However, the role of human pancreatic secretory processes is great challenge due to the limited access to human pancreatic ductal cells. The recently developed three-dimensional pancreatic organoid cultures (OC) may help to overcome this limitation. However, the ion secretary processes in pancreatic OC is not known.

Aims & Methods: Our aim was to characterize the ion transport processes in mouse pancreatic OCs. Mouse pancreatic ductal fragments were isolated by enzymatic digestion. The isolated ducts were grown in Matrigel on 37°C for a week in OC media. Changes of the intracellular pH was measured to characterize the ion transporter activities of the epithelial cells in OC.

Results: Basolateral administration of 20 mM NH4Cl in standard HEPES or CO2/HCO3- buffered solution resulted in rapid intracellular alkalinization, followed by a recovery phase. Removal of NH4Cl induced rapid acidification followed by regeneration to the resting pH levels. The regeneration phase was inhibited by the removal of extracellular Na+ . The administration of 10 mM CFTRinh-172, a selective inhibitor of cystic fibrosis transmembrane conductance regulator decreased the regeneration from alkali load. Basolateral administration of 20 mM amiloride and 20 mM H2DIDS decreased the intracellular pH suggesting the activity of Na+/H+ exchanger and Na+/HCO3- cotransporter on the basolateral membrane.

Conclusion: The ion transport activities in mouse OC are similar to those observed in freshly isolated primary tissue. This suggest that OC will be suitable to study human ductal epithelial ion transport.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0101 INVESTIGATION OF THE ORAII MEDIATED CA2+ ENTRY IN MOUSE PANCREATIC DUCTAL CELLS
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Introduction: Acute pancreatitis (AP) is the most common inflammatory disorder in the gastrointestinal tract with an overall mortality of 20-30% in severe cases. The treatment of AP is not resolved yet, urging the identification of novel drug targets. Toxic cellular Ca2+ overload was highlighted as a key event in pancreatic acinar and ductal cells during the pathogenesis of AP. In addition, the inhibition of Orai in pancreatic acinar cells markedly decreased the Ca2+ toxicity and the severity of AP. However, we have no information regarding the role of Orai in pancreatic ductal cellul physiology or pathophysiology.

Aims & Methods: Wild type FVB/N mice were used for the isolation of pancreatic ductal fragments. The intracellular pH and Ca2+ level of the pancreatic ductal cells (PDC) were measured by microfluorimetry. The effect of selective Orai inhibitors provided by CalciMedica was evaluated.

Results: The tests compounds dose-dependently inhibited Ca2+ influx through the carbachol induced Ca2+ signal in PDC. Inhibition was complete at a concentration of 10μM (CM-B: 99.87%, CM-C: 95.29%). Next, endoplasmic reticulum Ca2+ stores were depleted with cyclopiazonic acid and the inhibition of store-operated Ca2+ entry (SOCE) was investigated after the re-addition of extracellular Ca2+. Under these conditions CM-B and CM-C significantly, but not completely, decreased SOCE in PDC (55.96% and 55.03% respectively). The removal of extracellular Na+ to abolish activity of the Na+/Ca2+ exchanger had no effect on the inhibition of SOCE by CM-B or CM-C. We also showed that the inhibition of Orai has no effect on the basal secretion of HCO3- by PDC, which is the main physiological function of these cells.

Conclusion: We showed that Orai has a significant role in the Ca2+ signaling of PDC. In the next step we will evaluate the pathophysiological relevance of the channel.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0102 ACUTE PANCREATITIS OF UNKNOWN ORIGIN AND IDIOPATHIC JUVENILE PANCREATITIS IN SWEDEN
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In early stage of severe acute pancreatitis (SAP), the factors for predicting hospital mortality in adult patients admitted between 2010 and 2015. Patients with a previous episode of SAP were enrolled into either index- or scheduled cholecystectomy (IC vs. SC). IC was performed before discharge or scheduled 6 weeks from the initial episode. SC was planned after 6 week from randomization. The primary outcome was recurrent biliary events. Secondary endpoints were cholecystectomy complications within 1 months, the proportion of common bile duct stones at cholecystectomy requiring ERC and patients´ reported quality-of-life and pain. Secondary endpoints were cholecystectomy complications within 1 months, the proportion of common bile duct stones at cholecystectomy requiring ERC and patients´ reported quality-of-life and pain.

Results: Sixty-four patients between May 2009 and March 2017 were randomized in ITTRIAL. Twenty-three patients were enrolled into either index- or scheduled cholecystectomy (IC vs. SC). The primary outcome was recurrent biliary events. Secondary endpoints were cholecystectomy complications within 1 months, the proportion of common bile duct stones at cholecystectomy requiring ERC and patients´ reported quality-of-life and pain.

Disclosure of Interest: All authors have declared no conflicts of interest.

References


P0104 EARLY OR LATE CHOLECYSTECTOMY IN MILD GALLSTONE PANCREATITIS? RESULTS FROM RANDOMIZED TRIAL

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Introduction: Cholecystectomy during the index admission may reduce risk of recurrent biliary events but concerns have been raised about complications if surgery is performed to early. The objectives of this study were to compare gallstone- and cholecystectomy-related complications and patient reported quality-of-life and pain if cholecystectomy was performed before discharge or scheduled 6 weeks from the initial episode.

Aims & Methods: Patients admitted with biliary pancreatitis at the Karolinska University Hospital were assessed for eligibility. Patients with mild pancreatitis were enrolled into either index- or scheduled cholecystectomy (IC vs. SC). SC was performed when patients showed recovery and within 48 hours from randomization. SC was planned after 6 week from randomization. The primary outcome was recurrent biliary events. Secondary endpoints were cholecystectomy complications within 1 months, the proportion of common bile duct stones at cholecystectomy requiring ERC and patients´ reported quality-of-life and pain.

Results: Sixty-four patients between May 2009 and March 2017 were randomized in ITTRIAL. Twenty-three patients were enrolled into either index- or scheduled cholecystectomy (IC vs. SC). The primary outcome was recurrent biliary events. Secondary endpoints were cholecystectomy complications within 1 months, the proportion of common bile duct stones at cholecystectomy requiring ERC and patients´ reported quality-of-life and pain.

Disclosure of Interest: All authors have declared no conflicts of interest.

References


P0103 THE FACTORS FOR PREDICTING HOSPITAL MORTALITY IN EARLY STAGE OF SEVERE ACUTE PANCREATITIS

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Introduction: Severe acute pancreatitis has high mortality and needs intensive care. However it is difficult to stratify the severity of acute pancreatitis in early stage because revised Atlanta classification requires persistent organ failure lasting at least 48 hours.

Aims & Methods: We searched factors to predict hospital mortality in early stage of severe acute pancreatitis. This was a retrospective cohort study of all consecutive patients with severe acute pancreatitis who admitted at 44 institutions between June 1, 2009 and December 31, 2013. We evaluated ten factors which associated with mortality in previous study.

Results: The mortality was 12.7% (142/1114 patients). All ten factors were associated with mortality in univariate analysis. In multivariable analysis, four factors, namely, "partial pressure of oxygen in blood <60 mmHg (room air) or mechanical ventilation", "age ≥70 years", "blood urea nitrogen ≥40 mg/dL (or creatinine ≥2.0 mg/dL) or oliguria (daily urine output <400 mL even after acute intravenous fluid resuscitation)", and "lactate dehydrogenase ≥22 times upper limit of the normal range" were associated with mortality. The other factors, namely "base excess ≤-3.5 mmol/L", "platelet count ≤100.000/μm3", "serum calcium <7.5 mg/dL", "c-reactive protein ≥15 mg/dL", "number of positive measures in systemic inflammatory response syndrome criteria ≥3" and "computed tomography grade" were not associated with mortality.

Conclusion: Advanced age, respiratory failure, renal failure and high lactate dehydrogenase could predict mortality in early stage of severe acute pancreatitis. In patients with these factors require transport to a hospital with intensive care unit.

Disclosure of Interest: All authors have declared no conflicts of interest.

References


P0102 COMPARISON OF PREDICTIVE SYSTEMS TO PREDICT MORTALITY WITH SEVERE AND MILD PANCREATITIS ACCORDING TO THE REVISED ATLANTA CLASSIFICATION


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Introduction: The course of acute pancreatitis (AP) ranges from life threatening to mild disease, so accurately predicting its outcome is important. The revised Atlanta classification breaks this into mild/severe dichotomy, so the absence of predictors of severity does not preclude a mild course. Studies designed according to the new classification evaluating existing predictors are still scarce.

Aims & Methods: Our study aims at evaluating the diagnostic accuracy of easily available prognostic scores to predict mortality, persistent organ failure (severe AP) and mild AP. We analyzed a single-center retrospective cohort including all adult patients admitted between 2010 and 2015. Patients with a previous episode of AP in the six months before admission, with other primary diagnosis at discharge and those partially attended at other institutions were excluded. Severity and local complications were defined according to the 2012 Atlanta classification. Four different scores (BISAP, SIRS, APACHE II and HAPS) and the following predictors: C reactive protein (CRP) at 24 h, hematocrit and BUN at admission.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

and their evolution after 24 h were evaluated. Accuracy was measured using different methods for operating characteristic analyses.

**Results:** Of the 817 eligible patients, 118 were excluded, most for a previous episode before admission. We analyzed 699 patients with a median age of 57.5 years (IQR: 45.1–72.7), 57.4% males. Most frequent comorbidities were: diabetes (18.3%), hypertension (16.6%) and COPD (7.7%). Median length of stay was 7 (5–10) days. Most common causes were: biliary (53.9%), idiopathic (21.8%) and alcoholic pancreatitis (14.3%). A CT scan was performed in 56.1% identifying local complications in 36.2% of them, acute fluid collections in 16.8%. There were 42 (6%) severe and 196 (28%) moderately severe cases. Overall mortality was 2.4% (1.5–3.9%), 9.3% (9.6–9.4%). BUN at admission AUC: 0.89 [0.86–0.91], APACHE II (60) [0.67–0.69] and their evolution after 24 h were evaluated. Accuracy was measured using different methods for operating characteristic analyses.

**Conclusion:** The revised Atlanta classification accurately identifies those patients at higher risk of death. Among the available predictors of severity, BISAP and BUN at admission presented an excellent performance, with an AUC of nearly 1.0.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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**P0106 PANCREATIC DUCT ASCARISIS**

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**Introduction:** Although uncommon in the West, Ascaris lumbricoides is a common cause of acute pancreatitis in developing countries. The mechanism of acute pancreatitis in ascariasis may be due to obstruction of papilla of Vater, invasion of common bile duct (CBD) or pancreatic duct (PD). The invasion of pancreatic duct occurs rarely owing to its smaller calibre. Ultrasoundography (USG) is an effective tool for the diagnosis of biliary and pancreatic ascariasis; however, the diagnosis may be false negative in up to 30% of cases. Pancreatic ascariasis has been reported only in case reports. Only case reports have been described in literature. We present our retrospective data of last 10 years of 15 cases of pancreatic ascariasis.

**Aims & Methods:** During a study period of 10 years, 15 cases of pancreatic ascariasis were diagnosed by USG or endoscopic ultrasonography(EUS). EUS was performed with a linear or radial echoendoscope. 13 patients presented with symptoms of acute pancreatitis. Out of 13, 9 patients presented with first episode of idiopathic pancreatitis while 4 presented with idiopathic recurrent acute pancreatitis (IRAP). One patient had biliary colic and one patient presented with abdominal complaints. All the patients had mild pancreatitis while only one patient had necrotic pancreatitis. Patients were treated with parenteral fluids, analgesics, antibiotics, and albendazole. Only 2 cases were diagnosed with USG while 13 patients were diagnosed with EUS. The patients underwent side viewing endoscopy/ERCP under lignocaine 0.2% as well as EUS if EUS was not diagnosed. EUS showed biliary/pancreatic ascariasis. Out of 15 patients, 14 underwent side viewing endoscopy with removal of live multiple worms with rat tooth forceps/biopsy forceps/dormia basket in 13 patients. The managed conservatively with repeat USG showing absence of ascariasis. There were no complications.

**Results:** The patient characteristics are described in table 2. 2 patients had associated bile duct ascariasis. Sonographic characteristics of A. lumbricoides are single or multiple echogenic nonshadowing linear, tubular structures and curved strips with anechoic tubular central lines. EUS features were single or multiple linear hyperechoic structure without acoustic shadowing in the PD or CBD (“single-tube sign” or “strip sign”) or with central hypoechoic tube representing alimentary canal of the worm (“double tube sign” or “inner tube sign”) and movements of worms inside the duct. Live roundworms were removed from PD without undertaking sphincterotomy. In endemic areas, sphincterotomy facilitates the risk of migration of worms into the CBD or PD. Conclusion: Ascariasis-induced acute pancreatitis is usually cold and EUS is the investigation of choice. The recurrence is rare and treatment is side viewing endoscopy with removal of worms. EUS significantly improves the diagnostic yield for idiopathic acute pancreatitis (IAP). Our retrospective study shows that EUS is a highly sensitive method to diagnose the etiology of IAP with reference to biliary or pancreatic ascariasis. Although USG is quite sensitive for diagnosing BPA, its sensitivity significantly falls when the worm is thin, in the PD, or the CBD is non-dilated. EUS is more sensitive for diagnosis of ascariasis in the pancreatic duct than other radiological investigations. The probable reasons are excellent imaging of pancreas by EUS and in and out movement of ascaris which might be missed by other investigations. Endoscopic retrograde cholangiopancreatography, considered the gold standard for diagnosis of biliary ascariasis, should be reserved for therapeutic rather than diagnostic purposes as the endoscopy can lead to reentry of the worm into the common bile duct. EUS should be used early in the work-up of IAP after the first episode. We propose EUS to be investigation of choice for PD ascariasis. Most of the episodes are of mild pancreatitis with no mortality.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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**References**
Abstract No:P0109

Table 1a: AUC, sensitivity, specificity, positive predictive values and negative predictive values of scoring systems and biomarkers in predicting Severe Acute Pancreatitis. (SAP: Severe acute pancreatitis. AUC: Area under the curve. PPV: positive predictive value. NPV: Negative predictive value.

<table>
<thead>
<tr>
<th>SAP</th>
<th>Cut-off values</th>
<th>AUC (95% CI)</th>
<th>Sensitivity (95% CI)</th>
<th>Specificity (95% CI)</th>
<th>PPV (95% CI)</th>
<th>NPV (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BISAP</td>
<td>≥3</td>
<td>0.9 (0.83–0.97)</td>
<td>70.6% (46.9%–86.7%)</td>
<td>93.3% (89.5%–95.7%)</td>
<td>41.4% (25%–59.3%)</td>
<td>97.9% (95.3%–99.1%)</td>
</tr>
<tr>
<td>RANSON</td>
<td>≥4</td>
<td>0.85 (0.76–0.95)</td>
<td>88.2% (65.7–96.7%)</td>
<td>79% (73.5%–83.5%)</td>
<td>22.1% (13.8%–33.3%)</td>
<td>99% (96.4%–99.7%)</td>
</tr>
</tbody>
</table>

Table 1b: AUC, sensitivity, specificity, positive predictive values and negative predictive values of scoring systems and biomarkers in predicting Mortality. (AUC: Area under the curve. PPV: positive predictive value. NPV: Negative predictive value.

<table>
<thead>
<tr>
<th>Mortality</th>
<th>Cut-off values</th>
<th>AUC (95% CI)</th>
<th>Sensitivity (95% CI)</th>
<th>Specificity (95% CI)</th>
<th>PPV (95% CI)</th>
<th>NPV (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BISAP</td>
<td>≥3</td>
<td>0.97 (0.93–0.99)</td>
<td>100% (67.6%–100%)</td>
<td>92% (88%–94.7%)</td>
<td>27.6% (14.7%–45.7%)</td>
<td>100% (98.4%–100%)</td>
</tr>
<tr>
<td>RANSON</td>
<td>≥4</td>
<td>0.94 (0.89–0.99)</td>
<td>100% (67.6–100%)</td>
<td>77% (71.5%–81.7%)</td>
<td>11.8% (6.1%–21.5%)</td>
<td>100% (98.1%–100%)</td>
</tr>
</tbody>
</table>

References
Table 1a. AUC, sensitivity, specificity, positive predictive values and negative predictive values of scoring systems and biomarkers in predicting Severe Acute Pancreatitis. (SAP: Severe acute pancreatitis. AUC: Area under the curve. PPV: positive predictive value. NPV: Negative predictive value. BUN: Blood urea nitrogen measured on admission. CRP: C-reactive protein measured on admission.

<table>
<thead>
<tr>
<th>SAP</th>
<th>Cut-off values</th>
<th>AUC (95% CI)</th>
<th>Sensitivity (95% CI)</th>
<th>Specificity (95% CI)</th>
<th>PPV (95% CI)</th>
<th>NPV (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lactate</td>
<td>&gt;2.8mEq/L</td>
<td>0.79 (0.71-0.88)</td>
<td>58.8% (36%-78.4%)</td>
<td>83.3% (78.2%-87.4%)</td>
<td>19.2% (10.8%-31.9%)</td>
<td>96.8% (93.5%-98.4%)</td>
</tr>
<tr>
<td>Creatinine</td>
<td>&gt;1.4mg/dL</td>
<td>0.82 (0.71-0.93)</td>
<td>64.7% (41.3%-82.7%)</td>
<td>86.1% (81.3%-89.8%)</td>
<td>23.9% (13.9%-37.9%)</td>
<td>97.3% (94.3%-98.8%)</td>
</tr>
<tr>
<td>BUN</td>
<td>&gt;28mg/dL</td>
<td>0.83 (0.73-0.93)</td>
<td>64.7% (41.3%-82.7%)</td>
<td>86.9% (82.2%-90.5%)</td>
<td>25% (14.6%-39.4%)</td>
<td>97.3% (94.3%-98.8%)</td>
</tr>
<tr>
<td>CRP</td>
<td>CRP &gt; 47mg/L</td>
<td>0.72 (0.60-0.83)</td>
<td>70.6% (46.9%-86.7%)</td>
<td>69.7% (63.8%-75.1%)</td>
<td>13.6% (8%-22.3%)</td>
<td>97.2% (93.7%-98.8%)</td>
</tr>
</tbody>
</table>

Table 1b. AUC, sensitivity, specificity, positive predictive values and negative predictive values of scoring systems and biomarkers in predicting Mortality. (AUC: Area under the curve. PPV: positive predictive value. NPV: Negative predictive value. BUN: Blood urea nitrogen measured on admission. CRP: C-reactive protein measured on admission.

<table>
<thead>
<tr>
<th>Mortality</th>
<th>Cut-off values</th>
<th>AUC (95% CI)</th>
<th>Sensitivity (95% CI)</th>
<th>Specificity (95% CI)</th>
<th>PPV (95% CI)</th>
<th>NPV (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lactate</td>
<td>&gt;2.8mEq/L</td>
<td>0.87 (0.78-0.96)</td>
<td>87.5% (52.9%-97.2%)</td>
<td>82.7% (77.6%-86.8%)</td>
<td>13.5% (6.7%-25.3%)</td>
<td>99.5% (97.4%-99.9%)</td>
</tr>
<tr>
<td>Creatinine</td>
<td>&gt;1.4mg/dL</td>
<td>0.85 (0.70-0.99)</td>
<td>75% (40.9%-92.9%)</td>
<td>84.7% (79.8%-88.5%)</td>
<td>13% (6.1%-25.7%)</td>
<td>99.1% (96.8%-99.9%)</td>
</tr>
<tr>
<td>BUN</td>
<td>&gt;28mg/dL</td>
<td>0.83 (0.68-0.98)</td>
<td>75% (40.9%-92.9%)</td>
<td>85.4% (80.6%-89.2%)</td>
<td>13.6% (6.4%-26.7%)</td>
<td>99.1% (96.8%-99.9%)</td>
</tr>
<tr>
<td>CRP</td>
<td>CRP &gt; 47mg/L</td>
<td>0.62 (0.41-0.82)</td>
<td>62.5% (30.6%-86.3%)</td>
<td>68.1% (62.2%-73.4%)</td>
<td>5.7% (2.5%-12.6%)</td>
<td>98.5% (95.2%-99.4%)</td>
</tr>
</tbody>
</table>


**P0110 POST-ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY PANCREATITIS: MORBIDITY AND PREDICTORS OF SEVERITY**

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**Introduction:** Endoscopic retrograde cholangiopancreatography (ERCP) is increasingly used for therapeutic management of various biliary and pancreatic diseases¹. However, ERCP is not a procedure without morbidity². Post-ERCP pancreatitis (PEP) remains the most common and serious complication after ERCP³.

**Aims & Methods:** To detect risk factors for post-endoscopic retrograde cholangiopancreatography (ERCP) pancreatitis (PEP) and investigate the predictors of its severity. This is a prospective cohort study of all patients who underwent ERCP. Pre-ERCP data, intraoperative data, and post-ERCP data were collected

**Results:** The study population consisted of 996 patients. Their mean age at pre-ERCP test, BUN, CRP and venous gasometry including lactate were performed on admission. PEP is associated with higher morbidity and mortality beside its complication after ERCP⁴. The revision of Atlanta Classification in 2012 has established an important change in Acute Pancreatitis (AP) definitions, comprising 3 grades of severity depending on the presence and persistence of organic failure (1). Thereby, patients with severe acute pancreatitis (SAP) include the vast majority of deaths in this disease (2–4).

**Conclusions:** Biomarkers are quick but incomplete tools for SAP prediction, which can be easily obtained at any moment throughout the disease. Our study shows good values of specificity and AUC for BUN, Cr and lactate but not for CRP concerning SAP and mortality prediction on admission, but since they are low prevalent outcomes in our sample, PPVs are low and not very reliable. Although many of these parameters has been analyzed in previous studies, we predict lactate as a new biomarker with similar performance than that of Cr and BUN, suggesting a possible role for scores building or outcome monitoring.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**References**


POSTER PRESENTATIONS

P0112 COTTON VS. REVISED ATLANTA CRITERIA TO DEFINE SEVERITY OF POST-ERCP PANCREATITIS
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Introduction: The Cotton criteria (I) and the revised Atlanta classification (2) are associated with post-endoscopic retrograde cholangiopancreatography (ERCP) pancreatitis (PEP), severity (3). Whereas Cotton puts the emphasis on length of hospitalisation, Atlanta focuses on the presence of local (necrosis) and systemic (organ failure) complications. The number of hospitalization days may not be a proper representation of PEP severity, because it is influenced by other diagnoses such as ERCP complications and comorbidity. The goal of this retrospective cohort study is to compare the Cotton and Atlanta criteria for the severity of PEP.

AIMS & METHODS: All ERCP procedures from a Dutch university medical centre and a teaching hospital between 2012 and November 2016 were checked retrospectively for patients with PEP. Patients were eligible if they met the Cotton criteria or Atlanta criteria for acute pancreatitis. All records were checked up to 48 hours after ERCP to capture delayed PEP. Patients were excluded if they had acute pancreatitis prior to ERCP or had chronic pancreatitis. In the primary analysis, mild/moderate and severe PEP were compared between Cotton and Atlanta with Fischer’s exact test. Atlanta was regarded as the golden standard. Secondly, we compared the sensitivity and specificity of both definitions for mortality.

RESULTS: Out of a total 2156 ERCPs, 66 patients (3%) had PEP. Two patients were excluded due to missing data for hospital stay. Of the 64 patients analysed, 39 (60.9%) were female, mean age was 60.6 years and the most common indication for ERCP was choledocholithiasis (n = 39, 60.9%). Four patients (6.3%) developed organ failure, 3 patients (4.7%) died. The table below depicts the PEP severity distribution according to Cotton and Atlanta. No significant differences were found (p = 0.64). Of the 25 severe patients according to Cotton, 23 were categorized due to hospital stay exceeding 10 days, but were mild according to Atlanta. In 11 patients (44%), concomitant disease (syndrome of inappropriate antidiuretic hormone secretion, cholangitis, pneumonia, perforation or biliary leakage) was the cause for prolonged stay.

<table>
<thead>
<tr>
<th>Severity of PEP according to Cotton and Atlanta</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
<tr>
<td>Cotton</td>
</tr>
<tr>
<td>Mild-moderate</td>
</tr>
<tr>
<td>Severe</td>
</tr>
<tr>
<td>Total</td>
</tr>
</tbody>
</table>

All 3 patients that died had severe PEP according to Atlanta due to persistent organ failure. Cotton classified them as mild, moderate and severe based on hospitalization. Two patients died within 10 days of early multiple organ failure. None of the other Cotton criteria for severity was met. Thus, the Cotton criteria did not capture early deaths due to multiple organ failure. The sensitivity and specificity of Atlanta and Cotton for mortality were 100%, 98.4%, 33.3% and 60.7%, respectively.

CONCLUSION: The Cotton criteria for PEP overestimate disease severity, but under-estimate mortality. Therefore, the Atlanta criteria should be used for defining PEP severity.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P0113 RISKS FACTORS AND OUTCOMES OF INFECTED PANCREATIC NECROSIS: RESULTS FROM A COHORT OF 148 PATIENTS ADMITTED IN ICU FOR SEVERE ACUTE PANCREATITIS
C. Garret1, M. Péron2, A. Le Thua4, M. Le Rhun2, C. Guittot2, J. Gournay2, J. Reigner1, E. Corson2
1Loire Atlantique, CHU de Nantes, nantes/France
2Digestive Diseases Institute; University of Nantes Institute of Digestive Disease - Digestive Diseases Institute, University of Na, Nantes/France
3CH Le Mans, Le Mans/France

Contact E-mail Address: charlotte.garret@chu-nantes.fr

Introduction: Acute pancreatitis (AP) is a common but potentially lethal pathology due to the multiplicity and severity of its complications. Infected pancreatic necrosis (IPN) occurs in 30% of patients with necrotizing AP and is associated with an increase in mortality ranging from 15% to 39%. While interventional drainage and/or removal of the infected tissue remain the mainstay of therapy of IPN, important progresses have been achieved over the last decade and minimally invasive treatment has been developed. The aim of this study was to identify factors associated with IPN and to describe outcomes and management.

AIMS & METHODS: This was a retrospective study of collected data from all patients admitted to Intensive Care Unit (ICU) in a single centre from 2012 to 2015 for a severe AP. Baseline characteristics of the overall population were expressed as frequencies (percentages) for categorical variables, as mean ± standard deviation (SD) for continuous data. For the analysis of mortality, multi-vari-ate analysis with Cox proportional hazards regression modeling was used to identify independent predictors. Association between IPN and patients’ characteristics at baseline was evaluated using logistic regression.

RESULTS: In total, 148 patients were included in this study. Overall mortality was 17%. Body mass Index, computed Tomography Severity Index (CTSI) ans persistent (≥48H) organ failure (OF) were independently associated with overall mortality. Also, patients died in 16 patients died in 2 documented mesenteric ischemia during the early phase (≤8 days) and 3/10 patients during the late phase (>8 days). IPN was present in 62 patients (43%), all requiring an intervention (i.e. radiological, endoscopic, and/or surgical). 35% of patients (22/62) had only one modality of drainage (radiologic or transgastric) and did not required any necrosectomy. For 30 patients (48%), additional necrosectomy was needed because of lack of improvement after drainage alone. 10 patients (17%) had only necrosectomy without prior drainage procedure. Complications such as hemorrhage and perforation of visceral organ occurred more frequently in the IPN group (1.4% vs 19.4%, p < 0.001 and 9% vs 8.5%, p = 0.02 respectively). The late phase mortality (>8 days) was significantly higher in the IPN group (14.5% vs 1.4%, p < 0.01). In multivariate analysis factors associated with IPN were number of OF and portosplenomesenteric venous thrombosis (table 1). 39 patients (68%) received anticoagulants with a median time of 6 [3–6] months and among them, 25 patients developed cavernoma, irrespective of whether or not they receive systemic anticoagulation (p = 0.31).

Table 1: Multivariate analysis of factors associated with infected pancreatic necrosis

<table>
<thead>
<tr>
<th>Cause of pancreatitis</th>
<th>Alcohol Abused Others</th>
<th>OR_adjusted (IC95%)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cause of pancreatitis</td>
<td>Alcohol Abused Others</td>
<td>1.43 [0.79–7.45]</td>
<td>0.02</td>
</tr>
<tr>
<td>Number of organ failure (OF)</td>
<td>No OF or 1 OF multiple OF (≥3)</td>
<td>1.44 [1.07–18.40]</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Postplenomesenteric vein thrombosis</td>
<td>8.16 [3.06–21.76]</td>
<td>&lt;0.001</td>
<td></td>
</tr>
</tbody>
</table>

Conclusion: In conclusion, this study performed in routine practice conditions showed that IPN occurs in almost half of patients hospitalized in ICU for severe AP, and is associated with increased mortality and complications rates. Overall mortality was 17.6%, and factors associated with mortality were a high BMI, CTSI and persistent OF. Those results are consistent with previous studies1–3, but we reported a high rate of mesenteric ischemia (7/26 patients deceased) while this complication is occasionally described. IPN patients required an intervention for drainage of infected tissue removal, which was performed using minimally invasive techniques in the vast majority of cases, with no complication or severe side effect. 35% of patients were treated with drainage alone without any additional necrosectomy. Finally, PSMVT and early OF appeared to be associated with the risk of developing an IPN but anticoagulation for PSMVT did not protect for cavernoma occurrence and can expose to intestinal bleeding. Our results also suggest that the optimal and early management of OF and detection of PVSMT might prevent IPN and/or its complications. Such hypothesis will need to be tested in large multicentre prospective studies.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P0114 EARLY PREDICTORS AND OUTCOMES OF FLUID SEQUESTRATION IN ACUTE PANCREATITIS
S. Goyal
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Contact E-mail Address: drsundeepgoyal@gmail.com

Introduction: Although it is well known that some patients with AP have an increased need for fluid therapy, it is not clear who should get fluids aggressively. Changes in hematocrit, BUN and serum creatinine, has been documented to limit nephrotoxicity and improve outcome. The early prediction of fluid sequestration may help to select patients for more or less aggressive fluid resuscitation.

AIMS & METHODS: 1) To determine early variables as predictors of fluid sequestration in the first 48 hours. 2) To determine outcome associated with fluid sequestration. In this prospective cohort study, 300 consecutive patients of acute pancreatitis were included. Fluid sequestration was calculated by adding the total amount of fluid administered and subtracting the total amount of fluid lost in the first 48 hours of hospitalization. Local complications were defined

Disclosure of Interest: All authors have declared no conflicts of interest.
According to the revised Atlanta classification. Univariate and multivariate analysis were performed.

**Results:** The median fluid sequestration in the first 48 h after hospitalization was 4.7 liter (2.8–6.8 L). It was 3.2 (1.4–5.1), 6.4 (3.6–9.5) in those without necrosis and those with necrosis, and 7.5 (4.4–12) in those with persistent organ failure. The univariate and multivariate analysis showed that alcohol etiology, an increasing number of SIRS criteria and Hematocrit were significantly associated with increased fluid sequestration (Table). Body mass index, APACHE II score, sodium, creatinine and blood urea nitrogen levels did not help predict fluid sequestration. Patients with and without acute fluid collections had a median sequestration of 7.2 and 4.2 L (p < 0.001, respectively). Twenty patients died (7.3%); median fluid sequestration in the patients who died was 6.5 L compared to 4.2L among the patients who survived (p=0.05). Increased fluid sequestration was associated with prolonged hospital stay (p < 0.01, table) Association between variables determined at admission and fluid sequestration.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Fluid sequestration (48 hours) (L)</th>
<th>Univariate analysis, p value</th>
<th>Multivariate analysis, p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;35</td>
<td>5.3 (2.7–8.9)</td>
<td>0.06</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>35–45</td>
<td>5.6 (2.9–7.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>45–55</td>
<td>4.9 (3.1–7.9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>55–65</td>
<td>5.3 (2.7–6.9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;65</td>
<td>4.5 (2.7–6.2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>5.1 (2.7–8.9)</td>
<td>&lt;0.01</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Female</td>
<td>4.8 (2.8–7.4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Etiology</td>
<td></td>
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<tr>
<td>Alcohol</td>
<td>5.5 (2.7–8.8)</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Bilirubin</td>
<td>5.2 (2.4–8.1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Idiopathic</td>
<td>4.8 (2.8–7.2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Others</td>
<td>4.6 (2.7–6.4)</td>
<td></td>
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<tr>
<td>Hematocrit (%)</td>
<td></td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
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<tr>
<td>&lt;35</td>
<td>3.6 (2.7–4.9)</td>
<td></td>
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<td>35–40</td>
<td>3.3 (2.7–5.1)</td>
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<tr>
<td>40–45</td>
<td>3.8 (3.1–7.5)</td>
<td></td>
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<tr>
<td>&gt;45</td>
<td>4.7 (3.8–7.9)</td>
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<tr>
<td>SIRS score</td>
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<tr>
<td>0</td>
<td>5.3 (2.7–4.1)</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
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<tr>
<td>1</td>
<td>5.3 (2.2–4.4)</td>
<td></td>
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<tr>
<td>2</td>
<td>5.3 (2.9–6.5)</td>
<td></td>
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<tr>
<td>3</td>
<td>5.3 (3.1–7.2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>5.3 (3.8–8.9)</td>
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</table>

**Conclusion:** Alcohol etiology, increased number of SIRS criteria, hemococoncentration and younger age were independent predictors of increased fluid loss. Patients with increased sequestration of fluid are at higher risk of local complications and prolonged stay.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**References**


**Disclosure of Interest:** All authors have declared no conflicts of interest.

**References**


**P0116 AUTOIMMUNE PANCREATITIS CLASSIFIED AS NOT-OTHERWISE-SPECIFIED (NOS) ACCORDING TO THE INTERNATIONAL CONSENSUS DIAGNOSTIC CRITERIA: CLINICAL FEATURES AND OUTCOMES IN 47 PATIENTS**

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**Introduction:** Autoimmune pancreatitis (AIP) is a well-recognized fibro-inflammatory disease of the pancreas characterized by a dramatic response to steroid therapy. Three different types have been identified according to the International Consensus Diagnostic Criteria: type 1, type 2 and type not-otherwise-specified (NOS). Despite the significant number of studies published on AIP type 1 and 2, (3, 4) no studies have been focused on AIP type NOS and therefore very little is known about clinical features and long-term outcomes of these cases.

**Aims & Methods:** Aim was to investigate clinical features, risk of other organ involvement, risk of relapse and long-term outcomes of AIP type NOS patients. Patients classified by International Consensus Diagnostic Criteria (ICDC) as AIP type NOS at clinical onset included in our database prospectively maintained since 1995 have been evaluated. AIP type 1 (168 patients) and AIP type 2 (63 patients) were excluded. Epidemiological and clinical data have been collected and analyzed.

**Results:** 47 patients fulfilled inclusion criteria. Symptoms at clinical onset were malaise and weight-loss (40%, 5%), jaundice (34%) and pancreatitis (29.8%). Six patients (12.8%) had other organ involvement (5 proximal biliary involvement and 1 salivary involvement) and only two (4.3%) patients had serum IgG4 levels >140 μg/dL at clinical onset. Six patients (12%, 8%) developed ulcerative colitis (UC) during follow-up and were therefore reclassified as AIP type 2. The mean time between the clinical onset of AIP-NOS and development of UC was 14 months (range 4–48). Eight patients (17%) experienced a relapse after steroid treatment and two (4, 3%) needed immunosuppressive drugs (Azathioprine) because of recurrent relapse. None underwent functional or radiologic treatment despite 30 patients (63, 8%) had a focal pancreatic involvement of the pancreas at imaging. It is therefore a potential good candidate for PPS.

**Conclusion:** Patients suffering from AIP type NOS have own clinical features. The risk of relapse is low (17%) but not irrelevant, as well as the risk of developing UC (12%) during follow-up switching the diagnosis to AIP type 2.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**References**

Results: The purpose of EPDBD therapy for pancreatic stone was to use endoscopic procedures in the pancreatic duct and stone removal, and to reduce stone relapse rates. 568 cases of pancreatic stone were treated by EPDBD. They consisted of 90 cases treated by endoscopic method alone (via major papilla 62, minor papilla 28), and 478 cases treated by ESWL +/- endoscopic method (via major papilla 381, minor papilla 97). After EPDBD therapy, the stone free rate was 75.3%, the pain free rate 97.1%. The stone relapse rate was 5.7% - this is a much lower result compared to other reports. We think that EPDBD contributes to this good result. Complications of EPDBD therapy were only minor bleeding from orifice at the therapy and mild pancreatitis after therapy for several days. Case A; 22 y/o male, idiopathic chronic pancreatitis, pancreas stone: After 4th ESWL, small stones remained in the head duct which can’t be removed by basket catheter and severe pain continued, so EPBD was done under general anesthesia, but via the endoscope we saw that a stone remained in the neck duct. After dilatation of the duct with a bougie, the stone could be removed. Case B; 66 y/o male, alcoholic chronic pancreatitis, pancreas stone: ERCP revealed type 2 incomplete divisum. After EPDBD therapy, the relapse rate of pancreatic stone decreased, the stone free rate was 90%, the pain free rate was 97.1%. The stone relapse rate was 5.7% - this is a much lower result compared to other reports. We think that EPDBD contributes to this good result. Complications of EPDBD therapy were only minor bleeding from orifice at the therapy and mild pancreatitis after therapy for several days. Case C; 72 y/o male, alcoholic chronic pancreatitis, pancreas stone: ERCP revealed type 2 incomplete divisum. After EPDBD therapy, all stones were removed via minor papilla, then EPBD was placed into minor papilla successfully.

Conclusion: By EPDBD therapy, the relapse rate of pancreatic stone decreased, and the success rate of endoscopic drainage and stenting in pseudocyst and dilatation of the minor duct with mild complications, and their prognoses were good. EPDBD is a safe and favorable procedure for pancreatic diseases.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0118 ENDOCYTOSIC ULTRASOUND AS A PREDICTOR AND GUIDE TO SUCCESSFUL ENDOTHERAPY IN CHRONIC PANCREATITIS

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Introduction: Pancreatic calculi (PC) are a sequela of chronic pancreatitis (CP) and can cause problems due to duct obstruction leading to pain, pancreatitis, and a poor feature of CP. The rationale for endoscopic treatment of obstructing PC is based on the observation that pain subsides when the stone(s) is removed and drainage of pancreatic secretion is restored. Indications for endotherapy include stones <5 mm size, stones in head of pancreas which are not impacted and absence of downstream strictures. The assessment prior to the procedure is done by MRCP or CT. However, problems are encountered during ERCP clearance which are not anticipated despite MRCP/CT. The problems are, possible impacted stones, hard stones with acoustic sound shadowing, and duct strictures during ERCP. Hence, controversy exists. EUS can help by providing concordance or discordance with MRCP images and may help in further clarification.

Aims & Methods: We aimed to evaluate the role, feasibility and management challenges of EUS-guided ERCP in patients planned for endotherapy in CP. Another objective was to evaluate whether EUS features of pancreatic duct (PD) stones can serve as a predictor of successful removal during ERCP. The data of 412 patients during the study period (2009-2016) with CP was retrospectively reviewed. PD stones were associated with stones in head/papillary region of pancreas. Out of these, 75 were excluded and remaining 68 were evaluated by EUS using a linear/radial echo endoscope prior to ERCP. Results: Out of 68 cases, 48 were associated with hard stones with acoustic shadowing. While 20 were associated with soft stones without acoustic shadowing. In 20 soft stones cases, ERCP was successful in 18 patients. In 48 patients with hard stones, there was failure of endotherapy in 40 patients which required ESUL/surgery. The failing patients required multiple sessions of ERCP for successful removal. Three patients had ampullary/pancreatic stones which were removed with precut sphincterotomy with immediate relief of pain. Four patients had ventral duct obstruction by calculus and hence underwent ERCP through minor papilla with successful removal of stones in 3 patients. In three patients, there were calculus in pancreatic parenchyma and pancreatic duct simultaneous (ducto-parenchymal stones) and hence endotherapy was avoided. Three patients had pancreas divisum diagnosed on EUS and hence underwent minor papillotomy with stone removal. Three patients also had biliary obstruction with CBD stone/slagde and underwent biliary endotherapy. Four patients had pancreatic mass in head and underwent EUS-FNA with two patients diagnosed with pancreatic cancer who were referred for surgery. The remaining two were also referred for surgery. Four patients were found to have strictures on EUS and hence were referred for surgery. The presence of large (>5 mm), hard, immobile stones were negative predictors of successful endotherapy. Small (<5 mm), ampullary/pancreatic stones were positive predictors.

Conclusion: Present study suggests that EUS can differentiate "soft PD stones" (without an acoustic shadow) from "hard PD stones"(with an acoustic shadow). This differentiation can help in predicting success rate and stone free rate and stone relapse rate in 568 stone pancreatic cases treated by EPDBD. The progeny of 114 EPS-successful pseudocyst cases treated by EPDBD. The progeny of 16 EPS-successful divisum cases complete type 6, incomplete type 10 treated by EPDBD. Complications after EUS-FNA are an additional advantage of making a diagnosis of ampullary/papillary stones and biliary obstruction which can be treated endoscopically. It can guide whether endotherapy needs to be performed through major or minor papilla. EUS by diagnosing pancreatic tumour/strictures missed on other imaging modalities allows early diagnosis and hence improves long term prognosis. It can prevent unsuccessful attempts at endotherapy and its possible risks/costs. We conclude that EUS before endotherapy plays an important role regarding further management decisions in patients with CP.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0119 UTILITY OF SERUM APOPTOSIS INHIBITOR OF MACROPHAGE FOR DIFFERENTIATING IgG4-RELATED DISEASE FROM MALIGNANT DISEASE

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Introduction: IgG4-related disease (IgG4-RD) is characterized by the infiltration of inflammatory cells, such as plasma cells and macrophages, and fibrosis in tissues. We previously reported that apoptosis inhibitor of macrophage (AIM), which is secreted by macrophages, is related to the progression of hepatic fibrosis in chronic hepatitis C. Some studies have observed a relationship between IgG4-RD and malignancy. IgG4-RD is considered to represent a premalignant state or paraneoplastic condition.

Aims & Methods: To clarify the significance of the serum AIM levels in patients with IgG4-RD, we measured these levels in 22 healthy controls, 32 patients with IgG4-RD, and 36 patients with other pancreatic diseases (chronic pancreatitis [CP], intraductal papillary mucinous neoplasm [IPMN], pancreatic cancer [PC]). We also analyzed the prevalence of malignancy, the relationship between the appearance of malignancy and the diagnosis of 42 IgG4-RD, the type of cancer, and related factors, and we compared the age, gender, laboratory data, and AIM level.

Results: Fifteen malignancies were seen in 12 of 42 patients (28.6%). These diagnoses were made before the diagnosis of IgG4-RD for 10 malignancies in 8 patients (mean 4.8 years earlier, range 1–16 years), and after the diagnosis of IgG4-RD for 3 malignancies in 2 patients (mean 2 years later, range 1–3 years). Two malignancies in 2 patients were diagnosed at the same time as IgG4-RD, and 2 patients have IgG4-RD and malignancy. IgG4-RD is considered to represent a premalignant state or paraneoplastic condition.

Conclusion: Macrophages are reportedly related to IgG4 class switching in B cells and progression in IgG4-RD. The increased level of AIM in IgG4-RD, the increased level of AIM is related to cancer, and related factors, and we compared the age, gender, laboratory data, and AIM level.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference
Mera K, et al Serum levels of apoptosis inhibitor of macrophage are associated with hepatic fibrosis in patients with chronic hepatitis C. BMC gastroenterology 2014
This was done in consideration of the current knowledge about lesions mimicking cancer in the setting of a normal pancreatic parenchyma or existence of signs for pancreatic cancer.

**Aims & Methods:**

Retrospective analysis of prospectively collected data in our tertiary University center. From March 2007 to October 2015, 218 (124 men, 94 women; mean age: 79.3 years; age range, 85–100 years; mean tumour size, 29.6 ± 19.7 mm; tumour size range, 10–66 mm) were collected by EUS-FNA.

**Results:**

Pathological diagnoses showed 2 adenocarcinomas, 3 intraductal papillary mucinous neoplasms (IPMNs) not undergoing surgery if and whether that aids in deciding an appropriate treatment.

**References:**

mural nodules, it is useful to analyse genetic mutations of cystic fluids or walls. Currently, adequate samples from EUS-FNA were unavaiable in some cases, we could not make a pathological diagnosis. Even in such cases, genetic analysis and the subsequent diagnosis of malignant or benign tumours may be possible. We could identify several cancer-related genes, such as GNAS, KRAS, TP53, and BRAF.

Conclusion: In this study, we performed whole-genome sequencing of samples obtained from IPMN or PDA using EUS-FNA. Consequently, genetic analysis by NGS may be effective in addition to pathological diagnosis when deciding the management of pancreatic tumours.

Disclosure of Interest: All authors have declared no conflicts of interest.

References


P0124 CIRCHPK3 PROMOTES PANCREATIC CARCINOMA CELLS BXPC3 PROLIFERATION BY TARGETING MI-124/6 R/ STAT3 PATHWAY

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Introduction: Circular RNAs (circRNAs) are a novel class of noncoding RNAs commonly derived from the RNA precursors by a “back-splicing” mechanism. Increasing reports have shown that circRNA is dysfunction in neuro system diseases, cardiovascular diseases, human cancers and many other diseases. CircRNA have been demonstrated involved in tumorigenicity, proliferation, apoptosis, angiogenesis, migration, invasion and metastasis in human carcinoma. CircRNA can act as a microRNA (miRNA) sponge and regulate the targets of miRNA. Circular RNA HIPK3 (cIRCHPK3) is originated from second exon of HIPK3 gene, which is upregulated in gastric, liver, esophageal. However, the mechanism remains unclear. Previous studies revealed that signal transducer and activator of transcription 3 (STAT3) as an oncogene that was activated in pancreatic carcinoma.

Phosphorylation of STAT3 (p-STAT3) is a downstream target of interleukin 6 receptor (IL6R). Activation of STAT3 leads to malignancy of tumorigenesis, cell proliferation and migration. Knockdown STAT3 induces cell apoptosis by Bcl-xL, c-Myc, cyclinD1, etc. CircHIPK3 regulates BcPC3 cell proliferation through IL6R/STAT3 pathway. It may be a new target for the therapy of pancreatic carcinoma.

Aim & Methods: Our research is to study whether cIRCHPK3 can promote proliferation of pancreatic carcinoma cell line, BcPC3, and to explore the mechanism of cIRCHPK3 in cell proliferation. Cell viability was determined by cell counting kit-8 (CCK-8). Transient knockdown of cIRCHPK3 using specific siRNA targeting the conjunction of cIRCHPK3. Overexpression of miR-124 was transfected with synthetic miRNA mimic. Real-time quantitative reverse transcription-polymerase chain reaction (qRT-PCR) was performed to detect cIRCHPK3, miR-124 and miRNAs. The expressions of STAT3, p-STAT3, IL-6R were measured by Western blot. Overexpression of STAT3 was transfected with STAT3 plasmid. Dual-Luciferase Reporter Assay was performed to detect the interaction of cIRCHPK3 and miR-124.

Results: cIRCHPK3 was upregulated in BcPC3 compared to human pancreatic duct epithelial cells (HPDE6-C7). Knockdown of cIRCHPK3, which didn’t affect the linear transcript, significantly decreased cell viability of BcPC3. Bioinformatical analysis and lucerase assay demonstrated that cIRCHPK3 interacted with miR-124. qRT-PCR results showed that expression of cIRCHPK3 decreased during miRNA levels of STAT3 and IL-6R and protein levels of STAT3, p-STAT3 and IL-6R. Previous studies confirmed that miR-124 negatively regulates STAT3, IL-6R via interacting with 3’-UTR (untranslated region). In qRT-PCR and Western blot results confirmed that cIRCHPK3 and both STAT3, p-STAT3 and IL-6R were upregulated in BcPC3 cells than HPDE6-C7 cells while miR-124 was downregulated. MIR-124 was negatively correlated with cIRCHPK3 and STAT3, p-STAT3 and IL-6R.

In this study, we identified cIRCHPK3 promotes BcPC3 pancreatic carcinoma cell proliferation by targeting miR-124 and its target genes STAT3 and IL-6R. We found that miR-124 was a negative regulator of proliferation in BcPC3. And overexpression of STAT3 could attenuate the anti-proliferation of si-cIRCHPK3 and miR-124. These results demonstrated that cIRCHPK3 regulates BcPC3 cell proliferation by acting as miR-124 sponge.

Disclosure of Interest: All authors have declared no conflicts of interest.

References


P0125 CONCOMITANT PANCREATIC CANCERS ARISING ADJACENT TO INDEX INTRADUCTAL PAPILLARY MUCINOUS NEOPLASMS SHARE IDENTITY WITH MULTIPLE MI-124/6 R/STAT3 MUTATIONS AND ARE ASSOCIATED WITH A FAVORABLE PROGNOSIS


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Intraductal papillary mucinous neoplasms (IPMN) are precursors of pancreatic ductal adenocarcinoma (PDA) and are also associated with multifocal cancers (field defect), where concurrent de novo PDA, independent of index IPMN, can also develop. However, there are cases where PDAs arise adjacent to the index IPMNs, and occasionally they are pathologically indistinguishable whether the carcinoma developed from IPMN or was coincidental to the IPMN. A genetic approach can be useful to clarify the origin of each tumor compartment to determine if they shared molecular signatures.

This study, we performed whole-genome sequencing of samples obtained from IPMN or PDA using EUS-FNA. Consequently, genetic analysis by NGS may be effective in addition to pathological diagnosis when deciding the management of pancreatic tumours.

Disclosure of Interest: All authors have declared no conflicts of interest.

References


**Aims & Methods:** Twenty concomitant PDAs and IPMNs (39 samples, including concurrent lesions) from surgically resected patients were enrolled in this study. Resected pancreata were sliced at 5-mm intervals for whole-section histological analysis, and the distance between PDA and IPMNs was measured after precise pathological mapping. Target amplicon sequencing that covers 18 PDA-associated genes including KRAS, CTNNB1, GNAS, TP53, SMAD4, CDKN2A, 9/11, CTNNB1 and RNF43, was performed using Ion PGTM system (Thermo Fisher Scientific). The protein expression of TP33, SMAD4, p16, b-catenin, and RNF43 was also analyzed immunohistochemically.

**Results:** A total of 170 lesions were detected in 19/20 (95%) of PDAs and in 38/39 (97%) of IPMNs. “Adenomatous” concomitant PDAs, defined as those that are 5 mm or less away from the IPMN (n = 11), tended to harbor identical KRAS mutations as the index IPMNs (KRAS identical; n = 8, 72%, KRAS different; n = 3, 27%). Among cases with contiguous neoplastic lesions via the main duct between PDAs and IPMNs had identical KRAS mutations. In contrast, 7 of 9 “distant” concomitant PDAs, defined as those greater than 5 mm away from the IPMN (n = 9), possessed distinct KRAS mutations from the index IPMNs (7/9 = 78%). The KRAS mutations were demonstrated in 14/20 (70%) of index IPMNs and in 29/39 (74%) of all IPMNs, but not in PDAs, supporting de novo carcinogenesis rather than progression from the IPMNs. PDAs harboring identical mutations in KRAS as IPMNs were significantly closer to the IPMNs (KRAS identical: median 2 mm, HR = 1.1, 95% CI 1.0–1.2, p < 0.05). In contrast, the Pro/Pro genotype of the TP53 gene was significantly more common in IPMNs than in PDAs, with a relative risk of 1.6 (95% CI 1.1–2.4, p = 0.01). The Pro/Pro genotype was more common in IPMNs than in PDAs (53% vs. 23%), whereas the Pro/Arg genotype was more common in PDAs than in IPMNs (41% vs. 16%). The level of TNF-α was significantly lower in patients with PCa than in patients with CP. The level of IL-1β was significantly lower in patients with PCs than in patients with CP.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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**P0127 VALIDATION OF SERUM/PLASMA METABOLIC BIOMARKERS AGAINST PANCREATIC CANCER BY QUANTITATIVE TARGETED GC/MS**

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**Introduction:** Pancreatic cancer (PC) is one of the most lethal diseases due to the difficulty of early detection. There is no effective blood biomarker for screening. Recently metabolomics is considered to be a promising approach to discover disease biomarkers. We previously reported that the serum/plasma levels of metabolites were significantly changed compared with those of healthy individuals.

**Aims & Methods:** The aim of this study is to confirm and develop our candidate metabolomic biomarkers in blood of PC patients. Blood samples from PC patients and healthy individuals (HV) were collected by two independent groups consisting of multiple institutions. The 1st set was included 55 PC in stage I and II and 58 HV. The 2nd set was included 16 PC and 16 HV. Sixteen candidate metabolites were selected from previous report. Quantitative analyses were performed by gas chromatography/tandem mass spectrometry (G/C/MS/MS) together with their corresponding stable isotopes. In the 1st set, diagnostic models were constructed via multivariate logistic regression analysis. These results were validated using the 2nd set.

**Results:** In the 1st set, the levels of 4 metabolites differed significantly between PC and HV. Model Y consisting of 2 metabolites, i.e., histidine and xylitol showed high sensitivity (70.4%) than CA19-9. Furthermore, combination of model Y with CA19-9 increased its sensitivity (89.5%) and specificity (89.5%). In the 2nd set, combination of model Y with CA19-9 demonstrated high sensitivity (81.3%) and specificity (93.8%). In particular, it displayed very high sensitivity (100%) for PC in a resectable state.

**Conclusion:** Quantitative analysis using GC/MS/MS confirmed the possibility of metabolomics-based screening methods for PC.

**Disclosure of Interest:** All authors have declared no conflicts of interest.
P0129 VERIFICATION OF INTERNATIONAL CONSENSUS GUIDELINES FOR SURGICAL INTERVENTION FOR BRANCH DUCT INTRADUCTAL PAPILLARY MUCINOUS NEOPLASM OF THE PANCREAS (BD-IPMN) WITH WORRISOME FEATURES


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Introduction: In the revised international consensus guidelines for 2012 for the management of IPMN of the pancreas, resection is recommended for all main pancreatic duct IPMN. While in branch pancreatic duct IPMN (BD-IPMN), the indications for resection are more conservative. Cyst size >30 mm without “high-risk stigmata” can be observed without immediate resection. And EUS observation is recommended to decide a treatment strategy.

Aims & Methods: The present study was a retrospective investigation of surgical indication for BD-IPMN with worrisome features (WF). 466 patients with IPMN underwent pancreatic resection at 3 high volume centers in Japan between 1996 and 2014. Among them, 136 patients with BD-IPMN were enrolled this study. The investigation of predictors of malignancy was done for 10 factors: age at time of surgery, sex, presence or absence of symptoms, serum amylase, CA19-9, CEA, and cyst size of main pancreatic duct (MPD), and cyst size of branch pancreatic duct (BPD). In preoperative examination, endoscopic ultrasonography (EUS) and computed tomography (CT) were considered to be essential. For size of MN, EUS measurements were used in all 156 cases. For diameter of MPD and cyst size of BPD, the CT measurement values were used. In this study, BD-IPMN was defined as cases with cystic dilatation of BPD and the MPD diameter was considered <5 mm (International Consensus Guidelines 2012). According to the WHO histological classification of IPMN (2000), pathological diagnosis is classified as adenoma (IPMA), borderline (IPMB), and noninvasive and invasive carcinoma (IPMC). A central review of pathological diagnosis was done in the cases of IPMB and IPMC.

Results: Pathological diagnosis was benign IPMN in 91 cases (58%) and malignancy, and in ROC analysis AUC for these factors was 0.74 and 0.72, respectively. Among cases of IPMC, 12 patients had metastasis to nodes or liver, and 30 patients had regional lymph node metastasis. About 15% of cases had multiple lesions. In the cases of BD-IPMN, the median age was 65 (range: 41–80). The patients had a median cyst size of 30 mm (range: 15–130 mm) and a median procedural time was 30, 5 minutes (range: 17–58 minutes). We report a technical success rate of 85% (n = 17) - technical failure was only seen in transduodenal puncture (n = 3, 15%). Biopsies were generally of good quality and contributed to the diagnosis in 14 patients (clinical success of 82%). Among these, there were ten cases of intraductal papillary mucinous neoplasia, two serous cyst adenomas, and one mucinous cystadenocarcinoma, and one pseudocyst. Two mild adverse events were recorded (1%), a case of re-admission due to non-specific abdominal pain and a mild acute pancreatitis.

Conclusion: The use of micro-biopsy forces was until now only reported in case reports. This is a first large-scale feasibility study. We conclude that the use of the micro-forces seems feasible and safe with acceptable rates of technical and clinical success. However, prospective studies are needed in order to determine diagnostic potential of this instrument compared to the other modalities currently used.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P0130 USE OF A NOVEL THROUGH-THE-NEEDLE MICRO-BIOPSY FORCES IN DIAGNOSING PANCREATIC CYSTS – A MULTICENTER FEASIBILITY STUDY

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Introduction: The diagnosis of pancreatic malignancy can be performed by brush cytology of the common bile duct or main pancreatic duct (MPD) during endoscopic retrograde cholangiopancreatography (ERCP). This is a first large-scale feasibility study. We conclude that the use of the micro-forces seems feasible and safe with acceptable rates of technical and clinical success. However, prospective studies are needed in order to determine diagnostic potential of this instrument compared to the other modalities currently used.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P0131 PANCREATIC DUCTAL CYTOLOGY: AN UNDERUSED DIAGNOSTIC TOOL


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Introduction: The diagnosis of pancreatic malignancy can be performed by brush cytology of the common bile duct or main pancreatic duct (MPD) during endoscopic retrograde cholangiopancreatography (ERCP). This is a first large-scale feasibility study. We conclude that the use of the micro-forces seems feasible and safe with acceptable rates of technical and clinical success. However, prospective studies are needed in order to determine diagnostic potential of this instrument compared to the other modalities currently used.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
endoscopic ultrasonography fine needle aspiration. One patient developed mild pancreatitis (6.1%).

Conclusion: In patients with suspected cephalopancreatic adenocarcinoma referred for ERCP, MPD brush cytology may be performed beyond biliary cytology, as it may improve cytologic diagnosis of malignancy without increasing complications rate.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0132 ANALYSIS OF PROGNOSTIC FACTORS IN PANCREATIC METASTASES: A MULTICENTER RETROSPECTIVE ANALYSIS

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Introduction: Pancreatic metastases (PM) account for 1–2% of pancreatic tumors. Several cancer types metastasize to the pancreas, but even recently developed cross-sectional imaging modalities have difficulties distinguishing PM from primary pancreatic tumors. Moreover, their prognostic significance is poorly defined.

Aims & Methods: The aims of this study were to clarify the incidence of primary tumors leading to PM, the clinical characteristics, and prognoses, and to define the prognostic factors for survival. A retrospective analysis was performed at 39 Japanese tertiary referral hospitals between January 2005 and August 2015, after receiving approval from the institutional review board of each hospital. We identified the patients based on data obtained from each institutional database, and analyzed patient and tumor characteristics, and survival time. All the patients enrolled in the analysis were histopathologically or cytopathologically diagnosed with PM. Kaplan-Meier analysis and Cox’s proportional hazard models were applied to evaluate overall survival and survival analysis, respectively.

Results: We enrolled 159 patients (median age 74.5 years) with a pathologic diagnosis of PM. The most common primary tumor was renal cell carcinoma (38.4%, n = 61), followed by lung cancer (24.5%, n = 39), colorectal cancer (11.3%, n = 18), sarcoma (6.3%, n = 10), breast cancer (6.3%, n = 10), and other cancers (n = 21). At the time of the diagnosis of PM, 38 patients (24%) had at least one tumor-related symptom. Additional extra-pancreatic metastases were diagnosed in 94 patients (59%). Sixty-four patients (40%) underwent surgery. At the time of diagnosis, and no surgical resection was performed in 95 patients (60%). Additional therapies were chemotherapy (n = 69), chemoradiation (n = 4), radiation (n = 3), palliative care, and unclear (n = 2). Eight patients were lost during follow-up and 151 patients were included in the statistical analysis. All patients with PM had a median overall survival of 43.0 months, with 3- and 5-year survival rates of 52.5% and 42.6%, respectively. Among the five frequent primary sites of PM, prognoses of RCC, breast cancer, and colorectal were better than those of lung cancer and sarcoma. Univariate Cox proportional regression analysis identified four prognostic factors: pancreatic resection (hazard ratio [HR] 0.31, 95% confidence interval [CI] 0.18–0.57, p < 0.001), extra-pancreatic metastases (HR 3.07, 95%CI 1.71–5.51, p < 0.001), tumor-related symptoms at PM diagnosis (HR 3.88, 95%CI 1.29–6.56, p < 0.001), and pathologic diagnosis of primary tumors (p < 0.001). Multivariate Cox proportional regression analysis identified three independent prognostic factors: extra-pancreatic metastases (HR 2.13, 95%CI 1.11–4.07, p = 0.02), tumor-related symptoms at diagnosis (HR 5.39, 95%CI 2.92–9.91, p < 0.001), and pathologic diagnosis of primary tumors (p < 0.001).

Conclusion: Treatment strategies and prognoses for PM completely differ according to the primary tumor type. A definitive pathologic diagnosis of PM is essential for selecting the appropriate treatment.

Disclosure of Interest: All authors have declared no conflicts of interest.

References


P0133 LUNG METASTASIS IN PANCREATIC CANCER: SHOULD STAGING CHEST CT BE ROUTINELY PERFORMED?

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Disclosure of Interest: All authors have declared no conflicts of interest.

Introduction: National Comprehensive Cancer Network (NCCN) guidelines recommend chest x-ray or chest computed tomography (CT) for the staging of potential resectable pancreatic adenocarcinoma (PDA). However, there is limited data supporting these guidelines, and the prevalence of lung metastasis is not well defined on staging CT scans. We report our findings of patients with lung metastasis during initial staging and follow-up of patients with PDA.

Aims & Methods: Data was prospectively collected from May 2013 to September 2016 for PDA patients who were presented at a multidisciplinary pancreas center (MDPC) at a large tertiary-care center. All patients were staged with CT pancreatic protocol, CT chest and Endoscopic Ultrasound. Patients with findings of lung lesions on initial staging chest CT were followed prospectively. Metastatic lung lesions were determined based on definite imaging characteristics with clinical consensus or lung biopsy results.

Results: A total 278 PDA patients referred to MDPC were staged with CT chest (Table 1). Out of these, 36 (12.6%) patients were found to have either malignant (N = 6) or indeterminate (N = 30) lung lesions on initial staging CT chest. Out of the six malignant lung lesions, 5 (83.3%) patients had metastatic PDA lesions, and 1 (16.7%) patient had incidental primary lung cancer. On a follow-up of 30 patients with indeterminate lung lesions, 8 patients (26.7%) were later determined to be lung metastasis. The overall prevalence of definite lung metastasis was at least 4.8% (13/278). The prevalence of lung metastasis in pancreatic head cancer was 3.0%, while body and tail masses was 10.5%. Lung metastasis was almost four times more likely in the body, and tail masses (OR = 3.83, CI 1.2–11.8, p = 0.02) compared to head. Overall CT chest resulted in a change in management plan in 9 (2.5%) patients due to change in the stage to metastatic (8) and diagnosis primary lung cancer (1). Staging with CT chest changed otherwise resectable disease to unresectable/metastatic in 5 patients (1.8%) and borderline resectable to metastatic disease in 2 (0.7%) patients. Prevalence of isolated PDA lung metastasis without any other metastasis was 2.8% (8/278).

Table 1: Comparison of patient and tumor characteristics.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Patients without Lung metastasis N = 265</th>
<th>Patients with LungMetastasis N = 13</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs), mean (S.D)</td>
<td>68.8</td>
<td>64.8</td>
<td>0.22</td>
</tr>
<tr>
<td>Male (%)</td>
<td>48.4</td>
<td>69.2</td>
<td>0.14</td>
</tr>
<tr>
<td>Race, Caucasian (%)</td>
<td>90.2</td>
<td>100</td>
<td>0.36</td>
</tr>
<tr>
<td>Mass size (mm), mean (S.D)</td>
<td>26.9</td>
<td>31.1</td>
<td>0.16</td>
</tr>
<tr>
<td>Mass Location</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Head (%)</td>
<td>76.7</td>
<td>46.2</td>
<td>0.01</td>
</tr>
<tr>
<td>Body/Tail (%)</td>
<td>23.3</td>
<td>53.8</td>
<td></td>
</tr>
<tr>
<td>CA 19-9, mean (S.D)</td>
<td>899 (1528)</td>
<td>961 (482)</td>
<td>0.90</td>
</tr>
</tbody>
</table>

Conclusion: Our study showed that the prevalence of pulmonary metastasis in PDA was clinically relevant to mandate routine staging with CT chest. Prevalence was significantly higher for pancreatic body and tail cancers compared to the head. Staging CT chest resulted in a change in the stage of PDA and management decisions.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0134 VALUE OF EUS IN EARLY DETECTION OF TUMOR LESION IN THE REMNANT PANCREAS

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Disclosure of Interest: All authors have declared no conflicts of interest.

Table 1: Comparison of patient and tumor characteristics.
Introduction: New lesions (metachronous pancreatic cancer) and recurrence may develop after IPMN. The rate of new malignancies after initial surgery for IPMN and intraductal papillary mucinous neoplasms (IPMN). Endoscopic ultrasonography (EUS) is proved to be a more specific and sensitive method for pancreatic cancer. However, there is no report about EUS after pancreatectomy. If it is possible to observe the appearance of new lesions after pancreatectomy, the detection of new lesions could be estimated by the number of patients with EPMs among patients with and without EPMs by univariate analysis. We compared the distribution of IPMN in different anatomical parts and identified any of the demographics and clinical characteristics to significantly influence EPM occurrence among patients with IPMN.

Aims & Methods: The aim of this study was retrospectively to investigate the observation ability of EUS for renal pancreas. In this retrospective study, 44 patients underwent EUS for renal pancreas. In the surgical procedure, pancreaticoduodenectomy (PD) including pylorus-preserving PD (PPPD) and subtotal stomach-preserving PD (SSPPD) was 20 cases and distal pancreatectomy (DP) was 24 cases. Total observation of renal pancreas was possible in 41 cases (93%). Seven of 44 cases showed the lesion of recurrence in the remnant pancreas. Although CT or MRI was able to point out it in only 2 cases, EUS was able to point out it in the remnant pancreas of all cases. Stage of six cases were as follows, 1 case of stage 0, 2 cases of stage Ia, 3 cases of stage IIb. The other cases (28 cases) were able to perform EUS-FNA in lesion in the remnant pancreas in all cases. Pathological results were positive in 5 cases. One of the other 2 cases was negative (case IIb), but it was a recurrence by surgery. The other case was strongly suspected to recurrence by positron emission tomography (PET). Second pancreatectomy was performed in 3 of 7 cases. The sensitivity of EUS-FNA was 71.4% (5/7), the specificity was 85.7% (6/7) and the accuracy was 71.4% (5/7). In addition, a comparison of detection ability of EUS and CT or MRI findings showed that EUS was significantly superior to CT or MRI (P < 0.001).

Conclusion: EUS was able to observe renal pancreas in almost cases. We were able to perform EUS-FNA for lesion in the remnant pancreas. In addition, the detection ability of EUS was significantly superior to that of CT or MRI. We believe that EUS and EUS-FNA should be performed for lesion in remnant pancreas, and that remnant pancreatic cancer may be pointed out an early stage.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0135 PATIENTS WITH INTRADUCTAL PAPILLARY MUCINOUS NEOPLASMS OF PANCREAS (IPMNs) ARE AT INCREASED RISK OF RENAL CELL CARCINOMA, PROSTATE, COLORECTAL AND BREAST CANCER: A SINGLE CENTER ITALIAN EXPERIENCE

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Introduction: Number of studies reported that patients with intraductal papillary mucinous neoplasms of pancreas (IPMNs) are at the increased risk for occurrence of extrapancreatic malignancies (EPMs). We have conducted a study in order to assess the prevalence and incidence of EPMs in a cohort of Italian patients with IPMNs. The aim of this study was to determine the risk of EPMs in IPMN patients and to identify the risk factors for development of EPMs. We identified 72 EPMs in 63 patients with IPMN between December 2002 and March 2016, the enrolled patients were 44 who underwent EUS for renal pancreas. The demographics, clinical characteristics, treatment, previous, synchronous or metachronous in relation to IPMN diagnosis. We extracted for all the cases identified on demographics, clinical characteristics, treatment, survival for remnant pancreas observed from linear white line (anastomotic part) to opposite side pancreas, otherwise it was insufficient observation. We compared the detection rate of EUS findings and that of CT or MRI findings.

Results: Among the 395 patients who underwent pancreatectomy at the AOU Onofrio General Hospital between December 2002 and March 2016, the enrolled patients were 44 who underwent EUS for renal pancreas. In the surgical procedure, pancreaticoduodenectomy (PD) including pylorus-preserving PD (PPPD) and subtotal stomach-preserving PD (SSPPD) was 20 cases and distal pancreatectomy (DP) was 24 cases. Total observation of renal pancreas was possible in 41 cases (93%). Seven of 44 cases showed the lesion of recurrence in the remnant pancreas. Although CT or MRI was able to point out it in only 2 cases, EUS was able to point out it in the remnant pancreas of all cases. Stage of six cases were as follows, 1 case of stage 0, 2 cases of stage Ia, 3 cases of stage IIb. The other cases (28 cases) were able to perform EUS-FNA in lesion in the remnant pancreas in all cases. Pathological results were positive in 5 cases. One of the other 2 cases was negative (case IIb), but it was a recurrence by surgery. The other case was strongly suspected to recurrence by positron emission tomography (PET). Second pancreatectomy was performed in 3 of 7 cases. The sensitivity of EUS-FNA was 71.4% (5/7), the specificity was 85.7% (6/7) and the accuracy was 71.4% (5/7). In addition, a comparison of detection ability of EUS and CT or MRI findings showed that EUS was significantly superior to CT or MRI (P < 0.001).

Conclusion: EUS was able to observe renal pancreas in almost cases. We were able to perform EUS-FNA for lesion in the remnant pancreas. In addition, the detection ability of EUS was significantly superior to that of CT or MRI. We believe that EUS and EUS-FNA should be performed for lesion in remnant pancreas, and that remnant pancreatic cancer may be pointed out an early stage.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0136 CLINICAL CHARACTERISTICS OF SECOND PRIMARY PANCREATIC CANCER


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Introduction: Pancreatic ductal adenocarcinoma (PDAC) is known to have an extremely poor prognosis. Several studies reported the increased risk of second primary pancreatic ductal adenocarcinoma (2nd PDAC) in cancer survivors. However, data on the characteristics of 2nd PDAC are insufficient. Studies of PDAC in the setting of second primary cancer can provide etiologic clues to understand PDAC.

Aims & Methods: The aim of this study was to investigate the clinical characteristics of the patients with second primary PDAC compared to patients with first primary PDAC. This retrospective cohort study included 1759 patients with PDAC. They were classified as having 2nd PDAC or first primary PDAC (1st PDAC) according to a prior diagnosed cancer that originated from different organ and diagnosed at least 6 months before the diagnosis of PDAC. Comparative analysis and multivariated survival analysis were used to evaluate the characteristics of the 2nd PDAC.

Results: A total of 1759 patients with PDAC were included in the cohort. Forty-three patients were classified as having synchronous 2nd PDAC and excluded from the analysis. There were 110 patients (6.4%) with 2nd PDAC and 1606 (93.6%) patients with 1st PDAC. The median interval between the diagnosis of the 2nd PDAC and the diagnosis of the prior cancer was 8.4 years (range 0.7–31.4 years). The 2nd PDAC group. In the comparison of baseline characteristics between the 1st PDAC and 2nd PDAC groups, patients with 2nd PDAC presented significantly older age at diagnosis (66.5 vs. 62.2 years, p < 0.001), lower rate of alcohol consumption (25.5 vs. 36.8%, p = 0.017), higher rate of resectability of PDAC (26.4 vs. 15.9%, p = 0.004), and higher rate of receiving surgery as initial treatment (26.4 vs. 15.9%, p = 0.018) than patients with 1st PDAC. The most common origin of prior cancers was the stomach (22 of 110, 19.1%), breast (19 of 110, 17.3%), colon (12 of 110, 10.9%), and others. The overall survival (OS) was slightly longer in patients with 2nd PDAC; however, the difference was not significant (11.8 vs. 12.3 months, p = 0.068). Multivariated analysis without resectable status showed that 2nd PDAC (HR 0.73, 95% CI 0.56–0.94, p = 0.016), age at diagnosis (HR 1.02, 95% CI 1.01–1.02, p = 0.001), and alcohol consumption (HR 1.28, 95% CI 1.12–1.46, p = 0.001) were significantly related to OS (Table 1). When resectable status was included in multivariate analysis, age at diagnosis (HR 1.02, 95% CI 1.01–1.02, p < 0.001), alcohol consumption (HR 1.25, 95% CI 1.11–1.42, p < 0.001), and resectable status at diagnosis (HR 0.30, 95% CI 0.25–0.36, p < 0.001) were significantly associated with OS. However, 2nd PDAC (HR 0.85, 95% CI 0.66–1.09, p = 0.198) was no longer significantly associated with OS after adjusting for resectable status. This analysis suggested that the association between 2nd PDAC and survival was owing to the higher resectability rate. When subgroups were separately analyzed according to initial treatment modality, the effectiveness of surgery and chemotherapy were similar between 2nd and 1st PDAC. In the subgroup of patients who received curative surgery, the median OS was 28.5 months (95% CI, 23.0–34.1) in the 1st PDAC group compared to 12.3 months (95% CI, 5.0–19.5) in the 2nd PDAC group.
pared with 33.1 months (95% CI, 9.0–27.2) in the 2nd PDAC group (N: 259 vs. 201) (p = 0.001). The 5-year survival of the APT group was significantly higher than that in the no APT group (16.0% vs. 5.9%; p = 0.001). Postoperative bleeding occurred in seven and nine patients in the continuous single-LDA group (15.2%) and the continuous LDA on DAPT group (22.5%), respectively. In multivariate analysis, specimen size of ≥ 40 mm (odds ratio [OR] 3.19; 95% confidence interval [CI], 1.65–6.16; P < 0.001) was a sole independent risk factor for postoperative bleeding (Table 1). In subgroup univariate analysis among continuous LDA users, continuous single-LDA and continuous LDA on DAPT were not related to postoperative bleeding.

Table 1: Multivariate analysis for postoperative bleeding after ESD.

<table>
<thead>
<tr>
<th>Odds ratio</th>
<th>95% CI</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coronary artery disease</td>
<td>1.52</td>
<td>0.61–3.78</td>
</tr>
<tr>
<td>CKD with hemodialysis</td>
<td>3.21</td>
<td>0.97–10.60</td>
</tr>
<tr>
<td>Continuous LDA</td>
<td>2.13</td>
<td>0.83–5.45</td>
</tr>
<tr>
<td>Specimen size ≥ 40 mm</td>
<td>3.19</td>
<td>1.65–6.16</td>
</tr>
</tbody>
</table>

Conclusion: This study suggests that continuous LDA may be acceptable for gastric ESD in patients on DAPT. However, patients with continuous LDA on DAPT should be monitored carefully for postoperative bleeding after gastric ESD because the rate of postoperative bleeding in the continuous LDA on DAPT group was higher than that in the other groups.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
Introduction: Peroral endoscopic myotomy (POEM) has received wide acceptance as a safe and effective treatment for achalasia. Several large, multicenter randomized studies have confirmed the efficacy and safety of POEM in treating achalasia. However, the mechanisms underlying its treatment effects are poorly understood. Recent studies have reported that POEM significantly attenuates the acid reflux and improves the motility in patients with chronic gastrointestinal ischemia (CGI) in the absence of gastric atrophy. This study aims to investigate the potential mechanisms of POEM in treating achalasia in patients with chronic gastrointestinal ischemia (CGI).

Methods: Consecutive patients with chronic gastrointestinal ischemia (CGI) in the absence of gastric atrophy were included. A total of 50 patients were included. POEM was performed in all patients. The primary endpoint was the rate of the lesions that need hemostatic forceps was compared among the three groups (n = 50 for the lower gastric body atrophy and n = 43 for the antral intestinal metaplasia). The degree of correspondence between the observed differences between the three groups was compared using McNemar's test. A p-value < 0.05 was considered statistically significant.

Results: The mean age of included patients was 38.7 ± 15.6 years, they were 21 (42%) males and 29 (58%) females. 38 (76%) and 13 (26%) patients have peptic ulcer disease and intestinal metaplasia respectively. Overall, 41 (82%) and 9 (18%) patients have low and high gastric cancer risk respectively. The sensitivity of NBI in the diagnosis of Helicobacter pylori infection, gastric cancer and intestinal metaplasia were 96% (n = 48.50), 100% and 61.5% (n = 8/13) respectively. The degree of correspondence between the scores obtained by NBI and by histology was 58% (29/50) for the lower gastric body atrophy and 86% (n = 43/50) for the antral intestinal metaplasia. The degree of correspondence between the high risk and low risk groups determined on the basis of NBI endoscopy on one hand and histopathology on the other hand was 80% (n = 40/50).

Conclusion: NBI is able to approximate histopathological staging of gastritis to that of endoscopy. More studies and training will further improve the performance of our suggested new staging method.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

PO141 SAFETY ADVANTAGE OF THE NEW DEVICE (SPLASH-M KNIFE®) FOR ENDOSCOPIC SUBMUCOSAL DISSECTION OF EARLY GASTRIC CANCER:

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Introduction: Endoscopic submucosal dissection (ESD) is a standard treatment for early gastric cancer. Development of the ESD device has been conducted recently with a novel multifunctional knife device. New ESD device was invented to achieve complete ESD with a simple device. It achieves clear marking, better hemostasis and smoother operation during a procedure without replacing the knife.

Aims & Methods: The aim of this study was to investigate clinical outcome of ESD for early gastric cancer with a new device (SPLASH-M knife®). In total, early gastric cancer treated by ESD with a needle-type knife between January 2012 and August 2016 at Kitakyushu Municipal Medical Center were retrospectively reviewed. Lesions treated by ESD with a conventional needle-knife (ESD-C, n = 76) and by ESD with a new device (ESD-N, n = 73) were compared. Multivariate analyses and propensity score matching were used to compensate for the differences in age(≥75 years vs < 75 years), sex (male vs female), under-lying disease (none vs with cardiovascular or cirrhotic), antithrombosis drugs (not receiving or discontinuation vs continuation), tumor size (≥21 mm vs < 21 mm), lesion location (in the upper or middle third of the stomach vs in the lower stomach), lesion position (in the lesser curvature of the stomach vs others), macroscopic type (flat or depressed vs elevated), presence of ulceration (presence vs absence) and operator level (experience of ≥50 vs experience < 50). As primary endpoint, the rate of the lesions that need hemostatic forceps was compared

References
INCIDENCE, PREDICTORS AND FOLLOW-UP FINDINGS

Gastric cancer. It may contribute to reduce cost for ESD by reducing usage of Splash M-Knife

Conclusion: CI: 1.0–2.0 mg, p = 0.001), diagnostic yield (95% CI: 1.8–8.9, p = 0.001) and age (95% CI: 78.8%, 90.0%, respectively, for eradicated status, and 67.1%, 91.4%, 59.6%, 93.6% and 21.7, respectively, for infected status. High DORs were obtained for the following endoscopic findings: 32.2 for RAC, 7.7 for FGP and 4.7 for red streak in subjects as signs of infection. Further investigation for eradicated status, and 26.8 for diffuse redness, 13.3 for mucosal swelling, 10.2 for sticky mucus and 8.6 for enlarged fold in subjects with infected status.

Conclusion: The Kyoto classification is useful for diagnosis of HP infection status, the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and diagnostic odds ratio (DOR) for endoscopic findings were determined. This study was registered as a clinical trial in UMIN (UMIN000016674) and was conducted with the approval of the ethics committee in our institution.

Introduction: Since Helicobacter pylori (HP) eradication therapy is necessary to prevent the development of gastric cancer, evaluation of HP infection status (uninfected, infected, eradicated) by endoscopy has become important. For that purpose, the Japan Gastroenterological Endoscopy Society proposed the Kyoto classification for gastritis. However, the usefulness of the classification in daily clinical practice has not been sufficiently evaluated.

Results: The 498 subjects included 376 males and 122 females with a mean age of 53.1 years. HP status was uninfected in 315 subjects, eradicated in 104 subjects and infected in 79 subjects. The diagnostic accuracy rate was 82.9%. The sensitivity, specificity, PPV, NPV and DOR were 88.3%, 92.9%, 95.5%, 82.1% and 99.0%, respectively. For uninfected status, the false negative rate for endoscopy was 17/30 (56.7%), consisting of pharyngeal abnormalities (n = 9), dysmotility (n = 7) and no further findings (n = 1%).

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Aims & Methods: We retrospectively identified all gastroscopies performed at a district general hospital between August 2010–August 2016 from an endoscopy database, and reviewed cases with IF. We excluded patients who had achieved oesophageal intubation. Data on sedation use, endoscopy status, indications, radiological and endoscopic findings were recorded. Procedural limitations were classified into 2 groups: failure to tolerate (e.g. pulling out scope, anxiety) and ‘failure to progress’. Statistical analyses were made using Pearson’s chi² and Wilcoxon signed rank test.

Results: The incidence of IF was 0.95% (248/26130). 238 patients were identified, with a mean age of 63.2 (SD 16.1), with ‘failure to progress’ in 41 and ‘failure to tolerate’ in 197. Subsequent investigations included barium radiology (59.7%, n = 142), CT (21%, n = 50), repeat gastroscopy (29.4%, n = 70) and no further investigations (19.7%, n = 47). Structural pharyngeal abnormalities were diagnosed comprising of cuffed tongue, hyperplastic CPH (49%), Zenker’s diverticulum (ZD) (14.6%), pharyngeal web (12.2%), ZD with CPH (9.8%), cervical spondylosis (7.3%) and other (7.3%). Endoscopist status was a predictor of IF (OR for medical vs. non-medical endoscopist 0.7, 95% CI: 0.5–0.9, p = 0.007). Within the IF cohort, predictors of structural causes on barium radiology included: dysphagia (OR 5.5, 95% CI: 2.5–11.8, p < 0.001), failure to progress (OR 5.2, 95% CI: 2.3–12.0, p < 0.001) and age ≥ 65 (OR 4.0, 95% CI: 1.8–8.9, p < 0.001). Repeat gastroscopy was successful in 65/70 (2 using nasendoscopy) after increasing midazolam dosage (mean increase = 0.15 mg, HP eradicated: 1.0–2.0 mg, p < 0.001). Diagnostic yield for barium radiology, CT and repeat gastroscopy were 69.0%, 54.0% and 64.3% respectively. The concordance of endoscopic indication and pathology on further investigation for IF was 110/192 (57.5%). In patients undergoing barium radiology and repeat gastroscopy, the false negative rate for endoscopy was 17/30 (56.7%), consisting of pharyngeal pathology (n = 9), dysmotility (n = 4) and significant reflux (n = 4).

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference
1. Ponchon T, GIE, April 2000; 51(4): AB275

P0144 DIAGNOSTIC CAPABILITY OF ENDOSCOPY FOR HELICOBACTER PYLORI INFECTION

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Aims & Methods: The aim of this study was therefore to determine the usefulness of the Kyoto classification for diagnosis of HP infection status. A total of 498 subjects were recruited during the period from January to October in 2015 for this study after providing informed consent in writing. HP infection status was determined by the presence of HP-IgG antibody (E-plate II H. pylori antibody, Eiken Chemical Co., Ltd., Tokyo, Japan) and history of eradication therapy. HP infection status was judged to be “eradicated” if there was a definite history of eradication therapy. Without a history of eradication therapy, HP infection status was judged to be “infected” for an HP antibody titer of less than 3 U/ml, “eradicated” for an HP antibody titer of 3–10 U/ml and “infected” for an HP antibody titer of more than 10 U/ml. Seven endoscopists (5 well-experienced endoscopists and 2 trainees) who were blinded to history of eradication therapy performed endoscopy. Two following endoscopy recordings were made according to the Kyoto gastritis classification: diffuse redness, regular arrangement of collecting venules (RA), fundic gland polyph (FGP), atrophy, xanthoma, hyperplastic polyph, map-like redness, intestinal metaplasia, nodularity, mucosal swelling, white and flat elevated lesion, sticky mucus, depressive erosion, raised erosion, red streak, and enlarged fold. HP infection status was diagnosed on the basis of the findings. An Olympus H260 and Xp260NS were used for endoscopy. The diagnostic accuracy rate of the Kyoto classification and the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and diagnostic odds ratio (DOR) for endoscopic findings were determined. This study was registered as a clinical trial in UMIN (UMIN000016674) and was conducted with the approval of the ethics committee in our institution.

Results: The 498 subjects included 376 males and 122 females with a mean age of 53.1 years. HP status was uninfected in 315 subjects, eradicated in 104 subjects and infected in 79 subjects. The diagnostic accuracy rate was 82.9%. The sensitivity, specificity, PPV, NPV and DOR were 88.3%, 92.9%, 95.5%, 82.1% and 99.0%, respectively. For uninfected status, the false negative rate for endoscopy was 17/30 (56.7%), consisting of pharyngeal abnormalities (n = 9), dysmotility (n = 7) and no further findings (n = 1%).

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

P0145 A RETROSPECTIVE AUDIT OF OUTCOMES AND CURRENT CLINICAL PRACTICE POST-BALLOON TAMPONADE FOR ACUTE VARICEAL BLEEDING: HAVE THINGS IMPROVED OVER TIME?

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Introduction: Balloon tamponade, such as with Sengstaken-Blakemore tubes (SBT), remains the main immediate salvage therapy for acute variceal bleeding uncontrolled by variceal ligation or injection therapy. Previous cohort studies from the 1970–1980s report success rates of 40–94% for initial haemostasis but high re-bleeding rates of 40–70% on removal [1–3]. Despite guidelines recommending balloon tamponade as initial therapy in treating endoscopically uncontrollable variceal bleeding, specialists and trainees feel uncomfortable with SBT insertion [4] given the perceived difficulties and complications [5].

Aims & Methods: We aimed to describe the current practices surrounding SBT insertion of acute variceal bleeding, the outcomes and to identify areas requiring improvement. A retrospective audit of all patients from 2008–2016 who required SBT insertion for control of acute variceal bleeding was undertaken at Monash Health, a large tertiary Australian centre. These patients were identified from coding classifications. Details regarding their admission were obtained via electronic records.

Results: Approximately 14% of all patients with variceal bleeding required insertion of SBT. Of these 42% were inserted by junior doctors, the majority were males (71%), with a mean age of 55 years (range 34–78). Alcohol was the most common aetiology for cirrhosis (62%), with 65% actively drinking. Most patients had cirrhosis severity scores of Child-Pugh B (67%) or Child-Pugh C (29%) and a median MELD score of 16 (range 5–39). At the index variceal bleed, 43% were haemodynamically unstable and 29% were encephalopathic. All received standard medical therapy with octreotide or terlipressin, antibiotics and blood products as required. The time to initial endoscopy from 1st onset bleeding was prompt (median 6.6 hours). Most bleeding varices were oesophageal (90%). Initial ligation/injection was performed in 64% with the remaining patients having such large volumes of blood in the UGI tract that satisfactory views were unable to be obtained. The current practice surrounding SBT insertion is shown in the table.
below. Relook endoscopy post-SBT insertion was performed in 86% patients at a median of 39 hours after insertion with further endoscopic therapy in 47%. Complications of SBT insertion occurred in 31% and included minor oesophageal ulceration (9), significant oesophageal ulceration (3), aspiration pneumonia (4) and oesophageal perforation (1).

Current practice surrounding Sengstaken-Blakemore Tube insertion

<table>
<thead>
<tr>
<th>Variable</th>
<th>Results (n = 42)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indication for SBT insertion</td>
<td>Incomplete haemostasis 74%, poor view 30%</td>
</tr>
<tr>
<td>SBT insertion site</td>
<td>Oral 32, nasal 8</td>
</tr>
<tr>
<td>Confirmation of position</td>
<td>Direct endoscopic visualisation 13, imaging 25, none 6</td>
</tr>
<tr>
<td>Volume of balloon inflation</td>
<td>Gastric balloon - 306 ml mean (60-450 ml) Oesophageal balloon - 25-300 ml (n = 15)</td>
</tr>
<tr>
<td>Duration of balloon inflation (median hours)</td>
<td>Gastric balloon - 35.1 (1-140.3) Oesophageal balloon - 16 (1-62.8)</td>
</tr>
<tr>
<td>Time to re-look endoscopy after SBT (median hours)</td>
<td>39.3 (11.5-348.2)</td>
</tr>
</tbody>
</table>

Re-bleeding occurred in 45% patients during the admission despite SBT insertion, of which 79% did not survive. Seven other patients subsequently underwent a TIPS procedure for these still died. The median time to discharge and survival was 50% and 41% respectively. The median duration of hospitalisation, intensive care and mechanical ventilation was 13 days (1-56), 6.2 days (0.3-36.2) and 120 hours (1-708) respectively.

Conclusion: Primary haemostasis was achieved in 93% of patients; however, re-bleeding occurred in 45% and was associated with a poor survival rate of 20%. Short and longer-term survival has not significantly improved since studies in the 1970s-1980s despite advances in pharmacological therapy. Current practice for SBT insertion and re-bleeding is variable and would benefit from further education. Rates of direct visualisation of balloon position prior to inflation with endoscopy should be improved as with referrals for early TIPS.

Disclosure of Interest: All authors have declared no conflicts of interest.

References


P0146 CONSCIOUS SEDATION FOR ENDOSCOPIC SUBMUCOSAL RESSECTION BY USING DEXMEDETOMIDINE

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Introduction: To evaluate the feasibility and safety of the dexmedetomidine (DEX) for conscious sedation during endoscopic submucosal dissection (ESD). Aims & Methods: This study was a prospective trial, and was conducted at the Yamanashi University. Between January 2016 and December 2016, all 50 patients were enrolled in this study. The inclusion criteria for the study was the presence of esophageal, gastric or duodenal tumors. The criteria for exclusion from this study is as follows: patients who were allergic to the drugs used, a baseline heart rate less than 50 beats/minutes, patients who could not use anticholinergic drugs, and lack of patient’s consent. A total 50 patients who underwent ESD by using DEX for esophageal, gastric or duodenal tumor. The patients were sedated with DEX (an initial bolus infusion of 3.0 µg/kg/hour intravenously over 10 minutes, followed by a continuous infusion of 0.1 µg/kg/hour titrated). During sedation, midazolam (0.03 mg/kg) and pethidine (17.5 mg) were added intravenously as needed. If the level of sedation dropped to less than RASS -3, the intravenous DEX injection rate was reduced by 0.1 µg/kg/hour. If the patient's heart rate was less than 50 beats/minutes, the patient was intravenously infused with atropine sulfate hydrate (0.125 mg-0.25 mg). During procedure, the following parameters were measured continuously, and recorded every 5 minutes: heart rate, blood pressure, hemoglobin oxygen saturation (SpO2), respiratory rate and RASS. As the achievement rate of conscious sedation during procedure, the percentage of the time that the depth of sedation from RASS -1 to -3 during procedure were evaluated. Body movement leading to the interruption of ESD were recorded appropriately. After the procedure, all patients were intravenously infused with flumazenil (0.3 mg) and observed until the Aldrete score reached 9 points.

Results: During this study period, 50 patients with esophageal, gastric and duodenal tumors were identified as potentially eligible for participation. Of whom 37 males and 13 females, and the mean age was 67.5 ± 8.6 y. 27 patients regularly consumed alcohol and 5 patients use sleeping drugs regularly. Tumors were located in the following locations: 9 cases in the esophagus, 38 cases in the stomach. The mean tumor size was 23.8 ± 14.5 mm and the procedure time was 88.0 ± 59.5 minutes. The histologic results of ESD were squamous cell carcinoma (n = 9), adenoma (n = 17) and adenocarcinoma (n = 24). ESD by using DEX were successfully performed in all 50 tumors. No adverse events that were thought to be procedure occurred. The mean achievement rate of conscious sedation during procedure was 84.7 ± 16.5%. The median frequency of disturbance by patient’s movement was 0 times (range 0-3 times). 33 cases reduced and 14 cases discontinued a continuous infusion of DEX. In 23 cases heart rate was a decreased heart rate less than 50 beats/minutes. In 16 cases, the patient required an infusion of atropine sulfate hydrate. Thirty cases of 16 cases required an infusion of atropine sulfate hydrate after the procedure and 3 cases required it during procedure. The median time that the final administration of an atropine sulfate hydrate was 35 min (range 5-140 min) after procedure. There was no case in lowering of systolic blood pressure less than 80 mmHg. Although in 7 cases, the patient’s SpO2 level dropped to less than 90%, however, they recovered after the administration of oxygen to the nasal cannula. The mean time that the Aldrete score reached 9 or over was 7 ± 4 minutes. The median endoscopist and patient’s satisfaction score was 9 points (range 2-10 points) and 8 points (range 2-10 points). There were 30 patients (60%) who had oral intake after the procedure. None of the patients required any intervention during the period.

Conclusion: Conscious sedation with DEX is effective, safe and a high level of satisfaction for endoscopists and patients for upper gastrointestinal ESD.

Disclosure of Interest: All authors have declared no conflicts of interest.


References

P0148 IMPACT OF NEEDLE-BASED CONFOCAL LASER ENDOMICROSCOPY (NCLE) IN IMPROVING DIAGNOSIS OF Pancreatic Cystic Neoplasms: Single Center Experience
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Introduction: Endoscopic ultrasound (EUS) has been found to be an effective tool in diagnosing pancreatic cystic neoplasms (PCN). Carcinoembryonic antigen (CEA) tumor marker has also been used to differentiate PCN and is the most accurate marker of mucinous cystic neoplasms. Recently, needle-based confocal laser endomicroscopy (nCLE) has been increasingly used for the diagnosis of PCN. nCLE allows for evaluation of pancreatic cysts with results similar to that of a pathological diagnosis. In this study, we will compare our standard of care, EUS with combined CEA and nCLE to determine which combination of diagnostic modalities is a better predictor of PCN.

Aims & Methods: In this retrospective chart review, 22 patients with pancreatic cysts were evaluated. Specificity and Negative Predictive Value (NPV) of EUS alone or EUS with combined CEA and nCLE were evaluated and diagnostic accuracy was compared with pathology using McNemar's test. Worrisome features (increased cyst size, wall thickness, main pancreatic duct size, and presence of non enhanced mural nodules, abrupt changes, distal atrophy and lymphadenopathy) were tested by determining dissimilar calculations using Euclidian distance and later were used in hierarchical clustering to create two clusters based on Euclidian distance.

Results: Diagnosis of PCN using EUS alone had a specificity of 0.75 and a NPV of 0.88. EUS and CEA had a specificity of 0.95 and a NPV of 0.90. Finally, EUS with CEA and nCLE combined had a specificity of 0.80 and a NPV of 0.94. Worrisome features clustering was able to predict pathology, p = 0.000289.

Conclusion: We concluded that specificity and NPV of EUS predicting PCN are positively impacted by the addition of CEA and nCLE. We also found that clustering of worrisome features predicts pathology, however, a larger cohort is required for future studies.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P0149 FULL-SPECTRUM ENDOSCOPY FOR UPPER GASTROINTESTINAL SCREENING INCLUDING PRECISE OBSERVATION OF THE AMPULLA OF VATER AND THE ANAL VULVA OF THE PYLORIC RING
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Introduction: Endoscopic submucosal dissection (ESD) is accepted as the treatment of intestinal-type early-stage gastric cancer. However, ESD occasionally results in unfavourable outcome due to technical difficulties. Therefore, predictions of difficulties in ESD would preclude complications associated with ESD. Aims & Methods: The aim of this study is to determine the predictive factors of procedural difficulties in ESD. Between January 2009 and July 2016, 577 consecutive patients who underwent ESD for gastric neoplasms were enrolled. These patients were classified into 3 groups: group S, group L, and others. Group S comprised 30 patients who underwent ESD for the shortest duration (10–16 min). Group L comprised 30 patients who underwent ESD for the longest duration (149–215 min). Multivariate analysis was performed between Groups L and S using the following factors: location (cardia, posterior wall of angle, lesser curvature of lower gastric body and others), macroscopic type (protruded, depressed or mixed), size of the resected specimen, preoperative scar, number of preoperative biopsies, (others), and as predictor for submucosal fat tissue, body mass index, waist circumference, visceral fat tissue measurements on CT, blood test findings (glycated hemoglobin, triglyceride and total cholesterol), blood pressure, and heart rate before ESD.

Results: Significant differences were found regarding the number of biopsies (group L, 8.5; group S, 6.8; p = 0.0231), biopsy diagnosis (group L, 96.6%; group S, 90.7%; p = 0.0292), and location (p = 0.0268), biopsy visualization of SCJ was also local at 92.0% (81/88) with FUSE-EGD. VASs at insertion, during and after examinations were 51.2 (10–75), 46.9 (0–75), and 45.2 (10–50) points, respectively, which were equivalent to conventional EGD. The ampullary adenoma was observed in all 3 patients with FUSE-EGD and the openings of the biliary and pancreatic ducts of the ampulla of Vater were observed in all 2 cases with the ampullary tumors with FUSE-EGD. There were no adverse events associated with FUSE-EGD. Conclusion: FUSE-EGD seems safe and effective for upper gastrointestinal screening, especially when the diagnosis of the ampulla of Vater and/or the anal side of the pyloric ring is necessary.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
in the lesser curvature (43.9%, 284/647). Posterior EGC was more frequent in the mid-to-upper part of the stomach than the anterior part (20.4%, 31/157 vs. 16.4%, 11/67, respectively). For EGC characteristics compared between the lower and mid-to-upper parts, submucosal invasive EGC was found to be significantly different (odds ratio, 1.919; confidence interval, 1.014–3.623; p = 0.045).

Conclusion: Most of the EGCs resectable with ESD were found in the lesser part of the stomach and lesser curvature of the stomach. The incidence of the posterior part in the mid-to-upper part of the stomach was higher than that of anterior part. The EGc located in the mid-to-upper part of the stomach was found to have a higher incidence of invasive cancer.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0152 A STUDY OF THE RECOGNITION OF ESODONIC IMAGES BY MACHINE LEARNING WITH CONVOLUTIONAL NEURAL NETWORK AND DEEP LEARNING

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Introduction: The recognition of general images by machine learning (ML) with the convolutional neural network (CNN) and deep learning (DL) is good. However, the possibility of the recognition of endoscopic images by ML with CNN and DL is undetermined.

Aims & Methods: The aim of this study was to clarify the possibility of the recognition of endoscopic images by ML with CNN and DL. We selected 816 endoscopic images of 8 categories which include laryngopharynx (LP), thoracic esophagus (TE), abdominal esophagus (AE), gastric fundus (GF), proximal body (PB), corpus (CP), distal body (DB), and corpus (CD). The average of the number of images in each category was approximately 100 images. These images were randomly separated into two groups, 60% (489 images) for learning and 40% (327 images) for testing. We increased the learning group images to 833 by adding additionally rotated images of each five degrees. We made an ML model with three CNN layers, three Activation function layers, two Max-Pooling layers and two Dens layers by TensorFlow and Keras. We trained the ML model with the learning group images (n = 8313) and then tested it with the testing group images (n = 327) to determine whether it can recognize the endoscopic site. Two members of our hospital staff performed the same testing with the same images.

Results: It took 73 minutes for the ML model to learn and 6 seconds to answer the test. The percentage of correct answers of the ML model was 70.6% in all categories (n = 327), 71.1% in LP (n = 48), 91.5% in TE (n = 47), 64.4% in AE (n = 45), 73.8% in PB (n = 38), 65.7% in CP (n = 35), 56.2% in GF (n = 36), 65.6% in DB (n = 32) and 71.4% in DD (n = 42). The average percentage of correct answers of humans was 95.4% (n = 48), 91.5% in TE (n = 47), 64.4% in AE (n = 45), 73.8% in PB (n = 38), 65.7% in CP (n = 35), 56.2% in GF (n = 36), 65.6% in DB (n = 32) and 71.4% in DD (n = 42). The average percentage of correct answers of humans was 95.4% (n = 48), 91.5% in TE (n = 47), 64.4% in AE (n = 45), 73.8% in PB (n = 38), 65.7% in CP (n = 35), 56.2% in GF (n = 36), 65.6% in DB (n = 32) and 71.4% in DD (n = 42). The average percentage of correct answers of humans was 95.4% (n = 48), 91.5% in TE (n = 47), 64.4% in AE (n = 45), 73.8% in PB (n = 38), 65.7% in CP (n = 35), 56.2% in GF (n = 36), 65.6% in DB (n = 32) and 71.4% in DD (n = 42).

Conclusion: The proposed system is useful for the determination of DL.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0153 CONVENTIONAL VERSUS TRANSITION-ASSISTED ESODONIC DISSECTION FOR GASTRIC NEOPLASMS (CONNECT-G): A MULTICENTER, RANDOMIZED CONTROLLED TRIAL


Introduction: The recognition of endoscopic images by ML with CNN and DL is undetermined.

Aims & Methods: The aim of this study was to clarify the possibility of the recognition of endoscopic images by ML with CNN and DL. We selected 816 endoscopic images of 8 categories which include laryngopharynx (LP), thoracic esophagus (TE), abdominal esophagus (AE), gastric fundus (GF), proximal body (PB), corpus (CP), distal body (DB), and corpus (CD). The average of the number of images in each category was approximately 100 images. These images were randomly separated into two groups, 60% (489 images) for learning and 40% (327 images) for testing. We increased the learning group images to 833 by adding additionally rotated images of each five degrees. We made an ML model with three CNN layers, three Activation function layers, two Max-Pooling layers and two Dens layers by TensorFlow and Keras. We trained the ML model with the learning group images (n = 8313) and then tested it with the testing group images (n = 327) to determine whether it can recognize the endoscopic site. Two members of our hospital staff performed the same testing with the same images.

Results: It took 73 minutes for the ML model to learn and 6 seconds to answer the test. The percentage of correct answers of the ML model was 70.6% in all categories (n = 327), 71.1% in LP (n = 48), 91.5% in TE (n = 47), 64.4% in AE (n = 45), 73.8% in PB (n = 38), 65.7% in CP (n = 35), 56.2% in GF (n = 36), 65.6% in DB (n = 32) and 71.4% in DD (n = 42). The average percentage of correct answers of humans was 95.4% (n = 48), 91.5% in TE (n = 47), 64.4% in AE (n = 45), 73.8% in PB (n = 38), 65.7% in CP (n = 35), 56.2% in GF (n = 36), 65.6% in DB (n = 32) and 71.4% in DD (n = 42). The average percentage of correct answers of humans was 95.4% (n = 48), 91.5% in TE (n = 47), 64.4% in AE (n = 45), 73.8% in PB (n = 38), 65.7% in CP (n = 35), 56.2% in GF (n = 36), 65.6% in DB (n = 32) and 71.4% in DD (n = 42). The average percentage of correct answers of humans was 95.4% (n = 48), 91.5% in TE (n = 47), 64.4% in AE (n = 45), 73.8% in PB (n = 38), 65.7% in CP (n = 35), 56.2% in GF (n = 36), 65.6% in DB (n = 32) and 71.4% in DD (n = 42).

Conclusion: The proposed system is useful for the determination of DL.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
P0155 ENDOscopic TREATMENT OF FISTulas AFTER SLEEve GASTRECTomy: ASSESSMENT FOR SWITCHING TOWARDS INTERNAL DRAINAGE IN A REFERENCE CENTER

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Introduction: Post-sleeve gastrectomy fistulas (PSGF) are major complication of bariatric surgery. Endoscopic management evolved from a fistula closure to an internal drainage (ID) strategy within the 2013 year. The main objective of this study is to evaluate different endoscopic approaches.

Aims & Methods: This retrospective study included all patients treated for PSGF in a referral center. “Closure” management was defined as: initial treatment using covered-metal-stent and endoclips. ID management was defined as: initial management with OTSC and/or double-pigtail-steel. The failure was defined as: need for surgery, or death.

Results: Between 2007 and 2015, 101 patients (women: N=78; mean age: 42 ± 12years) were included. The mean delay between SG and the first endoscopy was 92 ± 58 days. Overall success of endoscopic treatment was 86% within 6 ± 2.7 months. Two patients died. Primary success of ID and closure management occurred in 19/22 (86%) and 49/77 (63%) patients, respectively. Among patients in failure of closure management, 22 had secondary ID (18 being successful). Success of initial management was significantly higher for ID (p = 0.016). Factors associated with failure of closure management were in multivariate analysis: collection > 5 cm (p = 0.013, OR = 3.89 [CI:1.3–10.9]). Factors associated with failure of management over 6 months were in multivariate analysis: reper- formation before endoscopy (p = 0.044, OR = 3.95 [CI:1.0–14.9]) and purulent flowing at endoscopy (p = 0.043, OR = 4.65 [CI:1.0–20.9]). Factors associated with post-2013 management were in multivariate analysis: first endoscopy within 30 days (p = 0.016). Clavien-Dindo-type 4 and 5 (p = 0.016), and absence of glue sealing (p = 0.027).

Conclusion: Endoscopic management of PSGF healed in 86% of cases. In case of collection greater than 5 cm, an internal drainage should be proposed first. A successful closure before endoscopy was associated with longer care. Management in our center has changed over time with earlier first endoscopy and management of more severe patients.

Disclosure of Interest: M. Barthel: Boston scientific consultant. All other authors have declared no conflicts of interest.

P0156 CLOSURE BY USING OVER-THE-SCOPE CLIPS AFTER ENDOscopic FULL-THICKNESS RESECTION

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Introduction: Endoscopic full-thickness resection (EFR) is a mini-invasive tech- nique for gastrointestinal subepithelial tumors, which enables a full-thickness resection of tumors and can provide a complete basis for pathological diagnosis. Gastrointestinal fistula closure after EFR is a challenge for endoscopists. In this study we introduced EFR with fistula closure using the over-the-scope clip (OTSC) system for gastrointestinal subepithelial tumors originating from the musculi- aris propria.

Aims & Methods: We aimed to evaluate the feasibility and safety of fistula closure with OTSC by a retrospective analysis on the cases of EFTR with defect closure associated with long-term care. In our center has changed over time with earlier first endoscopy and management of more severe patients.

Conclusion: Endoscopic management of PSGF healed in 86% of cases. In case of collection greater than 5 cm, an internal drainage should be proposed first. A successful closure before endoscopy was associated with longer care. Management in our center has changed over time with earlier first endoscopy and management of more severe patients.

Disclosure of Interest: M. Barthel: Boston scientific consultant. All other authors have declared no conflicts of interest.

References
Patients without polyposis syndrome who underwent cold polypectomy for sporadic SNADETs. In this study, we aimed to assess the dissection (ESD), compared with resection of other parts of the digestive tract.

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P0158  LONG-TERM OUTCOMES OF COLD POLYPECTOMY FOR SPORADIC SNADETS

Aims & Methods: Patients without polyposis syndrome who underwent cold polypectomy for one or more SNADETS ≤6 mm in size and were diagnosed with adenomas between March 2015 and November 2016, and were followed up by endoscopy for more than 1 year were analyzed. All patients subsequently underwent upper gastrointestinal endoscopy 3 months after the intervention. The presence of residual tumors was evaluated by conducting endoscopic examinations and histopathological tests with tissue samples obtained from the cold polypectomy scars. Subsequently, patients underwent upper gastrointestinal endoscopy annually, and when residual tumors could not be denied, biopsies were taken from the scars.

Results: A total of 43 lesions in 35 patients were removed using cold polypectomy in 20 patients with no complications. The mean follow-up period by upper gastrointestinal endoscopy was 13.1 (12–18) months. Of these 20 patients, 12 (60%) were men and the mean age of the subjects was 63 ± 11 years. The number of lesions were 5, 16, and 3 (21%, 60%, 8%) respectively, and 2, 3, 3, and 4 (2%, 13%, 17%, 8%) per macroscopic appearance (Isp, Is, Ia, Ia + Ilc, and Ilc), respectively. Nine lesions in 8 patients were resected using CFP, while 15 lesions in 12 patients were resected using CSP. Seven of 9 (78%) and 14 of 15 (93%) lesions were removed en bloc using CFP and CSP, respectively; the other 3 lesions were removed by piecemeal resection in 2 pieces. All specimens resected using both CFP and CSP were successfully retrieved.

Histopathologic analysis showed that 21 of 24 lesions (88%) were low-grade adenomas, while 3 (12%) were high-grade adenomas. The mean size of the adenomatous lesions was 4.0 ± 1.3 mm (2–6 mm). Eleven of 24 adenomas (46%) were R0 resections; 3 of 9 (33%) and 8 of 15 (53%) were R0 resections using CFP and CSP, respectively. Delayed bleeding and intraprocedural/delayed perforation were observed in one case respectively. The patient received a conservative therapy, complemented by a withdrawal of oral aspirin. A 48-year-old male was presented at the emergency room the next day. He was admitted to our hospital after an episode of hematemesis. The patient had a 22-year history of peptic ulcer disease and is diabetic. On admission he was tachycardic with a heart rate of 128 bpm. The computed tomography of the chest demonstrated a hydrothorax, as well as mediastinal free air. Due to the hemorrhage we performed an emergency upper endoscopy after we obtained the patient's consent. We observed an approximately 3 cm long, with a Mallory-Weiss tear at the distal lesser curvature. We clipped the visible vessel and decided to close the opening with clips (Figure 1). We used twelve clips and successfully stopped the bleeding while also closing the esophageal opening. Thoracic surgeons placed a thoracic drainage tube. The patient received 3 days after resuscitation because of heart failure. The patient received a conservative therapy, complemented by a withdrawal of oral intake and administration of broad spectrum antibiotics.

Conclusion: Cold polypectomy is a safe and effective treatment for diminutive and small sporadic SNADETs that have been subjected to long-term follow-up.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

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P0160  ARTIFICIAL INTELLIGENCE DIAGNOSIS OF HELICOBACTER PYLORI INFECION USING LINKED COLOR IMAGES (EGGD)

Aims & Methods: The aim of this study was to establish an AI diagnosis of HP infection using LCI. We designed a prospective study of all patients who underwent EGD and were tested for serum anti-HP IgG antibodies at our medical clinic. Subjects who had a history of HP eradication therapy were excluded in this study. A total of 230 examinees were candidates who underwent EGD and serum test of anti-HP IgG antibodies. The diagnosis of HP IgG antibodies positive examinees were 112. The HP IgG antibody titer of each subject was taken as the gold standard for HP infection status for this study. During EGD an endoscopist took 3 LCI pictures of the lesser curvature, greater curvature and antrum of the stomach by EG-L580NW (FUJIFILM Co., Japan). Finally, we used a total of 639 LCI pictures in the study. The specifications of the AI used in this study were as follows: Operating system: Linux (Ubuntu 14.04 LTS), Neural network: GoogleNet3, Framework: Caffe3, and Graphic processor unit: GeForce GTX TITAN X (NVIDIA Co., Japan). The AI was trained using the dataset. The AI was trained using the dataset.

Results: The area under the curve (AUC) of receiver operating characteristics (ROC) was 0.95 for the lesser curvature. Compared to this, the AUC of the greater curvature and antrum was 0.81 and 0.67, respectively. The AUCs obtained in the lesser curvature was significantly larger than that in the greater curvature and antrum (P < 0.01).

Conclusion: The results demonstrate that the AI has excellent ability to diagnose HP infection using LCI in the lesser curvature. The authors believe that AI technology with IEEs is likely to become a useful image diagnostic tool.

Disclosure of Interest: All authors have declared no conflicts of interest.

References


P0159  ENDOSCOPIC TREATMENT OF BOERHAAVE SYNDROME: A SURPRISINGLY QUICK HEALING

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Aims & Methods: A 48-year-old male was presented at the emergency room complaining of severe chest pain, which began after several episodes of vomiting, following a meal. Upon his arrival a severe episode of haematemesis was reported. A chest radiograph showed tachycardia with a ventricular rate of 128 bpm. The computed tomography of the chest demonstrated a hydrothorax, as well as mediastinal free air. Due to the hemorrhage we performed an emergency upper endoscopy after we obtained the patient’s consent. We observed an approximately 3 cm long, with a Mallory-Weiss tear at the distal lesser curvature. We clipped the visible vessel and decided to close the opening with clips (Figure 1). We used twelve clips and successfully stopped the bleeding while also closing the esophageal opening. Thoracic surgeons placed a thoracic drainage tube. The patient received 3 days after resuscitation because of heart failure. The patient received a conservative therapy, complemented by a withdrawal of oral intake and administration of broad spectrum antibiotics.

Conclusion: Boerhaave syndrome has an estimated mortality rate of 20% to 40%. The standard of care is multidisciplinary; surgical, endoscopic or conservative approaches are acceptable. No consensus exists regarding the best strategy.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference


P0161  ENDOSCOPIC GRADING FOR GASTRIC INTESTINAL METAPLASIA (EGGDM) AS AN ARTIFICIAL INTELLIGENCE (AI) technology

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Introduction: Current guidelines (MAPS) suggest that intestinal metaplasia (IM) should be staged using OLGIM 1 (Operative Link on Gastric Intestinal Metaplasia) and that patients with stages OLGIM 3 and 4 should be followed up. High-resolution narrow band imaging (HR-NBI) was previously shown to be accurate to diagnose IM 2. Recently a new endoscopic classification (Endoscopic Grading of Gastric Intestinal Metaplasia - EGDM) has been proposed to assess the risk phenotype of patients by the evaluation of IM in the antrum and in the corpus with the use of HR-NBI scopes 3. 4.

Aims & Methods: We aimed at determining the accuracy of EGDM classification, compared with the pathological evaluation of gastric biopsies expressed according to OLGIM classification. Two centers (Italy, Portugal) consecutively included 78 adult patients (female 56%); median age 61 (20–84) years: 8 with 1st degree family history of gastric cancer. All patients were evaluated by High-
Resolution White Light Endoscopy (HR-WLE) followed by HR-NBI. A careful evaluation of the antrum and corpus mucosa was performed and EGGM score was calculated. Five different areas were considered (lesser and greater curvature in the antrum, lesser and greater curvature in the corpus and incisura) and in each area 0 (no IM), 1 (focal IM, less or equal than 30% of the area) or 2 points (extensive IM in that area, more than 30% of the area) were attributed for a total of 10 points. Biopsies were taken where the endoscopists observed IM and, if IM was not present, random biopsies were taken using the updated Sydney System protocol. Biopsies from the different sites were sent for histopathologic evaluation.

Aims & Methods: The diagnostic performance of EGGM was then compared to OLGIM (gold standard) and sensibility, specificity, positive predictive value (PPV) and negative predictive value (NPV) were calculated. Results: IM was staged as OLGIM 0, 2, 3, and 4, respectively: 32 (41.0%), 23 (29.5%), 17 (21.8%), and 6 (7.7%) pts (no patients with OLGIM 1 were found). Table 1 shows detailed the EGGM scores compared to OLGA. Compared to OLGIM as gold standard for the evaluation of IM, sensitivity, specificity, PPV and NPV of EGGM classification were 97.8%, 81.2%, 88.2% and 96.3%, respectively. IM was observed in 6 patients who had positive results using the EGGM classification were H. pylori positive. Analyzing the subgroup of patients with OLGIM 3 and 4, the diagnostic performance of EGGM was: sensibility 95.6%, specificity 90.9%, PPV 81.5% and NPV 98.0%. Two of the 5 patients who resulted false positive using the EGGM classification were H. pylori positive. A high agreement between EGGM and OLGIM scores was observed (83.3%).

Conclusion: The EGGM classification showed a high diagnostic performance compared to OLGIM, in particular in patients with OLGIM 3 and 4. A possible confounding factor leading to overestimation of presence of intestinal metaplasia might be the presence of H. pylori infection. This approach could be used to simplify the surveillance of these patients.

Disclosure of Interest: All authors have declared no conflicts of interest.

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PO0163 COMPARISON OF PERCUTANEOUS ENDOSCOPIC GASTRODUODENOSCOPY VERSUS RADIOLOGIC GASTROSTOMY IN TERMS OF INDICATIONS, EFFICACIES, COMPLICATIONS; A RETROSPECTIVE ANALYSIS.

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Introduction: Gastrostomy is the current method of choice for medium and long-term enteral feeding. Available techniques include Percutaneous Endoscopic Gastrostomy (PEG) and Percutaneous Radiologic Gastrostomy (PRG). Both techniques are preferred over oral gastrostomy. Previous studies that have compared outcomes between PEG and PRG are limited due to small sample sizes, high risk of confounding and selection bias. Our primary aim was to retrospectively analyse data from our centre with respect to complications and mortality between PEG and PRG procedures in relation to indications. These data may help to predict which technique is best for an individual patient.

Aims & Methods: A retrospective analysis including all adult patients receiving initial PRG (January 2010 until April 2016) and PEG (January 2008 until April 2016) placement in our university hospital, was performed. Outcomes were complications (early (<30 days) and late), success rates and mortality (procedure related, 30-day, and overall). Chi2, Fisher’s exact and t-tests were used. Multivariable logistic regression and Cox proportional hazards regression analysis were performed.

Results: A total of 760 initial procedures (469 PRG and 291 PEG) were included in the analysis (62.9% male, mean age 62.8yrs [SD 12.6yrs]). Most common indications were: Motor Neurone Disease (MND, PEG 2.7%, PRG 9.8%, p < 0.001). Cerebrovascular Accident (CVA; PEG 13.7%, PRG 2.1%, p < 0.001) and Motor Neuron Disease (MND, PEG 2.7%, PRG 9.8%, p < 0.001). Success rates for placement were 91.2% for PEG (failure mostly due to absence of transillumination, n=14) and 97.1% for PRG (p = 0.001). Major complications (e.g. abscess, buried bumper, peritonitis) and infections did not differ amongst groups, neither did procedure-related mortality, which was 1.7% in PEG (n=5) vs. 0.4% in PRG (n=2, p = 0.113). One case of tumour (HN) seeding occurred after PRG placement. Tube related complications (including dislocation, obstruction, leak and tube defects) were lower in PEG than PRG, both within 30 days (2.7% vs. 26.4% of patients, p = <0.001 and after 30 days (8.6% vs. 31.5%, p < 0.001).

Conclusion: PEG appears favourable with respect to 30 day mortality while PEG appears favourable over PRG in terms of complications (such as dislocation, peritonitis and infection). A higher success rate and the possibility of placement in case of a narrow lumen favour PRG placement. More adequate patient selection and more thorough procedure selection prior to gastrostomy is therefore required.

Disclosure of Interest: All authors have declared no conflicts of interest.
P0165 COMPREHENSIVE EVALUATION OF THE LEARNING CURVE FOR PERORAL ENDOSCOPIC MYOTOMY: LESSONS FROM 1346 PATIENTS
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Introduction: Peroral endoscopic myotomy (POEM) is being increasingly performed worldwide. However, studies on the learning curve are limited. A comprehensive evaluation based on risk factors is needed.
Aims & Methods: This study was aimed to evaluate the impact of various factors on the learning curve of POEM. From August 2010 to July 2015, 1346 POEM procedures in our hospital were analyzed. The primary outcome of the study was a composite outcome of aborted procedures and complication. The secondary outcomes included procedure time and hospital stay. The impact of risk factors was assessed by backward conditional logistic regression on primary and secondary outcomes. The risk-adjusted CUSUM and moving average methods were used to evaluate the outcomes.
Results: Fifty-four (4%) patients had the composite outcome with 10 aborted procedures and 44 adverse events. The composite outcome was related to case number, faill-thickness myotomy and procedure time in the multivariate logistic regression. Adjusted for these risk factors, the CUSUM analysis showed that the composite outcome gradually decreased after 150 cases. The procedure time was higher in the early stage and decreased after 71 cases. Case number, in representative of the operative experience, is also an independent risk factor for a longer procedure time and hospital stay.
Conclusion: For POEM operators, seventy cases might be considered a threshold for faster operation, i.e., technical proficiency. A hundred-and-fifty cases might be considered a threshold for the decrease of aborted procedures and adverse events, i.e., technical reliability.
Disclosure of Interest: All authors have declared no conflicts of interest.

P0166 CLINICAL CURATIVE EFFECT ANALYSIS OF 162 GASTRIC STROMAL TUMORS RESECTED BY ENDOSCOPIC TREATMENTS
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Introduction: Gastrointestinal stromal tumor (GIST) is one of the most common tumors originating from mesenchymal tissue of gastrointestinal tract, which accounts for about 0.2% of gastrointestinal tumors. Gastric stromal tumors are more common, accounting for about 40%~70% of GIST. At present, the endoscopic treatments of gastric stromal tumors includes endoscopic submucosal dissection (ESD), endoscopic full-thickness resection (EFTR) and combined endoscopic and laparoscopic surgery.
Aims & Methods: Our study is aimed to assess the safeness and effectiveness of endoscopic treatments for gastric stromal tumor. Clinical data of 162 patients with gastric stromal tumor who underwent endoscopic treatments from June 1 to July 31st 2015 were analyzed retrospectively. The mean diameter of the tumors was 1.5 cm (0.3~5.0 cm). 104 patients received endoscopic submucosal dissection, 58 patients received endoscopic full-thickness resection. Among them, 4 operations were delayed under the monitor of laparoscopy.
Results: Complications were observed in 8 patients(4.9%): bleeding during operations: 3 patients, post-operation perforation: 3 patients, respiratory tract infection: 2 patients. The mean post-operation feeding time was 2.67 days (range 1~9 days) and post-operation hospital stays were 5.39 days (range 2~10 days). The mean time of follow-up was 26.4 months (range 5~51 months). The follow-up showed that 6 patients kept on treating with oral administration of imatinib. No patient was found recurrence or death.
Conclusion: Endoscopic treatments were demonstrated as safe and effective ways to resect gastric stromal tumors in this study.
Disclosure of Interest: All authors have declared no conflicts of interest.

References

P0167 GASTROENTEROLOGY REGISTRAR OF THE WEEK: A SOLUTION FOR AUGIB ENDOSCOPY TRAINING?
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Introduction: Much concern surrounds Gastroenterology Specialist Registrar (SIR) endoscopy training, especially in regards to endoscopic management of Acute Upper Gastrointestinal Bleeding (AUGIB). Recent evidence suggests that there has been a decline in experience and exposure in AUGIB endoscopy. In July 2013 our University Hospital introduced a Consultant-led and Registrar-supported Monday to Friday, 9 to 5 pm in-reach service. It comprises of a morning visit to the acute medical units and a daily inpatient emergency list. This study looked at registrar AUGIB endoscopy training after its implementation.
Aims & Methods: Endoscopy reports of patients presenting with haematemesis, melena or both who had undergone gastroscopy during the period of 1st of May to 1st August 2013 were retrieved using the endoscopy reporting tool Unisoft and analysed. Reports where SIRs were the primary operator were considered. Number of procedures, haemostatic intervention and nature of haemostasis was analysed. This was then compared to data from the year before implementation (01/03/2012 to 31/08/2012)
Results: A total of 7 SIRs (5 Full Time and 2 Less than Full Time) performed gastroscopies on AUGIB patients as first operators under Consultant supervision. Over the 6-month period a total of 166 gastroscopies were undertaken (Mean 24). On 26 occasions, endoscopic intervention (EI) was performed (Mean 4). On average, 16% of the AUGIB patients required EI. In cases of Non Variceal Bleeding, Dual therapy was applied in 87.5% of the cases. For Variceal cases Haemostatic banding was used. On average, patients were able to perform one case of oesophageal variceal banding and one case where Haemospary was utilised. Data from the 2012 cohort in comparison showed a total of 66 gastrosopies over 6 months with 13 EI. On average 13 procedures and 2.6 EIs were performed by each SIR. Dual therapy was applied in only 25.8% of the cases.
Conclusion: The introduction of the Registrar of the Week Service provides a valuable opportunity for SIRs to be trained in endoscopic haemostasis and acquisition of experience in AUGIB endoscopy. As per this study each SIR on an average performed endoscopy on 24 AUGIB patients. If this is extrapolated, each SIR will be able to perform 48 procedures in 1 year and 240 procedures over 5 years. In the case of EI, on average a SIR can perform around 4 interventions over 6 months, which comes to 8 per year and 40 in a 5 year program. This is significantly better than in the previous cohort and other centres. Hospitals should consider developing similar services not only to meet demands for 24/7 Consultant led AUGIB endoscopy service but provide adequate endoscopic training provision for current and future specialist registrars in order to ensure future competent and confident consultants.
Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

P0168 HIGH PERCENTAGE OF VISIBLE LESIONS IN PATIENTS WITH BARRETT’S ESOPHAGUS REFERRED TO DYSPLASIA IN RANDOM BIOPSY SAMPLES
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Introduction: Endoscopic recognition of dysplasia or early cancer in Barrett’s esophagus (BE) is difficult. Experience in recognition of early neoplastic lesions is thought to increase the detection of visible dysplastic lesions. A previous study reported that endoscopists in community hospitals detect neoplastic lesions at a significantly lower rate than referral centres. The aim of the study we want to assess the significance of dysplasia in random biopsies in BE, in the absence of reported visible lesions as well as the final outcome of pathology.
Aims & Methods: We retrospectively analysed all patients referred from 19 community hospitals to our tertiary referral centre with the diagnosis of BE with non-variceal bleeding. From February 2008 and April 2016. All patients underwent a dedicated imaging endoscopy with high-definition endoscopy supplemented with virtual chromoendoscopy and/or acetic acid staining at the discretion of the endoscopist. All procedures were performed by an endoscopist with extensive experience in the detection of early neoplastic lesions in BE. During endoscopy all visible lesions were noted and biopsied and/or removed by endoscopic resection (ER). Patients were included for analysis in case of absence of reporting visible lesions at referral.
Results: In total 184 patients were referred with dysplasia or EAC of which 82 patients (80.5% male, age 42–81 years (median 68) did not show a visible lesion upon referral endoscopy. Referral diagnosis of these 82 patients was 32 low-grade dysplasia (LGD), 43 high-grade dysplasia (HGD) and 7 EAC. In three of 32 patients (9.4%) referred with LGD, a visible lesion during imaging endoscopy was detected. Two cases of histology proved EAC and one confirmed LGD. In twenty-six of 43 patients (60.5%) referred with HGD, a visible lesion with histology specimens corresponding to HGD (10) and EAC (16) were found,
respectively. All cases of EAC were detected (7/7). In 18/75 (24%) patients referred with dysphasia (LG/DG/HGD) without a visible lesion, the referral diagnosis was thus upstaged to EAC. Overall, 41/82 (50%) lesions were found additionally.

Conclusion: The presence of any grade of dysphasia in random biopsies in BE screening in community hospitals is a potential marker for more severe final pathology after endoscopic work-up in an expert centre. Training in Barrett's imaging is mandatory for non-expert endoscopists.

Disclosure of Interest: All authors have declared no conflicts of interest.

TABLE 1: Demographics & Results

<table>
<thead>
<tr>
<th>Clinical failure</th>
<th>Clinical success</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients n = 22</td>
<td>n = 12</td>
<td>n = 10</td>
</tr>
<tr>
<td>Gender</td>
<td>Male/Female</td>
<td>6/6</td>
</tr>
<tr>
<td>Etiology</td>
<td>Post-surgery</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>Post-dilatation</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Post-radiation</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Post-invasive ventilation</td>
<td>3</td>
</tr>
<tr>
<td>Pulmonary localization</td>
<td>Trachea</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>Right bronchus</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Left bronchus</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Orifice size</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Punctiform</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Medium</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Large</td>
<td>6</td>
</tr>
<tr>
<td>Timing of closure</td>
<td>Resolution at 3 months</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Resolution at 6 months</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>No resolution at 6 months</td>
<td>12</td>
</tr>
<tr>
<td>Endoscopic treatment Mean number of esophageal stents</td>
<td>3.6 (±3.9)</td>
<td>2.3 (±2.7)</td>
</tr>
<tr>
<td></td>
<td>Mean number of OTSc</td>
<td>1.2 (±1.8)</td>
</tr>
<tr>
<td></td>
<td>At least one esophageal stent</td>
<td>11</td>
</tr>
<tr>
<td></td>
<td>At least one OTSc</td>
<td>6</td>
</tr>
</tbody>
</table>

Results: A total of 22 patients were included and analyzed. The etiologies of ERF were esophageal surgery in 12 patients (54.5%) and esophageal dilatation in 3 (13.6%), invasive ventilation in 3 (13.6%), radiation therapy in 2 (9.1%) and tracheostomy in 2 (9.1%). A total of 83 procedures were performed with a mean of number of endoscopies of 4.2±4.5 per patient. At some point of the management, twenty-one patients (95%) had esophageal stents placement, eight patients (36%) had over the scope clips (OTSC) placement and seven had OTSC associated with esophageal stent. The clinical success rate was 45.5% (n = 10), and 55% of the patients had a functional success (n = 12). Serious adverse events occurred in 9 patients (40%) such as gastrointestinal bleeding (4 patients, 18.2%), stent migration (4 patients, 18.2%), thoracic spondylodiscitis (2 patients, 9.1%) alimentary esophageal impaction (1 patient, 4.5%), stent mucosal impaction (1 patient, 4.5%), major chest pain (1 patient, 4.5%). Six patients died (27%). Clinical success was reached for 67% of punctum ERF (p = 0.193), 50% of medium ERF (p = 1) and 14% of large ERF (p = 0.17). The factor associated with the failure of endoscopic treatment was the persistence of the fistula after 6 months (OR = 44; IC95: 3.38–573, 4; p = 0.004 multivariate analysis).

Conclusion: Endoscopic treatment of ERF can lead to 45.5% of clinical success and 55.5% of functional success. However, this outcome appears directly dependent on the size of the fistula. Moreover, the absence of resolution after 6 months of endoscopic treatment dramatically decreases the chance for ERF healing. In conclusion, the endoscopic approach seems reasonable for small or medium orifices, and has to be attempted during six months. After this time or for larger orifices, surgery or palliative therapy should be considered.

Disclosure of Interest: All authors have declared no conflicts of interest.
emerging modality for refractory gastroparesis with promising preliminary results.

Aims & Methods: The aim of this prospective case series was to assess our first (single center) experience with POEP. Main outcomes were: 1) the efficacy defined by improvement of GCIS score; 2) gastric emptying evolution and 3) safety. From Nov 2015, a total of 7 patients underwent POEP. The etiology of gastroparesis was post-operative in 4, diabetic in 2 and idiopathic in 1 patient. One patient underwent POEP for gastroparesis following a multivisceral transplantation; one patient underwent both POEP and POEM (as a single procedure) for coexisting refractory gastroparesis and achalasia. All patients had severe gastroparesis as defined by elevated GCIS score and delayed gastric emptying scintigraphy. Follow visit at 3, 6, 12-months were completed in 7/7 (100%), 5/7 (71%) and 1/7 (14%) patients, respectively. Upper GI endoscopy and scintigraphy were performed 3 months after the procedure.

Results: POEP was successfully performed in all patients. Mean procedure time was 70 minutes (range 63–106). After POEP, mean GCIS decreased from 3.0 ± 1.2 to 0.8 ± 0.7 (at 3-months) and 0.9 ± 0.8 (at 6-months). One woman finished the 12-months follow maintaining excellent outcome. Treatment success was reached in 6/8 (75%) of patients, one female patient with diabetic gastroparesis did not have a major symptomatic improvement despite normalisation of gastric emptying study. Gastric scintigraphy normalized in all patients, mean half emptying time of 1.0 ± 0.3 h (from 1.8 ± 0.30 min to 62 ± 23 min) and mean bolus retention at 4 hours decreased from 17 ± 9.2% to 2.0 ± 2.0%. One patient developed bleeding ulcer 10 days after POEP, this adverse event was successfully managed endoscopically (clips) and by parenteral proton pump inhibitor.

Conclusion: We report our first experiences with POEP for refractory gastroparesis, demonstrating its feasibility and safety with promising clinical efficacy.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0173 TREATMENT OF MULTIPLE GASTROINTESTINAL SUBMUCOSAL TUMORS BY SUBMUCOSAL TUNNELING ENDOSCOPIC RESECTION

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Introduction: Submucosal tunneling endoscopic resection (STER) is a novel technique to remove the gastrointestinal submucosal tumors. Previous studies mainly focused on technical feasibility for patients with one single gastrointestinal submucosal tumor. No systematic studies about multiple upper gastrointestinal submucosal tumors synchronously removed by STER are addressed. The aim of this study was to evaluate the safety and outcome of STER in treatment of multiple gastrointestinal submucosal tumors.

Aims & Methods: From January 2011 to January 2017, 42 patients with multiple gastrointestinal submucosal tumors undergoing STER were included. Variables of each tumor and patient were analyzed. Detailed tumor characteristics included maximum size, sum of maximum size and number of tumors, and longest distance of tumor. While detailed technique information included number of tumors, tunnel length, hospital stay, procedure time, complication, follow-up, recurrence, and metastasis.

Results: Among all the cases, 96 lesions of upper gastrointestinal submucosal tumors were removed by STER. The median procedure time was 50 min (range 13.6–84.9 min). The median number of tumors was 2 (2–4). The median max size of each tumor was 1.8 cm (range 0.7–3.5 cm) and the median sum of max size of each patient was 3 cm (range 1.3–8.3 cm). Six patients had perioperative complications (14.2%), with 3 pneumothorax/hydrothorax (7.2%), 1 mucosal injury (2.4%), 1 pneumonia (2.4%), and 1 major bleeding (2.4%). Patients with different number of tumors had similar tumor characteristics and techniques. There were significant differences in longest distance of tumors comparing two groups (p = 0.001). No local recurrence or distant metasatasis was detected with a median follow-up of 33 months.

Conclusion: STER is a safety and feasible technique for multiple upper gastrointestinal submucosal tumors no matter in one tunnel or two tunnels resection. Based on the longest distance of tumors, different number of tunnels can be performed with similar procedure technique and prognosis.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
P0174 COMPARISON OF THE LINKED COLOR IMAGING (LCI) TECHNOLOGY AND CHROMOENDOSCOPY WITH ACETIC ACID FOR DIAGNOSIS OF BARRETT’S ESOPHAGUS

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Aims & Methods: The aim of this prospective study was to evaluate the recently introduced LCI technique compared to conventional dye spraying with acetic acid for diagnosis of Barrett’s esophagus. Therefore, consecutive patients with Barrett’s esophagus referred to the gastroenterology team. Individual physician and group results of key quality indicators were compared to the one already obtained by using LCI.

Conclusion: The newly introduced LCI technique is superior to high-definition white light endoscopy for diagnosis of Barrett’s esophagus and equally effective to acetic acid dye spraying. Therefore, the LCI technique has the potential to facilitate the diagnosis of Barrett’s esophagus and to overcome the limitations of a random 4-quadrant biopsy protocol.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0175 ALBERTA FAMILY PRACTICE ELECTRONIC ENDOSCOPE STUDY (APFEE)

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Aims & Methods: The Alberta Family Physician Electronic Endoscopic (APFEE) study aimed to examine the quality of colonoscopies performed by Family Physicians who perform colonoscopies. These endoscopists may improve access to colonoscopies for rural patients who require endoscopy and help improve provincial endoscopy wait times. Although some studies demonstrate that adequately trained Family Physicians are able to perform quality endoscopy, other studies question the quality of colonoscopies performed by non-gastroenterologists.

Results: In this six-month study, 9 Family Physicians performed 1769 colonoscopies in 11 rural Alberta sites. The proportion of successful cecal intubations; proportion of patients 50 years and older having a successful cecal intubation was 87.9% (95% CI: 97.2, 98.5). All physicians had over 90% successfully completed colonoscopies (ranging from 95.2 to 100%). The proportion of males and females 50 years old with an adenoma on a first-time colonoscopy was 67.4% (95% CI: 62.4, 72.7) and 51.1% (95% CI: 45.5, 56.7) respectively. All physicians achieved benchmarks of 30% of males and 20% for females having at least one adenoma. From all colonoscopies in the study there were 2099 pathologically confirmed adenomas or SSAs, 628 advanced adenomas and 17 cancers. Correlating to 120 adenomas, 36 advanced adenomas and 1 colon cancer per 100 colonoscopies. There were 2 post-polypectomy bleeds, no perforations and no deaths.

Conclusion: Alberta Family Physician colonoscopists are meeting benchmarks of the Canadian Society of Colonoscopy. Ongoing electronic collection of endoscopy quality markers should be encouraged. Supported and training rural Family Physicians who perform endoscopy may help alleviate current wait times and improve access for rural Canadian patients.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P0176 PREDICTORS OF ADENOMA DETECTION AT COLONOSCOPY AFTER BOWEL SCOPE SURVEILLANCE: RESULTS FROM A UK PILOT SCREENING CENTRE

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Aims & Methods: We prospectively collated data from all BS patients at our centre and identified those undergoing colonoscopy between August 2013–2016. We assessed conversion rates, compliance with BS protocol and correlated endoscopic and histological findings to identify predictors of detection of pathology at colonoscopy. Univariate analysis was performed using Pearson’s chi2.

Results: 11,711 bowel scopes were performed, with an adenoma detection rate (ADR) of 8.5%, and conversion to colonoscopy in 421 patients (3.6%). 386 were included for analysis after excluding incomplete colonoscopy/histology. All patients were aged 55 (64.8% male). Additional ADR at colonoscopy was 35.2%, with malignant diagnoses in 3% (all detected at BS). The adenoma miss rate at BS was 5.2%. On univariate analysis (Table 1), poly 40mm was the only indication associated with increased ADR at colonoscopy (OR 2.13, p < 0.001). Additional predictors identified included villous (not tubulovillous) histology (OR 4.41, p = 0.002) and male gender (OR 2.35, p < 0.001). These factors also significantly predicted new ≥ 10 mm adenoma. 57 (14.8%) underwent colonoscopy outside protocol, which reduced ADR (OR 0.29, p = 0.03). After exclusion of high risk indications, changing the conversion criteria from any villous to villous only histology altered sensitivity from 27.2% to 83.3%, and specificity from 84.3% to 80.5%.

Table 1: Indications for progression from BS to colonoscopy (in bold) and likelihood of new adenoma detection. *Patients in multiple categories are included multiple times. **p < 0.05

<table>
<thead>
<tr>
<th>Indication</th>
<th>N*</th>
<th>New adenoma</th>
<th>OR (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>At least 3 polyps</td>
<td>78</td>
<td>45 (57.7%)</td>
<td>1.46 (0.88–2.43)</td>
<td>0.14</td>
</tr>
<tr>
<td>Size at least 10mm</td>
<td>196</td>
<td>86 (43.9%)</td>
<td>2.13 (1.39–3.27)</td>
<td>&lt; 0.001 **</td>
</tr>
<tr>
<td>High grade dysplasia</td>
<td>16</td>
<td>5 (31.3%)</td>
<td>0.82 (0.28–2.41)</td>
<td>0.72</td>
</tr>
<tr>
<td>Any villous component</td>
<td>190</td>
<td>69 (36.3%)</td>
<td>1.09 (0.72–1.67)</td>
<td>0.66</td>
</tr>
<tr>
<td>&gt; 20 hyperplastic polyps</td>
<td>3</td>
<td>0</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>None of the above</td>
<td>57</td>
<td>9 (15.8%)</td>
<td>0.29 (0.14–0.62)</td>
<td>0.001 **</td>
</tr>
<tr>
<td>Villous only histology</td>
<td>10</td>
<td>7 (70.0%)</td>
<td>4.41 (1.12–17.36)</td>
<td>0.02 **</td>
</tr>
</tbody>
</table>

Conclusion: At BS, male gender, ≥10mm polyps, and villous histology are predictors of proximal colonic pathology. Further analyses are required to clarify the benefits of converting low-risk tubulovillous adenomas at BS to colonoscopy.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference
1. WS Atkin, Lancet 2010, 375:1624–33
Aims & Methods: A 70-item survey was sent by email to all Gastroenterology Departments in all Spanish hospitals. The rate of participation was 20.3% (341/1678). All physicians indicated their geographical location. In total, 341 Flemish digestive physicians responded to the survey; 30.7% were in academic centres, 51.9% were in teaching hospitals, and 17.4% were in non-teaching hospitals.

Results: Two hundred and seventy-one Flemish digestive physicians participated (response rate: 80%). The mean number of colonoscopies per week was 21 (60%) were males and 50% had more than 14 years in practice. The mean procedural time was 13.8 minutes. Rates of IPB were similar between the two groups (SL-CSP; 3.6%, EMR; 3.9%). There were marginally significant predictors correlating negatively with complete resection (37.3% vs. 28.1%, p = 0.05). By multivariate analysis, female gender (OR, 0.15; 95%CI, 0.02–1.06; P = 0.06) and Paris 0-IIa morphology (OR, 0.12; 95%CI, 0.01–1.19; P = 0.07) were marginally significant predictors correlating negatively with complete resection.

Conclusions: There is a remarkable heterogeneity in the techniques used for removal of polyps <20 mm among Spanish endoscopists. Cold forceps, hot biopsy forceps and EMR are the preferred techniques for removing small polyps. Cold snare polypectomy is the preferred technique for polyps <10 mm, respectively. The use of cold snare for removing small and diminutive polyps is most frequent among gastroenterologists with a greater dedication to endoscopy (cold polypectomy volume per week and performing advanced endoscopy) and among endoscopists with less than 10 years in practice.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0177 COLD SNARE POLYPECTOMY WITH SUBMUCOSAL LIQUID LIFT FOR 6-10MM COLONIC POLYPS: A RANDOMIZED NON-INFERIORITY TRIAL
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Introduction: Cold snare polypectomy is an established method for the resection of small colorectal polyps (SCPs); however, significant incomplete resection rates still leave room for improvement. We aimed to assess the efficacy of cold snare polypectomy, with liquid lift (SL) and EMR for sessile or flat colorectal polyps <20 mm. The aims were to determine any significant differences in resection rates, technical difficulties, and related morbidity for cold snare polypectomy (CSPP) and EMR when comparing small polyps (<10 mm) and polyps 11–20 mm.

Aims: To assess the efficacy of cold snare polypectomy for resection of sessile or flat colorectal polyps smaller than 20 mm.

Methods: A randomised controlled trial was performed at the University of Crete Medical School, Heraklion, Greece. Two different groups were compared: 1) Cold snare polypectomy with submucosal liquid lift (CSPL) and 2) EMR. Randomisation was performed by central allocation. No routine preprocedural computed tomography was performed. A total of 168 patients were included. The baseline characteristics were comparable between the two groups.

Results: A total of 168 patients were included. The mean number of colonoscopies per week was 21 ± 12.3. Half of participants performed endoscopies for ≥3 days per week and 49.6% did not perform advanced therapeutic endoscopy. The techniques used for the excision of polyps smaller than 20 mm by Spanish clinicians are summarized in Table 1. Significant differences were noted in the polypectomy techniques used for the resection of polyps 1–3 mm, 6–9 mm and 10–19 mm in diameter; being cold forceps, hot snare and endoscopic mucosal resection (EMR), the preferred techniques respectively for the different sizes. However, for polyps 4–5 mm in size, both the cold snare and cold forceps were the most commonly used techniques, though no method was use more often than the other. Years in practice, colonoscopy volume per week and performing advanced therapeutic endoscopy were associated with different choices of polypectomy technique. For polyps measuring 4–5 mm, cold snare was the most common among endoscopists who preferred ≥20 colonoscopies in week (≥20 colonoscopies/week < 20 colonoscopies/week, 42.4% vs. 26.6%, p < 0.05), among those who performed endoscopies ≥5 days/week (≥5 days/week < 3 days/week, 58.5% vs. 66.7%, p = 0.05) and among those who performed advanced endoscopy (advanced endoscopy vs no advanced endoscopy, 40.4% vs. 29.2%, p < 0.05). However, cold forceps was the preferred technique among endoscopists who performed endoscopies <7 days per week (38.9% vs. 23.1%, p = 0.05) and among those who performed <10 colonoscopies/week < 20 colonoscopies/week, 28% vs. 13%, p < 0.05). and among those with less than 10 years in practice (<10 years vs. >=10 years, 27.2% vs. 17.7%, p < 0.05). However, hot snare polypectomy was most frequent among endoscopists who performed more colonoscopies ≥20 colonoscopies/week < 20 colonoscopies/week, 28% vs. 13%, p < 0.05) and among those with more than 10 years in practice ≥10 years vs. <10 years, 54.5% vs. 44.7%, p < 0.05).

Conclusion: There is a remarkable heterogeneity in the techniques used for removal of polyps <20 mm among Spanish endoscopists. Cold forceps, hot biopsy forceps and EMR are the preferred techniques for removing small polyps, small polyps and measuring 10 to 19 mm, respectively. The use of cold snare for removing small and diminutive polyps is most frequent among gastroenterologists with a greater dedication to endoscopy (cold polypectomy volume per week and performing advanced endoscopy) and among endoscopists with less than 10 years in practice.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0178 COLONOSCOPIC POLYPECTOMY PRACTICE AMONGST SPANISH CLINICAL GASTROENTEROLOGISTS. RESULTS OF A NATIONAL SURVEY FROM THE SPANISH ENDOSCOPY SOCIETY ELECTROSCOPY SUBGROUP
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9Hospital Puerta de Hierro, Madrid/Spain
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Introduction: Colonoscopic polypectomy effectively reduce the incidence of colorectal cancer. Variations in the technique have been implicated in the effective- ness of the resection and in the complication rates. However, there is no consensus regarding the optimal polypectomy technique for diminutive (<5mm) colorectal polyps. There are scarce of data about polypectomy practices among European endoscopists.

Aims & Methods: To determine the different techniques used by Spanish endoscopists for resection of sessile or flat colorectal polyps smaller than 20 mm. A 70-item survey was sent by email to all gastroenterologists in all Spanish hospitals (1678 gastroenterologists). The survey was conducted from December 2015 to February 2016.

Results: The rate of participation was 20.3% (341/1678). All physicians indicated they were practicing gastroenterologist (none were trainees). Most respondents (60%) were males and 50% had more than 14 years in practice. The mean number of colonoscopies per week was 21 ± 12.3. Half of participants performed endoscopies ≥ 3 days per week and 49.6% did not perform advanced
colonoscope. Some operators participated in a follow up session in order to assess the learning curve. Results: On average, experts required the shortest time to reach the caecum, followed by video gamers, trainees then novices. Polyp detection rate (as a proportion of total number in the model simulator colon) was the highest in the novices (91.67%) followed by the experts (86.11%), then equally, trained and video gamers (79.17%). Four out of nine participants attended the second session where they were asked to repeat the procedure from the first session. Each participant had a lower caecal intubation time during session 2 in comparison with session 1, with a median improvement of 10% and 20%. Each of the participants also had the same or higher polyp detection rate with range of improvement between 0% and 25%. Qualitative assessment of feedback from all participants indicated that most operators felt that the role of the novel test was likely to be a diagnostic probe in an out of hospital setting. Expert operators felt that training in the device was easier but also provided less ability to torque steer due to automated sequences.

Conclusion: This project is the first step in identifying specific training needs and providing evidence for early diagnosis of cancer. This study also indicated the potential to reduce the length of time for skills acquisition associated with standard colonoscopy training through the use of semi-automated robotic devices.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

Introduction: To reduce costs of colorectal cancer screening, a reset and discard strategy has been proposed for small polyps. The American Society of Gastrointestinal Endoscopy (ASGE) recommends achieving a diagnostic accuracy >90%, before implementing it (1). Narrow band imaging (NBI) is increasingly available and the NICE classification is frequently used to reach real time histologic classification. Endoscopists usually rely on short sessions, online courses or self-education for training in NBI, so we evaluated the learning curve in subjects with no previous endoscopic experience and their subsequent performance in patients with polyps ≤7 mm.

Aims & Methods: Participants (4th or 5th year medical students) attended one two-hour session in which the NICE classification was taught, followed by a 1-week interval (session 2). Participants were divided in two groups: group A (expert group) underwent endoscopic training with M-NBI and endoscopic images were taken and recorded in a filing system. After the endoscopy was completed, a determination was made regarding the presence or absence of NBI on the endoscopic images. The morphology of the NBI was determined for cases in which NBI was present and in whom NBI was seen in more than half of the region before the results of histopathological examination of the lesions were known. The morphological characteristics of the lesions were classified as regular NBI or irregular NBI according to our previous report (1).

The primary endpoint was the diagnostic performance of morphologic analysis of the NBI (accuracy, sensitivity, specificity) for early colorectal cancer taking irregular NBI as an indicator. The secondary endpoint was the difference in the prevalence of irregular NBI between mucosal (M) or SMs-colonoscopy (submucosal invasion: ≥1000 micrometers) and SM-1 (submucosal invasion ≥1000 micrometers).

Results: During the two-hour intervention, eight of the 20 endoscopists were rated as ‘expert’ (as they achieved >90% accuracy in the NICE diagnosis) and 12 of the 20 endoscopists were rated as ‘novice’ (as they achieved ≤90% accuracy in the NICE diagnosis). The mean±SD (range) in the diagnostic accuracy for early colorectal cancer was 86.5±3.1% (79–94% in the expert group) and 70.8±4.5% (62–79% in the novice group), respectively. There was no significant difference in the prevalence of irregular NBI in M or SMs cancer and SM-m cancer (p = 0.727, chi-square test).

Conclusion: These findings suggest that in colorectal epithelial neoplasms in colorectal epithelial neoplasms visualized by magnification endoscopy, the morphology of the NBI was a useful marker in the differential diagnosis of adenoma and carcinoma using magnifying endoscopy.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P0012 NARROW BAND IMAGING OPTICAL DIAGNOSIS OF SMALL COLORECTAL POLYPS: LEARNING CURVE AND SUBSEQUENT DIAGNOSTIC ACCURACY IN UNEXPERIENCED EVALUATORS


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Introduction: To reduce costs of colorectal cancer screening, a reset and discard strategy has been proposed for small polyps. The American Society of Gastrointestinal Endoscopy (ASGE) recommends achieving a diagnostic accuracy >90%, before implementing it (1). Narrow band imaging (NBI) is increasingly available and the NICE classification is frequently used to reach real time histologic classification. Endoscopists usually rely on short sessions, online courses or self-education for training in NBI, so we evaluated the learning curve in subjects with no previous endoscopic experience and their subsequent performance in patients with polyps ≤7 mm.

Aims & Methods: Participants (4th or 5th year medical students) attended one two-hour session in which the NICE classification was taught, followed by a 1-week interval (session 2). Participants were divided in two groups: group A (expert group) underwent endoscopic training with M-NBI and endoscopic images were taken and recorded in a filing system. After the endoscopy was completed, a determination was made regarding the presence or absence of NBI on the endoscopic images. The morphology of the NBI was determined for cases in which NBI was present and in whom NBI was seen in more than half of the region before the results of histopathological examination of the lesions were known. The morphological characteristics of the lesions were classified as regular NBI or irregular NBI according to our previous report (1). The primary endpoint was the diagnostic performance of morphologic analysis of the NBI (accuracy, sensitivity, specificity) for early colorectal cancer taking irregular NBI as an indicator. The secondary endpoint was the difference in the prevalence of irregular NBI between mucosal (M) or SMs-colonoscopy (submucosal invasion: ≥1000 micrometers) and SM-1 (submucosal invasion ≥1000 micrometers).

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Conclusion: These findings suggest that in colorectal epithelial neoplasms in colorectal epithelial neoplasms visualized by magnification endoscopy, the morphology of the NBI was a useful marker in the differential diagnosis of adenoma and carcinoma using magnifying endoscopy.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
PHASE 3 TRIALS

Aims & Methods: Colon cleansing efficacy of NER1006 was compared to three currently used bowel preparations in patients aged ≤65 years and in patients aged >65 years. NER1006 was compared to sodium picosulfate + magnesium citrate (NaPic + MgCit), trisulfate and 2L PEG with ascorbate (2L PEG + Asc), in three multicentre randomised Phase 3 clinical trials: DAYB1, NOCT2 and MORA3, respectively. 2L PEG + Asc was administered over 2 days and in the MORA trial, the doses of NER1006 were administered either in 1 day morning-only (N1D) or, as with 2L PEG + Asc, split over 2 days (N2D). In the DAYB study, NER1006 was administered evening-only the day before colonoscopy (NDB). Treatment-blinded central readers rated colon cleansing according to the Harefield Cleansing Scale. Following segmental scoring, overall colon cleansing was graded from A to D. Grades A and B were judged as successful cleansing; grades C and D were judged as failed cleansing.

Results: Pooling the data from the three trials to assess colon cleansing in the two age groups showed successful cleansing in 80.5% (1158/1438) of patients aged ≤65 years and 68.9% (277/400) of patients aged >65 years (difference of 9.3%, P = 0.098; 95% CI: -3.7–5.6%). Within each trial the difference in colon cleansing in the age groups indicated that the effect of increased age on cleansing efficacy was less in the NER1006-treated patients than in patients treated with the active comparators (Table 1). For example, in patients treated with NER1006 the rate of successful colon cleansing in patients aged >65 was 5.2% higher than in patients aged ≤65, whereas in patients treated with NaPic + MgCit, there was 3.5% lower successful cleansing rate in patients aged >65 than in patients aged ≤65.

Conclusion: NER1006 was efficacious in successful colon cleansing in patients aged >65 (in whom successful colon cleansing is harder to achieve) as well as in patients aged ≤65. Statistical significance was not reached in these comparisons.

Disclosure of Interest: R. Jover: Received grants support from MSD; Advisory board participation for Norgine
R. Ng Kvet Shing: Employee of Norgine
All other authors have declared no conflicts of interest.

References
3. Bisschops R et al. Gastroenterology 2016; 150(4); S1269–70. Abstract Tu2084

Available at: http://www.upatients.com/pdf/2016/1589

P0184 ACHIEVING ADEQUATE LEVEL BOWEL PREPARATION WITH EVENING/MORNING OR MORNING-ONLY SPLIT-DOSING REGIMENS OF NER1006 VERSUS STANDARD 2L PEG WITH ASCORBATE: POST HOC ANALYSIS OF A PHASE 3 TRIAL

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Introduction: Effective colonoscopy requires effective bowel preparation. For detection of polyps larger than 5 mm, an ‘adequate’ segmental cleansing level has recently been defined as ≥2 or more on the Boston Bowel Preparation Scale (BBPS). The Phase 3 trial MORA compared NER1006 as an evening/morning split-dosing or a morning-only dosing regimen, against 2L PEG with ascorbate as an evening/morning split-dosing regimen (2L PEG + Asc). Treatment-blinded central readers assessed the bowel cleansing efficacy using both the Harefield Cleansing Scale (HCS) and the BBPS. This post hoc analysis shows the BBPS scores for the two primary endpoints, in those patients who had a readable colonoscopy.

Aims & Methods: In the MORA trial, 789 patients aged 18–85 were randomised to bowel preparation with morning-only or evening/morning split-dosing using either NER1006 or 2L PEG + Asc. Adequate level cleansing success was assessed according to the BBPS for both overall colon (all segments ≥2) and right colon cleansing (segmental score ≥2). The analysis includes all subjects for whom colonoscopy videos were available for assessment by central readers.

Results: A total of 792 patients were analysed. When using an evening/morning split-dosing, 249/262 (95%) patients on NER1006 achieved adequate level overall colon cleansing compared to 232/260 (89%) on 2L PEG + Asc (Table 1). Using morning-only dosing, 243/270 (90%) patients on NER1006 achieved the same. Using evening/morning split-dosing, 254/262 (97%) patients on NER1006 achieved adequate level right colon cleansing compared to 242/260 (93%) on 2L PEG + Asc. Using morning-only dosing, 253/270 (94%) patients on NER1006 achieved adequate level right colon cleansing. Adequate level cleansing success was achieved significantly more often with NER1006 evening/morning split-dosing than 2L PEG + Asc, both in the overall colon (P = 0.013) and in the right colon (P = 0.042). The slight improvement seen with NER1006 morning-only dosing in the cleansing rate of the overall colon and right sided colon was not statistically significant. Table 1: Adequate level cleansing of the overall colon and right colon (BBPS segmental scores ≥2) as determined by treatment-blinded central readers

Disclosure of Interest: R. Bisschops: Norgine: self: salary, speaking and teaching; funded attendance by Norgine for Investigator’s Meeting trip for the MORA trial
L. Clayton: Employee of Norgine

References

Available at: http://www.upatients.com/pdf/2016/1590

P0185 ASSESSMENT OF COLONOSCOPY QUALITY IN CLINICAL PRACTICE COMPARED WITH EUROPEAN SOCIETY OF GASTROINTESTINAL ENDOSCOPY PERFORMANCE INDICATORS

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8Aschaffenburg Hospital, Aschaffenburg/Germany

Abstract No: P0185

Patients with successful cleansing, n (%)

<table>
<thead>
<tr>
<th>DAYB (1:1)</th>
<th>NOCT (1:1)</th>
<th>MORA (1:1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NER1006 (NDB)</td>
<td>NaPic + MgCit</td>
<td>NER1006</td>
</tr>
<tr>
<td>Aged ≤ 65</td>
<td>127/196 (64.8)</td>
<td>115/205 (56.1)</td>
</tr>
<tr>
<td>N (%)</td>
<td>28/40 (70.0)</td>
<td>20/38 (52.6)</td>
</tr>
<tr>
<td>Difference (P-value)</td>
<td>0.102</td>
<td>0.555</td>
</tr>
<tr>
<td>95% CI (%)</td>
<td>0.001–0.839</td>
<td>0.001–0.839</td>
</tr>
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</table>

N.B. successful cleansing defined here as a Harefield Cleansing Scale grade of A or B (overall colon)
Abstract No: P0184

<table>
<thead>
<tr>
<th>NER1006 evening/morning split dosing</th>
<th>NER1006 morning only dosing</th>
<th>2L PEG + Asc evening/morning split dosing</th>
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<tr>
<td>Patients (N)</td>
<td>262</td>
<td>270</td>
</tr>
<tr>
<td>Patients with an adequate level</td>
<td>249 (95)</td>
<td>243 (90)</td>
</tr>
<tr>
<td>cleansing success of the overall col, n (%)</td>
<td></td>
<td>232 (89)</td>
</tr>
<tr>
<td>Patients with an adequate level</td>
<td>254 (97)</td>
<td>253 (94)</td>
</tr>
<tr>
<td>cleansing success of the right col, n (%)</td>
<td></td>
<td>242 (93)</td>
</tr>
<tr>
<td>patients with adequate bowel</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| preparation, defined as Boston Bowel Preparation Scale score ≥3. From our data, 81% (n = 1669) of procedures had adequate bowel cleansing (data unavailable for 96.4%). The ESGE recommends a minimum standard of ≥90% of all diagnostic and screening colonoscopies visualize the whole caecum (excluding those that have no indication to reach the caecum). Only 55% of practitioners routinely record cecal intubation rate. The caecum was the intended endpoint in 66% of procedures. For those diagnostic and screening colonoscopies where the caecum was the intended endpoint (n = 1390), 93% reached the endpoint but only 78% had this endpoint photo-documented. The ESGE recommends that adenoma detection rate (ADR) should be used as a measure of adequate inspection at screening or diagnostic colonoscopy in patients aged 50 years or more. ADR was routinely recorded by only 18% of practitioners. Polyp removal rate is routinely recorded by 30% of practitioners, and polyp retrieval rate by 23%. Conclusion: Our findings indicate that some important performance measures recommended by ESGE are not currently being achieved in practice. By providing a self-assessment tool and as a next step, by individual consultations with national Group members, ECQI hopes to improve clinical practice standards. Further information on the ECQI Group initiative can be found on www.ecqigroup.eu

Disclosure of Interest: E. Toth: Consultancy and Advisory Board participant for Norgine R. Jover: Consultancy and Advisory Board participant for Norgine C. Spada: Consultant fee by Norgine A. Agrawal: Consultancy and Advisory Board participant for Norgine P. Amare: Consultancy and Advisory Board participant for Norgine L. Brink: Consultancy and Advisory Board participant for Norgine W. Fischbach: Consultancy and Advisory Board participant for Norgine M. Húnger: Consultancy and Advisory Board participant for Norgine A. Ono: Consultancy and Advisory Board participant for Norgine L. Petruzziello: Consultancy and Advisory Board participant for Norgine A. Naidoo: Employee of Norgine J.F. Riemann: In terms of ECQI, consultant to Norgine, otherwise no conflict of interest

References


P0186 SEDATION IN GASTROINTESTINAL ENDOSCOPY: CURRENT PRACTICES OF GREEK GASTROENTEROLOGISTS

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Introduction: When it comes to gastrointestinal endoscopy, considerable heterogeneity is observed between gastroenterologists regarding the use of sedation and the preferred sedative agents. The sedation protocol used by a gastroenterologist may have a significant effect on endoscopic quality, patient cooperation and both the doctor’s and the patient’s satisfaction with the procedure.

Aims & Methods: The aim of this study was to document current endoscopic practices of Greek gastroenterologists and investigate whether they use sedation to perform gastrointestinal endoscopy and which pharmaceutical agents are usually involved. A 39-item online questionnaire was devised, addressing demographic data, use of sedation in endoscopy and monitoring practices. It was subsequently made available to 509 Greek gastroenterologists by e-mail.

Results: A total of 195 questionnaires were successfully completed (38.3%). 49 gastroenterologists did not use sedation to perform esophagogastroduodenoscopy (EGD) or colonoscopy (25.1%). The younger gastroenterologists were more likely to use sedation (p = 0.005). Among those using sedation, midazolam was the most frequently used agent in EGD (50%) and the combination of midazolam/fentanyl was the most frequently used in colonoscopy (24.6%). Followed by midazolam (21.9%). Out of 137 physicians using benzodiazepines (midazolam, diazepam) as part of their endoscopic sedation regimen, 91 (66.4%) used midazolam during the procedure. Medical issues (33%), inadequate training in the use of propofol (73%), training in the use of midazolam (21.9%), and other agents (30%) were cited as the main reasons for not using propofol. As for the medication used during the procedure, the majority of gastroenterologists used diazepam and oxygen saturation (96% and 97% respectively). Regarding the safety equipment, 145 (74%) used oropharyngeal airway devices or laryngeal airway masks, 92 (47%) to endotracheal intubation equipment and 86 (44%) to a defibrillator. When asked to rate their level of satisfaction with their preferred sedation regimen (or with not using sedation) in a scale of 1 to 10, 72 physicians rated their satisfaction level as 9 or 10 (36.9%) and 92 as 7 or 8 (47.1%). While there was no significant difference in terms of satisfaction between the doctors that used sedation and those who did not, there was a statistically significant difference between the gastroenterologists that used propofol and other sedation agents (p = 0.003). When asked on their preferred method of sedation, if they were themselves subjected to gastrointestinal endoscopy, 104 physicians opted for propofol-based sedation regimens (53.3%).

Conclusion: Gastrointestinal endoscopy is performed with the use of sedation by the majority of Greek gastroenterologists. Propofol-based regimens are seldom used in everyday clinical practice, despite a vast number of Greek gastroenterologists identifying them as their preferred regimen, in case they themselves should undergo endoscopy. Compared to a past survey, Greek gastroenterologists are still hesitant about using propofol. However, an increasing tendency towards administering propofol without the aid of an anesthesiologist is observed. Also, physicians using propofol seem to be more satisfied with their sedation practices than the doctors using other sedation regimens. Absence of a distinct legal framework, inadequate training and fear of cardiopulmonary complications are identified as the main reasons preventing Greek gastroenterologists from using propofol.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

Aims & Methods: We locally adapted a company reporting system for colonoscopy by adding in a dedicated tab, selected procedure indicators. Endoscopic QI data from reporting system DB and pathologic results from another DB were extracted and merged together in a separated DB. On a regular period basis or on request, key QI are calculated and extracted. It includes adenoma detection rate (ADR), polyp detection rate, caecal intubation rate, quality of bowel preparation score and type of sedation. During a first period of 6 months starting in January 2016, endoscopists were encouraged to fulfill the dedicated tab on a voluntary basis. In a second period, filling of QI was turned to be mandatory. The completeness of QI recording was evaluated across both periods, and results from second period are presented. Performance measures of all endoscopists were compared to global results of our department and to published targets.

Results: During the 6 months "mandatory-filling" period (July-December 2016), 1802 colonoscopies were performed with a QI tab fully filled in 100% of cases compared to 63.1% after the "free-filling period" (p<0.0001). The global caecal intubation rate for screening colonoscopy was 92.9%. Mean Boston bowel preparation score was 7.2 ± 0.76 with 86.9% of cases with adequate preparation (Boston score >5; 89.9% among outpatients and 81.9% among inpatients). Colonoscopies were performed under propofol sedation in 94.1%. During this second period, the global ADR was 32.4% (range: 0%-55.7%). The polyp detection rate was 44.4% with a mean of 1.19 polyp removed by colonoscopy.

Conclusion: This study illustrates that quality indicators for colonoscopy assessment in a Belgian tertiary hospital endoscopy unit could be easily implemented with limited human resources by adapting a company reporting system and link it to a dedicated database. Moreover, filling of QI items is mandatory for system implementation success. Our results were consistent with goals required by international guidelines. This system allows giving feedback to individual endoscopists for self-performance assessment and might be easily adapted in the future following guidelines updates.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
Aims & Methods: The aim of this study was to develop a computer-aided detection (CAD) algorithm for colonoscopy using deep learning. To evaluate the developed CAD algorithm, we retrospectively viewed colonoscopy videos from a previous randomized controlled study (UMIN000017083) conducted from April 2015 to October 2015. All examinations were performed using CF-H290ZI (Olympus Medical Corp., Tokyo, Japan). In this study, two endoscopists (M.M., Y.M.) manually annotated 43 colonoscopy videos with 238 min of 17,903,967 frames. These videos included 75 polyps (48 neoplasms, 27 non-neoplasms), and annotations were made on the presence or absence of polyps in every frame. Forty-three videos were divided into 300 short video for machine learning and validation process. Among 300 short videos, 246 were used for the machine-learning process. The remaining 54 (33 included a lesion used to validate the CAD algorithm and 21 without lesion) were tested with a modified version of Caffe with 3-Dimensional Convolutional Networks (a kind of deep learning) was used for the CAD algorithm. The validation samples were analyzed using the CAD algorithm and its output as the probability of the presence of a lesion in each video frame. The receiver operating characteristic (ROC) analysis was performed to evaluate the efficacy of the CAD algorithm.

Results: The mean probability of a poly-positive video was 62.1 ± 27.9%, whereas that of a poly-negative video was 18.1 ± 24.6% (P < 0.001). The area under the ROC curve was 0.887 and the positive probability 0.90 in full present. The present CAD algorithm could detect a polyp with 90.6% sensitivity and 76.2% specificity.

Conclusion: Our preliminary results showed that state-of-the-art artificial intelligence has the potential for achieving automatic detection of colorectal polyps. A prospective study is now planned after more machine-learning sessions.

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Disclosure of Interest: K. Mori: Kensaku Mori received research funding from Cybernet System Company and Olympus Company. All other authors have declared no conflicts of interest.

References

P0192 TREATMENT OUTCOMES OF COLD FORCEPS POLYECYTOMY FOR PATIENTS WITH DIMINUTIVE POLYPS: A PROSPECTIVE FOLLOW-UP STUDY

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Introduction: The results of the National Polyp Study are premised on the removal of all adenomatous lesions. Cold forceps polypectomy (CFP) using jumbo biopsy forceps is a simple and safe technique used for diminutive polyps (<5mm). The recurrence rate after CFP for patients with diminutive polyps has not been elucidated.

Aims & Methods: We have prospectively enrolled patients with diminutive polyps treated with CFP from June 2008 to March 2017. Magnifying colonoscopy was used for all procedures. The location, size, endoscopic findings and procedures were recorded. The patients who have undergone CFP had their follow-up colonoscopy in one year after CFP.

Results: CFP was performed for total 515 polyps from 277 patients. The size of the polyps was <3mm/4mm/5mm: 79%/54%/37%. The rate of one-bite polypectomy for adenoma was <3mm/4mm/5mm: 79%/54%/33%. There was no significant difference in the one-bite rate between endoscopists’ experience. No cancer was observed in histology. Rates of delayed bleeding after CFP was 0.19% (1/515). Concomitant use of anticoagulation use of antiplatelet drugs was found in 14% (72/508), and none of them experienced delayed bleeding. No perforation occurred. Seventy-five patients had their follow-up colonoscopy so far. There are no polyps on suspicious residual or recurrent lesion. Among 75 patients, 62 had less than two polyps removed at their first colonoscopy (Group A). On the other hand, 13 patients had more than three polyps removed at their first colonoscopy (Group B). Follow-up colonoscopy revealed that the rates of newly discovered polyps in the same segment were 8% and 23% in groups A and B, respectively. The rates of newly discovered polyps in the different segment were 27% and 61% in groups A and B, respectively. When the initial CFP was performed by the endoscopist with the experience of <5 years/5-9 years/10 years/more than ten years, the rates of newly discovered polyps found at follow-up colonoscopy was 54% (14/26)/42% (8/19)/37% (11/30), respectively.

Conclusion: The rate of one-bite polypectomy was significantly higher for diminutive polyps especially less than 3 mm. Importantly there are no polyps on suspicious residual in the follow-up colonoscopy. CFP is a safe and effective option for diminutive polyps (5mm). Although the rate of one-bite polypectomy was not related to the endoscopists’ experience, adenoma detection rate is seemed to be low in young endoscopists. Since achievement of “clean colon” is very important, the multiple colonoscopy examination are necessary to achieve “clean colon” especially if the patients have more than two polyps at the first examination.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P0193 EFFICACY OF Cimetropium Bromide on POLYP DETECTION DURING COLONOSCOPIC WITHDRAWAL: A DOUBLE-BLIND, RANDOMIZED, PLACEBO-CONTROLLED, CLINICAL TRIAL

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Introduction: Colonoscopy is the most effective method for preventing colorectal cancer, as it offers easy detection and resection of polyps. Cimetropium bromide was recently developed (Olympus Medical Systems Corporation, Tokyo, Japan) for sedation and external compression, patients’ pain and satisfaction, adenoma detection rate, and offers potential advantages over standard colonoscopy technique in terms of effective- ness and convenience of colonoscopy.

Disclosure of Interest: H. Neuhaus: Honoraria and consultancy fees from Olympus Medical Systems Corporation. All other authors have declared no conflicts of interest.

Aims & Methods: To evaluate the efficacy of the novel motorized spiral overtube. This may have advantages in cases of difficult standard colonoscopy to facilitate cecal intubation on the one hand and in all colonoscopies in safe and effective option for diminutive polyps (<5 mm). Although the rate of one-bite polypectomy for adenoma in EMR specimen was histologically proven to have R0 en-bloc resection. All other therapeutic interventions could also successfully be conducted (elip n=3, argon plasma coagulation n=1, tissue sampling n=2). Two mild adverse events were recorded (mild superficial mucosal lesions without delayed bleeding occurred). Conclusion: This study represents the first clinical evaluation of the novel motorized spiral endoscope for examination of the colon. Our data show that it is effective and safe for diagnostic and therapeutic colonoscopy. It may also have potential advantages over Tokyo, Far standard colonoscopy technique in terms of effective-
results in colonic spasmolysis and may improve polyp detection. We studied the effect of cimetropium bromide on polyp detection during colonoscopic withdrawal.

Aims & Methods: Patients undergoing colonoscopy for screening examinations were included and randomized at cecal intubation to receive either 5mg cimetropium bromide or placebo. We evaluated the polyp detection rate (PDR), adenoma detection rate (ADR), and advanced ADR (AADR) in the right side colon as well as in the colorectum.

Results: A total of 181 patients were analyzed in this study. Cimetropium group consisted of 90 patients, while placebo group consisted of 90 patients. PDR, ADR, and AADR were not significantly different in cimetropium and control groups (62.6% vs. 66.6%, P = 0.571; 51.6% vs. 47.7%, P = 0.603; 3.2% vs. 7.7%, P = 0.187; respectively). Similarly, PDR and ADR in the right side colon were not statistically different between the groups (46.1% vs. 47.7%, P = 0.827; 32.9% vs. 35.5%, P = 0.714; respectively).

Conclusion: Cimetropium bromide does not improve the PDR or ADR in the right side colon or the colorectum. Thus, administration of cimetropium bromide can be used during colonoscopic withdrawal.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference:
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P0195 WOMEN AWAKE FASTER THAN MEN AFTER EOG-MONITORED PROPOFOL SEDATION - FIRST PROSPECTIVE OBSERVATIONAL STUDY OF GENDER DIFFERENCES IN PROPOFOL DOSES AND RECOVERY TIMES FOR COLONOSCOPY

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Introduction: Sedation for colonoscopy by using intravenous propofol has become standard in many Western countries.

Aims & Methods: While gender-specific differences have been shown for general anesthesia used in dentistry, no such data exist as yet for gastrointestinal endoscopy. In a prospective observational study at an Academic teaching hospital of Hannover Medical School 219 patients (108 women and 111 men) scheduled for colonoscopy were included. Sedation was induced using EOG monitoring during a constant level of sedation depth (D0 to D2) performed by trained nurses or physicians after bodyweight adjusted loading-dose.

Main outcome measures: Primary endpoint was the presence of gender-specific differences in wake-up time (time from end of sedation to eye-opening and the complete orientation of the patient); secondary outcome parameters analysed were total dose of propofol, sedation associated complications (bradycardia, hypotension, hypoxia, apnoea), patient cooperation and patient satisfaction. Multivariate analysis was performed to correct confounding factors such as age and BMI.

Results: Women awaked significantly faster than men to a time of eye opening (26.2 ± 3.69 min. vs. 34.13 min. p = 0.005) and time until complete orientation 9.14 ± 3.88 min vs. 10.4 ± 3.71 min (p = 0.008); propofol dosage was not significantly different, with some trend towards more propofol per kg body weight in women (3.98 ± 1.81 mg vs. 3.72 ± 1.75 mg, p = 0.232, n.s.).

The effect of gender differences should be taken into account upon propofol induced sedation for gastrointestinal endoscopy. That includes adequate dosing for female as well as cautiousness regarding potential overdosing of male patients.

Trial registration: ClinicalTrials.gov (Identifier: NCT02687568). Data were presented at a national meeting (DGEBV) in Germany.

Disclosure of Interest: All authors have declared no conflicts of interest.

References


nontattooing group, both side injection group was better result (96.2% vs. 91.5%, p-value 0.029). Most results did not have statistical association with higher lymph node yield in colorectal cancer. But in T1 cancer, the rate of adequate lymph node harvest was higher in the both side injection group, statistically (94.7% vs. 81.0%, OR 4.235, p-value 0.047)

Disclosure of Interest: All authors have declared no conflicts of interest.

References

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Disclosure of Interest: Prevention of complications secondary to endoscopic resection techniques (EMR or ESD) requires avoiding deep thermal damage and increase mucosal healing. Platelet-rich plasma (PRP) has demonstrated efficacy in pre-clinical endoscopic resection models [1]. The EndoPRP study was a prospective single-center study to assess the efficacy of PRP on endoscopic resection of large sessile lesions (larger than 35 mm). (Study registered at ClinicalTrials.gov: NCT02931149)

Introduction: In the EndoPRP study patients (males and females, aged 52–80) were assigned to receive PRP (6–15 mL): 1) Endoscopic Shielding Technique (EST, n = 4), applying PRP as a shield after standard resection technique, or ii) Submucosal injection (SMI, n = 11), performing a submucosal injection of PRP prior to EMR or ESD. Patients were informed and accepted to participate with a written consent. PRP was obtained from a sample of patient’s blood (18–36 mL) drawn at the time of endoscopy. Patients underwent endoscopic follow-up after 4 weeks. The efficacy of PRP was assessed by the incidence of adverse events (delayed bleeding or perforation). Mucosal healing rate (MHR) was defined as a percentage of mucosal restoration after 4 weeks.

Results: Shielding technique with PRP performed in 4 lesions at rectum (Æ 53.7 ± 20.6 mm, range 35–80 mm). Submucosal injection of PRP was used in 11 lesions (2 at antrum, 3 at rectum, and 8 at colon) (Æ 41.6 ± 9.6 mm, range 35–70 mm). Delayed bleeding occurred after EMR of 1 lesion (no required blood transfusion or endoscopic treatment; 6.6% of all lesions: 1 patient at EST group, 0 patients at SMI group). MHR was significantly higher in patients treated with PRP vs. SMI than EST (87.5% vs. 78.6%; p = 0.03).

Conclusion: PRP applied as a shield over the scar or as submucosal fluid cushion has proved clinical efficacy in endoscopic resection of large lesions. Submucosal injection of PRP has showed better mucosal healing rate as compared with standard shielding technique.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference
with a defined AE. Treatment options, including none required, were taken from Spanish- and English-language guidelines examined included. Over 62% of providers were gastroenterologists and anaesthesiology nurses. Local guidelines determined practice in most cases, and propofol and midazolam were the main sedation agents employed. The most common AEs reported were hypotension and bradycardia, with 9% and 4% of respondents, respectively, estimating each to occur during >10% of procedures. Mean provider time required to treat AEs ranged from 1.7 minutes for mild desaturation in Germany to 3.10 minutes for cardiac arrest in the USA. Accounting for interventions and provider time, the mean direct costs per range from EUR 12 for bradycardia in Germany to USD 3,877 for cardiac arrest in the USA (Table). When costs were “fully loaded” these became EUR 39 and USD 19, 722, respectively. Although of low direct cost, bradycardia in Germany was reported to cause procedure termination or substantial delay in 3.3% of cases. In Euro countries, the median of direct costs for an AE was EUR 40 (IQR: 29–67). When costs of outcomes of AEs were included the median “fully loaded” cost reached EUR 301 (IQR: 115–738).

Table: Costs of select adverse events by country. FL: Fully-loaded (costs including hospital administration, time, inpatient stays, delays, and cancellations, but excluding legal costs).

<table>
<thead>
<tr>
<th>Country, currency</th>
<th>Mild Hypotension</th>
<th>Severe Hypotension</th>
<th>Cardiac arrest</th>
<th>Prolonged Apnoea</th>
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<td>US, USD 247</td>
<td>841</td>
<td>465</td>
<td>1529</td>
<td>1715</td>
</tr>
</tbody>
</table>

Conclusions: Costs of sedation-related AEs can be substantial regardless of country of origin. Disruption of patient flow and provider efficiency may add to the cost burden. Even relatively minor events may prompt additional intervention, increasing the overall cost of care.

Disclosure of Interest: R. Saunders: Rhodri Saunders is the owner of Coreva Scientific GmbH & Co KG, which received consultancy fees for designing and performing this research. J. Eisen: Jason Eisen is an employee of Coreva Scientific GmbH & Co KG, which received consultancy fees for designing and performing this research. R. Weissbrod: Rachel Weissbrod is an employee of Medtronic. D. Whitaker: David Whitaker received no remuneration for work on this research project. He has previously consulted for Medtronic and Vedad P. Kranke: Peter Kranke did not receive any remuneration for work on this research project. He has previously consulted for Medtronic and Covidien. KG, which received consultancy fees for designing and performing this research project. He has previously consulted for Medtronic and Covidien. R. Saunders: Rhodri Saunders did not receive any remuneration for work on this research project. He has previously consulted for Medtronic and Covidien.

Reference

P0200 COLORECTAL ENDOSCOPIC SUBMUCOSAL DISSECTION (ESD); KNIFE-ASSISTED SNARE RESECTION (KAR) AND SPAIN RECURRENCE RATE: A WESTERN EUROPEAN EXPERIENCE IN
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Introduction: To compare the recurrence rate after R0 and R1/Rx endoscopic resection (ER), on an ESD “intention-to-treat” basis, in a Western European setting where CR-ESD is performed by non-experts. 2.) To evaluate the impact of LM involvement on local recurrence when neoplasms without risk factors for lymph node metastasis are resected en bloc. We prospectively included 89 consecutive CR neoplasms planned for ESD from September 2008 to December 2015. When technical difficulties arose or for patient’s safety reasons, we performed a KAR. Kaplan-Meier survival curves were used to assess the recurrence rate over time. The end of follow-up was considered when a local recurrence occurred or at the end of the surveillance period in those patients who did not develop the event. Comparisons were made using the log-rank test. The recurrence rate during follow-up was stratified considering advanced histology, en bloc resection and R0 resection.

Results: The ER was aborted in 5 cases (perforation n = 3; technical difficulties n = 2). Surgical intervention was needed after ER because of submucosal or linfoc娠al invasion in 4 patients. Five out of the remaining 80 cases, were lost to follow-up. Finally, 75 CR neoplasms were included in 74 patients (43 male; 58.1%). Median age was 71 years (range: 37–93). Median size of the lesions was 32 mm (range 10–100). Histology was 26 (34.7%) Vienna category 3; 46 (61.3%) Vienna 4 and 3 (4%) sm1/Vienna 5. En bloc resections were obtained in 44 cases (58.7%); 33 ESD (48%) and 11 KAR (14.7%). The ER finished as an R0 resection in the 31 remaining lesions (41.3%). R0 resections (n = 23; 30.7%) were achieved in 18/33 ESD and 5/42 KAR [OR: 8.9 (CI 95%: 2.8–28.3); p < 0.0001]. The median follow-up period was 16 months (1–91). Local recurrence occurred in 11 cases; 9 of the latter throughout the first year (81.8%). No surgery was needed because of recurrence. The overall recurrence rate at 36 months was 15%. The recurrence rate at 3 years showed a statistical significant difference when R0 resections were compared with R1/Rx: 0% vs. 21.5% (p = 0.03). When results were stratified according to histology and en bloc resections, no significant differences were found in the recurrence rate. When en bloc resections in pTa/T1b (sm1); pT2: (sm2); pT3 (sm3) lesions (n = 44) were analysed separately; LM distribution in LM0 (52.3%), 18 LM1 and 3 LMx (6.8). There was a non-significant trend concerning the recurrence rate when LM0 (n = 23) lesions were compared with LM1/LMx (n = 21): 0% vs. 14.8% at 3 years; p = 0.06.

Conclusions: ESD R0 resections were 9 times greater than that of KAR on an ESD “intention-to-treat” basis. R0 resections were associated with lower recurrence rates in comparison with R1/Rx resections. LM involvement increased the recurrence rate but without a statistical significance when it was the only pathological risk factor for recurrence and the specimen was resected en bloc.

References

P0201 ASSOCIATION BETWEEN SIZE, LOCATION AND HISTOLOGICAL CHARACTERISTICS OF COLORECTAL LATERALLY SPREADING TUMORS

Introduction: Laterally spreading tumors (LST) are important precursors of colorectal cancer (CRC). The endoscopic characteristics of the LSTs, such as size and location, appear to correlate with the histological findings1, 2, which is an essential data for the decision of the best therapeutic procedure to be carried out.3

Aims & Methods: To determine the association between size, location and the histological characteristics of colorectal LSTs by reviewing of the colonoscopy and histopathological reports of the LSTs endoscopically removed between October 2013 and June 2015 at the digestive endoscopy department of a tertiary hospital. The Vienna revised classification was used for the adenomatous lesions5, and the World Health Organization (WHO) classification for the “sessile serrated adenomas” (SSA)6, 7. The regions of the colon were referred to

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as either "proximal" or "distal" colon. Thereafter the division into six anatomical segments was considered (cecum, ascending, transversal, descending, sigmoid and rectum). 

Results: A total of 218 LSTs were included in this study. Most patients (59.4%) were female. The mean age was 66.1 years, and the average size of the LSTs included was 1.6cm (±1.9). The most common proximal colon was the most common site (73.4%) of occurrence of the LSTs, with 34% being at the ascending colon. The most common histological type was the low grade dysplasia adenoma (Vienna 3), followed by the SSA without dysplasia with 21.6%. There was significant correlation between size and histology (p < 0.005), where the adenomatous lesions were found to be larger than the other categories. The SSAs, however, did not show this association. We identified association between location and histological type (p < 0.005): the adenomas with low grade dysplasia were most prevalent in the proximal colon. However, when the subdivision of the colon into anatomical segments was considered, the SSA without dysplasia was the most common type at the ascending colon.

Conclusion: There is association between the size and the histological characteristics of colorectal LSTs. In cases of high grade dysplasia were found to be larger than the other classifications. This association, however, is not observed between SSAs lesions. There is association between location and histology; with the SSAs without dysplasia being the predominant type at the ascending colon.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P0202 SAFE AND SUCCESSFUL RESECTION OF DIFFICULT GI LESIONS USING A NOVEL SINGLE-STEP FULL-THICKNESS RESSECTION DEVICE (FTRD)

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Introduction: Endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD) are well-established and effective techniques for the endoscopic resection of mucosal neoplasms along the gastrointestinal (GI) tract. However, these procedures are limited to superficial lesions. In the case of deeper ingrowth into the gut wall as well as anatomic sites prone to perforation, the novel full-thickness resection device (FTRD#) opens a new dimension of possibilities for endoscopic resection.

Aims & Methods: Sixty patients underwent therapeutic endoscopic full-thickness resection (eFTR) at our institution. The procedures were carried out as follows: First, the target lesion is marked with electrocautery and the endoscope is then retracted. The full-thickness resection device (FTRD, Ovesco® Endoscopy AG, Tübingen), is fitted onto a therapeutic endoscope. The endoscope with the FTRD# is advanced to the previously marked lesion. Grasping forceps are used to take hold of the target lesion and carefully pull it into the plastic cap of the FTRD#. Immediately after deployment of the OTSC®, eFTR is performed using the hyperthermic snare within the plastic cap. The full-thickness specimen is retrieved and processed for histopathological examination. Safety, learning curve, R0 resection rate and clinical outcome of all 60 interventions were studied.

Results: eFTR was performed for the following indications: 1. Recurrent adenomas (n = 22.3%) with a non-lifting sign after previous incomplete polypectomy and adenomas with a primary non-lifting sign on saline injection (n = 2.3%). 2. Non-lifting base after extensive piecemeal resection of a spreading adenoma (n = 0.7%). 3. Diverticulum (4.6%). 4. Polyph of the cecal appendix (5.8%). 5. Submucosal lesions (n = 5.8%). 6. Early carcinoma (n = 7.12%). 7. Follow-up resection of a malignant polyp (n = 0.6%). 8. FTR over endoloop resection (n = 2.3%). In 97% (58/60) of the interventions, the FTRD#-mounted endoscope reached the previously marked lesion and eFTR was performed (technical success). Full-thickness resection was achieved in 88% of the cases, with an R0 resection on histological examination in 79%. The clinical success rate based on follow-up histology was even higher (88%). The following adverse events occurred: Appendicitis of the residual cecal appendix after eFTR of an appendicular adenoma (1/58.2%). Minor bleeding at the eFTR site (2/58.3%). eFTR performed accidentally without proper prior deployment of the OTSC® (1/58.2%). There was no secondary perforation or eFTR-associated mortality.

Conclusion: In conclusion, after specific training, endoscopic full-thickness resection is a feasible, safe and promising resection technique. It allows complete resection of lesions affecting layers of the gut wall beneath the mucosa, without the risk of perforation. In the future, eFTR may become a valuable alternative to a surgical approach in cases where endoscopic resection was previously thought impossible.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0203 VASCULAR AND PIT-PATTERN ANALYSIS ACCORDING TO KUDO, SANO AND NICE CLASSIFICATIONS SIGNIFICALLY IMPROVES AFTER AN IMAGE-BASED TRAINING PROGRAM

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Introduction: Narrow Band Imaging (NBI) and chromoendoscopy with methylene blue are enhancing techniques which are helpful in differentiating vascular and pit patterns of colorectal neoplasms. Therefore, they have a key-role for the adequate management of the lesions which might be candidates for endoscopic resection.

Aims & Methods: The aim of our study was to measure the interobserver agreement and the diagnostic accuracy in an endoscopic unit using methylene blue and NBI for the evaluation of the pit and vascular pattern according to the Kudo, Sano and NICE classifications of colo-rectal neoplasms, before and after an image-based training program. We retrospectively collected consecutive endoscopic images (NBI and with methylene blue) of colo-rectal neoplasms from the internal database. The image set was then evaluated by our gold standard composed by two expert endoscopists. Their evaluation resulted confident with histology reports in 88% of cases. The images set was then evaluated by the 9 endoscopists of the unit, before and after a 30-minutes image-based training program on enhancing techniques and surface colorectal patterns. NBI and colonic neoplasms’ surface and vascular patterns. Interobserver agreement was calculated using the kappa statistic by Cohen. By using the gold standard evaluation as criterion standard, the accuracy of colo-rectal neoplasms’ evaluation before and after the training was also calculated using the McNemar test. A value of p < 0.05 was considered statistically significant.

Results: A total of 30 images were obtained (see Table). Before the training process, the interobserver agreement was minimal for Kudo (0.10 ± 0.03) and Sano (0.12 ± 0.04), and poor for the NICE classification (0.24 ± 0.05). Diagnostic accuracy was 0.33 ± 0.07, 0.54 ± 0.12 and 0.60 ± 0.10 for Kudo, Sano and NICE classifications, respectively. After the image-based training program, interobserver agreement moved to moderate for the Kudo classification (p < 0.0001) and to good for Sano and NICE classifications (p < 0.0001). Diagnostic accuracy increased significantly, too, with values of 0.60 ± 0.05, 0.76 ± 0.05, 0.80 ± 0.05 for Kudo, Sano and NICE classifications, respectively (p < 0.0001).

Disclosure of Interest: All authors have declared no conflicts of interest.
References

P0204 YIELD OF 2ND SURVEILLANCE COLONOSCOPY IN “INTERMEDIATE RISK” PATIENTS. COULD SURVEILLANCE INTERVALS BE REDEFINED?
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Introduction: Data regarding the yield of 2nd surveillance colonoscopy after index procedure findings of advanced colonic neoplasia (ACN) are limited. The yield of ACN at 2nd surveillance is associated with high risk index or 1st surveillance findings (1). However, previous studies are heterogenous and definition of ACN at 2nd surveillance might be increased as ACN is infrequently detected in this group. The objective of this study was to determine the safety of CSP in patients on antithrombotic medication. The safety of antithrombotic medication used during post-CSP bleeding in patients on antithrombotic medication (non-antithrombotic group). In the antithrombotic group, 106 patients with 283 polyps continued taking the antithrombotic medication; specifically, aspirin in 41 patients with 113 polyps, clopidogrel in 13 patients with 17 polyps, dual antiplatelet therapy (DAPT) in 13 patients with 18 polyps, antipatelet agents other than clopidogrel in 17 patients with 68 polyps, anticoagulant agents in 20 patients with 56 polyps, and antipatelet plus anticoagulant combination therapy in 2 patients with 11 polyps. Heperin bridging was used in 13 patients with 38 polyps. Post-CSP bleeding occurred in patients on other antiplatelet or anticoagulant agents, or on heparin bridging. Clipping after CSP was more likely used in the antithrombotic group (i.e., 13.5% vs. 4.6%; p < 0.01). No significant difference in post-CSP bleeding rate was observed between lesions with and without clipping (0% vs clipping vs. 0.34% without clipping; p = 0.55)
Conclusion: CSP is a safe procedure even in patients on antithrombotic medication; specifically, aspirin in one patient with one polyp (0.88%, 1/113), and aspirin and clopidogrel a patient with 2 polyps (11.1%, 2/18). No post-CSP bleeding occurred in patients on other antiplatelet or anticoagulant agents, or on heparin bridging. Clipping after CSP was more likely used in the antithrombotic group (i.e., 13.5% vs. 4.6%; p < 0.01). No significant difference in post-CSP bleeding rate was observed between lesions with and without clipping (0% vs clipping vs. 0.34% without clipping; p = 0.55)
Disclosure of Interest: All authors have declared no conflicts of interest.

P0206 OPTICAL ENHANCEMENT FOR THE IN VIVO PREDICTION OF COLORECTAL POLYP HISTOLOGY
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Introduction: Diminutive polyps are a common finding among surveillance colonoscopies without having high prevalence of advanced histology, making their standardized removal cost-, time- and risk-intensive. Based on these considerations, the American Society of Gastrointestinal Endoscopy (ASGE) proposed the so called PIVI statement, in which diagnostic thresholds are defined that new technologies used for the real-time assessment of colorectal polyp histology should meet. Optical enhancement (OE) is a novel endoscopic pre-processing optical filter technology, in which the spectrum of the emitted wavelengths is reduced, thereby leading to enhanced visualization of the mucosal and vascular pattern.
Aims & Methods: In this study we aimed to assess whether OE can accurately predict the histology of diminutive colorectal polyps according to the ASGE PIVI criteria. A total of 106 colorectal polyps from 49 patients undergoing diagnostic or surveillance colonoscopy were included. The in vivo histology prediction using OE was compared to results of histopathology as a reference standard.
Results: The overall accuracy of OE for real-time prediction of polyp histology was 94.3% with a sensitivity, specificity, positive (PPV) and negative prediction value (NPV) of 100%, 95.3%, 85.4% and 100%, respectively. When including only high confidence (HC) predictions, the accuracy of OE increased to 96.5%. Sensitivity, specificity, PPV and NPV were 100%, 94.5%, 91.2% and 100%, respectively. In distal colorectal polyps the accuracy was 93.3% with sensitivity, specificity, PPV and NPV being 100%, 91.3%, 80% and 100%, respectively. The post-polypectomy colonoscopy surveillance intervals were predicted correctly in ≥90% of patients with OE.
Conclusion: Optical enhancement allows to accurately predict the histology of diminutive colorectal polyps in vivo in real-time and meets the PIVI thresholds for resection and discarding endoscopic polyps without histological assessment and for leaving distal diminutive colorectal polyps in place. Hence, optical enhancement can potentially reduce time, risk and costs associated with removal and histopathological assessment of diminutive polyps.
Disclosure of Interest: All authors have declared no conflicts of interest.

P0207 BLUE LASER Imaging OPTICAL DIAGNOSIS OF COLORECTAL POLYPS: ACCURACY OF THE NICE, SANO AND WASP CLASSIFICATIONS
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Introduction: Blue Light Imaging (BLI) is a new image-enhanced endoscopic technique, meant, in association with magnification endoscopy, to help differentiate between neoplastic and non-neoplastic colorectal polyps. A variety of endoscopic classifications have been developed to guide optical diagnosis of colorectal polyps. The aim of our study was to evaluate NICE, WASP and Sano classifications for the optical diagnosis of colorectal polyps using BLI with and without magnification.

Aims: Between May 2014 and December 2015, 181 colorectal polyps in 65 patients were imaged and resected in our single center study. Each polyp was evaluated using white light endoscopy, BLI with and without magnification.

Conclusion: Our work suggests that BLI with magnification is a promising technique for the optical diagnosis of colorectal polyps with a diagnostic accuracy of 88%. Our study did not establish significant difference between the three classifications. However, the ASGE criteria for the implementation of the "resect and discard" strategy were met for the classifications of Sano and WASP with a negative predictive value for the diagnosis of adenoma beyond 90% in the resectosigmoid.

Disclosure of Interest: J. DREANIC: HOSPIRA Congress invitation
M. Barret: 3D Matrix scientific work, Life partners europe training sessions
M. Camus: Life partners europe, Medwork medical scientific work, Cook medical, Fujifilm France, Ipsi PHarma, Life partners europe, MSD, Olympus: training sessions.
M. Dior: Roche: congress invitation
B. Brieau: Amgen Ipsen pharma: congress invitation
S. Leblanc: Boston scientific, Medwork medical: scientific work, Ipsi Pharma, Olympus, Life partners europe: training sessions, Cook medical: Olympus congress invitation.

All other authors have declared no conflicts of interest.

References

P0208 AN INNOVATIVE 3D COLOSONOSCOPE SHAPE IMAGING SYSTEM BASED ON FIBER BRAG GRATING ARRAY
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Introduction: Colonoscopy is difficult procedure, largely due to unpredictable looping during insertion. If the endoscopist is able to see the colonoscope on the image display, fewer attempt is needed to straighten the shaft of the scope. A prototype Fiber Brag Grating (FBG) scope guided endoscopy provides a facility for continuous viewing on a monitor of the position of the colonoscope during examination.

Aims: The aim of this study was to evaluate the accuracy and feasibility of the innovative 3D Colonoscope using FBG. In the first part of the study, the FBG sensor was inserted into the working channel of a routine colonoscope in the first 70 cm from the tip of the scope. Then, the scope was placed in front of the monitor to confirm movement in all three dimensions. We evaluated loop formation such as N loop, alpha loop, reverse alpha loop, with the 3D imaging monitor. In the second part of the study, 5 patients underwent colonoscopy with a FBG sensor, the colonoscope can be displayed in anteroposterior or lateral view, or in both positions together. Fluoroscopy was used in all investigations for comparison.

Results: In the first part of the study, the results showed that the shape sensor was placed 90–150 mm from the tip of the scope. The average position error was 1.722 ± 1.678 mm, which corresponds to 1.50 ± 1.46% of the total length of the sensor. Scope movement and loops were detected correctly in all cases through the monitor. The prototype used in the second part of the study showed a high correlation and little discrepancy with the comparative findings at fluoroscopy.

Conclusion: Scope-guided endoscopy using FBG sensor can be successfully used to display colonoscope configuration. This flexible, thin and almost weightless shape sensor would be a novel technique for identification of colonoscope shape.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P0209 REAL-TIME MORPHOLOGIC CHANGE ON NUCLEI & MITOCHONDRIA OF CANCER CELL UNDER REVERSIBLE ELECTROPOREATION: DETECTED BY PROBE-BASED MULTIPHOTON MICROSCOPY
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Introduction: Irreversible electroporation (IRE) is a promising novel technique for tumor ablation using energy current pulses. IRE can effectively remove unordered cells without thermal damage surrounding normal tissues. Multiphoton microscopy for evaluated the response of cancer cell to IRE ablation and found apoptotic process after applying IRE.

Aims: By using multiphoton (MP) probes, that is ABI-Nu for nucleus and PMT for mitochondria, we were focusing on these two vital intra-cellular organelles for examining the real-time phenomenon of IRE-induced apoptosis. The study was conducted in three stages. Colon cancer cell lines and normal colon mucosa and colon neoplasm tissues obtained during colonoscopic biopsy from 10 patients were stained with multi-photon (MP) probes that is ABI-Nu for nucleus and PMT for mitochondria. We evaluated the feasibility of using multiphoton microscopy (MPM) to observe IRE response. First, the IRE responses of colon cancer cell lines were compared before and after IRE. Electrical pulses were administered with a Harvard apparatus, and the changes in the intensity of the nucleus and mitochondria were observed with time. The second, the IRE response of normal colon and colon cancer tissue obtained from same patient were evaluated before and after IRE same with previous method. Also, in order to determine whether IRE induced apoptosis, membrane blebbing of colon cancer cell lines were examined after apply IRE.

Materials & Methods: By using multiphoton (MP) probes, that is ABI-Nu for nucleus and PMT for mitochondria, we were focusing on these two vital intra-cellular organelles for examining the real-time phenomenon of IRE-induced apoptosis. The study was conducted in three stages. Colon cancer cell lines and normal colon mucosa and colon neoplasm tissues obtained during colonoscopic biopsy from 10 patients were stained with multi-photon (MP) probes that is ABI-Nu for nucleus and PMT for mitochondria. We evaluated the feasibility of using multiphoton microscopy (MPM) to observe IRE response. First, the IRE responses of colon cancer cell lines were compared before and after IRE. Electrical pulses were administered with a Harvard apparatus, and the changes in the intensity of the nucleus and mitochondria were observed with time. The second, the IRE response of normal colon and colon cancer tissue obtained from same patient were evaluated before and after IRE same with previous method. Also, in order to determine whether IRE induced apoptosis, membrane blebbing of colon cancer cell lines were examined after apply IRE.

Results: MPM images of cancer cells stained with MP probes revealed that ABI-Nu for nucleus and PMT for mitochondria, we were focusing on these two vital intra-cellular organelles for examining the real-time phenomenon of IRE-induced apoptosis. The study was conducted in three stages. Colon cancer cell lines and normal colon mucosa and colon neoplasm tissues obtained during colonoscopic biopsy from 10 patients were stained with multi-photon (MP) probes that is ABI-Nu for nucleus and PMT for mitochondria. We evaluated the feasibility of using multiphoton microscopy (MPM) to observe IRE response. First, the IRE responses of colon cancer cell lines were compared before and after IRE. Electrical pulses were administered with a Harvard apparatus, and the changes in the intensity of the nucleus and mitochondria were observed with time. The second, the IRE response of normal colon and colon cancer tissue obtained from same patient were evaluated before and after IRE same with previous method. Also, in order to determine whether IRE induced apoptosis, membrane blebbing of colon cancer cell lines were examined after apply IRE.

Conclusion: Here, we observed using MPM that nuclear staining occurred quickly due to increased cell membrane permeability and bleb was formed after electric pulse exposure. These results are expected to challenge the understanding of the
permeability process after IRE by providing the real-time images. Additionally, MRA can also serve in pancreatitis assessment and monitoring, e.g., with Annexin V FITC and PI staining. This MP probe protocol would dramatically increase the accuracy of diagnostic techniques by providing in vivo cell images.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0211 LARGE (>30MM) POLYP ENDOSCOPIC MUCOSAL RESECTION: OUTCOMES AND PREDICTORS OF SUCCESS
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Introduction: Endoscopic mucosal resection (EMR) is an established therapeutic option for large (>30 mm) colonic polyps. We aimed to assess characteristics and outcomes of this cohort. Primary outcomes consisted of rates, predictors and durability of EMR success, whilst secondary outcomes included complications, malignant risk, and conversion to surgery.

Aims & Methods: We prospectively identified patients referred for large polyp EMR from a polyp multidisciplinary team meeting between August 2008–2016 in a district general hospital with tertiary EMR expertise. Data on demographics, polyp site, morphology, size, accessibility (SMA), histology and follow-up endoscopy were retrospectively collected. Binary logistic regression modelling was performed using SPSS, with components comprising of year, individual SMA components, and histology. The Kaplan-Meier approach was used to measure durability of EMR success.

Results: Large polyp EMR was performed in 91 patients out of 125 MDT referrals (73%). Patients had a median age of 72 (interquartile range [IQR] 14.4), and were predominantly male (60%). Polyps were sessile (46%), flat (49%) or pedunculated (4%), with a median size of 40 mm (IQR 20.5 mm), and were left-colon in 81%. Bleeding occurred in 16.5%, all of whom achieved haemostasis. The 30-day complication rate was 1.1% (delayed bleeding in 1 patient), 54 (59%) were fully resected in one session, with overall EMR success in 75 (81.5%) after an average of 1.5 sessions. On multivariable analysis, significant predictors of complete resection at first attempt (Table 1) included: increasing year, sessile vs. flat morphology, and non-malignant histology. Malignant histology (p < 0.001) predicted overall EMR failure, but not age, gender, year of EMR, SMSA score, or concomitant argon plasma coagulation. Of the EMR failure group, 11/16 (69%) underwent surgical resection, of which 7/11 (64%) harboured adenocarcinoma. Of the 25 R0 EMR success group, 4/25 were malignan polyps with R0 endoscopic resection. The overall malignant histology rate in this cohort was 11/91 (12%). In this cohort, the R0 EMR success rates was 4/11 (36%), with no recurrence after 60 months of follow-up. The overall 12-month recurrence rates following complete EMR was 1.5%, with no significant factors affecting EMR durability identified.

Table 1: Predictors of complete resection on first EMR attempt. p-values derived from bivariate regression, with bold values significant if <0.05. Increase in OR for each increase in year. **p-value < 0.05 considered statistically significant.

<table>
<thead>
<tr>
<th>Factor</th>
<th>Odds Ratio</th>
<th>95% Confidence Interval</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Year</td>
<td>1.41*</td>
<td>1.04–1.90</td>
<td>0.048**</td>
</tr>
<tr>
<td>Size (3–3.9 cm vs. &gt;4.0 cm)</td>
<td>2.96</td>
<td>0.85–10.3</td>
<td>0.088</td>
</tr>
<tr>
<td>Site (left vs. right colon)</td>
<td>0.46</td>
<td>0.99–2.48</td>
<td>0.367</td>
</tr>
<tr>
<td>Access (easy vs. difficult)</td>
<td>1.39</td>
<td>0.38–5.14</td>
<td>0.619</td>
</tr>
<tr>
<td>Morphology (sessile vs. flat)</td>
<td>3.38</td>
<td>1.04–11.00</td>
<td>0.043**</td>
</tr>
<tr>
<td>Non-malignant histology</td>
<td>41.5</td>
<td>3.74–461</td>
<td>0.002**</td>
</tr>
</tbody>
</table>

Conclusion: Large polyp EMR is a safe and effective alternative to surgical resection of large polyps. Endoscopist experience, polyp morphology, and benign histology are important complete predictors at index EMR. Further data are required to evaluate the longer-term outcomes of malignant polyps.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0212 PROSPECTIVE RANDOMIZED CONTROLLED TRIAL COMPARING EFFICACY OF 1-L PEG-ASC WITH PRUCALOPRIDE AND 2-L PEG-ASC FOR BOWEL PREPARATION
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Introduction: Though numerous research has enabled decrease of the bowel preparation solution volume, it is still a major complaint of patients preparing colonscopy. There have been studied that additional administration of laxatives could lessen the amount of necessary formula with prokinetic effect. Prucalopride is a serotonin (5-HT4) receptor agonist which stimulate colonic mass movements and provide main propulsive force for defecation.

Aims & Methods: The aim of this study is to compare 2-L PEG-Asc and 1-L PEG-Asc plus prucalopride while preprey for quality of bowel cleansing while improving colonscopy and patient compliance. Two hundred patients were prospectively enrolled. Patients referred for colonscopy were divided into group A (the split-dose 2-L PEG-Asc) and group B (1-L PEG-Asc + prucalopride) randomly. During colonoscopy, each patient's bowel preparation quality was evaluated with The Boston Bowel Preparation Scale (BBPS) and Aronchick Preparation Scale (APS). The tolerability and satisfaction of patients was determined based on a questionnaire-based survey.

Results: One hundred patients received either 2-L PEG-Asc or 1-L PEG-Asc with prucalopride. Regarding colon cleansing outcome (BBPS and APS), the 1-L PEG-Asc with prucalopride group showed similar, but non-inferior results compared to the 2-L PEG-Asc group on both BBPS (7.65 ± 1.27 vs 7.52 ± 1.40, p = 0.586) and APS scales (93.1 ± 16.3 vs 95% ± 5.8%, p = 0.717). Tolerability was similar for both 1-L PEG-Asc with prucalopride and 2-L PEG-Asc.

Conclusion: 1-L PEG-Asc plus prucalopride preparation showed comparable result to traditional 2-L PEG-Asc preparation. 1-L PEG-Asc plus prucalopride preparation method could be an alternative method for bowel preparation which can relieve patient discomfort.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0213 IMPROVING SURVEILLANCE FOLLOW UP RATES AFTER COLONOSCOPY ENDOSCOPIC MUCOSAL RESECTION: A QUALITY IMPROVEMENT PROJECT
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Introduction: Endoscopic mucosal resection (EMR) is an effective and safe treatment for large (>20mm) laterally spreading colorectal lesions. Although colon EMR has been established as a minimally invasive technique for treatment of large colorectal lesions, risk of adenoma recurrence is the main limitation. Current guidelines recommend first follow-up at 3–6 months; however, there are no well-designed prospective-studies published establishing an optimal follow-up interval. Here, we evaluated the current scheduling process and developed strategies to standardize our endoscopy center practices.

Aims & Methods: Single tertiary referral center quality improvement project started in January 2017 and currently still in progress. We present here the interim data. Consecutive patients who had undergone or would have EMR of lesions ≥20mm were eligible for inclusion. The process of follow-up visits after EMR was divided at two levels: A dedicated team member reviewed follow-up patients who underwent EMR and would have follow-up visits. Evaluation of follow-up before EMR was generated a monthly report identifying patients who underwent colon EMR using our endoscopy procedure documentation program. The appropriate timeframe for follow-up after colon EMR was identified and orders and scheduling for the colonoscopy follow-up were carried out. Evaluation of follow-up: A dedicated team member reviewed the status of patients who underwent colon EMR six months prior to the start of the QI study. If patient did not show up on their scheduled follow-up, phone calls were placed to contact the patients. Patients who had followed-up with their local gastroenterologists were recorded. All the data in intervention group was compared retrospectively with nonintervention group who were not tracked through quality improvement process.

Results: Per-protocol 25 patients included in intervention group were compared to 60 patients in the nonintervention group. Mean age was 62 years in intervention group and 60 years in nonintervention group (p = 0.04). There were no differences in distribution in size of lesion, gender, EMR site, and polyp histology between two groups (Table 1). The mean follow-up time in intervention group was 8.2 months (±2.6) and nonintervention group was 10.4 months (±9.1). There was increase in rate of 6–9 months follow-up in intervention group when compared to the nonintervention group (88%, 95% CI [0.80%-0.94%] vs 64%, 95% CI [0.54%-0.73%]) (Table 1).

Table 1: Demographic, clinical characteristics, follow up rates

<table>
<thead>
<tr>
<th>Variables</th>
<th>Intervention group (n = 25)</th>
<th>Non-intervention group (n = 60)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, Mean (SD)</td>
<td>62 (8.7)</td>
<td>66 (10.5)</td>
</tr>
<tr>
<td>Sex, Male (%)</td>
<td>38% (10)</td>
<td>58% (35)</td>
</tr>
<tr>
<td>Size of polyp(mm)</td>
<td>35 (18)</td>
<td>30 (12)</td>
</tr>
</tbody>
</table>

(continued)
Table 1 Continued

<table>
<thead>
<tr>
<th>Variables</th>
<th>Intervention group (n = 25)</th>
<th>Non-intervention group (n = 60)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Site of polyp resection</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rectum</td>
<td>8% (2)</td>
<td>5% (3)</td>
</tr>
<tr>
<td>Sigmoid</td>
<td>4% (1)</td>
<td>7% (4)</td>
</tr>
<tr>
<td>Recto-sigmoid</td>
<td>0%</td>
<td>2% (1)</td>
</tr>
<tr>
<td>Descending colon</td>
<td>0%</td>
<td>3% (2)</td>
</tr>
<tr>
<td>Transverse colon</td>
<td>15% (4)</td>
<td>12% (7)</td>
</tr>
<tr>
<td>Hepatic flexure</td>
<td>15% (4)</td>
<td>8% (5)</td>
</tr>
<tr>
<td>Ascending colon</td>
<td>23% (6)</td>
<td>37% (22)</td>
</tr>
<tr>
<td>Mid ascending colon</td>
<td>0%</td>
<td>5% (3)</td>
</tr>
<tr>
<td>Cecum</td>
<td>23% (6)</td>
<td>13% (8)</td>
</tr>
<tr>
<td>Cecum with appendice orifice</td>
<td>8% (2)</td>
<td>0%</td>
</tr>
<tr>
<td>Ileoceleal valve</td>
<td>4% (1)</td>
<td>8% (5)</td>
</tr>
<tr>
<td>Polyp histology</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sessile serrated adenoma</td>
<td>23% (6)</td>
<td>30% (18)</td>
</tr>
<tr>
<td>Tubular adenoma</td>
<td>35% (9)</td>
<td>35% (21)</td>
</tr>
<tr>
<td>Tubular adenoma with HGD</td>
<td>8% (2)</td>
<td>2% (1)</td>
</tr>
<tr>
<td>Tubulovillous adenoma</td>
<td>31% (8)</td>
<td>32% (19)</td>
</tr>
<tr>
<td>Tubulovillous adenoma with HGD</td>
<td>4% (1)</td>
<td>0%</td>
</tr>
<tr>
<td>Adenocarcinoma</td>
<td>0%</td>
<td>2% (1)</td>
</tr>
<tr>
<td>Follow-up Rates</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median(range)</td>
<td>7.3 months</td>
<td>7.3 months</td>
</tr>
<tr>
<td></td>
<td>(6–15 months)</td>
<td>(6–66 months)</td>
</tr>
<tr>
<td>Mean (±SD)</td>
<td>10.4 months (9.1)</td>
<td>10.4 months (9.1)</td>
</tr>
<tr>
<td>Colon EMR follow-up rate of 6–9 months, % (n)</td>
<td>CI [0.8%–0.94%], CI [0.54%–0.73%], CI [0.8%–0.94%], CI [0.54%–0.73%], CI [0.8%–0.94%], CI [0.54%–0.73%], CI [0.8%–0.94%], CI [0.54%–0.73%], CI [0.8%–0.94%], CI [0.54%–0.73%], CI [0.8%–0.94%], CI [0.54%–0.73%], (22) (35)</td>
<td>(22) (35)</td>
</tr>
</tbody>
</table>

Conclusion: These preliminary results suggest significant improvement in SC1 compliance with our intervention. We believe that continuing these efforts and further refining the intervention process, requiring less personnel resources, may be helpful to improve the follow-up time until 3–6 months interval while also enduring as a sustainable change for our practice.

Disclosure of Interest: M.B. Wallace: Michael Wallace reports grant support from Boston Scientific, Medtronic, Cosmo pharmaceuticals, and equity interest in iLumen. Dr Wallace is a consultant to Aries Pharmaceuticals and Lumendi Inc.

References

P0214 META-ANALYSIS SUGGESTS: INSPECT TWICE TO INCREASE RIGHT COLON ADENOMA DETECTION RATE
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Introduction: Missed adenomas in the right colon are of major concern for interval colon cancer (CRC) development. There is evidence from cohort and randomized controlled studies (RCTs) that a second examination of the right colon – either in direct view or in retroflexion- increases the diagnostic yield of the procedure. However, data are not accepted unanimously.

Aims & Methods: The aim of this meta-analysis was to examine the effect of a second, back-to-back mucosa inspection on the diagnostic yield of colonoscopy in the cecum and the ascending colon. We performed literature searches in MEDLINE to identify studies evaluating the effect of a second pass endoscopic examination on adenoma detection rate (ADR) and advanced adenoma detection rate (AADR) in the right colon. Study outcomes effect sizes were calculated using RevMan 5.3 software fixed or random effect model, as appropriate, and they are presented as OR[95% CI]. Heterogeneity was measured using the I2 statistics. Publication bias for publication bias was detected in the direct view arm of the analysis. As compared to a single pass, the second right colon inspection significantly increased ADR (1.31 [1.15–1.49], I2 = 49%). The effect size of ADR was higher in the direct view second pass arm (1.73 [1.41–2.12], I2 = 0%) as compared to the retroflexion arm (1.17 [1.06–1.29], I2 = 0%). Sensitivity analysis with removal of one study each time did not identify a single study responsible for the detected heterogeneity. Our analysis did not show significant increase in right colon AADR (1.5 [0.76–1.56], I2 = 0%) after the second exam.

Conclusion: In comparison to a single pass, the second inspection of the right colon either in direct view or with scope retroflexion increases ADR in this colon segment. However, results should be interpreted cautiously due to the small number of meta-analyzed studies with mixed indications populations, and the detected moderate levels of heterogeneity and risk for bias.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P0215 ENDOSCOPIC FULL-THICKNESS RESECTION FOR T1 EARLY RECTAL CANCER: A CASE SERIES (WITH VIDEO)
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2Interventional Endoscopy Center, I. Medizinische Klinik Und Poliklinik, Universität Erlangen-Nürnberg, Mainz/Germany
3Asst Rhodense, Gastrofarm Milanesa/Italy

Disclosure of Interest: P. Soriani: Speaker fees, speaking fees and honoraria: Boston Scientific, Medtronic, Cosmo pharmaceuticals, and equity interest in iLumen. Dr Wallace is a consultant to Aries Pharmaceuticals and Lumendi Inc.
# Rectal site | Endoscopic features | Positive Ueno's criteria after en bloc EMR | Indication to EFTR | Pre-EFTR staging | Histology following EFTR | Follow-up after EFTR
--- | --- | --- | --- | --- | --- | ---
1 | Distal | Tumor budding, excision margin, Kikuchi’s level, width of submucosal invasion | unfit for surgery (ASA IV) | T0, N0 | R0, full-thickness resection; histology negative for residual disease | Endoscopy, EUS, and CT negative at 3 and 12 months; Endoscopy and EUS negative at 18 months.
2 | Distal | Tumor budding, Haggitt’s level, excision margin, depth and width of submucosal invasion | refusing surgery (ASA II) | T0, N0 | R0, full-thickness resection; histology negative for residual disease | Endoscopy, EUS and CT negative at 6 and 12 months.
3 | Distal | Haggitt’s level, excision margin, depth and width of submucosal invasion | refusing surgery (ASA III) | T0, N0 | R0, complete submucosal resection but no muscularis propria layer in the specimen; histology negative for residual disease | Endoscopy, EUS and CT negative at 6 and 12 months.
4 | Proximal | Haggitt’s level, excision margin | unfit for surgery (ASA IV) | T1, N0 | R0, full-thickness resection; histology positive for adenocarcinoma | Endoscopy, EUS and CT negative at 6 and 12 months; Patient died for severe cardiac disease at 8\*\* follow-up month.
5 | Distal | Low tumor differentiation grade, excision margin | unfit for surgery (ASA IV) | T0, N0 | R0, full-thickness resection; histology negative for residual disease | Endoscopy, EUS and CT negative at 6 and 12 months.
6 | Distal | Tumor budding, excision margin, width of submucosal invasion | refusing surgery (ASA III) | T0, N0 | R0, complete submucosal resection but no muscularis propria layer in the specimen; histology negative for residual disease | Endoscopy, EUS and CT negative at 6 and 12 months.

### Table 1: T1 early rectal cancer features, indications to endoscopic full-thickness resection, and follow-up.

<table>
<thead>
<tr>
<th>Complex(n=27)</th>
<th>No complex(n=27)</th>
<th>P Univ.</th>
<th>Odds ratioUniv.</th>
<th>PMultiv.</th>
<th>Odds ratioMultiv.</th>
</tr>
</thead>
<tbody>
<tr>
<td>SEX, n(%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male Female)</td>
<td>16 (59.2) 11 (40.8)</td>
<td>49 (60.4) 32 (39.6)</td>
<td>0.910</td>
<td>0.95 (0.39-2.31)</td>
<td></td>
</tr>
<tr>
<td>AGE, n(%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;70 years old ≥70 years old</td>
<td>17 (63) 10 (37)</td>
<td>51 (63) 30 (37)</td>
<td>1</td>
<td>1.00 (0.41-2.46)</td>
<td></td>
</tr>
<tr>
<td>SMOKER, n(%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No Yes Former smoker</td>
<td>12 (44.4)</td>
<td>4 (14.8) 11 (40.8)</td>
<td>0</td>
<td>1</td>
<td>1, 8 (0.50-6.43) 1, 2 (0.46-3.12)</td>
</tr>
<tr>
<td>ANTICOAGULANT-ANTIAGGREGANT/COAGULATION DEFICIT, n(%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No Yes</td>
<td>22 (81.4) 5 (18.6)</td>
<td>61 (75.3) 20 (24.7)</td>
<td>0</td>
<td>0</td>
<td>70 (0.23-2.07)</td>
</tr>
<tr>
<td>BODY MASS INDEX (obese), n(%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;30 ≥30</td>
<td>22 (81.4) 5 (18.6)</td>
<td>72 (88.9) 9 (11.1)</td>
<td>0.510</td>
<td>1.82 (0.55-6.00)</td>
<td></td>
</tr>
<tr>
<td>BODY MASS INDEX (overweight), n(%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;25 ≥25</td>
<td>10 (37) 17 (63)</td>
<td>36 (44.4) 45 (55.6)</td>
<td>0.500</td>
<td>1.36 (0.56-3.33)</td>
<td></td>
</tr>
<tr>
<td>ANESTHETIC RISK, n(%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low (ASA I-II) High (ASA III)</td>
<td>18 (66.6) 9 (33.3)</td>
<td>59 (72.9) 22 (27.1)</td>
<td>0.539</td>
<td>1.34 (0.53-3.43)</td>
<td></td>
</tr>
<tr>
<td>PREVIOUS COLORECTAL SURGERY, n(%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No Yes</td>
<td>23 (85.2) 2 (7.4)</td>
<td>68 (84.0) 13 (16.0)</td>
<td>0.261</td>
<td>0.418 (0.09-1.99)</td>
<td></td>
</tr>
<tr>
<td>CO2 insufflation, n(%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No Yes</td>
<td>15 (55.6) 6 (44.4)</td>
<td>16 (19.8) 68 (80.2) &lt;0.001</td>
<td>5.08 (1.99-12.94) 0.030</td>
<td>6.34 (1.20-33.57)</td>
<td></td>
</tr>
<tr>
<td>Size, n(%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;3.5 mm ≥3.5 mm</td>
<td>10 (37) 17 (63)</td>
<td>59 (72.8) 22 (27.2)</td>
<td>0.001</td>
<td>4.56 (1.81-11.46) 0.025</td>
<td>5.74 (1.26-25.33)</td>
</tr>
<tr>
<td>LOCATION, n(%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right Colon Left Colon Rectum</td>
<td>7 (63.5) 5 (18.5) 5 (18.5)</td>
<td>55 (67.9) 17 (21) 9 (11.1)</td>
<td>0.932 0.342</td>
<td>1.05 (0.3-3.2) 0.56 (0.1-1.8)</td>
<td></td>
</tr>
</tbody>
</table>
A CT scan was performed in the 2 patients requiring 100mcg of fentanyl, showing serositis in 1 patient and no abnormalities in the other. Both patients were admitted and managed conservatively (discharge day 6 and 2 respectively). The other 5 patients were discharged home on the same day after extended recovery. Predictors of PP were lesion size ≥45 mm (P = 0.003), Paris classification (P = 0.02) and intra-procedural bleeding requiring endoscopic control (IPB, P = 0.042). Lesion size ≥45 mm and IPB were also independent variables on multivariate analysis with an odds ratio of 2.8 (95% confidence interval 1.3–6.3, p = 0.012) and 2.3 (95% confidence interval 1.0–5.2, p = 0.042 respectively (Table 1).

Conclusion: Pain after EMR occurs in 20% of patients and is associated with larger lesion size and intraprocedural bleeding requiring endoscopic control in a multivariate analysis. If pain subsides after parenteral acetaminophen and does not recur the patient can be safely and confidently discharged to the step down recovery area and after medical review allowed to leave hospital. PP despite parenteral acetaminophen heralds a more serious scenario and imaging should be considered when stronger analgesics do not relieve the pain.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0218 QUALITY OF SINGLE-SESSION COLONOSCOPIC EXAMINATIONS INTENDING TO REMOVE ALL NEOPLASTIC POLYPS USING COLD POLYPECTOMY IN OUTPATIENT SETTING: RESULTS FROM CLINICAL PRACTICE DATA OF SINGLE CANCER CENTER HOSPITAL IN JAPAN


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Introduction: Some high-quality, large-scale cohort studies proved removals of colorectal neoplasms achieved prevention of colorectal cancer incidence and deaths. We introduced a strategy of removing all neoplastic polyps in single session colonoscopic examinations using cold polypectomy was started.

Aims & Methods: The aim of this retrospective study was to investigate about achievement of colorectal polyp remove in our clinical practice setting. Scheduled colonoscopic examinations for 40–79 years outpatients who had at least one colorectal neoplasm between January 2015 and December 2016 were collected from our endoscopic data base. Exclusion criteria were as follows: patients who had colorectal neoplasm larger than 20 mm, pre-examination of colorectal surgery or endoscopic submucosal dissection, inflammatory bowel disease, familial adenomatous polyposis, uncontrolled malignancies, by trainee endoscopists (<500 colonscopies), no agreements of polyp removal, and/or patients with continuation of anti-thrombotic agents. Outcome measurements were polyp removal rate (per-lesion analysis), complete polyp removal rate (per-patient analysis) and complications. Proportions of each endoscopic removal method according to size were also analyzed.

Results: A total of 2527 patients (mean age 66.8 ± 7.9 years) with 8203 colorectal neoplasms (CRNs) (7657 adenomas, 423 serrated polyps and 105 Tis and T1 cancers) who met inclusion and exclusion criteria were analyzed. Mean number of CRNs per patients was 3.2. Mean size was 4.7 (±2.9) mm. Polyp removal rates were 96.7% (8795/8203) and 94.7% (2394/2527), respectively. Post-polypectomy bleeding requiring endoscopic hemostasis occurred in 7 patients (0.27%) and all origins of bleeding were endoscopic mucosal resection (EMR) and hot snare polypectomy (HSP). Post electrocoagulation syndrome requiring admission was occurred in one patient (0.04%) after pre-cutting EMR. Mean procedure time was 27.4 ± (±13.3) min. Proportions of each endoscopic removal method according to size were presented in an attached table. In 1–4 mm CRNs, both cold snare polypectomy (CSP) (51.8%) and cold forceps polypectomy (CFP) (45.8%) for 1–4mm CRNs were main methods. In 5–9 mm CRNs, CSP was a leading method (73.8%) and EMR was the second one (24.1%). CRNs larger than 10 mm were almost removed by EMR (94.4%).

Disclosure of Interest: All authors have declared no conflicts of interest.
Disclosure of Interest: There are no disclosures of interest.

Proportions of each endoscopic removal method according to size

<table>
<thead>
<tr>
<th>Size (mm)</th>
<th>CFP</th>
<th>CSP</th>
<th>HSP</th>
<th>EMR</th>
</tr>
</thead>
<tbody>
<tr>
<td>1–4 (N = 5046)</td>
<td>45.8%</td>
<td>51.8%</td>
<td>0.5%</td>
<td>1.9%</td>
</tr>
<tr>
<td>5–9 (N = 2294)</td>
<td>0.6%</td>
<td>73.8%</td>
<td>15.2%</td>
<td>24.1%</td>
</tr>
<tr>
<td>10–20 (N = 612)</td>
<td>0%</td>
<td>4.9%</td>
<td>0.7%</td>
<td>94.4%</td>
</tr>
</tbody>
</table>

Conclusion: In our clinical practice setting, the polyp removal rates were satisfactory. A level ofSingolo single endoscopic examinations using cold polypectomy.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0219 META-ANALYSIS AND OWN EXPERIENCE IN THE TREATMENT OF RECTO-URETROGENITAL FISTULA USING THE OVER-THE-SCOPE CLIP (OTSC)

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2University Clinical Center Erlangen, Erlangen/Germany

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Introduction: The transmural OTSC is used to achieve a full-thickness, serosa-to-serosa apposition (emergency & elective cases) for closure of GI wall defects (perforation, leak, fistula) with reported mean closure rates of 62–100% (range 0–100%), depending on the size of perforation, type and nature of lesion and the endoscopists’ experience1-7. However, recto-uretrogenal fistulae are a particular type of fistula and are mostly leaky or fistula of chronic nature, rarely acute perforations with vital wound tissue. They may occur in Crohn’s disease, but can also be a consequence of abdominal surgery, traumatic lesions or post-radiation damage.

Aims & Methods: To further explore the role of the OTSC in this particular type of fistula we analyzed own cases and 21 reports from the literature dealing with any type of recto-uretrogenal fistula. In total, 25 patients, were identified with closure of a recto-uretrogenal fistula using the OTSC, but there was considerable heterogeneity, because of the fistula location (rectovaginal n = 2, rectovaginal n=10, rectourethral n = 7, rectourethral n=2, other rectal fistula n = 3).

Results: In most situations a previous interdisciplinary discussion was reported before an OTSC attempt, or patients refused to undergo re-operation. However, special characteristics of these leaks were reported to make more difficult the OTSC procedure compared with other GI locations, e.g. the site of the fistula is nearby located to L. dentata and anal sphincter, it includes a localization with nearby located to L. dentata and anal sphincter, it includes a localization with

Conclusion: In conclusion, recto-uretrogenal fistula may be a potential indication for OTSC application, after interdisciplinary consensus, when re-operation is avoided, to be deemed to be too risky or cumbersome. Although this type of fistula carries some difficulties because of little space, tissue tension and fibrous or postop changes, long-term success may be achieved in half of all patients. Further improvements should focus on increasing healing potential of the fistula or better after performing anastomosis creation (acrylic acid), to avoid postoperative recto-uretrogenal leaks.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P0221 ENDOSCOPIC SUBMUCOSAL DISSECTION (ESD) IN THE COLORECTUM: FEASIBILITY IN AN EUROPEAN SINGLE CENTER CASE SERIES

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31st Department Of Medicine, Ostall-Klinikum Aalen, Acad. Teaching Hospital University of Ulm, Aalen/Germany

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Introduction: While ESD in the upper GI tract is well established, it is as yet not standard of care in the colorectum. Contrary to Japan, western experience is limited and only relatively few case series have been published in Europe (e.g. Dessai et al. 2017).

Aims & Methods: For the period 5/2012-1/2017 the first fifty-one consecutive patients with colorectal (n = 18/17/16 rectum/left/right hemicolectomy) neoplasias (diameter ≤ 13 mm, ≥ 2 cm, high grade dysplasia: n = 18; serrated/submu-

Conclusion: In Spain, there is good compliance with the quality indicators of colonoscopies. All authors have declared no conflicts of interest.

Disclosure of Interest: There are no disclosures of interest.

References
Results: According to endoscopic or pathologic judgment resection was complete in 40 or 30 patients, respectively. During hospital follow-up (12–14; median 4 days) abdominal pain, fever or local peritonitis were noted in 6 and bleeding in 3 patients (hypotension in 1) with antibiotics/transfusions/surgery needed in 4/0 patients. There was no hospital mortality. Among those with histologic incomplete resection (n = 21), surgery or FTR was performed in 5 patients; endoscopic follow-up is pending in 7 and revealed no residual neoplasia in 9. Among those with cancelled ESD or endoscopic incomplete resection (n = 11), surgery or FTR was performed in 5, endoscopic follow-up is pending in 2 and revealed no residual neoplasia in 1.

Conclusion: After appropriate training, even in low volume European case series ESD in the colorectum appears to be safe and partially effective.

Disclosure of Interest: G. Kleber: Activity as tutor in ESD learning courses sponsored by Olympus Medical Systems, Hamburg, Germany. All other authors have declared no conflicts of interest.

References
Dessau A. et al. 2017; *Virchows Arch* 470:165

P0222 CLINICAL USABILITY QUANTIFICATION OF A REAL-TIME POLYP DETECTION METHOD IN VIDEOCOLONOSCOPY

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2Center Computer Vision, Universitat Autonoma de Barcelona, Barcelona/Spain
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Introduction: Colorectal cancer is the second leading cause of cancer death in US [1]. Its incidence can be mitigated by detecting its precursor lesion, the polyp, before it develops into cancer. Colonoscopy is still the gold standard for colon screening though some polyps are still missed. This can be explained by technical limitations of colonoscopes (camera orientation, field of view, etc.), but also by human factors (such as experience). Several computational systems, being the majority still-frame-based, have been proposed to assist clinicians in this task [2] but, to the best of our knowledge, none of them is being used in the exploration before it develops into cancer. Coloscopy is still the gold standard for colon screening though some polyps are still missed. This can be explained by technical

Results:

<table>
<thead>
<tr>
<th>Method</th>
<th>PDR</th>
<th>MPT</th>
<th>MNFP</th>
<th>Proc</th>
<th>Rec</th>
<th>F1</th>
<th>RT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Texture (Local Binary Patterns) [3]</td>
<td>100%</td>
<td>162 ms</td>
<td>0.7</td>
<td>29.88%</td>
<td>34.96%</td>
<td>32.22%</td>
<td>45.9 (1.8 sec)</td>
</tr>
<tr>
<td>Shape (Haar features) [5]</td>
<td>100%</td>
<td>21 ms</td>
<td>0.6</td>
<td>39.14%</td>
<td>42.56%</td>
<td>40.78%</td>
<td>27.3 (1.1 sec)</td>
</tr>
<tr>
<td>Combination</td>
<td>100%</td>
<td>185 ms</td>
<td>1.0</td>
<td>30.72%</td>
<td>51.00%</td>
<td>38.34%</td>
<td>17.4 (0.7 sec)</td>
</tr>
</tbody>
</table>

Conclusion: Work presented in this abstract shows how a real-time still-frame-based polyp detection method can be successfully adapted to video analysis. Clinical usability metrics along with a new fully annotated video database were introduced to completely assess method performance. Results show methodology potential regarding clinical deployment as it detects different polyps with a small RT. Results show that the sole use of shape features allows to meet real-time constraints but that a combination with a computationally efficient texture descriptor might improve frame-based performance.

Disclosure of Interest: X. Dray: Xavier Dray has received consultation fees from Covidien GI solutions.

P0223 REJECT AND DISCARD/DIAGNOSE AND DISREgard STRATEGY FOR COLONIC POLYPS: ARE WE READY TO START IT?


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Introduction: The use of Narrow Band Imaging (NBI) technology for in vivo histological prediction of colon polyps presents high accuracy in Referral Centers, particularly for diminutive polyps, which could be managed by the “reject and discard” strategy and, for sigmoid and rectum polyps, the “diagnose and disregard” strategy. However, the applicability of this practice in Community Hospitals still needs to be determined.

Aims & Methods: We aimed to determine the accuracy of NBI in predicting histology, according to NICE and WASP classifications, in a Center without previous NBI experience. This was a prospective study including patients submitted to colonoscopy between June 2016 and July 2017. Polyps characteristics: location, size, morphology (Paris Classification), NICE/WASP classification (hyperplastic, sessile serrated, adenoma, invasive carcinoma) and degree of confidence (low: <90% vs. high ≥90%). Comparison between NBI classification and histology SPSS 23.

Results: 163 polyps included (71 patients); mean polyp dimension of 6.1 mm (61.3% <5 mm); 91.4% sessile polyps; 62.6% on the left colon. Polyps classification according to NICE/WASP vs. histology: hyperplastic 49.7% vs. 42.9%; sessile serrated polyps 4.9% vs. 9.8%; adenoma 44.2% vs. 43.6%; carcinoma 1.2% vs. 0%; inflammatory reaction on histology – 3.7%. Adenoma diagnosis using NICE/ WASC classification presents an accuracy, sensitivity, specificity, positive predictive value and negative predictive value of 80.9%, 78.1%, 84.2%, 85% and 77.1%, respectively. For left colon <5 mm (n = 61) the accuracy and negative predictive value were of 81.2% and 82.3%, respectively, with 79.4% high confidence classifications. Multivariates analysis showed that high confidence predictions and ≥2 polyps/exam had a significant association with correct NBI classification (p < 0.05).

Conclusion: NBI utilization by inexperienced endoscopists presented moderate acuity in histological prediction. Despite promising results, acuity and confidence levels were lower than the thresholds recommended in guidelines (≥90%). These results justifying implement additional training and monitoring.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
P0224 THE EFFICACY AND SAFETY OF JUMBO FORCEPS BIOUS USING NARROW-BAND IMAGING ENDOSCOPY IN PATIENTS WITH DIMINUTIVE POLYPS

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Introduction: Cold forces polypectomy (CFP) is commonly used to remove diminutive colorectal polyps (~5mm). In addition, jumbo biopsy forceps are superior to standard forceps for removing colorectal polyps. However, problems remain for CFP with regard to residual adenomatous tissue on histological evaluation after a complete endoscopic cold forceps polypectomy.

Aims & Methods: The aim of this study was to evaluate the efficacy and safety of jumbo forceps biopsy using narrow-band imaging endoscopy in patients with diminutive polyps. In addition, we evaluated the factors related to one-bite resection.

Results: A total of 503 patients were prospectively assessed, and 1015 polyps were resected. The median age of the patients was 65 years. The patients comprised 329 men (65%) and 174 women (35%). The polyp morphologies were 0-Ia lesions in 242 cases (48.2%), 0-IIa lesions in 65 cases (12.9%), 0-Isp lesions in 63 cases (12.5%), and 0-IIsp lesions in 53 cases (10.5%). The complete resection rate was 99.3%. The rate of one-bite polypectomy was 71.8%, which included rates of 100%, 91.5%, 81.8%, 56.9%, and 40.5% for lesions 1, 2, 3, 4, and 5 mm in diameter, respectively. Delayed bleeding that required endoscopic hemostasis occurred in only one case, but no other adverse events occurred. The most important factor related to one-bite polypectomy was polyp size (~5 mm; OR: 5.58), followed by macroscopic type of polyps (non-Ia; OR: 1.95).

Conclusion: This study revealed the diagnostic characteristics of depressed-type colorectal lesions. In contrast, the depressed-type lesions were observed as EC3a (38.9%) and VI or VN pit patterns corresponding to carcinomas. As for endocytoscopy, depressed-type cancers have been revealed, which are considered to emerge from the adenoma-carcinoma sequence theory that has been in the mainstream. This "adenoma-carcinoma sequence" theory has been in the mainstream, which has been in the mainstream. This "adenoma-carcinoma sequence" theory has been in the mainstream, which has been in the mainstream. This "adenoma-carcinoma sequence" theory has been in the mainstream, which has been in the mainstream. This "adenoma-carcinoma sequence" theory has been in the mainstream, which has been in the mainstream. This "adenoma-carcinoma sequence" theory has been in the mainstream, which has been in the mainstream. This "adenoma-carcinoma sequence" theory has been in the mainstream, which has been in the mainstream. This "adenoma-carcinoma sequence" theory has been in the mainstream.
Digestive symptoms 5.8 (165/2832) 13.1 (5.8–29.6)

CRCDR

Direct screening 14.9 (82/550) 1.2 (0.9–1.5) 0.177 1.3 (1.1–1.8) 0.023

Results:

noscopy indication adjusted by sex, age, cecal intubation, adequate cleansing included in the QUALISCOPIA project, an observational, multicenter and prospective (AADR) and colorectal cancer detection rate (CRCDR) depending on the indication.

Introduction:

It remains unknown if colonic lesions detection rates as quality indicators of the colonoscopy, behave in the same way in relation to colonoscopy positive fecal immunochemical test (FIT).

TABLE 1

<table>
<thead>
<tr>
<th>ADR</th>
<th>% (n)</th>
<th>OR (95%CI)</th>
<th>p-value</th>
<th>aOR# (95%CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Post-polypotomy surveillance</td>
<td>49.3 (629/1275)</td>
<td>2.5 (2.2–2.9)</td>
<td>&lt;0.001</td>
<td>2.2 (1.9–2.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>FIT+</td>
<td>54.0 (928/1718)</td>
<td>3.0 (2.7–3.4)</td>
<td>&lt;0.001</td>
<td>3.0 (2.6–3.4)</td>
<td>0.001</td>
</tr>
<tr>
<td>Direct screening</td>
<td>31.6 (174/550)</td>
<td>1.2 (1.0–1.5)</td>
<td>0.085</td>
<td>1.4 (1.1–1.7)</td>
<td>0.005</td>
</tr>
<tr>
<td>Detrictive symptoms</td>
<td>28.0 (79/2832)</td>
<td>1.0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SDR</td>
<td>4.2 (53/1275)</td>
<td>3.5 (2.6–5.3)</td>
<td>&lt;0.001</td>
<td>3.4 (2.2–5.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Post-polypotomy surveillance</td>
<td>4.1 (52/1275)</td>
<td>3.5 (2.6–5.3)</td>
<td>&lt;0.001</td>
<td>3.4 (2.2–5.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>FIT+</td>
<td>1.9 (32/1718)</td>
<td>1.5 (0.9–2.5)</td>
<td>0.091</td>
<td>1.5 (0.9–2.5)</td>
<td>0.094</td>
</tr>
<tr>
<td>Direct screening</td>
<td>3.3 (18/550)</td>
<td>2.7 (1.5–4.8)</td>
<td>0.000</td>
<td>2.8 (1.6–5.0)</td>
<td>0.001</td>
</tr>
<tr>
<td>Detrictive symptoms</td>
<td>1.2 (35/2832)</td>
<td>1.0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AADR</td>
<td>23.1 (294/1275)</td>
<td>2.0 (1.7–2.4)</td>
<td>&lt;0.001</td>
<td>1.8 (1.5–2.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>FIT+</td>
<td>36.8 (632/1718)</td>
<td>4.0 (3.4–4.6)</td>
<td>&lt;0.001</td>
<td>3.9 (3.3–4.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Direct screening</td>
<td>14.9 (82/550)</td>
<td>1.2 (0.9–1.5)</td>
<td>0.177</td>
<td>1.3 (1.1–1.8)</td>
<td>0.023</td>
</tr>
<tr>
<td>Detrictive symptoms</td>
<td>12.8 (362/2832)</td>
<td>1.0</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>CRCDR</td>
<td>5.8 (165/2832)</td>
<td>13.1 (5.8–29.6)</td>
<td>&lt;0.001</td>
<td>11.6 (4.7–28.7)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Aims & Methods: We aimed to evaluate the usefulness and safety of sSBE for therapeutic ERP in patients with surgically altered anatomy.

Aims & Methods: We aimed to evaluate the usefulness and safety of the SpyGlass system for diagnosis and treatment of bile-duct disorders in a large-volume center. All patients undergoing SOC in our department between January 2013 and May 2016 were retrospectively identified from a prospectively collected database. The baseline characteristics, including age, gender, presenting symptoms, indication and others were recorded. Procedure-related parameters of SOC for detecting malignant lesions and the stone clearance rate were calculated.

Disclosure of Interest: All authors have declared no conflicts of interest.
P0230 DIAGNOSTIC AND THERAPEUTIC ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAHY (ERCP) IN INFANT AND CHILDREN: A LARGE RETROSPECTIVE STUDY

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Introduction: Endoscopic retrograde cholangiopancreatography (ERCP) is increasingly being used in the diagnosis and management of biliary and pancreatic disorders in pediatric patients.

Aims & Methods: To evaluate the indications, success rate, diagnostic and therapeutic yields, and complications of ERCP performed in Chinese children. A retrospective study was conducted in an academic, tertiary care, medical center, in which all children undergoing ERCP between 2005 to 2016 were identified from endoscopy databases. Data on demographics, indication, ERCP findings, ERCP interventions performed and complications were collected.

Results: A total of 288 children (mean age 9.3 years, range 1 month to 18 years) underwent 312 ERCP procedures. General anesthesia and sedation were performed in 48% and 52% of procedures, respectively. Indications for ERCP included common duct obstruction (n = 153, 54.2%), recurrent or chronic pancreatitis (n = 64, 22.2%) and others. ERCP was successfully performed in 267 of 288 cases (92.7%). The most common ERCP findings was choledocholithiasis (n = 146, 50.7%). A therapeutic intervention was performed in 70.8% patients (n = 204), including sphincterotomy (n = 97), stone extraction (n = 55), and stent insertion (n = 52). Complications occurred for only 13 patients (4.5%), including 12 cases of post-ERCP pancreatitis and 1 case of bleeding. No severe pancreatitis, or perforation was noted.

Conclusion: Diagnostic and therapeutic ERCP is effective and safe in the children population, with the high rates of technical success and low rates of complication.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0231 ENDOSCOPIC RETROGRADE CHOLANGIOPANCRETOGRAPHY IN PATIENTS WITH SURGICALLY ALTERED GASTROINTESTINAL ANATOMY: 11 YEARS’ EXPERIENCE AT A LARGE CENTER IN CHINA

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Introduction: It is technically challenging to perform endoscopic retrograde cholangiopancreatography (ERCP) in patients with surgically altered gastrointestinal anatomy.

Aims & Methods: The aims of this study were to investigate the yield, efficacy and safety of ERCP in surgically altered anatomy patients at a single tertiary-care center with a high volume of endoscopy. All patients with altered surgical anatomy who underwent ERCP at our center from September 2005 to July 2016 were retrospectively reviewed. Data regarding to patients baseline characteristics, procedure-related details and adverse events was recorded and analyzed.

Results: A total of 304 procedures were performed in 236 patients, including 108 cases (45.8%) with Billroth II gastrectomy, 45 cases (19.1%) with Billroth I gastrectomy, 52 cases (22.0%) with hepaticoduodenostomy, 18 cases (7.6%) with esophagogastrostomy and 13 cases (5.5%) with Roux-en-Y reconstruction. The most common indication was cholelithiasis (58.1%, 137/236). The overall success rate of reaching the papilla was 90.8% (276/304), including 91.3% (126/138) for Billroth II gastrectomy, 94.5% (52/55) for Billroth I gastrectomy, 89.9% (71/79) for hepaticoduodenostomy, 100% (19/19) for esophagogastrastomy and 61.5% (8/13) for Roux-en-Y reconstruction. The clinical success rate was 88.2% (268/304). Therapeutic interventions were performed in 194 patients successfully, including stone extraction (n = 146), sphincterotomy (n = 44), stent placement (n = 57), papillary balloon dilation (n = 27) and mechanical lithotripsy (n = 25). The adverse event rate was 7.2% (17/236). Mild pancreatitis occurred in 3% (7/236) of cases, perforation occurred in 2.5% (6/236) of cases, and asymptomatic hyperamylasemia occurred in 1.7% (4/236) of cases.

Conclusion: ERCP can be performed in surgically altered anatomy patients with a high success rate.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0232 IMPACT OF HIGH DEFINITION, NEAR FOCUS-IMAGING AND SYNDROME REVERSIBILITY TOOL (SERT) AFTER COLORECTAL ENDOSCOPIC MUCOSAL RESECTION: A PROPENSITY SCORE ANALYSIS

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Introduction: Risk factors for colorectal adenoma recurrence after Endoscopic Mucosal Resection (EMR) such as size ≥20 mm, high grade dysplasia, use of argon plasma coagulation (APC) and intraprocedural bleeding (IPB), have been well documented in literature. However, it is unknown if the latest generation dual-focus (DF) colonoscopes ability to visualize subtle residual neoplasia, has improved the rate of complete EMR.

Aims & Methods: We aimed to examine the efficacy of the newer 190 colonoscopes versus standard 180 colonoscopes for complete resection of lateral spreading lesions (LSL) ≥20 mm. A secondary aim was to identify risk factors for recurrence and the applicability of the Sydney EMR recurrence tool (SERT score) in our cohort.

This was a single-center retrospective study of patients who underwent EMR with 180 or 190 colonoscopy series from 2010 to 2016. Lesions ≥20 mm resected in a piecemeal fashion and patients with a surveillance colonoscopy after index EMR were included. A propensity score approach with inverse probability weighting (IPW) was used to control potential confounders affecting adenoma recurrence. Each lesion was graded according to SERT score and associations with recurrence were analyzed.

Results: 291 patients met inclusion criteria for the study. The rate of adenoma recurrence at the EMR site was 23.3% for the 180 colonoscope cases and 25.2% for the 190 colonoscope cases. Odds ratio (OR) for recurrence with 190 series was 1.06 (p = 0.85). Adenoma size (p = 0.002) and concomitant need for supplemental APC (p < 0.001) were risk factors for recurrence. SERT > 0 lesions had a higher risk of recurrence during follow-up (OR 1.71; 95% CI 1.00–2.92; p = 0.048) and a higher cumulative incidence for recurrence. Conversely, SERT = 0 lesions reached a plateau for recurrence after 12 and 18 months in Kaplan Meier curves. Odds ratio estimates for 190 colonoscopy effect on adenoma recurrence at different stages of adjustment.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0233 INCIDENCE AND RISK FACTORS FOR PANCREATITIS IN EMERGENCY ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY: A PROSPECTIVE MULTICENTER STUDY

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Introduction: Pancreatitis, or perforation was noted.

Aims & Methods: The aims of this study were to investigate the yield, efficacy and safety of ERCP in surgically altered anatomy patients at a single tertiary-care center with a high volume of endoscopy. All patients with altered surgical anatomy who underwent ERCP at our center from September 2005 to July 2016 were retrospectively reviewed. Data regarding to patients baseline characteristics, procedure-related details and adverse events was recorded and analyzed.

Results: A total of 304 procedures were performed in 236 patients, including 108 cases (45.8%) with Billroth II gastrectomy, 45 cases (19.1%) with Billroth I gastrectomy, 52 cases (22.0%) with hepaticoduodenostomy, 18 cases (7.6%) with esophagogastrostomy and 13 cases (5.5%) with Roux-en-Y reconstruction. The most common indication was cholelithiasis (58.1%, 137/236). The overall technique success rate of reaching the papilla was 90.8% (276/304), including 91.3% (126/138) for Billroth II gastrectomy, 94.5% (52/55) for Billroth I gastrectomy, 89.9% (71/79) for hepaticoduodenostomy, 100% (19/19) for esophagogastrastomy and 61.5% (8/13) for Roux-en-Y reconstruction. The clinical success rate was 88.2% (268/304). Therapeutic interventions were performed in 194 patients successfully, including stone extraction (n = 146), sphincterotomy (n = 44), stent placement (n = 57), papillary balloon dilation (n = 27) and mechanical lithotripsy (n = 25). The adverse event rate was 7.2% (17/236). Mild pancreatitis occurred in 3% (7/236) of cases, perforation occurred in 2.5% (6/236) of cases, and asymptomatic hyperamylasemia occurred in 1.7% (4/236) of cases.

Conclusion: ERCP can be performed in surgically altered anatomy patients with a high success rate.

Disclosure of Interest: All authors have declared no conflicts of interest.
Aims & Methods: This study aimed to identify the incidence and risk factors for PEP in emergency ERCP. We performed a prospective study of 2078 cases under-going diagnostic and therapeutic ERCP at five Japanese institutions between April 2015 and May 2016. Exclusion criteria were active pancreatitis, cholecystectomy, choledocholithiasis, inability to approach a papilla, and inspection aimed at only the pancreatic duct (PD). Emergency ERCP indicated unscheduled inspections performed within and outside duty hours in this study. PEP was considered when two of the following three conditions were met: (1) serum amylase level more than three times the upper limit of the normal range in each institution, (2) continuous abdominal pain for over 24 hours, and (3) presence of pancreatici tis findings on computed tomography. The first study involved comparison of the incidence of PEP and its characteristics between emergency and elective ERCP. The second study involved determining the predictive risk factors for PEP in emergency ERCP using univariate and multivariate analyses.

Results: A total of 1677 cases were enrolled in this study. Study 1: PEP developed in 20 of 429 cases (4.7%) from the emergency group and in 101 of 1248 cases (8.1%) from the elective group. The incidence of PEP was significantly lower in the emergency group than in the elective group (odds ratio [OR]: 0.56, 95% confidence interval [CI]: 0.32–0.92, P = 0.017). Endoscopic sphincterotomy, stone removal, papillary balloon dilatation, and intraduodenal ultrasound sonography were performed significantly more often in the elective group than in the emergency group (P < 0.001). Placement of a biliary stent was significantly more common in the elective group than in the emergency group. In addition, the procedure time was significantly longer (P < 0.001) and the number of endoscopic biopsies who had more than five years of experience was significantly higher in the elective group than in the emergency group. In addition, the median number of reinterventions required to achieve treatment success was significantly higher for the elective approach (1 vs. 2 [IQR = 1–2], P = 0.003). Multivariable logistic regression analysis revealed that the algorithmic approach was the only variable associated with treatment success (OR = 0.64, p = 0.02) when adjusted for patient demographics, lab parameters and disease/WON characteristics.

Conclusion: A structured, algorithmic approach to endoscopic necrosectomy results in successful treatment outcomes.

Disclosure of Interest: R. Hawes: Consultant for Boston Scientific Corporation and Olympus America Inc., S. Varadarajulu: Consultant for Boston Scientific Corporation and Olympus America Inc. All other authors have declared no conflicts of interest.
Four patients in EST group and 6 patients in EPS group suffered PEP after the procedure. Both groups had similar rates of technical success (OR: 0.55; 95% CI: 0.33–0.92). Post-ERCP pancreatitis (PEP) was no significantly different in the two groups: 24/392 patients (6.1%) in the no-EBS group versus 37/339 (10.9%) in the EBS group (OR: 0.55; 95% CI: 0.33–0.92). Late complications were not significantly different in the two groups: 30/392 patients (7.6%) in the no-EBS group versus 29/339 (8.6%) in the EBS group (OR: 0.87; 95% CI: 0.49–1.58).

Results: 14 papers were assessed via full text for eligibility. 8 articles were excluded leaving 6 prospective studies (total of 711 patients). Technical success: The overall rate of biliary stent insertion was not significantly different: 384/392 (98%) in the no-EBS group versus 333/339 (98.7%) in the EBS group (OR: 1.05; 95% CI: 0.42–2.63). Early complications: The overall early AEs developed in 34/392 (11%) of patients without EBS versus 68/339 (20.1%) of patients who received EBS, with a significantly difference (OR: 0.12; 95% CI: 0.03–0.45). The rate of duodenal perforation was not significantly different: 3/392 (0.8%) in no-EBS group versus 4/339 (1.2%) in the EBS group (OR: 0.62; 95% CI: 0.29–1.36). Early complications that occurred in the overall late adverse events in the two groups: 50/251 patients (19.9%) in no-EBS group vs 38/201 subjects (18.9%) in the EBS group (OR: 0.93; 95% CI: 0.56–1.53). No significantly differences in stent occlusion (11.6% in no-EBS group in vs 11.4% in EBS group) (OR: 0.99; 95% CI: 0.67–1.48). No significantly differences in stent migration (4% in no-EBS group vs 5.5% - OR: 0.81; 95% CI: 0.29–2.25). No significantly differences in late cholangitis (2.0% in no-EBS group vs 0% in EBS group - OR: 1.83; 95% CI: 0.17–19.85). Long-term mortality was not significantly different (2.5% in EBS group and 2.9% in the EBS arm - OR: 1.18; 95% CI: 0.22–6.29).

Conclusion: Our meta-analysis showed no significantly differences in technical success and in PEP. In consideration of the significantly increase of the overall AEs in the EBS group, in particularity of the bleeding and cholangitis, the EBS seems not be recommended in patients not suitable to surgery undergone biliary stenting.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

PO237 ENDOSCOPIC PANCREATIC SPHINCTEROTOMY COMBINED WITH PANCREATIC DUCT STENT CAN EFFECTIVELY PREVENT RECURRENCE OF ACUTE RECURRENT Pancreatitis Caused by Biliary Microlithiasis — A Single-Center Study from Beijing, China

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Introduction: Acute recurrent pancreatitis (ARP) refers to a clinical entity characterized by episodes of acute pancreatitis which occurs on more than one occasion. Biliary microlithiasis plays an important role in the etiology of ARP.BILE sludge may induce acute pancreatitis as a consequence of transient papillary edema that can obstruct the pancreatic juice flow. The established treatments for ARP include endoscopic sphincterotomy (EST) and empirical cholecystectomy. However, EST may increase the morbidity of biliary reflux or cholecystitis recurrence. We hypothesized that endoscopic pancreatic sphincterotomy (EPS) can save the function of biliary sphincter and prevent the recurrence of ARP.

Aims & Methods: The aim of this study is to evaluate the effectiveness of EPS combined pancreatic duct stenting for preventing ARP caused by biliary microlithiasis. 67 patients with ARP from 2005 to 2016 were diagnosed as biliary microlithiasis by endoscopic retrograde cholangiopancreatography (ERCP), bile microscopy or intraductal ultrasonography (IDUS). The whole was divided into two groups according to endoscopic therapy by EST or EPS with pancreatic stent. Rate of pancreatitis recurrence, early complication of post ERCP pancreatitis, and late complication (3 months after treatment) which included cholangitis, cholecystitis or cholelithiasis were compared between the two groups.

Results: (1) 38 and 29 patients were included in EST and EPS group, respectively. The mean age and follow-up duration of EST and EPS groups were 48.4±15.1yrs, 45.7±26.5months and 45.6±15.2yrs, 24.1±26.3months, respectively. (vary from 2months to 115months). (2) The mean episodes of ARP in EST and EPS group before endoscopic therapy were 3.9±3.3 times and 7.9±11.8 times. (3) Four patients in EST group and 6 patients in EPS group suffered PEP after the endoscopic therapy (P=0.418). (4) 15 patients in EST group and 3 in EPS group suffered recurrent pancreatitis. The efficiency in EST group and EPS group is 68.4% and 89.6% respectively (P=0.039). (5) The incidence of late complications was 18.4% in EST group and 10.3% in EPS group (P=0.567).

Conclusion: EPS combined with pancreatic stent is a promising strategy to prevent recurrence of ARP due to biliary microlithiasis.

Disclosure of Interest: All authors have declared no conflicts of interest.
C.W. Kim, J. H. Chang, J.H. Kim, T.H. Kim, I. S. Lee, and S.W. Han. Size Disclosure of Interest: has the ability to alter more often the initial ERC diagnosis or management technology, providing increased sensitivity and specificity for visual impression that DC was an easier procedure compared to FC. Underwent DC (44.8%) the initial diagnosis and clinical management was altered under FC (9.1%) biopsy confirmed the endoscopic diagnosis, in contrast with 10 cases was performed in 29 cases respectively. Cholangioscopy-guided biopsies for cholangioscopy. Fiberoptic cholangioscope was used in 39 cases and digital cholangioscope digital scope.

Introduction: Since the emergence of the fiberoptic single-operator cholangioscopy, the sensitivity for detecting bile duct lesions has been increased and the diagnostic criteria and severity grading of acute cholangitis. Acute cholangitis is a life-threatening disease, and the emergency biliary drainage procedure is necessary for moderate or severe cases, according to TG13. In recent years, with an aging society, necessity to perform endoscopic retrograde cholangiopancreatoscopy (ERC/P) in elderly patients is increasing. However, few studies have examined the efficacy and safety of emergency ERC/P in super-elderly patients.

Aims & Methods: In this study, we examined the efficacy and safety of emergency ERC/P in super-elderly patients with moderate to severe acute cholangitis, according to TG13. We performed 178 emergency ERC/P procedures in 132 patients during 3 years (June 2014–December 2016). We determined patients >90 years as “super-elderly” and those <90 years as “non-super-elderly.”

Evaluation criteria included comorbidities, oral administration of anticoagulants, cause of cholangitis, ERC/P procedure (examination time, endoscopic biliary sphincterotomy (EST)) pre-cut papillotomy, treatment success rate, presence or absence of peripapillary diverticula and papilla after EST, seldinger dilation, ERC/P-related complications (bleeding, perforation, post-ERC/P pancreatitis, ERCP pneumonia, death within 30 days after ERC/P procedure), and anesthesia-related complications (blood pressure decrease, pulse reduction, respiratory depression).

Results: We examined 69 males (52.3%) and 63 females (47.7%). Women accounted for a larger proportion in the super-elderly group (71% vs. 41%). The average age was 92.5 years (range, 90–97) in the super-elderly group and 77.9 years (range, 50–89) in the non-super-elderly group. The super-elderly group comprised 54 ERC/P procedures (moderate, 32; severe, 22) against 124 ERC/P procedures (moderate, 104; severe, 20) in the non-super-elderly group, and severe cases observed in the super-elderly group were statistically significant (p < 0.001). Regarding comorbidities, chronic heart and renal failure were statistically dominant in the super-elderly group. However, no difference was seen in the proportion of other diseases and receiving anticoagulant medication between the two groups. The causes of acute cholangitis were common in both groups with common bile duct stone (46% vs. 46%), followed by malignant obstruction (9% vs. 12%) and benign stenosis (0% vs. 5%), but no difference was found. Regarding the ERC/P procedure, the examination time was longer in the super-elderly group (37.4 ± 28.1 min vs. 29.2 ± 24.0 min, p = 0.044), but there was no difference in the procedure success rate (93% vs. 97%, p = 0.24) and the presence of papipapillary diverticula. The patients were sedated using midazolam (MDZ) plus pentazocine (PTZ). The amount of anesthetic used was less in the super-elderly group (MDZ 2.2 ± 3.3 mg, p < 0.001, PTZ: 3.1 ± 5.4 mg, p = 0.005).

Regarding (i) ERC/P-related and (ii) anesthesia-related complications, these were higher in the super-elderly group ([i] 15% vs. 9%, p = 0.293, [ii] 17% vs 7%, p = 0.004). Regarding the need for intravenous or surgical treatment was required. Conclusion: Acute cholangitis in super-elderly patients was more likely to become severe and the complications were higher than that in non-super-elderly patients. When performing an emergency ERC/P procedure in super-elderly patients, we should particularly pay attention to developing complications in patients with moderate or higher acute cholangitis, according to TG13.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
included 20 patients with low-grade dysplasia (DBG) or high grade (DHG) lesions. The specimens were performed by a gastrointestinal pathologist, in relation to a residual adenomatous bud after endoscopic ampullectomy for ampullary adenoma. The lesions should extend to a maximum length of 20 mm in the CBD. Endoscopic retrograde cholangio-pancreatectomy (ERCP) was performed by the endoscopist (EMcision, UK) (effective power 10Watts, 30 s). Biliary or pancreatic ducts were placed at the end of the procedure. The primary endpoint was the rate of residual neoplasia at 12 months after surgery; 3) adverse events. The endpoints were: 1) residual neoplasia at 6 months after treatment; 2) rate of recurrence at the end of the procedure. The primary endpoint was the rate of residual neoplasia at 12 months; 3) adverse events. The results: The mean age (±SD) of 67 years (±11), with 12 men and 8 women were included. RFA was performed on average (±SD) 1.9 years (±3.5) after ampullectomy. The mean resected adenoma size (±SD) was 24.9 mm (±10.2), and 7 patients had adjacent duodenal mucosectomy at the time of ampullectomy. The histology of the resected ampullary adenoma was DBG for 7 patients, DHG for 12 patients, and in situ carcinoma for 1 patient. Lateral margins were not assessable in patients with adenocarcinoma. CBD recurrence was diagnosed predominantly on ERCP and/or endoscopic ultrasonography surveillance procedures with an estimated mean infiltration height (±SD) of 11.2 mm (±4.5). The passage of the RFA probe was judged to be easy in 100% of cases with visibility of the radio-paque markers judged satisfactory to very satisfactory in 80% of the cases. All patients included had RFA without any technical problems. All patients had biliary stent (4 SEMS 10 mm, 16 plastic stents 10 French) implanted following RFA (25%) had a pancreatic stent. The residual rate of DBG, DHG, invasive carcinoma at 6 months and at 12 months after treatment were 25% (5/20, DBG, carcinoma) and 45% (9/20, DBG, carcinoma) respectively. The adverse events were as follows: 4 benign pancreatitis all medically treated, 2 patients had angiocholitis requiring biliary stent replacement, 1 patient had an episode of unexplained spontaneously resolved abdominal pain (normal CT scan, colonoscopy and biological tests). At MI2, one patient presented with a biliary stricture resolved by dilation and a calibration biliary stent. Conclusion: Endobiliary RFA performed on residual endo-biliary dysplastic buds after ampullectomy is an alternative to surgery, with a rate 55% dysplasia eradication at 12 months. The postoperative follow-up was not performed due to the high rate of recurrence. Multiple RFA sessions may be proposed in case of incomplete results. Disclosure Interest: All authors have declared no conflicts of interest.

P0242 EXPERT VALIDATION OF A NOVEL MECHANICAL CUTTING PAPILLA

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Introduction: Simulation-based training has become an important pillar in competence and learning in medicine, especially in training novice endoscopists. Several simulators have been validated and implemented in training curricula pertaining gastrointestinal endoscopy. Surprisingly, limited data are available on simulators in ERCP training, despite the fact that ERCP seems to be an ideal simulation-based training model due to its technical complexity. The available simulators are difficult to implement in training settings due to the lack of realism or use of live animals or ex-vivo specimens. Recently, the Boilskosti-Chicago Cutting Papilla was validated and considered a realistic training model for our study group. A novel mechanical papilla has been designed allowing to train (precut) sphincterotomy. The mechanical papilla is inserted into the simulator. A specific alloy allows for electrical conduction and cutting of the material using standard sphincterotomes and needle knives.

Aims & Methods: The aim of our study was to determine the expert validity of this cutting papilla and its didactic value for training sphincterotomy, as judged by experts. Expert participants with more than 2500 ERCPs lifetime were invited to perform an endobiliary experiment and fill out a questionnaire on the realism of the sphincterotomy procedure and it’s didactic value.

Results: A total of 40 ERCP experts were included. All experts were men, originating from 16 different countries with a mean age of 49.6 years (range 37–65). All participants were gastroenterologists (92.5%), 3 participants were surgeons (7.5%). The mean number of years of endoscopic experience was 20.9 (range 10–40). Experts’ opinion on realism of performing a sphincterotomy was rated 6.98 on a ten-point Likert scale, resemblance of the performed maneuvers 7.60 and tactile feedback 6.78. When asked if the cutting was perceived as expected, experts rated 6.35 and the cutting result was rated 7.30 on a ten-point scale. The potential as a training tool of the cutting papilla in training surgeons was rated 3.93 on a four-point scale, and there was a high agreement among the experts to include the papilla in the training of novices (3.93 on a four-point scale).

Conclusion: This is the first mechanical papilla available for training sphincterotomy on the Boilskosti-Chicago ERCP Trainer and demonstrates good expert validity. ERCP experts highly appreciated. The shapes of ampullary adenoma were divided into three groups: long nose (L/N), meaning a long protrusion, Dome (D), meaning a hemisphere and X-ray images were magnified sequentially 5–10 times each. The eligibility criteria were: it must be naive papilla and both of BD and PD must be visualized. The cases with IAC were evaluated. The shapes of the ampulla were divided into three groups: long (cERCP) with contrast medium, which provides images of IAC and leads to infundibulotomy or precut. We propose advantage of conventional ERCP (cERCP) with contrast medium, which provides images of IAC and leads to evaluate the difficulties in cannulation. The aim of this study is to recognize the morphology of intra-ampullary bifurcation of bile duct (BD) and pancreatic duct (PD). Its variation allows refractory access to bile duct (BD). IAC has small cyst within ampulla regulated by Oddi’s sphincter, so the BD axis has changed via IAC. The cases with IAC may be more difficult to cannulate. IAC has small cyst within ampulla regulated by Oddi’s sphincter, so the BD axis has changed via IAC. The cases with IAC may be more difficult to cannulate.

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Disclosure of Interest: Cholecudocheo has been rarely recognized. We focus on intra-ampullary cholecdocheo with contrast medium for evaluating technical difficulty in ERCP.

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Disclosure of Interest: All authors have declared no conflicts of interest.

P0244 VISUALIZATION OF INTRA-AMPULLARY CHOLEDOCHOCELE WITH CONTRAST MEDIUM FOR ASSESSING TECHNICAL DIFFICULTY IN ERCP

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P0243 MEDICO-LEGAL CLAIMS IN GASTROINTESTINAL ENDOSCOPY DOES PROCEDURE RISK RELATE TO SUCCESSFUL OUTCOMES?

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Introduction: Complications in endoscopy can lead to adverse clinical events. The likelihood of developing a complication depends on the degree of risk associated with a certain procedure. It is generally noted that riskier the procedure larger is the chance for a complication and higher the likelihood for medico legal issues. This is relevant as in the event of the risk materialising, patients make seek legal redress. The aim of this study was to investigate the degree of success of medico legal claims based on the nature of the endoscopic procedure and the outcome of the claims.

Aims & Methods: The National Health Service Litigation Authority (NHSLA) database in U.K. was searched using a Freedom of Information request (F:2409) to identify all cases of diagnosed endoscopically notifiable endoscopic complications notified to the NHSLA between 2010/11 and 2014/15. The terms "Gastroscopy", "Sigmoidoscopy", "Colonoscopy", "PEG" and "ERCP" were used to search the database. They were then analysed for procedure type, characteristics and outcomes. StatsDirect statistical software was used for statistical analysis.

OUTCOME OF ENDOSCOPY CLAIMS

<table>
<thead>
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<th>PROCEDURE</th>
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<td></td>
</tr>
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<td>PEG</td>
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<td>19</td>
<td>12</td>
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<tr>
<td>Sigmoidoscopy</td>
<td>17</td>
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</tr>
<tr>
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<tr>
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Results: A total of 291 claims were notified to the NHSLA during this period. 107 (36.7%) of claims still remain ‘open’. Analysing outcomes by procedures reveals a success rate of 44%, 44%, 37%, 36% and 34% (rounded up to the nearest whole figure) for Gastroscopy, PEG, Sigmoidoscopy, ERCP and Colonoscopy claims respectively. There is no statistical difference between the proportions comparing Gastroscopy and Colonoscopy (StatsDirect software used).

Conclusion: A significant number of claims remain open leading to concern and worry among endoscopists. The impact on practitioners after a successful claim is unknown and merits further investigation. Procedures considered as dangerous like ERCP and Colonoscopy have the least successful claims. It is imperative that clinicians remain vigilant. Performing Gastroscopy is dangerous and so is undertaking a Percutaneous Endoscopic Gastrostomy. Endoscopists should tighten their approach to all procedures.

Disclosure Interest: All authors have declared no conflicts of interest.
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Results: There were cases of 1223 naive papilla out of 2226 cases in total. The
success rate to access BD with naive papillae was 97.7% (1195/1223) and overall
post-ERCP pancreatitis (PEP) was 1.3% (29/2226). The eligible patients were 908
(505 male and 403 female), among whom IAC was identified in 6.0% (54/908).
The prevalence of IAC in the L/N, D and F types were 8.9% (48/542), 1.2% (4/
339) and 7.4% (2/27), respectively. IAC was significantly higher in the L/N
(p 5 0.01) and F (p 5 0.05) types than in the D type. The choledochocele
shapes of Sp, Sh and Ov were 59.3%, 13.0%, 27.8%, respectively. The average
size was 8.1 mm (3.7–18.3) in diameter. The location of IAC in Ac and Ab were
63.0% and 37.0%. The IAC in Ab was found with L/N shape only. Patients of
53.7%(29/54) required GW placement on PD to access BD. IAC was alternatively seen on MRCP in 10%(3/30).
Conclusion: Choledochocele is rarely seen on even cERCP, in addition the visualization of IAC has been rarely reported. IAC could be actually visualized with
prudent contrast medium injection. Our results showed miscellaneous variations
in the intra-ampullary images. IAC would require refractory pursuit of the axis
alignment due to its unexpected pathway within ampulla to access BD. Moreover
6.0% prevalence of IAC should not be ignored. IAC can be one of the factor of
refractory cannulation. cERCP with focus on ampulla could the difficulty in
cannulation. On the other hand, WGC would not do. The previous randomized
control trials showed no difference to access to BD between WGC and cERCP.
However, both procedures still remained cases with refractory cannulation. It has
been reported that refractory cannulation might cause PEP1). Therefore careful
attention should be paid while passing through IAC to avoid PEP. According to
ampulla shapes, especially of L/N and F, cERCP would be recommended to
identify the presence of IAC. It will be a warrant strategy to choose.
Disclosure of Interest: All authors have declared no conflicts of interest.
Reference

P0245 ENDOTHERAPIES FOR DUCT-TO-DUCT BILIARY
ANASTOMOTIC STRICTURE AFTER LIVER TRANSPLANTATION
(BASALT STUDY GROUP): INTERIM ANALYSIS AND MEDIUMTERM OUTCOMES OF A RETROSPECTIVE NATIONWIDE ITALIAN
SURVEY
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Introduction: Most appropriate endotherapy of biliary anastomotic strictures
(AS) remains to be defined.
Aims & Methods: Aim is to retrospectively report the endotherapy for duct-toduct AS in 2013, procedure related complications and medium-term outcome
results in Italy. A questionnaire was sent to the Endoscopy Units working with
Italian Liver Transplantation Centers (BASALT study group).
Results: At present sixteen of the 19 Units (84%) returned the questionnaire.
Complete endotherapy data and follow-up are available for 182 pts. One-hundred and two patients have been treated with plastic multistenting (PM), 27 with
fully covered SEMS and 53 with single stenting (SS). Radiological success was
achieved in 144 pts (79%), i.e. 86% of PM, 89% of fully covered SEMS and 60%
of SS (p 5 0.01 vs PM). Recurrence occurred in 31 pts, i.e. 21% of pts in whom
radiological success was achieved: 11% of PM (p 5 0.0001 vs SEMS and
p 5 0.05 vs SS), 41% of fully covered SEMS and 17% of SS. After failure of
first-line endotherapy (36) or recurrence (31), patients were re-treated with
endotherapy (75%), surgery (21%) or percutaneous balloon dilation (3%); one
patient dropped out because of death unrelated to endotherapy. Second-line
endotherapy was PM for 26%, fully covered SEMS for 52% and SS for 22%
of pts and radiological success was achieved in 82% of them (in 86%, 89%, and
60% with PM, SEMS and SS respectively). Procedure-related complications
occurred in 7.8% (51/656), i.e. 2.6% pancreatitis (1 severe leading to death),
4.1% cholangitis and 0.9% bleeding. Overall clinical success was achieved in
83% after a median f-up of 25 mos and no need of surgery in 92% of patients.
Conclusion: Endotherapy is confirmed as the preferred first-line and rescue
option for AS. Progressive plastic multi-stenting is most frequently used. Single
stenting has suboptimal results and should be abandoned. Use of SEMS is effective, but recurrences seem to be frequent, although a larger patients’ sample
needs to be evaluated.
Disclosure of Interest: All authors have declared no conflicts of interest.

P0246 COMPARATIVE EVALUATION OF TWO PORCINE EX-VIVO
MODELS FOR TRAINING IN ENDOSCOPIC ULTRASOUNDGUIDED DRAINAGE OF PANCREATIC FLUID COLLECTIONS
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Introduction: EUS-guided Cysto-Enterostomy (EUCE), technique indicated for
drainage of symptomatic pancreatic pseudocysts and other peri-enteric fluid collections, requires specific skills for which dedicated models are needed. Based on
a compact EASIE model (Erlangen Active Simulator for Interventional
Endoscopy) we developed two ex-vivo porcine models of retrogastric cysts and
evaluated learning performance within the frame of a structured training
program.
Aims & Methods: The first model was made of porcine colon (i.e. ‘‘natural cyst’’),
and second one was made with an ostomy bag (i.e. ‘‘artificial cyst’’). All procedures were achieved with EUS scope under fluoroscopy. Both models were evaluated prospectively over a 2-days session involving 14 students and 5 experts.
Results: ‘‘Natural cyst’’ and ‘‘artificial cyst’’ were prepared respectively within 10
and 16.5 minutes (p ¼ 0.78). More than 10 EUCE procedures were done in each
model. Model grading (analogic scale) showed no significant difference for primary endpoint of global satisfaction (p ¼ 0.06). Regarding secondary endpoints,
difference was not significant for overall impression of realism (p ¼ 0.75) whereas
it was significant favoring ‘‘artificial cyst’’ in terms of ability to teach procedural
steps (p ¼ 0.01) and ease of puncture (p ¼ 0.03) because of less elasticity.
Moreover, experts considered ability to improve students’ proficiency superior
with ‘‘artificial cyst’’ (p ¼ 0.008)
Conclusion: Both ‘‘artificial and natural cysts’’ are efficient for EUCE training in
terms of global satisfaction. However, the ‘‘artificial cyst’’ model appears to
make procedure easier and better to teach procedural steps improving students’
proficiency. Larger applications of this model are needed to validate as a standard of training.
Disclosure of Interest: All authors have declared no conflicts of interest.

P0247 A COMPARATIVE STUDY OF SUCTION METHODS
DURING ENDOSCOPIC ULTRASOUND-GUIDED FINE-NEEDLE
ASPIRATION (CONVENTIONAL SUCTION VERSUS CAPILLARY
SUCTION)
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Introduction: Endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) is an established procedure for obtaining a pathological specimen. However, detailed techniques of EUS-FNA vary substantially across medical centers. There is a need to establish more efficient method for better diagnostic accuracy and adequate sample. In the present study, we investigated the suction method for collecting specimens by EUS-FNA.

Aims & Methods: The aim of our study was to compare conventional suction using a 20mL syringe and capillary suction during EUS-FNA. Patients who required suction for solid mass lesions were prospectively enrolled. We performed EUS-FNA with two needle passes and applied each pass of different techniques which were randomly allocated. The diagnostic accuracy, the quantity of samples (0-5.5 represents sufficient material for adequate for histological interpretation) and quality (sampling without degree of contamination, and the amount of blood (0-2.2 represents significant amount of blood) were compared between conventional suction and capillary suction. Further analysis was carried out in the patients with pancreatic cancer. For patients with negative EUS-FNA, surgical specimen evaluation, results of other diagnostic investigations and/or long term clinical follow-up (6 months) were used to establish the definitive diagnosis.

Results: During the study period, 96 patients underwent EUS-FNA were enrolled and 7 patients were excluded due to loss of follow-up. Finally 89 patients (averaged 68.5 y/o, M:F=47:42) were analyzed. There were 60 pancreatic lesions (42 pancreatic cancer, 6 neuroendocrine tumor, etc.), 17 lymph adenopathy, 6 sub-acute pancreatitis, 7; organizing pancreatic pseudocyst, 4; IPMN, 1). Adequate tissue sampling was successfully achieved in 97% (199/206). Of 199 patients with successful tissue sampling, sensitivity, specificity and accuracy for malignancy were 98% (175/179), 95% (19/20) and 97% (194/199). The diagnostic accuracy of PDC using by HE and PAS staining was 76% (129/170) (Class V 91; IV 36; III 6; IIb 2). Moreover, by using immunocytochemical staining, the accuracy of PDC was 98% (167/170) (Class V 112; IV 50; IIIb 5). In the cases of highly suspicious NET, all samples were stained by chromogranin A or synaptophysin and the diagnostic accuracy of NET was 100% (6:6). No procedure-related complications occurred.

Conclusion: EUS-FNA of a pancreatic mass with the CB method showed high accuracy for definitive diagnosis.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0249 DIAGNOSTIC EFFICACY OF ENDOSCOPIC ULTRASOUND-GUIDED FINE-NEEDLE ASPIRATION FOR A Pancreatic MASS USING THE CELL BLOCK METHOD WITHOUT RAPID ON-SITE CYTOLOGY

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Introduction: Endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) has been shown to be efficient for diagnosis of pancreatic masses. Only with smear method, however, its diagnostic efficacy may vary greatly depending on the amount of proficiency of cytopathologists. On the other hand, cell block (CB) method allows cytological and/or histological evaluation with hematoxylin and eosin (HE) staining and with immunostaining for serial sections if necessary.

Methods: The aim of this study was to evaluate the diagnostic efficacy of EUS-FNA for a pancreatic mass using the CB method without rapid on-site cytology retrospectively. A total of 206 patients with pancreatic masses (head: 87, body: 86, tail: 33) who underwent EUS-FNA using a GF-L240P or GF-U240P Olympus Medical Systems Ltd., Tokyo, Japan between June 2005 and November 2016 were included in this study. The needles used were 22/25G needles. At least two passes were made during the procedure (mean 3.0±0.9 passes). Adequate specimens were regarded to be those in which whitish flagging were macroscopically achieved. The samples were immediately fixed in 10% formalin and processed by the cell block method using sodium alginate. Rapid on-site cytology was not performed. All samples were stained by hematoxylin and eosin, periodic acid Schiff and Alcian-blue, and immunohistochemistry. All samples were reviewed by 8 cytopathologists.

Results: From March 2013 to January 2016, a total of 114 patients (57 in a S- group and 60 in the PTBD group) were included. There were no significant differences in technical success (100% vs. 100%, P=1.00), the mean number of needle passes (6.8 vs. 7.0, P=0.556), or complication (0% vs. 3.5%, P=0.496) between the S- group and the PTBD group. The S- and PTBD groups exhibited comparable outcomes with respect to cytologic diagnostic yield (91.2% vs. 93.0%, P=1.000), histologic diagnostic yield (87.7% vs. 88.0%, P=1.000), and needle malfunction (7% vs. 0%, P=0.118). The procedure time was significantly shorter in the S-group than in the PTBD group (32 vs. 39.7 min, P=0.001).

Conclusion: EUS-guided tissue acquisition using a 25G-core biopsy needle without a stylet did not decrease the diagnostic yield for malignancy and is associated with shorter procedure time.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0250 A COMPARATIVE STUDY BETWEEN EUS-GUIDED BILIARY DRAINAGE AND PERCUTANEOUS BILIARY DRAINAGE IN PATIENTS WITH MALIGNANT BILIARY OBSTRUCTION AND FAILED ERCP

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Introduction: Patients with malignant biliary obstruction conventionally undergo percutaneous transhepatic biliary drainage (PTBD) after failed endoscopic retrograde cholangiopancreatography (ERCP) (1). While PTBD is efficacious, it is associated with significant morbidity, such as bile leakage, bleeding, and pneumothorax, and involves uncomfortable external drainage (2). Endoscopic ultrasound-guided biliary drainage (EUS-BD) is a minimally invasive endoscopic treatment increasingly offered as a potential option for malignant biliary obstruction after failed ERCP (3). Although a recent meta-analysis reported better clinical efficacy and superior safety of EUS-BD when compared to PTBD (4), the definitive diagnostic accuracy of NET was 100% (6:6). No procedure-related complications occurred.

Aims & Methods: We aimed to compare efficacy and safety of EUS-BD to PTBD in patients with malignant biliary obstruction after failed ERCP at a single tertiary referral center from mainland China. From November 2011 through December 2015, consecutive patients undergoing EUS-BD or PTBD for malignant biliary obstruction after failed ERCP were included. Demographical, biochemical, and outcome data were registered for each group. The primary outcomes included technical success rate and incidence of complications, the secondary outcomes included clinical success rates and re-intervention rate.

Results: A total of 93 patients (mean age 68±13.5 years, 49 males) were included, 33 in the EUS-BD group and 60 in the PTBD group. Both groups were similar in terms of age, gender, baseline bilirubin and functional status. Technical success was achieved in 32 (97.1%) of 33 patients in the EUS-BD group and in 57 (95.0%) of 60 patients (p>0.05) in the PTBD group. The clinical success (juvenileileuc: reduction in serum bilirubin by 50% within the first month) was achieved in all patients with technical success (32,32, 100% EUS-BD vs. 57,57, 100% PTBD). Procedure-related complication rates were higher in the PTBD group (58, 31.6%: 5 bleeding, 5 catheter site infection, 4 bile leaks, 2 cholangitis, and 2 tube malfunction) than in the EUS-BD group (3, 9.4%: 2 bleeding and 1 cholangitis) (p=0.018). Rate of re-intervention appeared to be lower in the EUS-BD group (2, 6.3%: 2 stent occlusion) than in the PTBD group (17, 29.8%; 6 stent occlusion, 5 catheter site infection, 4 bile leaks, and 2 tube malposition) (p=0.009).

Conclusion: Despite similar high technical and clinical success rates compared with PTBD, EUS-BD was associated with reduced rates of procedure-related complications, required fewer re-interventions. EUS-BD seems to be a better alternative than PTBD for malignant biliary obstruction after failed ERCP.

Disclosure of Interest: All authors have declared no conflicts of interest.
PD0251 A PROSPECTIVE COMPARATIVE STUDY OF EFFICACY OF EUS GUIDED FNA VERSUS ERCP GUIDED BRUSH CYTOTOLOGY IN ATTAINMENT OF HISTOPATHOLOGY OF DISTAL CBD MASSES

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Introduction: Distal CBD masses have always been a diagnostic dilemma. They are difficult to diagnose with any modality used. Brush cytology under ERCP guidance was used until now and also intraductal biopsies were used. The yield was hardly around 60% using all together. We started doing EUS localization of these difficult to identify distal CBD masses and took FNA from them. We devised a protocol to see the results of EUS FNA and brush cytology in the diagnosis of these masses.

Aims & Methods: We aimed to study the efficacy of EUS guided FNA for obtaining tissue from distal CBD masses and comparing it to ERCP guided brush cytology from the same masses. 56 cases with distal bile duct mass with obstructive jaundice in the last 3 years were taken for the study. The protocol we followed first- EUS was done using a linear echoendoscope, mass was identified and FNA performed with a 25 G needle making 2 to 5 passes and material sent for cytology. Same patients subjected to ERCP. A wide papillotomy was performed and over the wire cytology brush was used and brush cytology was obtained. Two passes were made and material taken on a slide and sent for cytology after wet fixation.

Results: Total number of cases 56 Age (range) 57.2 ± 13.6 Male to Female 40: 16 Total Serum Bilirubin (90 mg/dl) 5.9 Total number of cases 56 Age (range) 57.2

Results:
- FNA (47) Brush Cytology (34)
  - Malignancy 38 (80.8%) 23 (67.6%)
  - Suspicious Of Malignancy 5 (10.6%) 7 (20.5%)
  - Benign 4 (8.5%) 4 (8.5%)

Diagnosis in Positive Cases
- Metal (n = 31)
- Plastic (n = 29)

Conclusion: Except for shorter procedural duration, there was no significant difference in treatment outcomes between patients treated with LAMS or plastic stents. Given the faster resolution of WON, to minimize adverse events, patients undergoing LAMS placement should undergo post-intervention imaging at 3 weeks followed by stent removal if the WON has resolved.

Disclosure of Interest: R. Hawes: Consultant for Boston Scientific Corporation and Olympus America Inc. S. Varadarajulu: Consultant for Boston Scientific Corporation and Olympus America Inc. All other authors have declared no conflicts of interest.

PD0253 TRANS AORTIC ENDOSCOPIC ULTRASOUND GUIDED FNA IN THE DIAGNOSIS OF LUNG CANCERS AND MEDIASTINAL LYMPH NODES

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Introduction: Obtaining a tissue diagnosis from a lung tumour or a mediastinal lymph node located lateral to the aorta (para-aortic) is a diagnostic challenge because of the interposition of the aorta. Invasive surgical procedures like mediastinoscopy, thoracotomy, or video-assisted thoracic surgery is required for the diagnosis of these lesions. lymph node stations immediately anterior to the aortic arch and lateral to the descending aorta are difficult to access. Lymph nodes on the “far-side” of major blood vessels can be visualized by endoscopic ultrasound(EUS), however Fine needle aspiration(FNA) is avoided due to concern for bleeding complications. Tumours and mediastinal lymph nodes located in the para-aortic region can easily be visualized by esophageal EUS, because the aorta provides an excellent medium to transfer ultrasound waves.

Disclosure of Interest: All authors have declared no conflicts of interest.

PD0252 RANDOMIZED TRIAL COMPARING THE LUMEN-APPROXIMATING METAL STENTS (LAMS) AND PLASTIC STENTS FOR EUS-GUIDED DRAINAGE OF WALLED-OFF NECROSIS (WON)

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Introduction: Although lumen-apposing metal stents (LAMS) are being increasingly used for drainage of walled-off necrosis (WON), their advantage over plastic stents is unclear.

Aims & Methods: We aimed to compare the efficacy of LAMS and plastic stents for drainage of WON.

Symptomatic patients with WON (>20% necrosis) were randomized to undergo transmural drainage using LAMS (Hot AXIOS, 15 mm x 10 mm) or two double pigtail plastic stents (7Fr x 4 cm). Reintervention in persistently symptomatic patients included additional stent placement, percutaneous drainage and/or endoscopic necrosectomy. Treatment success was defined as symptom relief in conjunction with resolution of WON on CT at 6-week follow-up. Main outcome measure was to compare the no. of reinterventions. Secondary outcome measures were to compare treatment success, procedural duration, resolution of systemic inflammatory response syndrome (SIRS), clinical and stent-related adverse events, readmissions and length of hospital stay. Sample size to detect a difference in the no. of reinterventions performed at 90% power was calculated at 58 patients.

Results: 60 patients were randomized to LAMS (n = 31) or plastic stent (n = 29) placement. While there was no significant difference in the no. of reinterventions (median 1 [IQR 1–2] for both stent types, p = 0.78), the procedural duration was significantly shorter (15 vs. 42.5 mins, p < 0.001) and stent-related adverse event rate was significantly higher with LAMS placement (32.3 vs. 6.9%, p = 0.02). At an interim audit, significant adverse events (delayed bleeding [n = 3], buried stent [n = 2], biliary structure [n = 3]) were observed in the LAMS cohort after 3 weeks post-intervention. This necessitated an amendment to the study protocol whereby a CT scan was obtained at 3 weeks followed by LAMS removal if the WON had resolved. After protocol amendment, no difference in stent-related adverse events was observed between the cohorts (LAMS 6.5 vs. plastic 6.9%, p = 0.9). Also, there was no significant difference in treatment success, SIRS resolution, clinical adverse events, readmissions or length of hospital stay between the cohorts (Table).

Disclosure of Interest: The authors have declared no conflict of interest.

References

PD0249 METAL VERSUS PLASTIC STENTS FOR THE TREATMENT OF DISTAL BILIARY OBSTRUCTION

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Introduction: Distal bile duct obstruction is a diagnostic dilemma. They are difficult to diagnose with any modality used. Brush cytology under ERCP guidance was used until now and also intraductal biopsies were used. The yield was hardly around 60% using all together. We started doing EUS localization of these difficult to identify distal CBD masses and took FNA from them. We devised a protocol to see the results of EUS FNA and brush cytology in the diagnosis of these masses.

Aims & Methods: We aimed to study the efficacy of EUS guided FNA for obtaining tissue from distal CBD masses and comparing it to ERCP guided brush cytology from the same masses. 56 cases with distal bile duct mass with obstructive jaundice in the last 3 years were taken for the study. The protocol we followed first- EUS was done using a linear echoendoscope, mass was identified and FNA performed with a 25 G needle making 2 to 5 passes and material sent for cytology. Same patients subjected to ERCP. A wide papillotomy was performed and over the wire cytology brush was used and brush cytology was obtained. Two passes were made and material taken on a slide and sent for cytology after wet fixation.

Results: Total number of cases 56 Age (range) 57.2 ± 13.6 Male to Female 40: 16 Total Serum Bilirubin (90 mg/dl) 5.9 Total number of cases 56 Age (range) 57.2

Results:
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  - Malignancy 38 (80.8%) 23 (67.6%)
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  - Benign 4 (8.5%) 4 (8.5%)

Diagnosis in Positive Cases
- Metal (n = 31)
- Plastic (n = 29)

Conclusion: Except for shorter procedural duration, there was no significant difference in treatment outcomes between patients treated with LAMS or plastic stents. Given the faster resolution of WON, to minimize adverse events, patients undergoing LAMS placement should undergo post-intervention imaging at 3 weeks followed by stent removal if the WON has resolved.

Disclosure of Interest: R. Hawes: Consultant for Boston Scientific Corporation and Olympus America Inc. S. Varadarajulu: Consultant for Boston Scientific Corporation and Olympus America Inc. All other authors have declared no conflicts of interest.

References
Aims & Methods: We aimed to evaluate the feasibility, yield, and safety of EUS-guided drainage of lung tumours using FCSEMSs. We undertook a retrospective case series of 12 consecutive patients with suspected lung cancer or tuberculosis who underwent transaortic FNA during a study period of 7 years. In all cases, the para-aortal lesion was the only site suggestive of tumour on non-invasive imaging (either lesion/lymph node if present were negative). Based on CT/PET imaging, a transaportal FNA performed through the aorta was considered as the only option to diagnose or stage these patients by means of a minimally invasive procedure. Seven patients had left-sided lesions, seven had right-sided lesions. Four were located in left lower lobe and three in left upper lobe. Four patients have enlarged para-aortic lymph node (mean size 18 mm, range 8–22 mm), suspicious for IASLC stations 5 (n=1) and 6 (n=3). One patient had anterior mediastinum maso. EUS was performed with a linear echoendoscope. All aspirations were obtained under real-time US guided FNA by using a 22/25-gauge needle. A single real-time FNA of the lung mass or lymph node was performed. The para-aortal area was observed on EUS for 5 minutes to assess for immediate procedure-related complications.

Results: The final diagnosis was known in 11 patients (5 non-small-cell lung carcinoma [NSCLC], 2 small-cell lung carcinoma [SCLC], 3 tuberculosis and 1 thymolipoma). EUS-FNA established diagnosis in 9 of 12 patients (75%) (4 NSCLC, 1 SCLC, 3 tuberculosis and 1 thymolipoma). One aspiration revealed reactive nodal tissue, and one demonstrated nonrepresentative material. One procedure was abandoned due to complication. Three patients in whom diagno- sis was not established by transaortic FNA underwent subsequent surgical staging (1 thymoma, 1 mediastinotomy, and 1 VATS), and malignancy was found in 2 of the 3 patients. Transthoracic FNA was found to be safe. In one patient, EUS images after FNA were suspicious for a small para-aortic hema- toma. This patient recovered without any adverse event.

Conclusions: This study demonstrates the feasibility and probable safety of single EUS guided transaortic aspiration in para-aortic lesions. The diagnostic yield is 75 percent. Clearly, further study and very careful selection by expert EUS operators is needed before this procedure can be routinely recommended. Advantages of this procedure includes day care procedure, less invasive than surgical procedures, low cost, good diagnostic yield and can be performed in poor surgical candidate. Limitations includes single centre study, require EUS expertise, more data is required. At present, Transthoracic FNA should only be performed in the absence of alternative minimally invasive diagnostic procedures.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0254 ULTRASOUND-GUIDED ENDOSCOPIC TRANSDUODENAL PANCREATIC FLUID COLLECTIONS

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Introduction: Ultrasound-guided endoscopic transduodenal drainage (EUSTD) of pancreatic fluid collections (PFCs) by using double-pigtail plastic stents (DPPS) reduces the risk of multiple stents and can be restricted by inadequate drainage and leakage risk. Recently, the use of fully covered self-expanding metal stents (FCSEMSs) has been reported as an effective alternative.

Aims & Methods: We aimed to evaluate the successful placement of stents, the complete resolution of PFCs at 6-months, adverse events, and recurrence of EUSTD of PFCs using DPPS and FCSEMSs. This was a single-centre retrospective study (2012–2016) on 50 patients with symptomatic PFCs who underwent EUSTD. Endoscopic PFCs were drained using DPPS and FCSEMSs (Hanarostent BCF and Hot AXIOS system).

Results: We included 42 cases of pancreatic pseudocysts (PP), and 5 wall-ed off necrosis ( WON), drained using FCSEMSs in 51% of cases. The remaining cases (49%) were drained using DPPS exclusively. Eighteen (27%) patients had a prior failed drainage attempt. Median follow-up time was 88 weeks (IQR: 42–140); 19 patients were lost to follow-up (6 deaths during follow-up). The median size of lesions was 92 mm (IQR: 74–120). The overall technical success rate was 78% (74% for PP and 100% for WON; p < 0.05). Six patients required additional drainage with a different modality (surgery/pectacutaneous drainage) and 8 cases required another EUSTD attempt. Complete resolution of PFCs with DPPS was achievable in 7 cases of PP and in none of WON (p < 0.05); the recurrence was higher in the DPPS group than in the FCSEMS group (43% vs. 13%; p > 0.05).

Conclusion: EUS-TGD of PFCs using FCSEMSs improves clinical outcomes with similar adverse events compared with DPPS.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0255 ENDOSCOPIC ULTRASOUND-GUIDED TISSUE SAMPLING WITH A NEW 20G BIOPSY NEEDLE FOR THE CHARACTERIZATION OF GASTROINTESTINAL SUBEPITHELIAL LESIONS

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Introduction: Histological examinations and immunohistochemical stains (IHC) are necessary for the differential diagnosis of gastrointestinal subepithelial lesions (SLEs). Endoscopic ultrasound-guided fine needle biopsy (EUS-FNB) is the primary modality in the diagnosis of SLEs, but still has limited accuracy. A new 20 gauge (G) biopsy needle with a core-trap technology (EchoTip ProCore®, Cook Medical) has been developed with a large core size and enhanced flexibility.

Aims & Methods: The aim of this multicenter study was to determine the feasibility, efficacy and safety of EUS-FNB with the new 20G needle in diagnosing SLEs. Data retrieved from a prospectively collected database at five medical centers were analyzed and all consecutive patients with SLEs undergoing EUS-FNB with the 20G needle were included in the present study. The reference standards for the final diagnosis were histology on surgical specimen or clinical follow-up.

Results: A total of 50 SELs in 50 patients (22 males, mean age 61.5 ± 14.8 years) were included. The mean lesion size was 43.1 ± 17.5 mm. The lesion locations were esophagus (n=1), stomach (n=37), distal duodenum (n=5), rectum (n=6), and colon (n=1). The procedure was technically feasible in all patients. Mean number of passes required to reach a diagnosis was 2.2 (range 1–4). Definitive diagnosis with full histological assessment including IHC was obtained in 88% (44/50) of the patients. Diagnosis of EUS-FNB showed 36 (72%) malignant SELs (32 GISTs, 1 metastasis from breast cancer, 1 leiomyosarcoma, 1 carcinoid, 8 SEL-like adenomatoid tumors), 6 (12%) benign SELs (3 leiomyomas, 4 schwannomas, and 1 lipoma), and 6 (12%) indeterminate SELs. Considering malignant vs. benign lesions, the sensitivity, specificity, PPV, and NPV were 85% (95% CI 70.2–94.3%), 100% (95% CI 58.7–100%), 100% (95% CI 55.1–100%), and 62.5% (95% CI 27.7–84.8%), respectively. No major complications requiring additional care were observed.

Conclusion: In this multicenter study, we found that EUS-FNB with the new 20G core needle is an effective and safe method for the diagnosis of SELs with a high rate of producing adequate histological material and high diagnostic accuracy even from difficult-to-access anatomical locations. Comparative studies with different needle sizes are awaited.

Disclosure of Interest: All authors have declared no conflicts of interest.

References


P0256 COMPARISON OF NATURAL COURSE VersUS EUS-GUIDED ETHANOL ABLATION FOR CYSTIC PSEUDOTUMOURS

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Introduction: Endoscopic ultrasonography(EUS)-guided ethanol ablation for pancreatic cystic lesions (PCLs) is a recently introduced treatment option for PCLs. The aim of this study was to compare the clinical outcomes of EUS-guided ethanol ablation with those of the natural course of PCLs.

Aims & Methods: We performed retrospective study of patients with PCLs divided in two groups: EUS-guided ethanol ablation group (n=118, performed between June 2006 to August 2015) and natural course group (n=458, diagnosed between January 1993 to August 2015). The propensity score-matching analysis
between the two groups was applied in order to minimize the effect of selection bias. There was a rate of significant reduction in size (≥20% of initial size). The secondary outcomes were the rate of significant growth in size (>10 mm), complete remission rate, and surgical resection rate. Results: In a propensity matched analysis of 88 pairs, the mean initial cystic size of EUS-guided ethanolic ablation group and natural course group was 23.72 ± 10.99, 23.16 ± 13.15 mm and the mean follow-up duration was 75.45 ± 38.12, 82.12 ± 59.06 months respectively. Significant reduction in size was detected in 53 (60.2%) of the EUS-guided ablation group and 17 (19.3%) in the natural course group (p < 0.01). Significant growth in size was detected in 6 (8.9%) of ablation group and 11 (12.5%) of natural course group. (p = 0.20). Seven patients (7.95%) underwent surgical resection in the EUS-guided ablation group and 17 patients (19.3%) in the natural course group. (p = 0.028) during follow-up. Overall 28.8% patients (34 of 118) who underwent EUS-guided ethanolic ablation had achieved the complete remission. Conclusion: PCLs that underwent EUS-guided ethanolic ablation can be seen the likelihood of getting clinical benefits such as reduction of the cystic size, the clarity in decision in comparison to the natural course of them. It is also expected to achieve a certain level of complete remission for PCLs. Disclosure of Interest: All authors have declared no conflicts of interest.

P0257 RANDOMIZED TRIAL COMPARING THE FRANSEEN AND FORK-TIP NEEDLES FOR EUS-GUIDED FINE NEEDLE BIOPSY
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Introduction: EUS-FNA needle tissue compaction and desmoplastic stroma is required for molecular profile-based personalized chemotherapy in pancreatic cancer. Recently, a three-plane symmetric needle with Franssean geometry and a Fork-tip biopsy needle have been developed for histologic tissue preservation. Aims & Methods: We aimed to compare tissue acquisition between the 22G Franssean and 22G Fork-tip needles in patients undergoing EUS-guided sampling of pancreatic masses. Patients with pancreatic masses were randomized to undergo EUS-guided sampling using the 22G Franssean and 22G Fork-tip needles. Two dedicated passes were first performed using both needles in individual patients for cell block. Subsequent passes were then performed for rapid onsite evaluation (ROSE), using both needles only until a diagnosis was established. The main outcome measures were to compare total tissue volume and presence of desmoplastic stroma in pancreatic cancer. Secondary outcome measures were to compare rates of diagnostic cell block and diagnostic adequacy at ROSE. Results: In 50 patients randomized to undergo EUS-guided sampling, the diagnosis was pancreatic cancer in 43, neuroendocrine tumor in 2, lymphoma in 1 and chronic pancreatitis in 4 patients. There was no significant difference in total tissue area (median 6.1mm2 [IQR 3.5–10.5] vs. 8.2mm2 [IQR 4.0–13.0], p = 0.93), presence of desmoplastic stroma in tumors (100 vs. 83.3%, p = 0.23), rates of diagnostic cell block (96.0 vs. 92.0%, p = 0.68) and diagnostic adequacy at ROSE (94.0 vs. 98.0%, p = 0.06) between the Franssean and Fork-tip needles, respectively. Conclusion: Both the Franssean and Fork-tip needles appear equally effective in yielding histologic tissue. By virtue of their ability to yield a diagnostic cell block in greater than 90% of patients, the new generation FNB needles may obviate the need for ROSE during EUS-guided tissue sampling. Disclosure of Interest: S. Hebert-Magee: Consultant for Boston Scientific Corporation R. Hawes: Consultant for Boston Scientific Corporation and Olympus America Inc. S. Varadarajulu: Consultant for Boston Scientific Corporation and Olympus America Inc. All other authors have declared no conflicts of interest.

P0258 THE SUCCESS RATE OF DOUBLE BALLOON ENDOSCOPIC CHOLANGIOPHOTOGRAHY IN PATIENTS WHO UNDERWENT THEIR INITIAL SURGERY AS INFANT IS SIGNIFICANTLY LOWER THAN OTHER PATIENTS
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Introduction: To evaluate the success rate of double-balloon endoscopic retrograde cholangiopancreatography (DBERC) to reach the anastomosis in patients with surgically altered gastrointestinal anatomy. Aims & Methods: We review 346 patients with surgically altered anatomy who underwent DBERC from April, 2002 to December, 2016 (47 patients with biliary atresia (BA), 146 with portal vein thrombosis, 141 with liver transplantation). We evaluate the success rate according to the type of gastrointestinal anastomosis, age, and age at surgery. Results: The success rate for reaching the biliary anastomosis (or papilla of Vater) in all 346 patients (66.0 ± (3–91)) was 83%. The rate in 47 patients with BA after LDLT (12y.o (3–39)) was 57%. In the remaining 299 patients the rate was 87%. The success rate of reaching the biliary anastomosis in patients with BA after LDLT was significantly lower than other patients (p < 0.01). There was no significant difference between the success rate in the patients over or under 13 years at the time of ERCP (90% vs 56%, p = 0.70). The success rate was lower in patients who underwent initial surgery as an infant (Kasai hepatoportoenterostomy) than in those past infancy (54% vs 88%, p < 0.01). When reaching the biliary anastomosis is successful, the success rate of cannulation in the patients after LDLT is high (92%). Conclusion: The success rate for reaching the biliary anastomosis in patients with BA after LDLT is significantly lower than other patients. The age at the time of ERCP did not affect the success rate of reaching the biliary anastomosis, but the success rate was lower in patients who underwent their initial surgery as infants. Disclosure of Interest: All authors have declared no conflicts of interest.

P0259 EUS-GUIDED RADIOFREQUENCY ABLATION OF DIFFICULT SITES IN THE LIVER: A PRECLINICAL STUDY
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Introduction: Liver tumors such as hepatocellular carcinoma and liver metastases sometimes occur in positions in which treatment using percutaneous radiofrequency ablation (RFA) is difficult, such as the caudate lobe and surface of the left liver. EUS-guided RFA (EUS-RFA) can offer an alternative treatment by accessing these tumors through the stomach or duodenum. To the best of our knowledge, only one report has described EUS-RFA of the liver in an animal model, using a 19-gauge EUS-FNA needle with an umbrella-shaped array at the tip. Aims & Methods: We examined whether a novel 19-gauge RFA needle can be introduced to ablate the liver in a porcine model under EUS guidance. Two pigs were used in this study. All procedures were carried out under general anesthesia. EUS-guided 19-gauge needle and a VIB Combo generator (Taewoong Medical, Gimpo city, Korea) were used for the procedures. Three kinds of RFA needles (10-, 15-, and 20-mm exposed tips) were used. After the echoendoscope was advanced to the stomach, the RFA needle was inserted into the surface of the left lobe. EUS-RFA was performed at 340 W for 2-6min in general mode. In each pig, three RFA needles with 10-, 15-, or 20-mm exposed tips were serially used for insertion and ablation. Subsequently, the RFA needle with the 10-mm exposed tip was used in the quadrate lobe of the gallbladder through the bulb of the duodenum. Results: All procedures were technically successful. After the procedure, the liver of the pig was removed, and visible RFA effect was evaluated macroscopically. Histology with hematoxylin and eosin (HE) staining showed coagulative necrosis in the ablated area, corresponding with the macroscopic ablated area. Conclusion: In this experimental study, EUS-RFA could be performed technically not only in the surface of the left lobe, but also in the adjacent to the gallbladder of the porcine liver. Further studies are required to confirm the efficacy and safety. Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

P0260 CYANOACRYLATE INJECTION THERAPY OF SMALL BOWEL VARIES BY DOUBLE-BALLOON ENTEROSCOPY (DBE): A TERTIARY CENTRE EXPERIENCE
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Introduction: Small bowel varices (SBV) occur as a consequence of portal hypertension and may result in life-threatening mid-gut bleeding. First line management usually involves radiological intervention (RI) (e.g. TIPSS, stenting of occluded mesenteric veins +/- embolisation of culprit varices). In cases where RI is impossible, management options become very limited. Aims & Methods: This case series evaluated the usefulness of DBE facilitated cyanoacrylate injection of SBV. Retrospective review of DBE facilitated cyanoacrylate injection of SBV at our institution (December 2015 to August 2016). Demographic, clinical, endoscopic and radiological findings, interventions and follow-up data were analysed. Results: Seven DBEs were performed in 3 patients (3 women, median age 73-years). Four patients had previous surgery (hepatic/hepatectomy (n = 2); SB resection (n = 2)); one patient had a history of intra-abdominal sepsis in childhood causing portal vein thrombosis. No radiological or surgical options were deemed feasible in any case. SBV were diagnosed at capsule endoscopy and triple phase CT mesenteric angiography. At DBE, a total of 10 nests of SBV were identified.
and injected with cyanoacrylate glue. There were no haemorrhagic or embolic complications. No patient developed an anastomotic leak, nor a candidal urinary cyst, which was treated successfully with antibiotics. All patients underwent DBE via the anterograde route and 1 patient required bi-directional DBE for treatment of both proximal and distal SBV and another patient required a 2nd anterograde DBE for treading of further patent proximal SBV. At 30-day follow-up post-therapy, only 1 patient had experienced a mild recurrence of mid-gut bleeding.

Conclusion: Cyanoacrylate injection therapy of SBV at DBE appears to be a safe and effective management strategy for this condition when other first-line options have failed.

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P0261 MAGNIFYING NARROW-BAND IMAGING FINDINGS EFFICACY FOR INFLAMMATORY ACTIVITY EVALUATION IN SMALL INTESTINAL CROHN'S DISEASE WHEN USING NEWLY DEVELOPED MAGNIFYING ENTEROSCOPY: A PILOT STUDY

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Introduction: The development of balloon endoscopy and capsule endoscopy has made observation of the small intestine possible in clinical practice. The usefulness of magnifying endoscopy has already been reported in observing the pharynx, esophagus, stomach and colon. A single-balloon enteroscopy (SBE) with 80x magnification has been recently developed.

Aim & Methods: The aim of this pilot study was to assess the efficacy of narrow-band imaging (NBI) magnifying findings for evaluating the severity of inflammation in small intestinal crohn's disease (CD). The study was conducted in Showa University Northern Yokohama Hospital. We included CD patients who underwent enteroscopy with magnification from September 2013 to February 2015. NBI images and a biopsy specimen were obtained from small intestinal mucosa for CD patients with use of SBE (Y-0007, Olympus, Tokyo). Magnifying NBI was performed, and the images were evaluated by assessing visibility, increased vascularity, and the increased caliber of capillaries into three grades as follows: Normal, Visible and Irregular. Normal was indicative of inactive disease, while Visible and Irregular were indicative of acute inflammation in our study. The outcome measures included the diagnostic ability of magnifying NBI findings to distinguish active CD from inactive CD on the basis of histological activity.

Results: Twenty-four patients were enrolled. There was a correlation between magnifying NBI findings and the histological assessment (Spearman's ρ = 0.54 for sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of magnifying NBI findings for diagnosing acute inflammation were 88.2%, 71.4%, 88.2%, 71.4%, and 83.3%, respectively.

Conclusion: The NBI magnifying findings in the small intestinal mucosa had a correlation with histological inflammation and could help in distinguishing between active and inactive CD.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0262 SINGLE-INCISION LAPAROSCOPIC-ASSISTED DOUBLE BALLOON ENTEROSCOPY: A NOVEL TECHNIQUE TO MANAGE SMALL BOWEL PATHOLOGY

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Introduction: Double balloon enteroscopy (DBE) has revolutionised the diagnosis and treatment of small intestinal conditions. However, even in expert hands, deep small bowel (SB) insertion can be challenging, especially in patients with a history of abdominal surgery. Moreover, if the findings at DBE are not amenable to endoscopic therapy, a further surgical procedure is usually required to provide definitive treatment. Laparoscopic-assisted DBE (LA-DBE) using a standard multi-port technique has previously only been reported in a small series of 3 patients with Peutz–Jeghers Syndrome (PJS) 1.

Aims & Methods: This case series reports the development of LA-DBE using single-incision laparoscopic surgery (SILS) applied to a wide range of clinical indications. Retrospective review of LA-DBE procedures performed in a single tertiary centre over a 6 year period. Demographics, indication, findings, diagnosis and therapeutic interventions were recorded. Completion, complication rates and hospital length of stay were also captured.

Results: 17 procedures were performed over 6 years in 17 patients who had failed standard DBE. Mean (range) age was 40 (17-73) and 41% of patients were male. The enteroscopic approach was oral in 13/17 patients and rectal in 4/17. Laparoscopic approach was standard (multipor) in the first 4 cases, SILS was then used in all subsequent patients (13/17). The mean (range) procedure time was 147 (84-210) mins. Indications were PJS (n = 10), suspected submucosal/ intramural polypoid lesion at small bowel imaging (n = 5) and obscure gastrointestinal bleed (OGBB) with vascular abnormalities seen at capsule endoscopy (n = 2). In 15/17 procedures the target pathology was reached using laparoscopic assistance only and 1/17 was converted to intraoperative enteroscopy (IOE). In 1/17 the suggested pathology at magnetic resonance enterography (MRE) was not identified. Therapy was applied in 15/17 (88%) cases. 7 underwent endoscopic therapy of which 6 polypectomy and 1 ablation with argon plasma coagulation (APC). 4 required limited SB resection and 4 underwent both endoscopic polypectomy and small bowel resection for a second polyp that could not be removed endoscopically. A total number of 57 polyps were removed with the largest measuring 40 mm. The range of length of surgically resected SB was 4-17 cm. Diagnoses were PJS polyps (n = 9), neuroendocrine tumour (NET) (n = 2), PJS polyp with additional NET (n = 1), transmural arteriovenous malformation (n = 1), angiectasia (n = 1), inflammatory polyp (n = 1), leiomyoma (n = 1), Meeckel's diverticulum (n = 1). Median length of stay post procedure was 2 (1–19) days. 8/17 patients were discharged at 24 hours. 3/17 patients developed complications: 1 post procedure ileus, 1 partial bowel obstruction which resolved with conservative management.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

P0263 GASTRIC EMPTYING IN CROHN'S DISEASE – EVALUATION BY SMALL BOWEL CAPSULE ENDOSCOPY

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Introduction: The complex relationship between inflammatory bowel disease (IBD) and motility disorders of the digestive tract is a complex area of study, so far inadequately elucidated. The association between Crohn’s disease and gastric emptying time modification has been relatively less studied. However, there is no single standardized method to study gastric emptying, one particular investigation that could bring direct information in this field being the small bowel capsule endoscopy (SBCE).

Aims & Methods: We aimed to study gastric emptying by small bowel capsule endoscopy in patients with suspected and confirmed Crohn’s disease. We evaluated gastric passage time showed by SBCE in patients with small bowel Crohn’s disease, compared to patients without IBD, investigated by SBCE (PillCam), following recognized indications, in the Institute of Gastroenterology and Hepatology of Iasi, tertiary center in North-East of Romania.

Results: 144 SBCE studies were included, 24 were cases of suspected and confirmed Crohn’s disease. The mean time of gastric passage in patients with Crohn’s disease was 51±21.9 minutes, longer than in patients without inflammatory bowel disease, in which the mean gastric passage time was 24±16.6 minutes.

Conclusion: Gastric passage time, evaluated by SBCE, is prolonged in patients with inflammatory bowel disease compared to patients without IBD, suggesting a relationship between chronic inflammation and gastric motor disorders. Globally, the values correlated with those considered as physiological by other exploration methods. SBCE studies may provide additional data on gastric motility and in general gut motor disorders, with special usefulness in some individual cases, as particular symptoms or variations in the bioavailability of small bowel-released drugs.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0264 META-ANALYSIS SHOWS THAT PURGATIVE PREPARATION INCREASES SMALL BOWEL VIDEO CAPSULE ENDOSCOPY DIAGNOSTIC YIELD AND IMPROVES THE QUALITY OF SMALL BOWEL MOVEMENTS: A META-ANALYSIS

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Introduction: The value of purgative preparation (PBP) before small bowel video capsule endoscopy (VCE) remains controversial and it has been recently challenged.

Aims & Methods: The aim of this meta-analysis was to examine the effect of PBP on small bowel VCE outcomes. We performed literature searches in MEDLINE and Cochrane Library to identify randomized-controlled trials (RCTs) evaluating the effect of small bowel preparation –purgative (PEG, sodium phosphate,
others) vs. clear liquids diet on VCE outcomes. Examination’s diagnostic yield (DY) was meta-analytically primary endpoint and posed small bowel visualization quality (VQ), VCE completion rate (CR), gastric (GTT) and small bowel (SBTT) transit times comprised the secondary endpoints. Study outcomes effect sizes were calculated using RevMan 5.3 software fixed or random effect model, as appropriate, and they are presented as OR[95%CI] or mean difference[95%CI], respectively. Heterogeneity was measured using the I² statistics. Publication bias was assessed by Funnel plots inspection and the quality of the meta-analyzed studies was assessed using the Jadad criteria.

Results: We identified 9 eligible RCTs with 12 sets of data, including 1029 subjects. They were of high quality and no publication bias was detected. As compared to clear liquids diet, PB1 significantly increased small bowel VCE DY (1.44 [1.14–1.83], I² = 39%). However, a sensitivity analysis that excluded studies with sodium phosphate preparation (abandoned nowadays) and PBPs different (not widely used) than PEG showed no benefit of PEG preparation over clear liquids (1.31 [0.79–2.17], I² = 54%). VQ significantly improved after PB1 (2.05 [1.49–2.82], I² = 45%), without any significant effect on VCE CR (0.98 [0.73–1.33], I² = 53%) and SBTT (1.21 [1.21–1.73], I² = 49%). On the contrary, VCE SBTT was statistically lower by ~15.06 [–25.52–6.61] min (I² = 90%) after PBP.

Conclusion: In comparison to clear liquids diet, PB1 increases small bowel VCE DY and improves VQ without affecting exam’s CR. However, the positive effect of PB1 on VCE SBTT is mainly derived from two relative small, old (2004 and 2009) RCTs and does not appear if only PEG preparation studies are meta-analyzed.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0265 INTER-OBSERVER AGREEMENT IN BROTZ CLEANING SCALES FOR CAPSULE ENDOSCOPY
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Introduction: The diagnostic yield of capsule endoscopy (CE) depends on the adequate visualization of the mucosa. As with colonoscopy, cleaning scales should be described in the report in order to better interpret results. In 2009, Brotz et al proposed and validated 3 different cleansing scales in 40 patients.

Aims & Methods: A hundred CE videos (Mirocam®) were reviewed by 2 authors at a fixed frame rate of 100 frames per second in quadruple view (Miroview Client). The CE were evaluated according to Brotz scales: (1) Overall adequacy assessment (adequate/inadequate) (2) Qualitative scale (excellent, good, fair, poor) and (3) Quantitative scale (0–10 score, graded from 0–2 visualization of the mucosa, fluids, bubbles, bile and luminosity). The aim of this study was to evaluate the inter-observer variability of this cleaning scales. The kappa coefficient was used to calculate the inter-observer agreement in overall adequacy assessment and the intra-class correlation coefficient was used to evaluate the concordance of the qualitative and quantitative scales.

Results: In overall adequacy assessment, the quality of bowel preparation was classified as adequate by observer 1 in 100% and by observer 2 in 73%, with an inter-observer kappa index of 0.76 (p < 0.001) suggesting strong agreement. In the qualitative scale, most of the bowel preparations were considered reasonable (40% observer 1 vs 36% observer 2), with an intra-class coefficient of 0.89 (p < 0.001). In the quantitative scale, the mean score of the two observers was 6.5 and 6.7, resulting in an intra-class agreement of 0.78 (p < 0.001).

Conclusion: The optimization of quality of bowel preparation and the diagnostic yield of CE require a well-validated cleaning scale. Brotz’s rating scales have strong inter-observer agreement. The qualitative scale is easier to apply and has better inter-observer agreement, so the authors propose that it should be used routinely in the CE report.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

P0266 PILOT STUDY OF THE EFFECTS OF IMAGE QUALITY ON LESION VISUALISATION IN SMALL BOWEL CAPSULE ENDOSCOPY
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Introduction: Capsule endoscopy (CE) is the prime mode of investigation for small bowel (SB) pathology. However, as an entirely visual medium it depends heavily on image quality. The definition of optimal image quality remains to be ascertained between studies and poses significant limitations to the quality of study reporting. As yet, there is no widely-accepted or integrated method for scoring SB cleanliness during CE reporting. This pilot study aimed to quantify the image properties contributing to adequate visualisation quality in CE images.

Aims & Methods: Five clear images of SB pathology were obtained using Miracam® (Intromedic, South Korea), image resolution 320×320 pixels(px): P1 and P2 angioectasias, ulcer, aphtha and polyph. Each image was processed using GIMP2 image editing software (www.gimp.org) for 3 parameters: (1) opacity (opacity filter matched in colour to commonly-seen SB contents, 10–90% in 10% increments), (2) blur (Gaussian blur, radius 1–10px), (3) contrast (±50% to ±50% in 10% increments). Gaussian blur was used to simulate the effects of rapid capsule movement as well as to affect image definition. A set of 5 original and 190 edited images was obtained. A web-based survey was created using Google Forms and 9 expert CE readers were asked to indicate whether each image was adequate or not for diagnosis. The order of images was randomised for each reader. For each type of pathology, we determined the threshold of image quality for diagnosis. As the threshold was deemed inadequate for diagnosis.

Results: For image opacity, both aphtha and the polyloid lesion were adequately visualised below 40% opacity whereas the threshold was lower for both the ulcer and aphtha (10% opacity). Increasing blur radius significantly impacted the acceptability of images for reaching a diagnosis with confidence; for most images, blur radius 3px was the threshold for adequate visualisation but even 1px of blur radius decreased the visualisation quality of the aphtha image. The aphtha image was also affected the most by decreased contrast; conversely the ulcer was deemed more inadequately visualised with higher contrast. The other images were generally adequately visualised at ±10% contrast. Results are detailed in the table below.

Disclosure of Interest: All authors have declared no conflicts of interest.
P0267 EVALUATION OF A NEW PAN ENTERIC CAPSULE SYSTEM IN PATIENTS WITH SUSPECTED OR ESTABLISHED INFLAMMATORY BOWEL DISEASE - ASSESSING THE SYSTEM FUNCTIONALITY TO VISUALIZE AND ASSESS THE SMALL AND LARGE BOWELS

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Introduction: Chronic bowel diseases (IBD) are chronic inflammatory diseases that may affect the whole gastrointestinal (GI) tract, mainly the small bowel and colon. Endoscopic evaluation of these parts is essential to assess disease extent and severity. The small bowel capsule endoscopy (SBC-CE) system is a new system composed of a two-headed capsule with a panoramic field of view and adaptive frame rate, customized for complete coverage of IBD lesions in the entire bowel, data recorder and new disease specific software, allowing assessment and follow-up over time of disease severity and extent.

Aims & Methods: The aim was to evaluate SBC-CE system functionality in suspected or established IBD patients. This was a prospective 5 center feasibility study assessing the feasibility of the new capsule and software. Subjects enrolled into the study ingested the new capsule after standard bowel preparation plus boosts.

Results: (1) Six patients were men and three were women (mean age, 50.1 years). (2) During capsule ingestion in accordance to the video reading methodology. Secondary end-scoring was performed in terms of video creation and reproduction, subjective video reading time 3.9 (unconfident to confident), image quality 6.1 (unsatisfactory to satisfactory) and duration diathermy procedures because of a risk of pancreatitis.

Conclusion: Transpapillary diathermic dilation is a relatively safe and effective salvage procedure for severe MPD stricture due to chronic pancreatitis. This should be taken in cases that require multiple times and long duration diathermy procedures because of a risk of pancreatitis.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
**P0270 OUTCOME OF ENDOSCOPIC REINTERVENTION FOR MALIGNANT HILAR OBSTRUCTION TREATED BY STENT-IN-STEM DEPLOYMENT**

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**Introduction:** Endoscopic biliary decompression is widely used for advanced hilar cholangiocarcinoma. Bilateral stenting has become more feasible with more experienced endoscopists and the development of new devices. However, stent dysfunction develops in 3% to 45% because of tumor ingrowth, overgrowth, or debris as disease progresses. Endoscopic reintervention is difficult and complex with worsening bile duct strictures. The present study aimed to evaluate a suitable reintervention procedure for stent malfunction after stent-in-STEM (SIS) deployment for malignant hilar obstruction.

**Aims & Methods:** From September 2009 to June 2016, a total of 52 patients who underwent stent-in-STEM at Pusan National University Yangsan Hospital were enrolled in this study. Among them, 20 patients who underwent reintervention due to stent malfunction were analyzed. Reintervention was performed endoscopically or percutaneously. Technical and functional success rates were evaluated retrospectively.

**Results:** Technical and functional success rates of endoscopic reintervention were 83% (10/12) and 80% (8/10), respectively. Endoscopic biliary and unilateral stent dysfunction rates were 75% (6/8) and 100% (4/4), respectively. Functional success was observed in 8 out of 10 patients (80%) who achieved technical success. For bilateral reintervention, either plastic or plastic and metal stents were used. PTBD was performed in 8 patients because of duodenal stenosis (2 patients) and other conditions.

**Conclusion:** Endoscopic reintervention could be considered in the case of stent malfunction and fair patient conditions after SIS placement for malignant hilar obstruction. Decisions regarding bilateral or unilateral drainage and type of stents should depend on the conditions of the disease and the patient.

Disclosure of Interest: All authors have declared no conflicts of interest.

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**P0271 LONG-TERM OUTCOMES OF ENDOSCOPIC ULTRASOUND-GUIDED RIGHT INTRAHEPATIC DUCT DRAINAGE WITH TRANSMURAL COVERED METAL STENT**

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**Introduction:** Endoscopic ultrasound-guided biliary drainage (EUS-BD) has been regarded as an effective alternative in cases of endoscopic retrograde cholangiopancreatography (ERCP) failure or inaccessible papilla. However, EUS-BD for right intrahepatic duct obstruction (EUS-BDR) remains challenging, although recent studies showed promising result. The aim of current study was to evaluate the feasibility and long-term outcomes of EUS-BD with transmural covered metal stents for right intrahepatic duct obstruction.

**Aims & Methods:** Retrospective study, a total of 24 consecutive patients who underwent EUS-BDR after failed ERCP were enrolled. The patients were consisted of 12 cases of benign strictures and 12 cases of malignant strictures. The biliary stents used in this study was covered metal stent with anchoring flaps or partially covered metal stent with anchoring flaps. The technical success rate, clinical success rate and adverse events were evaluated.

**Results:** The mean diameter of right intrahepatic duct was 6.5 (4–30) mm. A fully covered metal stent was used in 22 patients and partial covered stent in 2 patients. Early adverse events developed after EUS-BDR in 2 patients (1 case of cholangitis and 1 case of liver abscess in patients with malignant biliary stricture). Late adverse event that stent occlusion was observed in 5 patients. No proximal peritoneal stent migration or spontaneous distal stent migration was observed during follow-up periods. The stent patency duration was 275.2 (147.8–402.7) days. During follow-up period, stent revision due fistula tract was successful and additional percutaneous biliary drainage for right intrahepatic duct obstruction was not required in all patients who achieved clinical success.

**Conclusion:** EUS-BD using transmural covered metal stent with antimigration properties for right intrahepatic duct obstruction may be technically feasible, effective and relatively safe for both benign and malignant strictures by expert hands. Furthermore, the route of hepatoduodenostomy created by covered metal stent was durable and endoscopically easily managed.

Disclosure of Interest: All authors have declared no conflicts of interest.

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**P0272 EUS-GUIDED GALLBLADDER DRAINAGE REDUCES LATE ADVERSE EVENT AND NEED FOR RE-INTERVENTION COMPARED WITH PERCUTANEOUS CHOLECYSTOSTOMY IN PATIENTS WHO ARE NOT ELIGIBLE FOR SURGERY**

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**Introduction:** Endoscopic ultrasound guided transmural gall-bladder drainage (EUS-GBD) has become increasingly used to treat patients with acute cholecystitis who are not a candidate for surgical treatment. However, there are limited data comparing long-term outcomes of EUS-GBD with covered metal stent and conventional percutaneous cholecystostomy.

**Aims & Methods:** Retrospective study comparing long-term outcomes of EUS-GBD and percutaneous cholecystostomy in patients who are not suitable for cholecystectomy. Data about the patient who underwent EUS-GBD for acute cholecystitis is obtained from prospective collected EUS database at Pusan National University Yangsan Hospital. The electronic medical record of patients who underwent percutaneous cholecystostomy was reviewed and analyzed. Demographics and procedure related outcomes including early, late adverse events and need for re-intervention in each group was compared.

**Results:** A total of 181 patients (74 in EUS-GBD group and 107 in percutaneous cholecystostomy group) were enrolled in this study. The cause of cholecystitis and ASA class were similar in both groups. The technical/clinical success rate was 100%/98.6% in EUS-GBD group and 99.1%/97.2% in percutaneous cholecystostomy group (P = 0.591). Early adverse events were also similar between two groups (6.8% in EUS-GBD group vs. 15.0% in percutaneous cholecystostomy group, P = 0.103). However, late adverse events including migration of stent or dislodgement of drainage tube, stent or tube occlusion, tract inflammation around percutaneous tube, bile leakage and recurrence of cholecystitis was more frequently observed in percutaneous cholecystostomy group (5.74% in EUS-GBD group and 21/107 in percutaneous cholecystostomy group, P = 0.017). Percutaneous cholecystostomy tube was indwelled for...
median 20 days (14.0–45.2) after the procedure. A total of 7 patients in EUS-GBD intervention for reverse stents and all of them were conducted successfully. The patients who underwent percutaneous cholecystostomy more frequently received re-intervention for adverse event or recurrence of cholecystitis after removal of cholecystostomy. (7/4 vs. 2/106; P = 0.041).

Conclusion: EUS-GBD and percutaneous cholecystostomy were both effective interventions to urgent drainage for acute cholecystitis. However, EUS-GBD might be beneficial than percutaneous cholecystostomy in long term management for the patients with acute cholecystitis who are not suitable for cholecystectomy.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0274 ENDOCOSCOPIC TREATMENT OF ANASTOMOTIC BILIARY STRICTURES IN PATIENTS WITH LIVING DONOR LIVER TRANSPLANTATION: MULTIPLE PLASTIC STENTS VS FULLY COVERED SELF-EXPANDABLE METALLIC STENTS
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Introduction: The “fully covered self-expandable metallic stents”(FcSEMS) were found to be non-inferior to multiple plastic stents (MPSs) for the treatment of anastomotic biliary strictures after orthotopic liver transplantation (OLT). However, there is scarce data about their efficacy in the treatment of anatomic biliary strictures after living donor liver transplantation (LDLT). We aimed to compare the efficacy of FcSEMS and MPSs for the treatment of anastomotic biliary strictures after LDLT.

Aims & Methods: We retrospectively analyzed the data of LDLT patients with duct-to-duct anastomotic biliary strictures who underwent endoscopic treatment at our center within the last 3 years. FcSEMS were inserted in 23 patients (13 male, 10 female, mean age 53 ± 9 years) and 79 MPSs were placed with MPSs insertion (Group-2). In Group-1, secondary branch ducts were prophylactically drained with insertion of plastic stent(s) in order to prevent the development of cholangitis due to their occlusion. FcSEMS and plastic stent(s) were left in place for 2 months. In Group-2, maximum number of plastic stents were inserted and replaced every 3 months. Patients with a follow-up duration of at least 3 months after stenting were included to the study. Primary endpoints were the number of endoscopic procedures and the time required for stricture resolution. The secondary end-point was the recurrence rate of the stricture.

Results: FcSEMS were successfully deployed in all cases. The diameter of the Fc-SEMS were 10 mm in 22 patients and 8 mm in 1 patient. The length of the Fc-SEMS were 8 cm in 13 patients, 10 cm in 8, and 12 cm in 2 patients. Secondary branch ducts were prophylactically drained with a single plastic stent in 12 patients, 2 plastic stents in 8 patients, and 3 plastic stents in 3 patients. The median number of endoscopic procedures was 2 (2–4) in Group-1 and 4 (2–9) in Group-2. The time required for stricture resolution was shorter in Group-1 (65.7 ± 18.2 days) than in Group-2 (240.1 ± 183.4 days) (p < 0.001). The recurrence rates were similar in Group-1 (17.4%) and Group-2 (15.6%) (p = 0.87) after a follow-up period of 315 ± 290 and 378 ± 36 days, respectively. Conclusion: FcSEMS is an effective method for the treatment of anastomotic biliary strictures after LDLT, with a lesser number of endoscopic sessions and a shorter stenting duration required for the resolution compared to MPSs.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0275 PROSPECTIVE RANDOMIZED STUDY FOR EFFICACY OF AN DOUBLE BARE STENT COMPARED A DOUBLE COVERED STENT IN MALIGNANT COLORECTAL OBSTRUCTION
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Introduction: Colorectal stenting is a minimally invasive, reliable and effective intervention in patients with malignant colorectal obstruction, associated with a low complication rate compared to surgical intervention. One of the actual problems associated with colorectal stenting is the recurrence of symptoms of obstruction. The most common cause is migration of covered stents and ingrowth of uncovered stents1-3. The aim of our study was to compare the results of the use of stents of a new design, the development of which was aimed at preventing these complications.

Aims & Methods: We aimed to evaluate the results of the use of the new design (double uncovered and dual coated colorectal stents). Between December 2012 and April 2017,71 patients with colorectal malignant obstruction were implanted 78 stents (39 bare, 39 covered EGIS Colorectal stent, S&G Biotech Inc., South Korea). A double uncovered stent has a two-layer structure created by crossing two stents, resulting in a smaller cell size. Such a design theoretically can reduce stent migration and reduce tumor ingrowth. The core tumor is coated with a silicone membrane between two layers of a metal mesh with distal, uncovered ends of 5 mm each. The role of the membrane is to prevent the ingrowth of the tumor, localization and uncovered edges prevent the migration of the stent. All interventions are performed by one operator using endoscopic and radiological control. Groups of patients using coated and uncovered stents were comparable in terms of sex, age, duration of symptoms of obstruction, and stenosis localization. The reasons for the obstruction were primary tumors of the colon 97.4%. The localization of the tumor is most common in the sigmoid colon - 54%. Debridement was provided to 43 (55.8%) patients, «bridge to surgery» - 34 (44.7%) patients.

Results: Clinical success was achieved in 74 (96.1%) patients. In two cases, when using covered stents, the symptoms of obstruction could not be relieved, the intervention was repeated. In one case, 18 hours after stenting with an uncovered stent, was diagnosed perforation due to obstructive colitis. The average stay in hospital after the intervention was 3 days; the difference between the groups was statistically insignificant. 30 day mortality was 5.2%, the difference was statistically significant. Complications were detected in 3 patients in the group of bare stents and in 1 patient in the group of covered stents, the difference was statistically insignificant. One patient with the carcinoma of a sigmoid colon with invasion in anterior abdominal wall noted the appearance of subcutaneous emphysema without pneumoperitoneum. In 3 (3.8%) patients the occlusion of the stents. The reasons for obstruction of the stents were occlusion by the obstruction from stool (fibers) on the 83rd day (the endoscopic recanalization was performed) and tumor overgrowth by 165 days (endoscopic «stent-in-stent» placement). In one patient, the cause of obstruction is unknown, operated in another hospital 34 days after stenting - a transversostomy was performed, died on the 4th day after the operation.

Conclusion: Double bare and double covered colorectal stents were feasibility and efficacy for relieving malignant colorectal obstruction. Reobstruction was rare complication and not different in both groups stent groups. Necessary to continue to research for the accumulation of material from other centers.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P0276 THE FEASIBILITY OF NEW ENDOSCOPIC GASTROINTESTINAL BYPASS STENT FOR WEIGHT REDUCTION: EXPERIMENTAL STUDY
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Introduction: Endoscopic therapy has been emerged as alternative treatment to bariatric surgery for reducing weight. We developed a new endoscopic gastrointestinal (GI) bypass stent and designed a preclinical study to assess the safety in a porcine model.

Aims & Methods: The aim of this study is to investigate the feasibility of our GI bypass device in animal. Before animal study, we performed an experimental study for durability test under simulated intestinal fluid flow. And next, we performed an animal study with 10 Yorkshire pigs. The stents were placed on pylorus with fixation by clippings or on duodenal bulb without fixation. Follow up endoscopy was done per one week after implantation. After they were sacrificed, gastric, duodenal, and jejunal tissues were harvested and examined for histologic assessment of any device or procedure-related effects.

Results: Our new GI bypass stent showed a good durability in simulated solution flow. No breakage or migration of stent occurred under continuous water flow in simulation system setting. In animal study, the mean starting weight was 30.1 ± 1.5 kg. Delivery of the implant took an average of 19.86 min (range, 11–32.1 min). The pylorostomy stent group and jejunal stent group required an average clamping time of 10.8 min (range, 8–14 min). Followed for stent migration after implantation, the mean patency duration was 3.0 ± 0.7 weeks. One pig was died due to small bowel perforation and peritonitis after stenting. In histologic finding, there were moderate degree of mucosal erosions, but no definite ulceration on pylorus and duodenum.

Conclusion: New GI bypass stent has a good physiocompatibilities in simulated intestinal system. In animal, all stents were successfully deployed but migration of stent occurred in this study. Compared with endoscopic suture machine and modification of stent would be required. Disclosure of Interest: All authors have declared no conflicts of interest.
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Introduction: Dysphagia may occur due to benign pharingo-esophageal strictures, often due to previous treatments. The aim was to access long-term efficacy of pharingo-esophageal dilations due to anastomotic or post-radiation strictures.

Aims & Methods: Retrospective study on patients suffering of dysphagia due to radiotherapy (Group 1) or anastomotic (Group II) placed pharingo-esophageal benign strictures submitted to endoscopic dilation between January 2013 and December 2015. The long-term efficacy (after a minimum follow-up of 12 months) was prospectively assessed by telephone interview: a) dysphagia improvement or b) resolution (grade 0 or 1 of Mellow-Pinkas scale), c) absence of further dilations and d) absence of PEG. Additional therapy (PEG or prophylaxis placement, electroincision or surgery) was considered inefficiency criteria and these patients were excluded from the interview. Post-procedure complications were registered. Efficacy predictive factors were assessed.

Results: Forty-eight patients (296 dilations) were evaluated (median of 4 dilations/patient): 85% were male, mean age of 62 years-old, 60% belonging in Group II. Thereafter between 2 and 12 dilations (mean 3.5 dilations) were performed within 5 weeks. The endoscopic dysphagia Mellow-Pinkas score and luminal calibre were 3±1 and 7±2, 8mm, respectively. Twenty-eight patients (out of 30 live patients non-submitted to additional therapies) answered to the interview: a) 96% had improved, b) 60% had resolved dysphagia, c) 75% didn’t need additional dilations, d) 89% without PEG, with a combined efficacy of 58, 3%. Nine patients required additional therapy (6 PEGs, 2 prophylaxis, 1 electroincision). Overall, 1 out with 21 previous PEG were able to resume feeding per os. Fifteen and 29% presented Kochen criteria (mean 65 days), respectively. There were two post-procedure complications (<1%): one deep laceration and one pharingo-esophageal fistula. Overall mortality was of 20% (10 patients died of non related procedure causes). Mean follow-up was 29, 2 months. Number of dilations and initial luminal calibre were significant predictors of combined efficacy in the univariate analysis; radiic strictures predicted a greater final dysphagia in the uni- and multivariate analysis; recurrent/refractory stenosis didn’t significantly predict global efficacy.

Conclusion: Our dilution programme presents relevant benefit to these patients and a low rate of complications. Patients with post-radiation strictures presented a worse prognosis. Even though retrospective we present the longest follow-up and focusing not only in objective measures but also in patient perception of relief.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P0278 OUTCOMe AFTER THE USE OF SX-ELLA DANIS BLEEDING STENTS FOR refractory VARICeAL BLEEDING – A VIENNA MULTICENTER EXPERIENCE

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Introduction: Current guidelines favour the use of bleeding stents over balloon tamponade for esophageal variceal bleeding (EBV). However, data on the efficacy of and outcomes after the placement of an SX-ELLA “Danis-Stent” are limited.

Aims & Methods: Retrospective multicenter study including cirrhotic patients receiving Danis-Stents for massive/refractory EBV at 4 tertiary care centers in Vienna (Medical University of Vienna, Krankenanstalt Rudolfstiftung, Wilhelminenspital and Krankenhaus Hietzing). Rates of bleeding control (5 days), bleeding-related mortality (6 weeks) and overall mortality were assessed.

Results: Among 35 patients, 13 patients had an unsuccessful endoscopic band ligation (EBL) prior to Danis-Stent placement. Danis-Stent controlled EBV in 80% (28/35) of patients. In the remaining uncontrolled bleeders (n=7), 3 patients had subsequent EBL, while in 3 patients the stent had to be replaced and 1 patient received a Linton- tube. Among these patients with initial Danis-Stent failure, 4 died of uncontrolled EBV, 2 experienced early bleeding-related mortality, and only 1 patient achieved a successful long-term bleeding control. In total, early-rebleeding within 6 weeks occurred in 14.3% (including n=1 while Danis-Stent was still in place and n=5 after Danis-Stent was removed): 3 underwriters received a subsequent Danis-Stent, and 1 patient was treated with a Sengstaken tube. Moreover, among n=14 patients without early rebleeding within 6 weeks, only n=3 (21.4%) showed rebleeding later during follow-up: n=2 patients were treated with a Sengstaken- Tube (both experienced bleeding-related death) and n=1 had another Danis-Stent placed (successful bleeding control). Only n=11 (31.4%) patients did not experience any rebleeding after Danis-Stent removal, while n=8 patients died with the Danis-Stent in situ. Notably, “early-TIPS” was performed in this study, but 4 (11.4%) received not Danis-Stent, but 6 NIPS during follow-up (n=1 of 6 patients (16.6%) died due to uncontrolled bleeding (≤5days) and n=10 died within 6 weeks (bleeding-related mortality 28.6%). Overall, n=22/35 (62.9%) patients died. The median survival was 10.5 (IQR[82]) days after Danis-Stent placement. Median Danis-Stents dwell time was 5 (range: 0–13) days. The most common adverse events were stent dislocation (n=13; 37.1%), while ulcers/nectrosis of the esophageal mucosa were seen in only 4 (11.4%) patients.

Conclusion: Danis-Stent controlled refractionary massive EBV in 80% of patients but bleeding-related mortality was as high as 45%. While stent dislocations are frequent, ulcers/nectrosis of the esophagus were rare with a dwell time of 5 days. The implementation of an early-TIPS strategy might improve the overall outcome, pending further experience.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P0279 A NOVEL METHOD WITH SELF-EXPANDABLE METALLIC STENT FASTENED WITH CLIP AND LOOP FOR THE TREATMENT OF ANASTOMOTIC STRICUTURE AFTER SUBTOTAL GASTRECTOMY

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Introduction: Benign anastomotic strictures are common adverse events of gastrointestinal tract surgery. And, they are difficult to be managed conservatively. The first choices of treatment of anastomotic strictures are balloon dilatation and bouginisation. But, they are requiring repeated sessions. Self-expandable metallic stent (SEMS) placement has continuous expanding effect for a long period. But, It has problem of frequent stent migration, because of slow stent expanding, 2–3 days. Therefore the new method to inhibit stent migration is needed for more successful management of anastomotic stenosis.

Aims & Methods: The aim of this study was to evaluate the clinical feasibility of new method to inhibit stent migration in postoperative anastomotic stricture. From May 2013 until February 2015, patients with benign anastomotic stricture after subtotal gastrectomy were enrolled at a single tertiary referral hospital, prospectively. The Niti-S ComVi pyloric stents (Taewoong Medical, Korea), double-layered covered, were inserted. We made two nylon thread loops at the proximal bared section of the stents. After stent placement, stent fastening with loop and clip method was performed. Patients' symptoms and oral intake were assessed once or twice a week with a clinical check-up or telephone interview. After two weeks, the loop and stent removals were done. All patients were successfully inserted and stent patency were confirmed (technical success rate, 100%). The obstructive symptoms were subsided in 12 of 13 patients (clinical success rate, 92.3%). Stent migration was found in a follow-up endoscopy on 14 days (1 of 13, 7.7%). Anastomotic restenosis occurred in two patients 14 and 20 days after stent removal. However, obstructive symptoms were relieved by stent reinserterion.

Conclusion: The new method with fastening the stent with loop and clip can reduce the risk of stent migration.
Our fastening method can be feasible and useful technique for postoperative anastomotic stricture in sub-total gastrectomy. A large-scale prospective research is needed to validate the clinical effectiveness of our method and to determine the appropriateness.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0280 Efficacy and tolerability of biodegradable stents for recurrent benign oesophageal strictures: The Leeds Experience

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Introduction: The optimum management of refractory or recurrent oesophageal strictures (RBES) despite repeated attempts at dilatation is controversial. An accepted method includes temporary stent placement. Most commonly temporarily fully covered self-expanding metal stents (FC-SEMS) are used but these require removal some 8–12 weeks later. Oesophageal biodegradable stents (EBS) have the advantage that they do not require removal. However, there is a lack of good-quality evidence in support of their use. We aimed to review the safety and efficacy of a large series of single and multiple EBS insertions for benign RBES in a single tertiary referral centre.

Aims & Methods: A retrospective review of insertion of EBS (SX-ELLA) between April 2008 and October 2016 was conducted. Patients with one or more EBS insertions were included. The data and clinical data extracted from the hospital database. 30 day safety and efficacy for all stent insertions and 12 month efficacy and median time to further intervention (MTTFI) for first stents were analysed using the Stata package.

Results: 20 patients (13 m, 7 f; age 44–93; Charlson index range 2–8, median 4) with 37 stents were included. Stricture aetiology included peptic (55%), radiotherapy (20%), post-surgical (20%) and post EMR (5%). Dysphagia score ranged from 2–4 (median 3). The total median number of dilatations prior to first EBS was 6 (range 0–17). 15(75%) patients had previously had a FC-SEMS placed with subsequent recurrence of symptoms. 30-day technical success and symptom improvement was 100%. 30 day adverse events included 4(11%) stent migrations and 12(32%) with significant pain, 3 patients requiring in-patient pain control (<3 days). There were no significant bleed or perforations. 12 months following first EBS insertion 18/90(20%) required further endoscopic intervention due to recurrent symptoms; 5(25%) had further dilatation, 9(45%) had either a FC-SEMS (2 patients) or a further EBS (7 patients) or NG tube insertion and (5%) patient died of unrelated illness. 2(10%) were symptom free after one stent at 12m. MTTFI was 139 days (range 75–517) and was not dependent on aetiology (peptic vs. non-peptic; 135 vs. 127 days, p=0.54). There was a significant reduction in median number of interventions in the 12m following EBS insertion compared to the preceding 12m (2 vs. 7 respectively, p=0.0003). 7(35%) patients received multiple EBS (range of stent insertions 2–9). 3 of these (43%) have subsequently required no further intervention, 3(43%) continue to receive intermittent EBS, inserted on a symptomatic basis, 1(14%) patient continues to receive treatment for RBES, but has declined further EBS after 2 EBS inserted in discomfort.

Conclusion: Use of EBS for RBES in our centre was safe and well tolerated but there was short-lived pain in a significant number. In this highly selected cohort of difficult strictures, EBS led to short-term benefit in all patients but sustained efficacy and median time to further intervention (MTTFI) for first stents was analysed using the Stata package.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
Seventy of intractable and intraabdominal lymphadenopathy: mediastinal lymph nodes at 19 (52.2%) and 20 (33.9%) patients, combined of 38 (64.6%) and 35 (59.3%). At pre-operated staging mostly met advanced form of cancer: T4N1 at 16 (27.1%), T4N2 at 23 (38.9%). Sensitivity in staging of tumor 89.8%. Long-term results: 1-year survival at 1 group 96.1%, 3-year is 42.5%, 5-year 106% in II group 1-year survival 6.45%

Conclusion: The use of 3D-modeling performed using MRI, spiral CT and EUS, allows to planning the optimal surgery and lymph node for locally common form of esophageal cancer, and improve the results of survival.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0283 INFLUENCE OF CONTINUOUS ADMINISTRATION OF LOW-DOSE ASPIRIN FOR INTRAOPERATIVE BLEEDING ON GASTRIC ENDOSCOPIC GASTRIC DISSECTION: A PROSPEKTIVE SCORE MATCHING ANALYSIS

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Introduction: Endoscopic submucosal dissection (ESD) was a promising method for treatment of esophageal gastric divisional carcinoma. However, antiplatelet and anticoagulant agents has increased for first or secondary prevention of cardiovascular or cerebral disease. Continuous administration of low-dose aspirin (LDA) during ESD was recommended in American, British and Japanese guidelines. However, the influence of this drug for the hemostasis condition during ESD procedure is still unclear. Therefore, we performed this study for addressing intraoperative bleeding risk without cessation of LDA.

Aims & Methods: In this retrospective study, we assessed the hemostasis condition during ESD that were treated for superficial gastric lesions between January 2014 and March 2017. Patients with antithrombotic therapy by LDA (n = 42) and those with no antithrombotic therapy (n = 187; Control) were compared using propensity score matching. Primary outcome was frequency of intraoperative major bleeding. Secondary outcomes included procedure time, Hb reduction rate, En blos resection rate, and adverse event rate.

Results: The propensity score analysis yielded 39 matched pairs. Adjusted comparison between the two groups showed similar with regards to major bleeding, median (range) 0% vs 2.6% (0%–16.7%), procedure time, median (range) 95 (70–125) vs 75 (50–100) min, and adverse event rate (0% vs 0%). Procedure time was prolonged in Aspirin group by 16.7% without significant differences. Other aspects were the same in both groups with low incidence of adverse events; perforation (0%), thromboembolism (0%).

Conclusion: This study indicated the feasibility of gastric ESD with continuous administration of LDA including little intraoperative bleeding and adverse events.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0284 WEEKDAY OF CANCER SURGERY IN RELATION TO PROGNOSIS

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Introduction: Later weekday of surgery seems to reduce the prognosis in oesophageal cancer, while any such influence on other cancer sites is unknown. This study aimed to test whether weekday of surgery influences prognosis following commonly performed cancer operations.

Aims & Methods: This nationwide Swedish population-based cohort study from 1997-2014 analysed weekday of elective surgery for 10 major cancer groups in relation to disease-specific and all-cause mortality. Cox regression provided hazard ratios with 95% confidence intervals (CI) adjusted for the covariates age, sex, year, calendar volume, calendar year, and tumour stage.

Results: Included were 228,927 patients. Later weekday of surgery (Thursday and even more so Fridays) was associated with increased mortality rates for gastrointestinal cancers. The adjusted hazard ratios for disease-specific mortality comparing surgery on Friday with Monday were 1.57 (95% CI 1.31–1.88) for oesophago-gastric cancer, 1.49 (95% CI 1.17–1.88) for liver-pancreatic-biliary cancer, and 1.53 (95% CI 1.44–1.63) for colorectal cancer. Excluding mortality during the initial 90 days of surgery made little change to these findings, and the all-cause mortality was similar to the disease-specific mortality. The associations were similar in analyses stratified for covariates. No consistent associations were found between weekday of surgery and prognosis for the head-and-neck, lung, thyroid, breast, kidney, bladder, prostate, or ovary-uterus.

Conclusion: Later weekday of surgery in relation to surgery for gastrointestinal cancer may be an approach to improve the prognosis in gastrointestinal cancer surgery. Besides that, the postoperative severe complications are thought to be the poor prognostic factor. Present study assessed the prognostic impacts of severe postoperative complications and perioperative oncological treatments in gastrointestinal cancer patients.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0285 IMPACT OF POSTOPERATIVE COMPLICATIONS AND PERIOPERATIVE ONCOLOGICAL TREATMENTS FOR GASTRIC CANCER PATIENTS AFTER GASTRECTOMY

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Introduction: Recently, multidisciplinary treatments such as perioperative chemo/ radiation treatments have been implemented to improve the prognosis of gastric cancer surgery. Besides that, the postoperative severe complications are thought to be the poor prognostic factor. Present study assessed the prognostic impacts of severe postoperative complications and perioperative oncological treatments in gastric cancer patients.

Aims & Methods: Consequent gastric cancer patients who underwent curative gastrectomy in Karolinska University Hospital between 2006 and 2016 were enrolled. Patients’ characteristics, surgical data, postoperative courses and prognostic factors were evaluated according to Clavien-Dindo classification. The significance of postoperative severe complications and perioperative oncological treatment for overall survival (OS) was evaluated by the Cox proportional hazard model.

Results: In total, ninety-six-nine-sixty-six patients were examined in this study. 89 (52.7%) and 66 (39.1%) patients had neoadjuvant and adjuvant treatment, 85 (50.3%) and 84 (49.7%) underwent distal total and gasterectomy, respectively. 24 (14.2%), 16 (9.5%) and 5 (3.0%) were diagnosed as grade III, IV, V complications.

Conclusion: The prognosis of the patients with grade III or higher complication was significantly worse (3-year OS: 66.6% vs 47.3%, P < 0.001). Subgroup analysis by pathologic stage showed that the prognosis of pStage III/IV patients with postoperative complications was significantly poorer than the patients with grade III or higher complications (3-year OS: 45.3% vs 7.5%, P < 0.001). For the patients who had either neoadjuvant or adjuvant treatment, however, no obvious prognostic worsening was seen by the existence of complications (3-year OS: 70.6% vs 52.9%, P = 0.13). Multivariate analysis identified that severe complication was independent risk factor for OS (hazard ratio 1.82; 95% confidence interval 1.08–3.05), especially in pStage III/IV gastric cancer (hazard ratio 3.00; 95% confidence interval 1.53–5.86).

Disclosure of Interest: All authors have declared no conflicts of interest.

P0286 ENDOCOSOPIC PAPILLECTOMY OF DUODENAL PAPILLARY TUMOR: A REPORT OF 75 CASES

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Introduction: Duodenal papillary tumor as rare gastrointestinal neoplasm is essential for curative therapy due to its malignant potential. Endoscopic papillectomy is accepted as an alternative approach to surgery in select cases. Endoscopic papillectomy is considered a difficult endoscopic technique mainly performed by experienced endoscopists. Multicenter standard endoscopic procedures for endoscopic papillectomy have not been established.

Aims & Methods: We aimed to investigate the clinical value of endoscopic papillectomy for duodenal papillary tumor based on the endoscopic and clinical characteristics. Between 2006 and 2017, seventy-five patients with duodenal papillary tumor under endoscopic papillectomy in the gastrointestinal endoscopic center of Chinese PLA General Hospital were included. These patients were diagnosed of duodenal papillary tumor by the clinical manifestations, laboratory tests, CT, MRCPE, endoscope, EUS, ERCP along with biopsies and histopathologic tests. During the detailed clinical assessment combined with patients’ wishes, endoscopic papillectomy and followed ERCP procedures were performed successfully, and the clinical data of these patients were retrospectively analyzed.

Results: 75 patients (50 males and 25 females) with a median age of 58.6 yrs (range 27 to 82 yrs) were evaluated. The main clinical symptoms were predominated by abdominal pain followed by cholestasis and cholangitis, but nine cases with no abdominal symptoms. Endoscopic papillectomy was technically feasible in all these patients, and was mainly performed by four experienced endoscopists. The majority of excised tumors were exogenous (90.7%, 68/75), and the tumor size ranged between 8 and 55 mm. The final histopathological diagnosis included adenoma (44.7%, 33/75), carcinoma (37.3%, 28/75), adenosquamous with high-grade intraepithelial neoplasia (18.7%, 14/75), adenoma with low-grade intraepithelial neoplasia (26.7%, 20/75), adenoma combined with local carcinoma (16%, 12/75), and neuroendocrine tumor (1.3%, 1/75). In blos resection was achieved in 55 cases (70.7%) and the per-rectum biopsion was performed in 22 cases (29.3%). After endoscopic papillectomy, the ERCP procedures were performed in 70 cases (93.3%). The prophylactic pancreatic duct stent was placed in 30 cases (40%) for preventing pancreatitis, the biliary plastic stent or nasobiliary drainage tube in 16% (12/ 75), the stent placed in both in 17.3% (13/75), and no stent placement in 28.7% (21/75). Moreover, intraoperative hemostasis was performed in 47 cases (62.7%), including pure endoscopic clip placement, followed by injection therapy, thermal therapy or in combination. Regarding to the postoperative adverse events,
hemorrhage was identified in 11 patients (14.6%) but mainly cured by endoscopic hemorrhoidectomy, followed by perianal sepsis (9.3%, 7/75) but cured with medical treatment. 

Conclusion: Endoscopic papillotectomy can be considered as a feasible and reasonable treatment option for suitable patients with tumors of duodenal papilla.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0287 PROPHYLACTIC COLECTOMY WITH EXTENDED INDICATION OF RECTAL PRESERVATION IN RELATED APC FAMILIAL ADENOMATOUS POLYP SYNDROME: SYSTEMATIC REVIEW

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Introduction: Prophylactic surgery of familial adenomatous polyposis (FAP) ranges from total colectomy with ileorectal anastomosis (IRA) to proctocolectomy with ileoanal anastomosis and J pouch (IAA). Rectal resection is based on studies that did not include systematic endoscopic treatment that we perform. The objective was to compare IRA to IAA in terms of oncological safety and quality-of-life.

Aims & Methods: Between January 1965 and November 2015, all consecutive prophylactic colectomies were performed on grey literature. Outcomes were compared between IRA and IAA using endoscopic follow up in our unit: systematic endoscopic treatment of adenomas (argon, mucosectomy), were prospectively included. MYRH-related polyposes and patients who underwent abdomino-perirenal resection were excluded from analysis.

Results: 296 patients were included: 92 proctocolectomy with IAA (31.1%), 197 total colectomy with IRA (66.5%), and 7 abdomino-perirenal resections (2.4%). Mean (SD) number of preoperative rectal adenomas was 24.7 (33.9) in the IRA group and 12.9 (18.8) in the IAA group (p = 0.06). Mean number of lower endoscopies was 3.2 (5.1) in the IRA group vs. 2.3 (3.7) in the IAA group (p = 0.4). Median time to resection was 15 months (IQR 6-36) in the IRA group vs. 11 months (IQR 6-29) in the IAA group (p = 0.02). Mean adenoma recurrence in the IRA group was 3.1% (n = 9). Mean (SD) follow-up was 16.6 (11.9) years, during which the mean (SD) number of lower endoscopies was 3.4 (2.5) in the IRA group vs. 3.4 (2.5) in the IAA group (p = 0.9); mean (SD) number of treated adenomas was 17.8 (20.8) in the IRA group vs. 12.9 (18.8), respectively (p = 0.06); secondary cancer incidence was 6.1% vs. 11% (p = 0.06). The 15-year recurrence-free and overall survival (IR vs. IAA) were respectively 99.5% vs. 100% (p = 0.09) and 98.9% vs. 98.8% (p = 0.08).

Conclusion: Combination of aggressive endoscopic treatment and extended rectal preservation appears to be a safe alternative to ileoanal anastomosis and J pouch.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0288 ANAL PROBLEMS DURING PREGNANCY AND POSTPARTUM: A PROSPECTIVE COHORT STUDY

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Introduction: Many pregnant women have anal symptoms during pregnancy and postpartum. The most common proctologic problems reported are haemorrhoids, fissures, and anal incontinence. Literature about this problem is scarce.

Aims & Methods: The aim of this study is to determine the prevalence of anal problems and constipation during the second and third trimester of pregnancy, in the immediate postpartum and up to three months after childbirth. We also want to identify the risk factors for the development of anal symptoms. This is a prospective cohort study. Women between their 19th and 25th week of pregnancy are included. High-risk pregnancy and non-Dutch speaking are exclusion criteria. Nineteen questions were followed by a symptom questionnaire in the second and third trimester, in the immediate postpartum (within 3 days) and three months postpartum. Descriptive data were obtained from the patient files. A specific proctologic diagnosis was presumed on the basis of combined symptoms (rectal bleeding, anal pain and swelling). Constipation was defined by the Rome III criteria. Statistical analysis was performed with SPSS and risk factors were identified using multivariate analysis with binary logistic regression.

Results: Sixty-eight percent of the women developed anal symptoms during the whole study period. Anal symptoms occurred in 50% of the women during pregnancy, in 56.2% in the immediate postpartum and in 62.9% during the three months postpartum. The most prevalent symptom was anal pain. Constipation was reported by 60.7% during the whole study period. Most prevalent haemorrhoids were haemorrhoidal thrombosis (immediate postoperative hemorrhoidal prolapse (3rd trimester and immediate postpartum) and anal fissure (not episode-related). Anal incontinence was only reported in 2% during the postpartum. Multivariate analysis identified constipation and a history of anal problems as significant risk factors for the development of anal complaints postpartum and postpartum.

Conclusion: Two-thirds of pregnant women deal with anal symptoms during pregnancy or postpartum, especially haemorrhoidal complications and anal fissures. This high prevalence emphasises the clinical importance of this problem. The most important risk factor is constipation. Therefore, prevention of constipation in pregnant women is recommended.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0289 SURGICAL TREATMENT OF DIVERTICULITIS AND ITS COMPLICATIONS: A SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMIZED CONTROL TRIALS


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Introduction: Diverticulitis is a common gastrointestinal disease in developed countries, especially among elders. It is classified into five stages according to the severity of the inflammation with stage 5 involving peritonitis as a consequence of perforation and abscess formation, with 30-day mortality reaching 32%. This indicates that acute diverticulitis is an emergency case requiring rapid management. However, the surgical interventions of divertiitis vary according to its grade and severity, there is a controversy about the preferable surgical procedure of these different complications in acute divertiitis.

Aims & Methods: We aimed to systematically review and meta-analyze randomized controlled trials (RCTs) comparing outcomes and complications between different surgical approaches for acute diverticulitis and its complications. Nine electronic databases, including PubMed, Scopus, Google Scholar, ISI Web of science, WHO Global health library (GHL), POPLINE, Virtual health library (VHL), NYAM (New York Academy of Medicine), and SIGLE (System for information retrieval in life sciences) were searched. We included 148 articles, only 77 were used for the meta-analysis. The risk of bias was assessed using the Cochrane Collaboration tool. The pooled risk ratio (RR) and 95% confidence interval (CI) were calculated in the meta-analysis using the RevMan platform. The protocol was registered in PROSPERO (CRD42015032290).

Conclusion: RCTs comparing laparoscopic sigmoid resection (LSR) (n = 247) versus open sigmoid resection (ORS) (n = 237) for treatment of acute complicated diverticulitis with minimal heterogeneity. For short-term outcomes, there was no significant difference in postoperative overall morbidity (RR = 0.89, 95% CI [0.61–1.31]; P = 0.56), all major postoperative morbidity (RR = 0.79, 95% CI [0.12–5.07]; P = 0.80), and minor postoperative complications (RR = 0.98; 95% CI [0.62–1.57]; P = 0.94). Similarly, there was no difference between the two procedures regarding the long-term postoperative morbidity (RR = 0.84, 95% CI [0.57–1.21]; P = 0.39) and mortality (RR = 0.78, 95% CI [0.46–1.31]; P = 0.34), and mortality (RR = 0.95, 95% CI [0.04–24.59]; P = 0.98). In other four RCTs compared laparoscopic lavage with resection (sigmoidectomy) for treatment of perforated diverticulitis with peritonitis, the postoperative mortality rate was non-significant in both short-term (RR = 1.55, 95% CI [0.79–3.04]; P = 0.21) and long-term (RR = 0.67, 95% CI [0.29–1.58]; P = 0.36) follow up. Interestingly, the short-term reoperation rate and long-term preence of intra-abdominal abscesses were significantly higher in LSR group (RR = 1.74, 95% CI [1.01–2.97]; P = 0.03) and (RR = 1.52, 95% CI [1.03–5.92]; P = 0.04) respectively. The remaining five RCTs compared between different procedures, like primary anastomosis versus non-restorative resection, RP-LASR versus NRP-LASR, and primary versus secondary resection, for different situations and reviewed qualitatively.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0290 NLR AND PLR IN DIAGNOSING SYNCHRONOUS LIVER METATASES IN PATIENTS WITH CRC

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Introduction: There has been enormous progress in diagnosing and treatment of colorectal cancer (CRC), however a great number of patients is nevertheless diagnosed in an advanced disease stage. It is of great interest to develop a less invasive, inexpensive, prognostic, diagnostic, and treatment predicting biomarkers in early diagnostics of CRC considering its incidence worldwide. There are studies suggesting that the systemic inflammation play an important role in CRC tumor stage development, which can be reflected by the levels of neutrophil to lymphocyte ratio (NLR) and platelet to lymphocyte ratio (PLR).

Aims & Methods: This study was designed to investigate the efficiency of preoperative NLR, PLR as a tool for the assessment of synchronous lymph nodes
and liver metastases in newly diagnosed patients with CRC. Three hundred patients with CRC undergoing curative resection were included in this cross-sectional study. Complete blood counts with automated differential counts were performed preoperatively. The NLR was calculated by dividing the absolute neutrophil count by the absolute lymphocyte count; also PLR was calculated by dividing the absolute platelet count by the absolute lymphocyte count. The diagnostic performance of NLR and PLR was estimated by ROC curve.

Results: Our results suggest that there was high statistically significant difference between NLR (p = 0.003), PLR (p = 0.002) and tumor stages (I to IV). ROC curve analysis showed high diagnostic specificity of NLR (AUC 0.774, 95%CI = 0.683–0.790) and PLR (AUC 0.698, 95%CI = 0.663–0.742) for syn-
chronous lymph node and liver metastases. Also combination of NLR and PLR improved diagnostic efficacy (AUC 0.841, 95%CI = 0.811–0.863) for synchronous liver and lymph node metastases.

Conclusion: Our results suggest that NLR and PLR could be useful diagnostic CRC biomarkers, and could have potential use in early recognition of different stages of CRC.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

Disclosure of Interest: This research was funded by the Ministry of Science and Technology of Thailand.

References

Disclosure of Interest: This research was funded by the Ministry of Science and Technology of Thailand.

References
P0294 FULL-SCALE INTRODUCTION OF RADICAL LAPAROSCOPIC SURGERY FOR INGUINAL HERNIA EMPLOYING THE TRANSABDOMINAL PREPERITONEAL (TAPP) REPAIR AND EARLY OUTCOMES

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Introduction: Ger reported the first laparoscopic hernia repair in 1982 by approximating the hernia with stainless-steel clips. The first radical laparoscopic transabdominal preperitoneal (TAPP) repair was a revolutionary concept in hernia surgery and was introduced by Arregui and Dion in the early 1990s. Institutions performing radical laparoscopic surgery for inguinal hernia have been rapidly increasing since the NIH point was amended in Japan. However, in the 12th JAPAN SOCIETY FOR ENDOSCOPIC SURGERY questionnaire survey, the recurrence rate after surgery employing the TAPP method was reported to be 4%, posing a problem regarding the thoughtless introduction of the TAPP method. Our institution began with surgery employing the TAPP method only in November 2015 until April 2016, but treatment of inguinal hernia was integrated, the indication was established in May 2015, and laparoscopic surgery employing the TAPP method has been performed for the indicated cases. In this study, we investigated the current state of inguinal hernia treatment at our hospital. Surgical indication of inguinal hernia in our department is as follows. Symptomatic inguinal hernia is treated using the TAPP method when there is only one POSSUM score-based risk factor. When 2 or more risk factors are present or the patient has undergone surgery of the prostate, the anterior approach is employed (the UHS and Mesh Plug methods for internal and external inguinal hernia, respectively). Treatment under local anesthesia is prioritized for patients aged 90 years or older and patients with PS2 or higher. Arrangement in operating room is that the operator and assistant stand at the left and right sides of the patient, respectively, an anesthesiologist stands at the patient’s head, and a nurse stands caudal to the assistant.

Aims & Methods: In this study, we investigated the current state of inguinal hernia treatment at our hospital. The subjects were 120 patients who underwent radical surgery for inguinal hernia before and after the full-scale introduction of the TAPP method (early period: October 2014-April 2015 (7 months), late period: May 2015-October 2015 (7 months), 47 and 73 patients were treated in the early and late periods, respectively). Changes in the surgical procedure, complications, and duration of hospital stay were investigated in 120 patients.

Results: The median age was 70 years (19-91 years old). There were 114 male and 6 female patients. A total of 132 hernias (isulated in 103; right: 60, left: 48; and bilateral in 12). The hernia classification (Japanese Hernia Society) was 1, 2, 3, 4, 5 in 91, 11, 7, 3, 0, and 1 lesions. Surgery was performed under local anesthesia in 43, lumbar anesthesia in 1, and general anesthesia in 76. A laparoscopic left colectomy was performed using a linear stapler inserted through a trocar at the left abdomen. The median operative time was 102 minutes. Early Period was 4 days (4–24), Late Period was 3 days (3–9) for median duration of hospital stay. In Early period, complications, and duration of hospital stay were investigated in 120 patients. The incidence of Clavien Dindo Grade 3 or higher did not occur. In the early and late periods, respectively. Changes in the surgical procedure, complications, and duration of hospital stay were investigated in 120 patients.

Conclusion: Our institution began with surgery employing the TAPP method only in November 2015 until April 2016, but treatment of inguinal hernia was integrated, the indication was established in May 2015, and laparoscopic surgery employing the TAPP method has been performed for the indicated cases. In this study, we investigated the current state of inguinal hernia treatment at our hospital. Surgical indication of inguinal hernia in our department is as follows. Symptomatic inguinal hernia is treated using the TAPP method when there is only one POSSUM score-based risk factor. When 2 or more risk factors are present or the patient has undergone surgery of the prostate, the anterior approach is employed (the UHS and Mesh Plug methods for internal and external inguinal hernia, respectively). Treatment under local anesthesia is prioritized for patients aged 90 years or older and patients with PS2 or higher. Arrangement in operating room is that the operator and assistant stand at the left and right sides of the patient, respectively, an anesthesiologist stands at the patient’s head, and a nurse stands caudal to the assistant.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P0295 EFFECTIVENESS OF PURE LAPAROSCOPIC LEFT COLECTOMY WITH PRIMARY ANASTOMOSIS AND LOOP ILEOSTOMY FOR THE TREATMENT OF COMPLICATED HINCHEY 3 CATEGORY DIVERTICULITIS
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Introduction: The effectiveness of laparoscopic left colectomy with primary anastomosis and loop ileostomy in the treatment of complicated acute diverticulitis with diffuse purulent peritonitis (Hinchee 3), also considering the lack of evidence about this topic due to the difficulty of carrying out comparative trials with the laparoscopic washing/drainage technique.

Aims & Methods: A consecutive unselected series of 44 patients undergone emergency surgery for acute complicated Hinchee 3 diverticulitis from January 2012 to December 2016 was retrospectively evaluated. All patients were treated by pure laparoscopic left colectomy with primary colorectal anastomosis and temporary loop ileostomy. All the procedures were performed by the same surgeons (IS, ADL, FR). Perioperative care plan, operative steps and surgical instrumentation were standardized. We collected patients-, surgery- and hospital stay-related data, as well as short-term outcomes. Complications were classified using the Clavien-Dindo classification system.

Results: There were 31 men (70.4%) and 13 women (29.6%) with a mean age of 57.8 ± 11.9 years. The mean body mass index was 28.3 ± 3.1 kg/m2. No conversion to open surgery was registered. The mean operative time and estimated blood loss were 184.3 ± 32.7 minutes and 81.2 ± 72.7 ml, respectively. All the specimens showed diverticulitis with peridiverticulitis. Length of hospital stay was 7.8 ± 2.8 days and we have not recorded any readmissions in patients discharged within 60 days after surgery. The rates of postoperative complications were 6.8% for grade 3A and 5 according to the CDChC respectively.

Conclusion: Laparoscopic left colectomy with primary anastomosis and loop ileostomy seems to be a good technique that resulted in encouraging short-term outcomes. In expert hands it represents an effective technique for the treatment of acute diverticulitis complicated by diffuse purulent peritonitis.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
lower abdomen. The bowel extraction was performed by invagination transrectal through the posterior rectal wall incision in the CM was moved to the lower abdomen. The anastomotic region was completed by applying a circular stapling device transrectally, assisted by a transcutaneous inserted grasper. Function testing was performed by the colonoscope. Gastric access closure was performed by OTSC clip.

Results: The procedure was successful in all animals with operation time ranging from 4.5 to 6 hours. After weight gain in all cases, the animals were sacrificed after postoperative day 42 and the workup showed competent anastomotic healing with a stenosis and consecutive prestenotic dilatation in one case. These anastomotic prestenotic abscess beside the anastomosis. Gastric closure was healed and the OTSC clip still in sit in all animals. In one case we used two OTSC clips for gastric closure, there were severe adhesions with two perigastric abscesses.

Conclusion: The use of an operating platform like the Anubiscope has the advantage of flexible preparation in opposite position of the instruments. The disadvantages are the only two degrees of freedom of the flexible instruments and the rotation-like movements. Flexible colonoscopy provided a fixed reference frame for observation and dissection. For resection and anastomosis, an additional transcutaneous access was necessary.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0298

ASCITES, COMPLEX ADNEXAL MASSES AND RAISED CA-125 IN POST-MENOPAUSAL WOMEN: OVARIAN CANCER OR TUBERCULOSIS?

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Introduction: Post-tubal tuberculous (TB) peritonitis is a late complication of pelvic inflammatory disease and a chronic form of peritonitis. Peritoneal TB is a notifiable disease in many countries. The disease is not uncommon among post-menopausal women presenting with abdominal symptoms mimicking ovarian cancer.

Methods: The aim of this study was to analyze patients’ characteristics, laboratory investigations, radiological and surgical findings in post-menopausal women with pelvic TB who were diagnosed after laparotomy or laparoscopy for suspected ovarian cancer. We report twenty-one cases of pelvic-peritoneal TB in post-menopausal women who presented with mimicking ovarian malignant from 2004 to 2014 in a Tunisian center.

Results: The mean age was 59.8 (46–87 years). Three patients have personal or family history of TB. All women presented with abdominal pain and distension and were admitted to the hospital for diagnosis and treatment. Symptoms such as weight loss, reduced appetite, and dull abdominal pain are already common to these two entities.

Aims & Methods: The aim of this study was to analyze patients' characteristics, laboratory investigations, radiological and surgical findings in post-menopausal women with pelvic TB who were diagnosed after laparotomy or laparoscopy for suspected ovarian cancer. We report twenty-one cases of pelvic-peritoneal TB in post-menopausal women who presented with mimicking ovarian malignant from 2004 to 2014 in a Tunisian center.

Conclusion: The diagnosis of a functional ileus may be made preoperatively and peritoneal TB can be confirmed by histology and pathogenesis in all patients. The diagnosis of post-tubal TB is a challenge for the gynecologist. The treatment of pelvic TB is surgical and associated with a high risk of recurrence. The standard treatment for pelvic TB should be tailored to each patient.

Disclosure of Interest: All authors have declared no conflicts of interest.

MONDAY, OCTOBER 30, 2017

09:00-17:00

IBD I - HALL 7

P0299

INSULIN-LIKE GROWTH FACTOR IGF-I AND INFLAMMATORY RESPONSE IN THE COLONIC MUCOSA IN ULTERRATIVE COLITIS

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Introduction: Peptide growth factors including the IGF family are expressed in the colorectal epithelium and proliferative activity of the intestinal epithelium in ulcerative colitis (UC) and Crohn’s disease (CD). At the same time, IGF-1 is one of the main triggers behind the immune-inflammatory process in the colonic mucosa (CM) in UC, and its level may be of prognostic value in determining the illness course.

Aims & Methods: The aim of the study was to identify the role that IGF-I plays in colonic inflammation in 35 patients with different clinical (Rahmilevich index) and endoscopic (Mayo index) activity of UC. The treatment was administered in the form of lower UC; 20 healthy volunteers were the control group. IGF-I levels in peripheral blood were determined by ELISA (Mediagnost, Germany).

The results were expressed as mmol/l. The spontaneous and E. Coli LPS-induced synthesis of IL-8 in rectal biopptic samples were studied via ELISA. The results were expressed as picograms per 1 mg of wet tissue (pg/mg).

The severity of the IGF-I in peripheral blood was divided into three groups: with a level of inflammatory factors (in %) in the lamina propria. The study implied that the IGF-I levels in the blood plasma, on one hand, and indicators of the UC clinical, endoscopic activity and the intensity of the inflammatory infiltrate in the CM, on the other. Direct relationship was found between the level of spontaneous production of the IL-8 chemokine and the density of the inflammatory infiltrate in the CM of patients with active UC. Through the period of the clinical remission development (an average of 8 weeks) the IGF-I levels increased to 94.25 ± 28.18 mmol/l (P < 0.05), yet have not reached the control value (P < 0.05 to control). Induction of the clinical remission was associated with a decrease to the level of the control values for spontaneous and LPS-induced IL-8 production, regardless of UC activity.

Conclusion: The intensity of the inflammatory process in the CM depends on the level of IL-8 produced by relevant cells. Evidently, IL-8 has a capacity of inhibiting the production of IGF-I at the peak of inflammation (acute UC). Improvement of IGF-I and reduced IL-8 in remission facilitates regeneration of the damaged mucosa.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0300

REGULATORY B CELLS CONTRIBUTE TO THE ALLEVATION OF COLITIS INDUCED BY DEXTRAN SULPHATE SODIUM AFTER H. PYLORI INFECTION

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Introduction: Epidemiological studies have shown that there was an inverse relationship between Helicobacter pylori (H. pylori) infection and the incidence of inflammatory bowel disease (IBD). Our previous research indicated that the regulatory immune responses induced by H. pylori infection were not limited to gastric mucosa, IL-10-producing B cells and Foxp3+ Treg cells expanded in spleen and mesenteric lymph nodes (MLN), the balance of intestinal mucosal immunity was influenced to a skewed regulatory immune response.

Aims & Methods: A murine model with H. pylori infection and acute and chronic colitis induced by dextran sulphate sodium (DSS) was established to explore the function of the Breg cells in the alleviation of H. pylori infection on acute and chronic colitis induced by DSS. A C57BL/6 mice model of acute and chronic colitis was induced by 3% DSS with or without H. pylori infection in advance, the colitis performances were assessed by disease active index (DAI), colon length shortening, colon histological inflammatory scores. The CD19+IL-10+ Breg cells and CD4+CD25+Foxp3+ Treg cells in blood, spleen, MLN and gastrointestinal mucosa were measured by flow cytometry, immunohistochemistry and immunofluorescent staining. The anti- and pro-inflammatory cytokines were also detected at mRNA level by real-time PCR.

Results: Compared with the DSS treated acute colitis group, H. pylori/DSS treated acute colitis group: (1) DAI and colonic histological scores reduced (9.25 ± 2.83 vs 16.00 ± 2.00, P = 0.025) and colon length shortening (6.56 ± 0.63 vs 5.40 ± 0.54, P < 0.001). (2) The percentages of CD19+IL-10+ Breg cells detected by flow cytometry expanded in different tissues: blood: 5.05 ± 0.68 vs 2.89 ± 0.55, P = 0.001; spleen: 4.32 ± 0.56 vs 3.17 ± 0.20, P = 0.03; MLN: 5.89 ± 0.54 vs 4.94 ± 0.65, P = 0.047; PP: 6.95 ± 1.67 vs 5.39 ± 0.88, P = 0.005, respectively. (3) The percentages of CD4+CD25+Foxp3+ Treg cells expanded in different tissues: spleen: 13.50 ± 1.37 vs 10.73 ± 1.13, P = 0.008; MLN: 17.50 ± 0.82 vs 14.87 ± 1.53, P = 0.001; PP: 17.20 ± 3.24 vs 8.58 ± 1.71, P = 0.001. The numbers of CD4+CD25+Foxp3+ cells per 106 cells in colon: 3.44 ± 0.40 vs 2.58 ± 0.34, P = 0.004. (4) mRNA expression in colonic mucosa: IL-10 (P = 0.001) mRNA relative expression upregulated and IFN-γ (P = 0.04) mRNA relative expression downregulated significantly. Compared with DSS treated acute colitis group, the expression level of H. pylori infection was not limited to gastric mucosa, IL-10-producing B cells and Foxp3+ Treg cells expanded in spleen and mesenteric lymph nodes (MLN), the balance of intestinal mucosal immunity was influenced to a skewed regulatory immune response.

Disclosure of Interest: All authors have declared no conflicts of interest.
Conclusion: (1) H. pylori infection can alleviate the acute and chronic colitis induced by MMP9 in pre-treated mice. (2) CD4+CD103+ Foxp3+ Treg cells expanded significantly in H. pylori/DSS co-treated acute colitis mice. (3) CD4+IL-10+Breg cells expanded while CD4+CD25+Foxp3+Treg cells reduced significantly in H. pylori/DSS co-treated chronic colitis mice. The potential protective effect of H. pylori infection on acute and chronic colitis induced by DSS may pass through the expansion and function of CD19+IL-10+Breg cells.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0301 Fungal Composition and Fungi-Bacteria Correlation in IBD Patients with Different Treatment Strategies

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Introduction: The microbial dysbiosis plays a pivotal role in the pathogenesis of inflammatory bowel disease (IBD), however, the role of fungal microbiota in IBD was unclear. The aim of our study was to clarify the gut fungal composition in IBD patients with different treatment strategies.

Aims & Methods: 73 IBD patients were divided into three groups, Untreatment (n = 21), Antiinflammation (n = 43) and Immunosuppression (n = 9). Antiinflammation was defined as treatment with 5-aminosalicylic acid (5-ASA), salazosulfapyridine (SASP) and Immunosuppression as treatment with Glucocorticoid (GC), azathioprine (AZA), biologics and thalidomine.

Noninflamed and inflamed mucosae were acquired for 16S and ITS sequencing to investigate the bacterial and fungal composition. Inflamed mucosa was used for RNA extraction and real-time PCR to detect the expression of lba:-associated biomarkers, such as TNF-alpha, IL-17A, MCP-1, etc. Analysis of Spearman’s correlation was performed to estimate the fungi-bacteria and microbe-biomarker correlation.

Results: Compared with noninfamed mucosa, lower diversity and evenness were observed in inflamed mucosa in all IBD patients, but no significance in noninfamed (or inflamed) mucosa of different treatment strategies. Beta diversity showed a treatment-dependent clustering in inflamed mucosa. Fungal microbiota was constituted by fungi from Ascomycota, Basidiomycota and Zygomycota in inflamed mucosa of different treatment strategies. Beta diversity significantly altered fungi-bacteria correlation patterns in noninflamed mucosa (p < 0.001). Additionally, IL-17A, IL-22, IL-8 and MCP-1, and treatment altered microbiota biomarkers correlation.

Conclusion: Treatment strategies affect fungal composition. To some extent, IL-22, IL-8 and MCP-1, and treatment altered microbiota biomarkers correlation. Additionally, IL-17A tended to be the main mediator for bacteria to induce inflammation in IBD.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0302 Investigating the Microbiome in a Phase 1b Study of Andecaliximab in Ulcerative Colitis

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Introduction: MMP9 is involved in the degradation of the extracellular matrix and its expression is elevated in the inflamed tissue of patients with ulcerative colitis (UC) [1-3]. Pre-clinical models of colitis demonstrate a therapeutic benefit for antibodies to inhibiting MMP9 in pre-existing colitis [4]. Andecaliximab (previously GS-5745) is a high-affinity IgG4 monoclonal antibody against human Matrix Metalloproteinase 9 (MMP9). In a 36-day Phase 1b study in UC, andecaliximab demonstrated clinical efficacy relative to placebo treatment [5]. Here we describe bacterial microbiota analysis of stool samples collected during the Phase 1b study of andecaliximab in UC.

Aims & Methods: The objective of this study is to examine changes to the bacterial microbiota pre- and post-andecaliximab treatment and relative to therapeutic response. Fecal pool was collected in a randomized treatment (Baseline) and all treatment arms (Day 36). Clinical response was defined as a Mayo score reduction ≥3 point and ≥30% reduction from baseline score; accompanying decrease in rectal bleeding sub-score of ≥1 or an absolute rectal bleeding sub-score of 0 or 1, DCA was extracted from fecal samples using a modified CTAB method and 16S rRNA amplicon sequencing was performed on 59 samples (27 paired and 5 unpaired samples). Alpha diversity, beta diversity (calculated in QIIME), and taxonomic differences were examined between placebo and andecaliximab-treated patients, and between responding and non-responding patients.

Results: Compared to placebo-treated patients, those who received andecaliximab trended towards decreased alpha diversity (p = 0.06) at 36 days post-treatment. These changes in alpha diversity were not dose related. At Day 36, a trend towards a significant difference in community beta-diversity was observed between the andecaliximab-treated group relative to placebo (p = 0.07). Andecaliximab treatment was also associated with differences in bacterial taxonomy relative to placebo (p = 0.07). Specifically, the genera Clostridia and Akkermansia represented some of the top organisms enriched post andecaliximab treatment relative to placebo. Andecaliximab treatment exhibited a non-significant expansion of Akkermansia from Baseline to Day 36 (p = 0.15). Amongstandecaliximab-treated subjects, a trend of increased relative abundance of Akkermansia muciniphila was detected (p = 0.08).

Conclusion: Akkermansia muciniphila is the most consistently enriched organism for subjects treated with andecaliximab who respond to treatment. These preliminary results show that the potential pro-inflammatory role of A. muciniphila in ulcerative colitis may be associated with response to andecaliximab. Analysis of a larger study population would be required to verify these observations. Recent Phase 2 studies of andecaliximab in UC and Crohn’s disease failed to demonstrate clinical efficacy. These preliminary biomarker results are unlikely to be pursued in relation to andecaliximab treatment effects, but may be beneficial as a reference for future trials in inflammatory bowel disease.

Disclosure of Interest: B. Lamere: Microbiome data was analyzed and interpreted by UCSF and funded by Gilead Sciences.
E.R. Wendt: Employee of Gilead Sciences, Inc.
B. Kanwar: Employee of Gilead Sciences, Inc.
S.V. Lynch: Consultant for Theravance Sponsored research projects from Sloan Foundation, UC Foundation and inflammation-related IP licensed to Gilead Royalties for IP licensed by KaloBios Inc. Founder and Board of Directors, Siolta Therapeutics

References

P0303 MUCOSAL CYTOKINE PROFILE IN INFLAMMATORY BOWEL DISEASE PATIENTS: A LASER CAPTURE MICRODISSECTION APPROACH

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Introduction: Crohn’s Disease (CD) and Ulcerative Colitis (UC) are inflammatory Bowel Disorders (IBD) with a complex etiology, including an immune response against microbial and autologous antigens and an imbalance between pro-inflammatory and anti-inflammatory mediators. Different approaches have been used to study the pattern of cytokines in IBD and few data are available on cytokines production in different intestinal compartments. Laser Capture Microdissection (LCM) is a powerful tool for the isolation of specific tissue compartments (1).

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through the expression of Wnt ligands (Mucosal Immunology, 2016). We have recently reported that STAT6 deficiency favours fibrosis in a murine model of TNBS colitis (P031, ECCO 2016).

**Aims & Methods:** We aim to characterize here the functional relevance of the macrophage phenotype in fibrosis development. WT or STAT6 (−/−) mice were given TNBS (0.5, 0.5, 0.5, 0.5, 1, and 1 mg) intracolitically or saline weekly and they were sacrificed 3, 5 or 7 weeks after the first TNBS administration. The percentage of CD206, CD16, and CD86 positive cells was analyzed by flow cytometry in F4/80+ macrophages isolated from the intestinal mucosa. The mRNA expression of CD16 and fibrosis markers were evaluated in the colonic mucosa. The number of fungi decreased significantly in inflamed mucosal tissue compared to controls

**Disclosure of Interest:** All authors have declared no conflicts of interest.

Reference

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Introduction: Although the etiology of ulcerative colitis (UC) has yet to be characterized, it is increasingly accepted that the cause of UC might well be related to commensal enteric bacteria in a genetically susceptible patient. Anti-inflammation therapy using probiotics is usually prescribed for UC treatment, and we previously demonstrated that triple antibiotic combination therapy with oral amoxicillin (1500 mg/day), tetracycline (1500 mg/day) or fosfomycin (3000 mg/day), and metronidazole (750 mg/day) (ATM/AFM), for two weeks, induces remission in more than 27% of patients with active UC including those with steroid-refractory or dependent disease, suggesting ATM/AFM to possibly be effective for achieving UC remission.

**Aims & Methods:** Thirty-two patients with UC given ATM/AFM therapy for two weeks on average were enrolled in this study. The clinical conditions of these UC patients were evaluated by Mayo score. Fecal samples were obtained prior to, after therapy and at three months after treatment completion. Gut microbiota were compared employing metagenomic analysis of fecal samples.

**Results:** Of the 32 patients, 17 and eight, respectively, experienced complete and partial remission over three months in response to ATM/AFM therapy, whereas ATM/AFM showed no efficacy in seven patients. The metagenomic analysis revealed abundant human DNA to correlate positively with the disease activity indicated by the Mayo score. Furthermore, dramatic gut microbiota changes were observed at an early stage, i.e. just two weeks after starting ATM/AFM therapy (P0306).

**Conclusion:** The expression of Wnt ligands from CD16 positive cells, which are accumulated in the mucosa, may be involved in murine intestinal fibrosis.

Reference


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Reference


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Reference


**Disclosure of Interest:** All authors have declared no conflicts of interest.

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**Disclosure of Interest:** All authors have declared no conflicts of interest.

Reference


**Disclosure of Interest:** All authors have declared no conflicts of interest.
before treatment in the active stage to possibly be associated with increased proliferation of bacteria. Neutrophil extracellular traps (NETs) are fibrous structures released by activated neutrophils upon stimulation. NETs consist of chromatin and cytoplasmic proteins, which are released extracellularly during a process called NETosis. Tissue factor (TF) is the main in-vivo initiator of coagulation and is expressed on NETs in a plethora of neutrophil-mediated thromboinflammatory conditions [1–3]. Ulcerative colitis (UC) is characterized by infiltration of neutrophils into the affected mucosa and increased risk of thromboembolic events; however the mechanism behind the thrombophilic state of UC has not been clearly elucidated yet [4].

Aims & Methods: We aimed to investigate for the first time the role of neutrophils/NETs through TF expression in the pathophysiology of UC. Neutrophils, sera and colon biopsies were obtained from 10 naive patients with active UC (6 male, mean age 34.6 ± 19.1 years, mean Mayo score 8.5 ± 1.4) and from 10 native patients suffered from active Crohn disease (CD) (7 male, 3 female, mean age 34.2 ± 18.5, CDAI > 220). Additionally, 10 sex- and age-matched healthy subjects, were served as control subjects (5 male, 5 female, mean age 38.9 years). Ex-vivo findings regarding NETs and TF expression in peripheral blood leukocytes and colon tissue specimens were verified using appropriate in-vitro stimulations of control neutrophils with corresponding sera and intestinal tissue-conditioned media, respectively. Identification and quantification of NETs were performed with immunofluorescence confocal microscopy (IFC), flow cytometry and MPO/DNA complex ELISA. The expression of TF on neutrophils/NETs was determined using ICM, qRT-PCR and western blot analysis. The bioactivity of TF on NETs was assessed by measuring thrombin-antithrombin complex levels with ELISA.

Results: Neutrophils from patients with active UC are characterized by increased NET formation in both the peripheral blood and affected colonic mucosa, compared to healthy controls. Furthermore, NETs are decorated with functional TF and the amount of TF-bearing NETs was reduced from the inflamed to normal colon. In-vitro stimulations of controls neutrophils with sera or intestinal tissue-conditioned media corroborated the findings obtained ex-vivo. Co-localization of NETs expressing functional TF may be involved in the induction of intestinal inflammation and systemic thrombosis in UC probably constituting a novel candidate diagnostic and/or therapeutic target.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
Concomitantly, these cells were positive for the WNT ligand WNT10A and autophagy/mitophagy-associated LC3, suggesting autoregulatory mechanisms for the maintenance of the stem cell niche and mitochondria-associated functional alterations, respectively.

Conclusion: Our results indicate that mitochondrial function not only reflects IEC phenotypic changes but seems to be the driving force in differentiation processes. Mitochondrial function might therefore represent a key player at the edge of intestinal tissue homeostasis and repair/healing processes in the context of diseases.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P0310 METABONOMIC PROFILING OF ULCERATIVE COLITIS PATIENTS: RESULTS FROM AN INCEPTION COHORT TIME SERIES ANALYSIS
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Introduction: Previous studies have shown differences in disease phenotype of ulcerative colitis (UC) in South Asian (SA) migrants compared to Caucasians with pan-colonic phenotype predominant. The gut microbiota differs in ulcerative colitis (UC) in South Asian (SA) migrants compared to Caucasians. Previous studies have shown differences in disease phenotype of UC. For the UC cohort, robust models were obtained by OPLS-DA between SAs and Caucasians (HC). There was no significant difference between SA and Caucasian at time point 2 months (HC). OPLS-DA model between South Asian (SA) and Caucasians with UC. *compound is increased or decreased in SA compared with Caucasians respectively.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0311 BASELINE CLINICAL AND ENDOSCOPIC FEATURES OF ULCERATIVE COLITIS PATIENTS ARE RELEVANT GUIDE FOR SELECTING RESPONDENTS TO SELECTIVE DEPLETION OF MYELOID LINEAGE LEUCOCYTES AS REMISSION INDUCTION THERAPY
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Introduction: Patients with active inflammatory bowel disease have elevated myeloid lineage leucocytes1 including the CD14⁺ CD16⁻ DR⁻ e phenotype known as proinflammatory monocytes, and a major source of tumour necrosis factor-α.² Accordingly selective depletion of myeloid leucocytes by granulocyte/monocyte apheresis (GMA) is expected to promote remission or enhance drug efficacy. However, studies in ulcerative colitis (UC) patients have reported contrasting efficacy outcomes, ranging from an 85%³ to statistically insignificant level.³ Patients’ baseline demographic features may guide to selecting responder patients.
Aims & Methods: In a retrospective and single-centre setting we aimed to under-
stand if patients’ baseline clinical and endoscopic features were relevant guide for iden-
tifying likely responders and non-responders to adsortive GMA. The sub-
jects were 145 consecutive UC patients who had undergone GMA with the Adacolumn as remission induction therapy between 2012 and 2016. Seventy-
three patients were steroid naive, 70 were steroid dependent, and 2 patients were steroid refractory. Patients had received up to an 11 GMA sessions over 10 weeks. At entry and week 12, patients were clinically and endoscopically evaluated, allowing each patient to serve as her or his own control. Clinical activity index was defined as remission. Biopsies from endoscopically detectable inflamed large intestinal mucosa were processed to see the impact of GMA on leucocytes within the mucosal tissue.

Results: At entry, the average CAI was 12.8, range 10–17. Ninety-three patients (64.1%) had responded to GMA, 52 of 73 steroid naïve (71.2%), 40 of 70 steroid dependent (57.1%), and 1 of the 2 steroid refractory cases. On average remission was sustained for 8.6 months in steroid naïve patients and for 10.4 months in steroid dependent subgroup. Observations on mucosal tissue biopsies showed that the most responsive histopathologies were mostly mucosae and mononucleuses. There was a marked reduction of infiltrating leucocytes in responder patients. Patients with extensive deep UC lesions together with loss of the mucosal tissue at the lesions were non-responders. Patients with the first UC episode were identified as the best responders (100%) as compared with steroid naïve patients. Additionally, a short duration of active UC prior to GMA marked a patient as a likely responder. Further, all patients who achieved remission were steroid free at week 12.

Conclusion: First episode and steroid-naïve cases which responded well to GMA attained a favourable long-term clinical course. Additionally, GMA was more effective if applied immediately after a relapse than after a lag time. In general, GMA is favoured by patients for its safety profile and for being a non-drug remission induction therapy. Patients with extensive deep ulcers, with long dura-
tion of UC refractory to multiple pharmacologicals are unlikely to benefit from GMA. In therapeutic settings, knowing baseline clinical and endoscopic features, which may identify GMA responder patients should guide to stop futile use of medical resources.

Disclosure of Interest: A.R. Sanabia: Dr. Sanabia has a non-Regular em-
ployment position at JIMRO
All other authors have declared no conflicts of interest.

References
**P0314** A COMBINED ADMINISTRATION OF AMPICILLIN AND VANCOMYCIN INDUCES MILD COLON DYSBIOSIS – A DIVERSITY OF GUT MICROBIOTA AND PERTURBATION OF GLUTAMINE AND SHORT CHAIN FATTY ACID METABOLISMS

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Introduction: Antibiotics sometimes have an influence on colitis negatively. Although it is well known that dysbiosis is one of the major disturbances to the gut environment, the molecular mechanisms underlying the pathogenesis remains unclear.

Aims & Methods: We aimed to clarify how antibiotics affect the gut microbiota and the pathology of colitis. Mice were gavaged with ampicillin (ABPC), vancomycin (VCM), neomycin, or a combination of ABPC and VCM (A-V) for three consecutive days. Colitis was assessed by fecal occult blood test (FOBT) and mRNA level of cytokines. Fecal microbiota was characterized by 16sRNA sequencing. In the gluteal and ileal areas, the glucose (Gln) metabolites and SCFA including butyric acid (SCFA) in the feces were measured by a chromatography-tandem mass spectrometry. Fecal mucus was characterized by hexosamine and fucose. In the gluteal area, (Gln) treatment experiment, the mice were given 30mg/mL of Gln in drinking water ad lib for six days, and additionally gavaged A-V for the last three days.

In vitro experiments: colon cancer cell line cell line CT26 and macrophage cell line RAW264.7 were stimulated by butyric acid.

Results: ABPC and VCM, but not other antibiotics, resulted in FOBT-positive and IL-6, IL-12p40 and MPO overexpression. The treatment caused colitis-like changes evaluated in the A-V mice. Moreover, Gln metabolites and SCFA including butyric acid were decreased and family S247 and order Clostridiaceae were less abundant in the feces of A-V mice. Interestingly, Gln treatment improved the antibiotics-induced colitis. Reduced mRNA expression of pro-inflammatory cytokines in RAW264.7 and induced expression of antimicrobial peptides (secretory leucocyte protease inhibitor and lactoferrin) in CT26.

Conclusion: A-V treatment induced mild colitis with reduced abundance of family SCFA and other SCFA, which might diminish Gln and SCFA metabolisms.

Disclosure of Interest: All authors have declared no conflicts of interest.

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**P0315** ANTI-INFLAMMATORY EFFECTS OF G-PROTEIN-COUPLER DOPAMINE RECEPTOR 18 – A NOVEL POTENTIAL THERAPEUTIC TARGET IN INFANTILATORY BOWEL DISEASE

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Introduction: Inflammatory bowel disease (IBD) is a group of gastrointestinal tract diseases consisting mainly of Crohn’s Disease (CD) and Ulcerative Colitis (UC). Various etiological factors contribute to the pathogenesis of IBD, including modulation of microbiota, epithelial barrier disruption, genetics and environmental factors. Recently, the treatment of IBD comprises several groups of drugs the choice of which is made based on disease activity and extent. The treatment options include: analogs of 5-aminosalicylic acids, glucocorticoids and other immunosuppressive drugs such as azathioprine. Biological therapy with anti-tumor necrosis factor alpha (TNFα) are considered when conventional therapy fails. In portion of patients surgical approach is necessary. Therefore novel pharmacological targets are sought in order to improve the remission rate and avoid the disabling procedures. G protein-coupled receptor 18 (GPR18) belongs to the G-protein coupled cannabinoid system which already earned its place in the pathogenesis of IBD. GPR18 was found to be implicated in protecting against bacterial infection and organ injury. Reports indicate that it may also be connected to the obesity/diabetes-related inflammation. As we lack data regarding its association with intestinal inflammation we attempted to shed some light on this phenomenon.

Aims & Methods: The aim of the study was to assess the anti-inflammatory and anti-nociceptive actions of GPR18 in the intestinal inflammation. The anti-inflammatory activity of GPR18 agonist PSB-KK-1415 and antagonist PSB-CBS (1–5 mg/kg, i.c., once daily) was characterized in two mouse models of colitis, induced by 2, 4, 6-trinitrobenzenesulfonic acid (TNBS) and dextran sulfate sodium (DSS). The extent of inflammation was evaluated based on the microscopic score, quantification of myeloperoxidase (MPO) activity and alpha (TNFα) in colonic tissue. The expression of GPR18 gene in colonic samples from patients with IBD was quantified using real-time RT PCR and Western blot analysis. GPR 18 was localized in human colonic samples using immunohistochemistry methods.

Results: The results of our study with lower doses of GPR18 ligands in the semiliquid TNBS model of colitis showed a non-significant decrease in macroscopic score, ulcer score and a significant decrease in MPO activity (p < 0.05) in mice injected with PSB-KK-1415 compared with TNBS-treated mice. PSB-CBS increased inflammation indices. Study in the mouse model of TNBS-induced colitis with higher dose of PSB-KK-1415 presented a pronounced reduction in the indices after treatment with the agonist. We also showed that GPR18 is expressed in the colon of patients with IBD.

Conclusion: We demonstrated potential ability of the GPR18 agonist PSB-KK-1415 to alleviate inflammation in the mouse models of colitis and showed that GPR18 is expressed in the human colon. We conclude that GPR18 is another receptor of the endogenous cannabinoid system family which may be implicated in the pathogenesis of IBD and intestinal inflammation overall.

Disclosure of Interest: All authors have declared no conflicts of interest.

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**P0316** THE MECHANISM OF PROTECTIVE ROLE OF D3 Dopamine Receptors in Pathogenesis of Ulcerative Colitis

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Introduction: Our previous study showed that activation of D3 dopamine receptors (D3R) had the beneficial effect in experimental colitis treatment while the mechanism of this effect is unclear [1]. The disruption of surface colon mucosa layer is the subsequent activation of local immune response by the bacterial infection into the inner layer of the mucosa are the key pathogenic mechanisms of ulcerative colitis progression and perpetuation. We found the localization of D3R on the goblet cells in colonic mucosa [2].

Aims & Methods: We hypothesized that activation of D3R improves colonic mucous secretion during experimental colitis. Study was done on male Wistar rats (180–230). Experimental colitis was induced by 6% iodoacetamide (IA) (0, 1 ml, enema). Selective D3 agonist 7-OH-DPAT (0.1 mg/kg, s.c.) was injected i.p. 5 h prior to IA enema. Rats were euthanized 0, 5 and 2 h after IA enema. During the autopsy 7 cm colon from the anus has been removed. Surface mucous layer was separated from epithelial cells with N-acetyl-L-cysteine and glycoproteins were measured by periodic acid/Schiff (PAS) staining or by the reaction with Folins reagent. The content of heoxine, fucose and hexosamine were determined by standard biochemical assays.

Morphometric analysis was performed to evaluate the histological changes of colonic epithelial and goblet cells. Oxidative metabolism and arginase activity (analyzed by colorimetric method) in peritonal macrophages were investigated.

Results: Pre-treatment with 7-OH-DPAT did not affect the glycoprotein levels in normal mucosa, but significantly increased total levels of glycoprotein (1, 6-fold, p < 0.05) and hexose (1, 1-fold, p < 0.05) during IA-colitis. Furthermore, 7-OH-DPAT significantly increased the content of hexosamine in macrophages in 0, 5 h (1, 6-fold, p < 0.05) and in 2h (1, 3-fold, p < 0.05) after IA enema. Pre-treatment with 7-OH-DPAT decreased the mucosal thickness 1, 1-fold (p < 0.05), crypt depth 1, 1-fold (p < 0.05) and goblet cell cell lesion area 1, 2-fold (p < 0.05) after IA enema.

Conclusions: Pre-treatment with D3R agonist increased levels of mucus secretion and activated natural immune response by macrophage activation during experimental colitis, which could indicate about the protective role of D3R.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

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**P0317** INFLAMMATION AT DISTAL ILEOCAecal RESECTION MARGINS INCREASE THE RISK OF POSTOPERATIVE CROHN’S RECURRENCE

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Introduction: Guidelines advise limited resection for Crohn’s terminal ileitis, as previous literature did not demonstrate clinical benefit from more extensive resections. Recently, some cohort studies identified positive resection margin as an independent risk factor for postoperative Crohn’s recurrence. But it is difficult to draw clinical conclusions, as non-uniform pathological definitions have been used. The aim of this study was to assess the incidence of non-radical resections by a validated pathological score, and correlate pathological findings to clinical outcomes.

Aims & Methods: H&E stained slides from proximal (ileum) and distal (colon) resection sites were scored according to the modified Geboes score from all consecutive patients undergoing primary ileocecal resection between January 2002 and September 2009. Endpoints were clinical recurrence (defined as recurrent disease activity demonstrated by endoscopy or MRI) requiring upsaling medical treatment or surgical recurrence.
Results: Of 104 ileocecal resections, 30 (29%) and 15 (14%) had inflammation at the proximal and distal resection margins, respectively. After a median follow-up of 8.6 years, clinical recurrence was seen in 57%, and surgical recurrence in 26%. A significantly increased recurrence rate was seen in patients with active inflammation at the distal resection margin whereas recurrence rates were comparable for inflammation at the proximal site and radical resections (87%, 61%, and 50% resp., p < 0.001). Active inflammation at the distal resection margin (HR: 3.189 (1.635–6.220); p = 0.001) and smoking (HR: 2.502 (1.331–4.703); p = 0.004) were the only independent predictors for clinical recurrence. The incidence of surgical recurrence was small to perform in AIEC screening.

Conclusion: Inflammation at the distal (colon) resection margin, and not the proximal ileum, after ileocecal resection was associated with significantly increased risk of clinical recurrence. This unexpected finding suggests that radioclinical staging, in correctly diagnosed terminal ileitis (I1 disease), while it is of crucial importance to exclude colonic (L3 disease). As this different phenotype is unlikely to benefit from more extensive surgery, pathological finding of positive distal resection margin should be regarded as a risk factor, warranting prophylactic drugs or close monitoring.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P0319 LIPOSMAL FORMULATION AS A NEW DRUG DELIVERY SYSTEM FOR CROHN’S DISEASE – VALIDATION IN THE MOUSE MODEL OF TNBS-INDUCED COLITIS

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Introduction: Crohn’s disease (CD) is a chronic inflammatory condition of the intestine, characterised by clinical symptoms of inflammatory bowel disease (IBD), constitutes a significant healthcare burden, in the developed societies. Current methods of treatment are only partially effective and/or associated with major adverse effects. New therapeutic solutions are needed to ameliorate the effects of medical therapy, reducing complications and improving patients’ quality of life.

Aims & Methods: The objective of the study was to assess the effectiveness of delivery of anti-inflammatory drugs encapsulated in the liposomal formulation. Liposomes were prepared using thin-lipid hydration method. 0.9% sodium chloride was used as a solvent. The hydration solutions contained an aminosalicylate mesalazine (5-ASA), two recently validated plant-derived anti-inflammatories with low bioavailability, chlorogenic acid (CGA) and berberine, and pure solvent as negative control. CGA was administered by a single intra-colonic (i.c.) administration of 2, 4, 6-trinitrobenzene sulphonic acid (TNBS) on Day 0. Liposomal suspensions containing 5-ASA (5 mg/kg), CGA (20 mg/kg), berberine (5 mg/kg) and the solvent were administered i.c. twice daily from Day 3 to Day 6. Mice were sacrificed on Day 7 and colonic damage was evaluated.

Results: The microscopic scoring system included the evaluation of the colon length and bowel thickness as well as the presence of ulcers, haemorrhage, faecal blood and diarrhea. Additionally, tissue myeloperoxidase (MPO) activity was determined and body weight was measured. The obtained results indicate that the best anti-inflammatory effect was obtained when liposomal suspension with berberine was used, while the treatment with 5-ASA was less effective. Surprisingly, CGA administration caused a detrimental effect as demonstrated by higher macroscopic score and increased MPO activity.

Conclusion: Drug-loaded liposomes may enhance the penetration of active compounds through the gut wall and therefore allow for increased bioavailability and effectiveness of the treatment at lower doses. We also showed that plant-derived compounds with low bioavailability, such as berberine and CGA, provide a new direction in the search of anti-inflammatory substances. However, increased bioavailability of anti-inflammatories due to liposomal formulation may result in adverse effects.

Disclosure of Interest: All authors have declared no conflicts of interest.

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1. Rutgeerts P, Geboes K, Vantrappen G, et al. Predictability of the postoperative finding of positive distal resection margin should be regarded as a risk factor, warranting prophylactic drugs or close monitoring.

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incidence rate of microscopic colitis appeared to increase with time (Table). The incidence of microscopic colitis in 2016 was twice that observed in 2009 (incidence rate ratio 1.86; 95% CI 1.41, 2.46). There was a strong, independent graded association between the incidence of microscopic colitis and the number of lower GI endoscopy procedures undertaken (p = 0.03).

Conclusion: Microscopic colitis diagnosis is becoming more common. It is unclear whether microscopic colitis itself is increasing or greater numbers of lower GI endoscopy are being undertaken causing an ascertainment bias. Further work is required to explore environmental exposures such as drugs associated with microscopic colitis and to observe its natural history.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

P0321 EXTRA-INTESTINAL MANIFESTATIONS AT DIAGNOSIS IN PAEDIATRIC- AND ELDERLY-ONSET ULCERATIVE COLITIS ARE ASSOCIATED WITH A MORE SEVERE DISEASE OUTCOME: A POPULATION-BASED STUDY

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Introduction: Data on extra-intestinal manifestations (EIM) and their impact on disease course of ulcerative colitis (UC) in population-based cohorts are scarce, particularly in paediatric- and elderly-onset UC patients.

Aims & Methods: The aims of this population-based study were to assess 1) the occurrence of EIM in paediatric- and elderly-onset UC; and 2) their impact on long-term disease outcome. Paediatric-onset (<17 years at diagnosis) and elderly-onset UC patients (>60 years) from a French prospective population-based Registry (EPIMAD) were included. Data on EIM and other clinical factors at diagnosis and at maximal follow-up were collected.

Results: 158 paediatric- and 470 elderly-onset UC patients were included (median age at diagnosis 14.5 and 68.8 years; median follow-up 11.2 and 6.2 years, respectively). EIM occurred in 8.9% of childhood- and 3% of elderly-onset patients at diagnosis and in 16.7% and 2.2% of individuals during follow-up (p < 0.01). The most frequent EIM was joint involvement (15.8% of paediatric-onset and 2.6% of elderly-onset). Presence of EIM at diagnosis was associated with more severe disease course (need for immunosuppressive or biologic therapy or colectomy) in both paediatric- and elderly-onset UC (HR = 2.0, 95% CI: 1.0-4.2 and HR = 2.8, 0.9-7.9). Extensive colitis was another independent risk factor in both age groups.

Conclusion: Elderly-onset UC patients had lower risk of EIM either at diagnosis or follow-up than paediatric-onset UC. EIM at diagnosis predicted more severe disease outcome including need for immunosuppressive or biologic therapy or surgery in both paediatric- and elderly-onset UC.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0322 LONG-TERM NATURAL HISTORY OF MICROSCOPIC COLITIS: A POPULATION-BASED STUDY


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Introduction: Data on long-term natural history of microscopic colitis (MC), including collagenous (CC) and lymphocytic colitis (LC) are lacking.

Aims & Methods: All new cases of MC diagnosed in the Somme area, France between January 1st, 2005 and December 31th, 2007 were prospectively included. Colonic biopsies from all patients were reviewed by a group of 4 expert gastrointestinal pathologists to assess the diagnosis of CC or LC. Demographic and clinical data were retrospectively collected from diagnosis to February 31th, 2017.

Results: One hundred and thirty cases of MC, 87 CC and 43 LC were included (median age at diagnosis 70 and 48 years, respectively). The median follow-up was 9.6 years (Q1: 7.6; Q3: 10.6). By the end of follow-up, 37 patients (28%) relapsed after a median time of 3.9 years (1.2; 5) since diagnosis, without significant difference between CC and LC (30% vs 25%, p = 0.47). Twenty patients (15%) were hospitalized for a disease flare and 32 (25%) presented with another autoimmune disease. Budesonide was the most widely used treatment (n = 31, 25%). Median duration of budesonide treatment was 92 days (70; 168) and no adverse event to budesonide were reported. Sixteen patients (22%) developed steroid-dependency and 4 (5%) were corticorestant. Only one patient was treated by immunosuppressants (azathioprine). No colorectal cancer was reported during follow-up. Any of the death (n = 25) observed during follow-up were linked to MC. In multivariate analysis, age at diagnosis (HR 1.03; 95%CI: 1.00-1.06; p = 0.02) and budesonide exposure (HR 0.40; 95%CI: 0.18-0.90; p = 0.03) were significantly associated with relapse.

Conclusion: This population-based study showed that after diagnosis, two third of patients with MC observed long term clinical remission. Age at diagnosis and budesonide exposure were associated with a risk of relapse.

Disclosure of Interest: M. Fumery: Lecture fees or consultant fees: Abbvie, Ferring, MSD, Takeda
All other authors have declared no conflicts of interest.

P0323 IBD-INFO QUESTIONNAIRE: A MULTICENTER FRENCH UP-TO-DATE SURVEY OF PATIENT KNOWLEDGE IN INFLAMMATORY BOWEL DISEASE

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Introduction: It has been demonstrated in many chronic conditions, including inflammatory bowel disease (IBD), that better patients’ knowledge about pathology and treatment improves the course and management of disease. The aim of this study was to develop an updated self-questionnaire to assess patients’ level of knowledge of IBD.

Aims & Methods: The IBD-INFO included 3 parts: an original part (Q1), and 2 parts from the translation of the pre-existing questionnaires Crohns’ and Colitis Knowledge score (CCKNOW) (Q2) and Crohn’s and Colitis Pregnancy Knowledge score (CCPKNOW) (Q3). The reliability and discriminatory ability of the questionnaire were validated with 3 groups of non-IBD volunteers with various theoretical knowledge levels. The final questionnaire (64 validated questions) was then tested on 364 in- and out- IBD patients from 4 French university hospitals. The score for each part of the questionnaire was calculated and factors associated with low scores were identified by uni- and multivariate logistic regression analyses.

Results: The scores obtained by the 3 non-IBD volunteer groups differed significantly (p < 0.0001) and the IBD-INFO questionnaire showed excellent internal reliability and consistency (α = 0.98). The median total score obtained by the IBD patients was 27.64 [0–59], and scores for Q1, Q2 and Q3 were, respectively, 10/23
Aims & Methods: In total 1814 patients with histologically confirmed IBD were evaluated. Medical records from 705 UC and 1022 CD patients as well as from 77 UC-PSC and 10 CD-PSC patients were assessed. Data were evaluated using standard statistical methods. In matched-pair analyses, IBD patients with and without PSC were matched at the ratio of 3:1 by sex, disease entity, age at disease onset and higher risk for extensive disease manifestation as well as increased risk for colorectal dysplasia development.

Disclosure of Interest: All authors have declared no conflicts of interest.
P0326 OPIATE USE IN INFLAMMATORY BOWEL DISEASE. PRESCRIPTION TRENDS AND MORTALITY IN AN ENGLISH PRIMARY CARE COHORT FROM 1990–2014

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Introduction: Chronic abdominal pain is a common symptom in inflammatory bowel disease (IBD). Pain management is complicated by clinically important gastrointestinal side effects of many of the available analgesics, particularly opioids. Opiate prescribing for cancer and non-cancer pain has increased dramatically in recent years but there is a paucity of data on prescription trends for individuals with IBD. The only population-based study is from Canada where 5% of subjects with IBD became heavy opiate users after 10 years of diagnosis and there was a strong association between heavy opiate use and mortality (OR 2.91, 95% CI 1.58–5.02). In this study we explore trends in the prescription of opiate medications and assess the association between opiate prescription and mortality in English primary care cohort of patients with IBD.

Aims & Methods: We used the English primary care database ResearchOne for this study which holds records from approximately 6 million individuals (>10% of the total population). We extracted relevant clinical codes and prescription data on all patients with IBD, and separated out those with ulcerative colitis (UC) and Crohn’s disease (CD). We created 4 categories of opiate medication use, namely; any opiate medication, codeine only, tramadol, and strong opiates. We defined 3 groups of prescription density as none/infrequent users, moderate, and heavy users as <1, 1–3, and >3 prescriptions per calendar year respectively.

We examined the trend in opiate prescriptions for all IBD patients in 4 year blocks from 1990–2014 using chi2 for trend as a significance. Separate trends were produced for each of our opiate classes. We calculated a propensity score estimating the conditional probability of being prescribed an opiate medication based on pre-defined characteristics which may influence the prescription of opiates. All-cause mortality in opiate users and non-users was compared in a propensity score matched, Cox proportional hazards regression analysis to produce hazard ratios (HR) and 95% confidence intervals (CI). All analyses were performed for each opiate medication class in CD and UC patients.

Results: We included 3517 patients with CD and 5349 with UC. Opiate prescriptions increased from 10% in 1990 to 30% in 2014 (chi2 for trend p < 0.005). There was a similar, significant increase for codeine (chi2 for trend, p = 0.008), tramadol (p < 0.003) and strong opiates (p < 0.005) when analyzed separately. Table 1 shows the association between opiate use and all-cause mortality in patients with IBD. Any opiate use in patients with UC was associated with increased mortality (HR 1.67, 95% CI 1.25–2.23). The strongest associations were for heavy users of strong opiates in patients with CD (HR 2.18, 95% CI 1.20–3.95) and UC (HR 3.30, 95% CI 1.77–6.18). There was no association for prescriptions of tramadol at any prescription density in CD or UC.

Table 1: The association between opiate prescriptions and all-cause mortality in patients with inflammatory bowel disease in the English primary care database Research One. Propensity score matched, Cox proportional hazards regression analysis.

Table 1 Continued

<table>
<thead>
<tr>
<th>Biological therapy</th>
<th>Surgery</th>
<th>Hospitalization</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1 year</td>
<td>3 years</td>
</tr>
<tr>
<td>Crohn’s disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eastern Europe</td>
<td>4 (5%)</td>
<td>6 (7%)</td>
</tr>
<tr>
<td>Western Europe</td>
<td>80 (20%)</td>
<td>110 (27%)</td>
</tr>
<tr>
<td>Ulcerative colitis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eastern Europe</td>
<td>1 (1%)</td>
<td>6 (5%)</td>
</tr>
<tr>
<td>Western Europe</td>
<td>28 (5%)</td>
<td>53 (9%)</td>
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</table>

Conclusion: Our study is the largest population based study of opiate use in patients with IBD. We have shown a significant increase in the prescription of opiates since 1990, with 30% being prescribed an opiate medication between 2010 and 2014. Prescriptions of codeine in UC and strong opiates in both CD and UC were associated with increased all-cause mortality. There appears to be a dose association as heavy users of strong opiates had the largest association with mortality. Observational studies are not proof of causality and there may be residual confounding. A dose response is a strong indicator that opiates could be responsible for the associations seen, which is consistent with other studies investigating opiates used for non-cancer pain in chronic disease. Randomised controlled trials would be unethical and not feasible to investigate this potential effect so population-based observational studies may provide the best estimate. Opiate prescriptions are increasing worldwide for chronic non-cancer pain, and individuals with IBD can now be included. Clinicians managing pain in individuals with IBD should consider the potential implications of prescribing, or continuing with opiate prescriptions as they are a marker for increased mortality.

Disclosure of Interest: All authors have declared no conflicts of interest.

References: See abstract.

P0327 PATIENTS WITH INFLAMMATORY BOWEL DISEASE HAVE AN INCREASE RISK OF PERIODONTAL DISEASE IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Introduction: We aimed to: (1) evaluate the prevalence of periodontitis in patients with inflammatory bowel disease (IBD), (2) assess the impact of IBD activity and IBD therapy on periodontal outcomes.

Table 1: Continued

<table>
<thead>
<tr>
<th>Biological therapy</th>
<th>Surgery</th>
<th>Hospitalization</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1 year</td>
<td>3 years</td>
</tr>
<tr>
<td>Crohn’s disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hazard ratio (95% CI)</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Ulcerative colitis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hazard ratio (95% CI)</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

Any opiate medication

none/infrequent use (<1 prescription per year) 1
Moderate use (1–3 prescriptions per year) 0.94 (0.64–1.39) 0.83 (0.56–1.21)
Heavy use (>3 prescriptions per calendar year) 1.15 (0.85–1.55) 1.67 (1.25–2.23)

Conclusion: We have shown a significant increase in the prescription of opiates since 1990, with 30% being prescribed an opiate medication between 2010 and 2014. Prescriptions of codeine in UC and strong opiates in both CD and UC were associated with increased all-cause mortality. There appears to be a dose association as heavy users of strong opiates had the largest association with mortality. Observational studies are not proof of causality and there may be residual confounding. A dose response is a strong indicator that opiates could be responsible for the associations seen, which is consistent with other studies investigating opiates used for non-cancer pain in chronic disease. Randomised controlled trials would be unethical and not feasible to investigate this potential effect so population-based observational studies may provide the best estimate. Opiate prescriptions are increasing worldwide for chronic non-cancer pain, and individuals with IBD can now be included. Clinicians managing pain in individuals with IBD should consider the potential implications of prescribing, or continuing with opiate prescriptions as they are a marker for increased mortality.

Disclosure of Interest: All authors have declared no conflicts of interest.

References: See abstract.
Aims & Methods: In a prospective 6-months study, dental examination was performed in IBD and in 19 healthy controls. IBD related variables were prospectively collected, as well as markers for periodontitis including gingival bleeding (BOP index, marker of periodontal inflammation), gingival recession (REC index, marker of cumulative periodontal destructions) and probing depth (PD) at the severity of the process. Additional dental examination was proposed 3 months after to all patients diagnosed with periodontitis.

Results: Among the 54 included patients, 44 had Crohn disease (81%) and 31 were women (55%). At the time of dental examination, median age was 33 years (Q1 = 26; Q3 = 41), 20 (36%) were smokers and the median IBD duration was 8.4 years (3.4-16.3). Eleven (20%) were treated by corticosteroids, 27 (49%) by anti-TNF, 6 (10%) by other biologics and 8 had no IBD treatment. IBD was significantly associated with periodontitis (81% vs 27%; Odds Ratio 2.9, 95% CI 3.6-2.3). Mild, moderate and severe periodontitis were respectively observed in 34 (63%), 8 (15%) and 3 (5%) IBD patients. As compared to healthy controls, IBD patients had significant increase of BOP index (p = 0.008), probing death (p = 0.03), and REC index (p = 0.01). Patients with active IBD (Harvey-Bradshaw index >1) had a significant increase of BOP index (p = 0.007) as compared to patients with inactive disease. A significant correlation between BOP and Harvey-Bradshaw index was observed (r = 0.44, p = 0.0018). Anti-TNF therapy was significantly associated with lower BOP index (p = 0.02). All patients with diagnosis of periodontitis were treated by periodontal debridement and subgingival irrigation with povidone-iodine which led to a significant decrease of BOP index three months after diagnosis.

Conclusion: Inflammatory bowel diseases were associated with an increased risk of periodontitis. Gingival inflammation was correlated to disease activity and anti-TNF therapy was associated with a lower risk of active periodontal disease.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P0328 DETECTION OF MUTATIONS IN NOD2/CARD15 GENE IN ARAB PATIENTS WITH CROHN’S DISEASE

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Introduction: Crohn’s disease is a chronic, immune mediated inflammatory condition which affects the gastrointestinal tract. NOD2/CARD15 mutations have been linked to an increased risk of Crohn’s disease and to some of its phenotypes. This study aimed to determine the presence of the above mutations in Arab patients suffering from Crohn’s disease in Kuwait.

Aims & Methods: Blood samples were obtained from 103 Arab patients with Crohn’s disease and 100 Arab control subjects. The genomic DNA was isolated from the samples using Qiagen DNA Blood mini kit. The isolated DNA were amplified in 54 patients with IBD and in 19 healthy controls. IBD related variables were prospectively collected, as well as markers for periodontitis including gingival bleeding (BOP index, marker of periodontal inflammation), gingival recession (REC index, marker of cumulative periodontal destructions) and probing depth (PD) at the severity of the process. Additional dental examination was proposed 3 months after to all patients diagnosed with periodontitis. As compared to healthy controls, IBD patients had significant increase of BOP index (p = 0.008), probing death (p = 0.03), and REC index (p = 0.01). All patients with diagnosis of periodontitis were treated by periodontal debridement and subgingival irrigation with povidone-iodine which led to a significant decrease of BOP index three months after diagnosis.

Results: Inflammatory bowel diseases were associated with an increased risk of periodontitis. Gingival inflammation was correlated to disease activity and anti-TNF therapy was associated with a lower risk of active periodontal disease.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0329 GENETIC ASSOCIATIONS OF INFLAMMATORY BOWEL DISEASE IN SRI LANKA: A CASE-CONTROL STUDY OF PHENOTYPES AND SELECTED GENETIC POLYMORPHISMS

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Introduction: There is limited data on genetics of inflammatory bowel disease (IBD) in populations where the condition is emerging, especially from South Asia.

Aims & Methods: A case [histologically confirmed ulcerative colitis (UC) and Crohn disease (CD) of 2+1 year duration] control [unrelated, healthy, gender matched] study was conducted at four major gastroenterology centres in Sri Lanka. Phenotypic data (type, location, severity, treatment types, response to treatment and complications) of cases were obtained. Cases and controls were genotyped for 16 selected variants with known IBD disease associations in Western and East Asian populations [IL12B:rs1045431, IL23R:rs11805303, ARPC2:rs12612347, IRGM:rs13361189, IL26:rs1558744, IL10:rs282785, IL10:rs3024505, PTGER4:rs1631763, IL17REL/PIM3:rs9268853, HLA-DRB5, DQA1, DRB1:rs9268853, MST1, UBA7, APEH:rs9822268]. Genotypes of all variants were compared with corresponding phenotypes: IL23R:rs11805303 with IBD-153 (37.2%), males-50.3% and 465 (males-50.5%) controls. The following variants were associated with corresponding phenotypes: IL12R:rs1045431 with upper gastrointestinal (UGI) CD (p = 0.001); IL17REL/PIM3:rs9268853 with relapsing IBD (p = 0.003); IRGMR:rs13361189 with UC (p = 0.003); IRGMR:rs13361189 with UC (p = 0.003); IL17REL/PIM3:rs5771069 with treatment-refractory IBD (all cases) (p = 0.005).

Conclusion: This study confirms the association of genetic variants of IBD previously reported in other populations, with clinical, prognostic and treatment phenotypes of IBD in a Sri Lankan (South Asian) population.

Disclosure of Interest: All authors have declared no conflicts of interest.

Table 1. Mutations in SNP5, SNP8, SNP12 and SNP13 of the NOD2/Card15 gene.

<table>
<thead>
<tr>
<th>Mutation</th>
<th>Patients (n 103)</th>
<th>Any mutation (n 100)</th>
<th>p-value</th>
<th>Homozygous mutation (n 100)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>SNP5</td>
<td>17</td>
<td>32</td>
<td>&lt;0.05</td>
<td>6</td>
<td>10</td>
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<td>NS</td>
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<tr>
<td>SNP12</td>
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<td>10</td>
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<td>10</td>
<td>10</td>
</tr>
<tr>
<td>SNP13</td>
<td>0</td>
<td>0</td>
<td>NS</td>
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</tbody>
</table>
P0330 VDR GENE BSM I POLYMORPHISM AND ULCERATIVE COLITIS

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Introduction: Among the numerous genetic factors associated with ulcerative colitis (UC), an increasing attention has been paid to the polymorphisms of the vitamin D receptor gene (VDR) associated with disorders of innate and adaptive immunity as well as the barrier function of the intestinal epithelium. However, the results of studies on the prevalence, clinical, diagnostic and prognostic significance of polymorphisms of the VDR gene in different populations are ambiguous and contradictory. In particular, associations of Bsm I polymorphism of the VDR gene with UC in the Chinese population and in the Jewish Ashkenazi has been found, while in the Irish population, with a sufficient prevalence of Bsm I polymorphism, this association is absent [1–3]. In the Russian Federation, there is no data on the prevalence, clinical, diagnostic and prognostic significance of Bsm I polymorphism of the VDR gene with UC. These circumstances determined the purpose and objectives of this study.

Aims & Methods: The purpose is to assess the clinical, diagnostic and prognostic significance of the Bsm I polymorphism of the VDR gene (rs154440) among the residents of the Kemerovo region of the Russian Federation. The study included 76 patients with UC and 85 controls. Genotyping was performed by PCR method (“SNP-express” reagents, Lytech Co. Ltd., Russia) with electrophoretic detection of amplification products. Statistical analysis was performed using the t-test and Mann-Whitney tests. In the presence of statistically significant differences (p < 0.05), odds ratios (OR) with 95% confidence interval (CI) were calculated.

Results: It was found that the frequency of the allele B polymorphism of the VDR Bsm I gene was higher among patients with UC than in the control group (44% vs. 26%, p = 0.02), which increases the risk of this pathology by 2.2% (95% CI: 1.2–4.1). In the case of carriers of the B/B genotype, the risk of developing UC increased up to 3.5 times in comparison with the control group (21% vs. 7%, p = 0.02, 95% CI: 1.4–8.6), whereas in b/b genotype the risk of UC decreased (33% and 54%, respectively, p = 0.02, OR = 0.4, 95% CI: 0.2–0.7). Significant differences between carriers of the B allele Bsm I polymorphism and the features of the clinical course of the UC have not been established. However, it has been shown that in carriers of allele B, the clinical implementation of UC develops significantly later than in patients with the b/b genotype (43 and 28.5 years, respectively, p = 0.04).

Conclusion: Genotype B/B polymorphism of the VDR gene has a protective effect in the development of ulcerative colitis among the residents of the Kemerovo region of the Russian Federation.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P0331 GENETIC AND SEROLOGICAL PROFILE AS MARKERS OF DISEASE SUSCEPTIBILITY IN SIBLINGS OF CHILDREN WITH INFLAMMATORY BOWEL DISEASE

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Introduction: DNA methylation is an important epigenetic modification mechanism of gene expression. Several studies have shown an association of impaired methylation with inflammatory bowel diseases (IBD) pathogenesis. DNMT3A and DNMT3B are two of the three members of the family of de novo DNA methyltransferases. Variants in these proteins are responsible for the establishment of de novo genomic methylation patterns and initiation of normal development as well as in many diseases. However, it is unknown if DNMT3A may play a role during the mechanism involved in this abnormal methylation pattern and consequently the development of diseases.

Aims & Methods: To assess the function of DNMT3A in intestinal epithelial cells (IECs), human Caco-2 colon carcinoma cells were transfected with siRNA targeting DNMT3A, DNMT3B and DNMT3L. Gene expression analysis and DNA methylation analysis using qRT-PCR, RNA sequencing and 850k methylation arrays were performed. For long-term experiments, we used a CRISPR/Cas9 genome editing to delete DNMT3A gene in Caco-2 cells. DNMT3A knockout Caco-2 cells were grown in a 3D-Matrigel culture system and after 2 weeks, spheroids cells were stained for actin/nuclei and subjected to confocal microscopy analysis.

Results: From the RNA sequencing data, approximately 1000 genes were found to be differentially expressed between cells lacking DNMT3A and controls. The KEGG pathway analysis identifies differentially regulated genes associated with several functional categories comprising extracellular matrix receptor interaction, focal adhesion and MAPK signalling pathway. In contrast, we observed no difference in DNA methylation between the groups. Furthermore, loss of DNMT3A induces abnormal spheroids formation by reducing spheroids diameter and defect in actin organization and lumen formation. Thus, the observed morphological phenotype may be linked to the differentially regulated genes involved in the previous analysed pathways.

Conclusion: Rapidly inactivating DNMT3A in IECs promotes changes in gene expression, but does not change global DNA methylation. The absence of DNMT3A induces abnormal, defective spheroids formation in 3D culture system. Hence, our data provide a preliminary overview of DNMT3A in intestinal epithelial cells and its potential role in maintaining intestinal homeostasis.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P0332 ROLE OF DNMT3A IN INTESTINAL EPITHELIAL CELLS

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Introduction: DNA methylation is an important epigenetic modification mechanism of gene expression. Several studies have shown an association of impaired methylation with inflammatory bowel diseases (IBD) pathogenesis. DNMT3A and DNMT3B are two of the three members of the family of de novo DNA methyltransferases. Variants in these proteins are responsible for the establishment of de novo genomic methylation patterns and initiation of normal development as well as in many diseases. However, it is unknown if DNMT3A may play a role during the mechanism involved in this abnormal methylation pattern and consequently the development of diseases.

Aims & Methods: To assess the function of DNMT3A in intestinal epithelial cells (IECs), human Caco-2 colon carcinoma cells were transfected with siRNA targeting DNMT3A, DNMT3B and DNMT3L. Gene expression analysis and DNA methylation analysis using qRT-PCR, RNA sequencing and 850k methylation arrays were performed. For long-term experiments, we used a CRISPR/Cas9 genome editing to delete DNMT3A gene in Caco-2 cells. DNMT3A knockout Caco-2 cells were grown in a 3D-Matrigel culture system and after 2 weeks, spheroids cells were stained for actin/nuclei and subjected to confocal microscopy analysis.

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Conclusion: Rapidly inactivating DNMT3A in IECs promotes changes in gene expression, but does not change global DNA methylation. The absence of DNMT3A induces abnormal, defective spheroids formation in 3D culture system. Hence, our data provide a preliminary overview of DNMT3A in intestinal epithelial cells and its potential role in maintaining intestinal homeostasis.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
(IRE1), double-stranded RNA-dependent protein kinase (PKR)-like ER kinase (PKR-like endoplasmic reticulum kinase, PERK), and double-stranded RNA-dependent protein kinase (PKR)-like ER kinase (PKR-like endoplasmic reticulum kinase, PERK). Defective IRE1 and PERK response have been shown to predispose to chronic inflammatory bowel disease (IBD). Genome-wide association studies identified disease susceptibility loci in or adjacent to several UPR related genes including XBPI and ORMDL3. Aims & Methods: The objective of this study was to determine the function of ORMDL3 in UPR signaling to gain insights into the molecular mechanisms promoting chronic intestinal inflammation. Using molecular cell biology approaches, we studied the effect of ORMDL3 on ATF6, PERK and IRE signaling. ORMDL3 overexpression induced the increased cleavage of ATF6 and augmented ERSE promoter activity. Mechanistically, we show that ORMDL3 colocalizes and directly interacts with ATF6. Furthermore, ORMDL3 overexpression induced the PERK pathway by elevating its downstream protein levels. In contrast, we observed an inhibition of IRE1 signaling exerted by ORMDL3 proteins as shown by reduced XBPI splicing and decreased UPR promoter activity. ORMDL3-deficient mice showed an increased susceptibility to acute DSS-induced colitis compared to their wild-type littermates. These results are in concordance with what was published by Pariente B et al. (1)

Conclusion: This study demonstrates for the first time the modulatory functions of ORMDL proteins as regulators of all three UPR signaling pathways. Aims & Methods: In the present study, we aimed to precisely fine-tune the mechanism of the UPR determining cell fate decisions in response to ER stress.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

P0334 THE USE OF LÉMANN SCORE TO EVALUATE THE DAMAGE TO THE DIGESTIVE TRACT CAUSED BY CROHN’S DISEASE IN AN EGYPTIAN COHORT

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Introduction: Lémann scores have assessed Crohn’s disease (CD) according to disease activity using clinical, laboratory & radiological activity indexes; but few have analyzed the damage the disease bring about on the GI tract. Lémann score was designed to develop a comprehensive assessment of the structural bowel damage, including strictureng lesions, penetrating lesions (fistulas and abscesses), and surgical resection. (1)

Aims & Methods: To calculate Lémann score in a cohort of Egyptian patients to determine its ability to assess the structural damage caused by CD in Egyptian patients. Lémann score was calculated using the computer software based on the original paper by Pariente. B et al (1) in a cohort of Egyptian patients with CD followed from April 2013 - August 2015. The temporal relation between Lémann score and disease duration was also assessed.

Results: A total of 141 patients with CD were enrolled, 69% males and 31% females. Median age was 32 years, 36% were smokers. The clinical presentation varied between abdominal pain occurring in 90% followed by 69% with chronic diarrhea, 52% with weight loss. Few patients (26%) presented with extraintestinal manifestations. According to ECCO classification of disease severity 73% of our patients had mild disease, 17% had moderate disease, 10% had severe disease. According to Montreal classification, 25% of patients were class II, 55% class IV, 35% class I, 7% class III, 12% L3, 63% B1, 5% B2, 26% B3, & only 4% had perianal disease. According to CDAI, 83% were in clinical remission, 11% mild “CDAI 150-220”, 4% moderate “220-450”, 2% severe “CDAI >450” disease activity. When assessing structural damage of upper GI, 4% had strictureing lesions, 2% grade 1 & 2% grade 2 lesions. The small bowel showed strictureing lesions in 65%; 39% grade 1, 23% grade 2, 3% grade 3 lesions. 25% of patients had grade 3 penetrating lesions, 5% had surgery which was resection in all the cases. As regards the assessment of strictureing lesion in the colon, 11% colon showed strictureing lesion of this structure, 3%, 2%, grade 3, 3% grade 4 lesions; ascending colon showed stricture lesions in 20%, with 7% grade 1 lesions, 11% grade 2 & 2% grade 3 lesions; transverse colon showed stricture lesions in 1%; sigmoid colon showed stricture lesions in 2%; rectum showed stricture lesions in 1; while in only 1% whole colon showed grade 1 strictureing lesions affecting the 6 segments. In addition, 12% had grade 3 penetrating lesions while 9% had history of surgery mainly intestinal resection. In the anal canal, only 3% of patients had grade 3 penetrating lesions. The mean Lémann score was 19.19 in the median abdominal Lémann score was statistically positively correlated with disease duration of ≥2 years & >2 ≤10 years and ≥10 years respectively. (r2 = 0.343 & p < 0.001) (KW = 9.235(0.01)). The current study showed that affection of the GI tract was (5%, 92%, 41%, and 3% with upper tract, small bowel, colon/rectum, & anus CD location, respectively). There is an increase in median Lémann score with increase in disease duration (global test p<0.001): 0.60, 2.50, 6.40 for disease duration of ≤2 years & >2 ≤10 years and ≥10 years respectively; these results are in concordance with what was published by Pariente B et al (1).

Conclusion: Crohn’s disease affection pattern in our Egyptian cohort is mainly in the small bowel (92%) followed by the colon (41%) with the upper GI and the anal canal representing only 5% and 3% respectively. Lémann score designed by

Disclosure of Interest: All authors have declared no conflicts of interest.

P0335 FINAL RESULTS ON IMMUNOGENICITY PROFILE AND PREDICTORS OF ADA DEVELOPMENT OF BIOSIMILAR INFliximab DURING THE FIRST 12 MONTHS OF THE THERAPY: RESULTS FROM A PROSPECTIVE NATIONWIDE COHORT


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Introduction: Biosimilar infliximab CT-P13 received EMA approval in June 2013 for all indications of the originator product and its use is mandatory in all anti-TNF naïve IBD patients in Hungary since May 2014. Aims & Methods: In the present study we aimed to prospectively evaluate the immunogenicity profile of the biosimilar infliximab and predictors of TDM in IBD during the first year of therapy in a nationwide, multicentre cohort. Demographic data were collected and a harmonized monitoring strategy was applied. Clinical and biochemical activity were evaluated at weeks 14, 30 and 54. Routine therapeutic drug monitoring (TDM) was applied. Trough level (TL) and anti-drug antibody (ADA) concentration were measured by ELISA (LT-005, TheraDia [France]) at baseline, week 2, 14, 30, 54 and 54 weeks right before anti-TNF administration during the induction treatment.

Results: 353 consecutive IBD patients (209 CD patients and 144 UC patients) were included in the present cohort. 23.4% of CD patients and 19.4% of UC patients had received previous anti-TNF therapy. None of the patients had received infliximab within 12 months prior to initiation of the biosimilar infliximab. 60/51% of CD/UC patients received concomitant immunosuppressives at baseline. Mean TLs were 18.9, 17.3, 7.4, 4.3 and 5.3 μg/ml at weeks 2, 14, 30 and 54 in CD and 19.1, 11.8, 5.0, 3.9 and 4.5 μg/ml in UC. Previous anti-TNF therapy was associated with lower early TL-s in both CD (week 2, 14, and 30, p < 0.05) and UC (week 2 and 6, p = 0.03) ADA positivity rates were 4.3%, 12.0%, 20.9% and 28.6% in naïve patients at weeks 0, 14, 30, and 54 (difference 266, 312, 290 and 210). ADA positivity at week 14 was associated with lower TLs in all CD (week 2, 14 and 30, p < 0.007 for all) and UC (week 6, 14 and 30, p < 0.001 for all) patients. Concomitant IS use prevented ADA formation in anti-TNF naïve patients (week 14, 30 and 54, p = 0.01, 0.02 and 0.004) in CD but not in UC and did not affect clinical remission or response rates. 32 (8.9%) patients had infusion reactions during induction or maintenance treatment, of which 16 patients had received previous infliximab treatment. Conclusion: TLs and ADAs in IBD patients until week 54 were in line with results from previous studies. Increased immunogenicity profile with previous exposure to anti-TNFs had lower early TL coupled with ADA positivity and were more likely to develop infusion reactions. Concomitant IS use prevented ADA development in anti-TNF naïve patients.

Disclosure of Interest: All authors have declared no conflicts of interest.

A275

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P0336 RECONSIDERING THE PROGNOSTIC VALUE OF TRADITIONAL SEROLOGIC ANTIBODIES IN CROHN’S DISEASE – IMMUNOGLOBULIN CLASSES TO TAKE THE CENTRE STAGE

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Introduction: The most relevant scope of serologic antibodies in Crohn’s disease (CD) is to stratify the risk of complicated disease course. Significance of distinct antibody class and their characterisation was rarely considered. We aimed to address these concerns.

Aims & Methods: Sera of 266 well-characterised CD patients (mean±SD: 25 yrs, BMI±SD: 20–80%) and 155 controls were assayed for traditional serologic IgA (anti-OMP IgA (ascA), Omp IgA), Omp IgG, ASCA IgG, Endoantigen core IgA (EndoCAb) and a panel of non-specific immunoglobulins (IgA1.54 [0.97–2.44]; 0.066 1.37 [0.82–2.28]; 0.23 1.25 [0.67–2.34]; 0.475

Regression analysis comprising relevant clinical factors. Performance OMP IgA was equal to ASCA IgA, however sIgA not. Anti-perianal penetration (PP) with IgG type ASCA (p LogRank = 0.019 2.08 [1.28–3.38]; 0.003 1.13 [0.63–2.01]; 0.692

Conclusion: The absence of serologic healing (ulcerative disease; SES-CDa ≤ 5) was an independent risk factor for clinical relapse (Hazard ratio [HR] = 4.78; 95% CI: 1.94–11.80; P = 0.001) and serological relapse (HR = 2.84; 95% CI: 1.63–4.98; P = 0.001), respectively. For the ASCA IgA Meier analysis, patients who did not achieve serologic healing were at a significant risk of worse outcomes (clinical relapse, P < 0.001; serological relapse, P < 0.001). MR ulcer healing (MaRIA score <11) showed a high sensitivity (82.5%; 95% confidence interval (CI): 74.9%–88.2%) and specificity (85.5%; 95% CI: 79.2%–90.6%) for detection of serologic healing. On Cox’s proportional hazards analysis, MRE findings of ulcer healing were associated with a low risk of clinical relapse (Hazard ratio [HR] = 0.24; 95% CIs: 0.11%–0.54%; P = 0.001) and serological relapse (HR: 0.47; 95% CIs: 0.29%–0.78%; P = 0.003).

Conclusion: The absence of serologic healing (ulcerative disease) were seen in a considerable number of CD patients who were in clinical-seromimetic remission, preinflammatory lesions were at risk factor for worse prognoses. MRE could evaluate both serologic healing with a high diagnostic accuracy, and could predict patient outcomes.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P0338 USEFULNESS OF DOUBLE BALLOON ENDOCOPY IN DIAGNOSIS AND TREATMENT OF SMALL BOWEL CROHN’S DISEASE

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Introduction: In Crohn’s disease (CD), accurate evaluation of location and small bowel involvement are necessary at the time of diagnosis for prognostic concern and planning of treatment strategy. Since Double Balloon Endoscopy (DBE) enables us to examine deep small bowel either oral or anal it could be of great utility in the management of Crohn’s disease patients.

Aims & Methods: We aimed to evaluate the diagnostic yield and therapeutic impact of DBE on small bowel CD. The medical records of 180 CD patients, from October 2009 to April 2012 were retrospectively reviewed. Patients were included if they had known CD based on clinical, colonoscopic and histological findings and had been subjected to DBE. If one patient underwent more than one DBE examination only the first examination was considered. The primary end point of our study was to evaluate small bowel involvement that is beyond the reach of conventional colonoscopy. The secondary endpoints were to determine the impact of DBE findings on management strategy of CD. The diagnostic yield of DBE in small bowel CD was determined. In addition, the changes in medical treatment, endoscopic intervention and surgical procedures, within three months after DBE, were analysed.

Results: Among 180 patients with CD, 90 patients underwent 168 DBE examinations and were included. The mean age of included patients was 40 ±13.6 years. They were 63 males and 27 females. Eighty-six (91%) patients with established CD underwent DBE for evaluation of small bowel involvement and 8 (9%) patients underwent DBE because of suspicion of CD and had been newly diagnosed. The overall diagnostic yield of DBE was 69%. DBE revealed small bowel involvement proximal to the terminal ileum in 40 (64.5%) patients; of them 17 (42.5%) patients had isolated small bowel CD. Within 3 months after DBE examination the management strategy of CD changed in 47 (52.2%) patients, based on DBE findings. The medical treatment was escalated in 20 (22%) patients, and decreased in 17 (11%). Fourteen (24%) patients underwent DBE-assisted balloon dilatation, and 6 (9.6%) patients underwent CD-related surgery.

Conclusion: DBE is able to detect small bowel involvement in a significant proportion of CD patients. The DBE findings modified the management strategy in at least one half of CD patients.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

References

P0339 AGE AND SMOKING KEY TO ADHERENCE IN INFLAMMATORY BOWEL DISEASE: LOW ADHERENCE CAN SERIOUSLY LIMIT DRUG EFFECTIVENESS IN YOUNG PATIENTS
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Introduction: Therapeutic adherence is crucial in the management of patients with inflammatory bowel disease (IBD). Poor adherence may lead to suboptimal treatment.

A total of 181 patients were evaluated. The median age was 47 years (range: 16–78) and 118 (64.8%) were men. The median duration of IBD was 16 years (range: 0.5–42 years). Eighty (43.5%) patients were taking mesalazine, 2.8% steroids, 29.3% immunomodulators, and 30.4% biologics. Activity was evaluated using Harvey-Bradshaw index in Crohn’s disease (CD) and Partial Mayo Score in Ulcerative colitis (UC). Anxiety and depression were estimated by the Goldberg Anxiety and Depression Scale and modified Morisky Medication Adherence Scale (MMAS-8) was used to assess adherence (6, 7–8 points indicate low, medium and high adherence, respectively). In statistical analyses, Chi-square and Student’s t-test were performed to determine the statistical significance with a p-value < 0.05.

Results: On MMAS-8, almost half of our patients 84 (46.4%) had high adherence to IBD treatment, 35.9% were taking mesalazine, 2.8% steroids, 29.3% immunomodulators, and 30.4% biologics. Activity was evaluated using Harvey-Bradshaw index in Crohn’s disease (CD) and Partial Mayo Score in Ulcerative colitis (UC). Anxiety and depression were estimated by the Goldberg Anxiety and Depression Scale and modified Morisky Medication Adherence Scale (MMAS-8) was used to assess adherence (6, 7–8 points indicate low, medium and high adherence, respectively). In statistical analyses, Chi-square and Student’s t-test were performed to determine the statistical significance with a p-value < 0.05.

Conclusion: This study demonstrated the feasibility of applying the CDMRIS score in clinical practice, to evaluate its variability after the initiation or optimization of an anti-TNF treatment, and to measure its correlation with an evaluation of clinical activity. Patients with known small bowel disease who underwent push and pull enteroscopy examinations at least 30 days were included between 2010 and 2015. Each exam was interpreted twice and the CDMRIS score was calculated on both exams in addition to classical criteria. All patients had a clinical evaluation over time, separating them in two groups: “active” and “inactive” disease.

Results: Seventy-two patients were included, with a mean CDMRIS of 3.4 at baseline, decreasing to 2.6 (p = 0.052) independently of clinical activity of disease. The median interval between the two MRIs was 15.4 months, and there was a significant larger decrease in the CDMRIS score when the interval was above 12 months. Two other radiological parameters decreased significantly: the rate of patients with a mural T2-hyperintensity (36.1% to 20.8% p = 0.042), with a good chincoradiological correlation, and mean wall thickness (5.5 to 4.4 mm, p = 0.047).

Conclusion: This study demonstrated the feasibility of applying the CDMRIS score in clinical practice, but sensitivity was too low to detect early changes. Accuracy for a long-term monitoring needs to be tested. Wall thickness and mural T2-hyperintensity emerged as the two most reliable radiological factors, significantly associated with the disease activity, allowing monitoring of the short-term efficacy of biotherapies.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P0340 IS THE CDMRIS USEFUL TO MONITOR PATIENTS WITH CROHN’S DISEASE BY MAGNETIC RESONANCE IMAGING?
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Introduction: Magnetic resonance enterography is now recognized by the European Crohn’s and Colitis Organization (ECCO) as a reference procedure to assess the intestinal involvement of Crohn’s disease (CD), including extra-intestinal manifestations, as well as to monitor patients under treatment. A new MRI index of severity was developed in 2015 by the GETAID consortium, specifically to evaluate lesions located in the small intestine. This score, labeled CDMRIS (Crohn’s disease Magnetic Resonance Imaging Severity index), was validated, for each 20-cm small bowel segment, the intensity of relative contrast enhancement (mild–moderate or severe), deep ulceration without fistula, “comb sign”, any fistula, and abscess. Although well standardized, this index has not yet been validated, either for the initial assessment of CD at diagnosis, or for monitoring patients under treatment. Its feasibility in routine practice has never been tested.

Aims & Methods: The aims of this study were to evaluate the feasibility of applying the CDMRIS score in clinical practice, to evaluate its variability after the initiation of an anti-TNF treatment, and to measure its correlation with an evaluation of clinical activity. Patients with known small bowel disease who underwent push and pull enteroscopy examinations at least 30 days were included between 2010 and 2015. Each exam was interpreted twice and the CDMRIS score was calculated on both exams in addition to classical criteria. All patients had a clinical evaluation over time, separating them in two groups: “active” and “inactive” disease.

Results: Seventy-two patients were included, with a mean CDMRIS of 3.4 at baseline, decreasing to 2.6 (p = 0.052) independently of clinical activity of disease. The median interval between the two MRIs was 15.4 months, and there was a significant larger decrease in the CDMRIS score when the interval was above 12 months. Two other radiological parameters decreased significantly: the rate of patients with a mural T2-hyperintensity (36.1% to 20.8% p = 0.042), with a good chincoradiological correlation, and mean wall thickness (5.5 to 4.4 mm, p = 0.047).

Conclusion: This study demonstrated the feasibility of applying the CDMRIS score in clinical practice, but sensitivity was too low to detect early changes. Accuracy for a long-term monitoring needs to be tested. Wall thickness and mural T2-hyperintensity emerged as the two most reliable radiological factors, significantly associated with the disease activity, allowing monitoring of the short-term efficacy of biotherapies.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P0341 CONCORDANCE OF STOOL FREQUENCY AND ABDOMINAL PAIN MEASURES WITH SIMPLIFIED ENDOSCOPIC SCORE FOR CROHN’S DISEASE
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2University of Leuven, Leuven/Belgium
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Introduction: Sphincter-saving surgery (ASS) in Crohn’s disease (CD) is not a simple procedure and is associated with a high risk of remission failure after surgery.

Primary Outcome Measures and Analysis: The primary outcome was the CD activity index (CDAI) at 30 weeks and 6 months postoperatively. The analysis was performed on an intent-to-treat basis.

The authors concluded that ASS is associated with a high risk of remission failure after surgery and may not be a suitable option for all CD patients. Further research is needed to identify factors that can predict remission failure after surgery to improve patient outcomes.

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**P0344 BOWEL PREPARATION QUALITY OF NER1006 VERSUS ORAL TRISULFATE SOLUTION AS ASSESSED BY COLONOSCOPTISTS AT SITE: A POST HOC ANALYSIS FROM A RANDOMISED CONTROLLED TRIAL**

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**Introduction:** The success of colonoscopy is dependent on efficient bowel cleansing. Inadequate bowel cleansing may decrease diagnostic sensitivity, necessitate repeat procedures and potentially delay appropriate treatment. The increasing frequency of the incidence of colorectal cancer arising in the ascending colon necessitates effective cleansing of this area; additionally these cancers are often associated with poorer prognoses. Data suggest that detection in the ascending colon is more dependent on higher grades of cleansing, perhaps due to the nature of polyps present, which may be more likely to be sessile or serrated. NER1006 is the first 1L polyethylene glycol (PEG)-based bowel preparation, a patented combination optimised for effective bowel cleansing. The NOCT study (a multicentre randomised Phase 3 clinical trial investigating bowel cleansing efficacy of NER1006 vs trisulfate solution) reported bowel preparation quality assessed by central readers.

This post hoc analysis shows the cleansing assessment by site colonoscopists, who typically guide clinical decision making; hence this study may be more relevant for clinical practice than previous studies.

**Aims & Methods:** In the NOCT study 621 patients (males and females, aged 18–85) were randomly assigned in a 1:1 ratio to receive either NER1006 or trisulfate solution, each administered as an overnight split-dose. Data from the 523 patients who underwent a colonoscopy and had a site colonoscopist assessment were used in this analysis. Colonoscopists were blinded to the preparation administered. Cleansing was assessed according to the Harefield Cleansing Scale;3 following segmental scoring, cleansing of the overall colon was graded from A to D; grades A and B were judged as successful cleansing. Cleansing judged as high-quality cleansing was achieved in 12% more patients who received NER1006 than who received trisulfate.

**Results:** As Table 1 shows, the bowel preparation quality of NER1006 when assessed by site colonoscopists did not show a statistically significant difference to trisulfate for the overall colon (93% vs 94%, P = 0.681; 95% CI: -5.1–3.3%) or ascending colon (80 vs 74%, P = 0.079; 95% CI: -0.7–13.6%). There was, however, a numerical advantage in favour of NER1006 on the proportion of patients achieving high-quality cleansing success in the right colon.

**Table 1:** Successful colon cleansing rates when treated with NER1006 or trisulfate solution.

<table>
<thead>
<tr>
<th>bowel preparation</th>
<th>N</th>
<th>Patients with successful cleansing N (%)</th>
<th>difference (%)</th>
<th>P-value</th>
<th>95% CI (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall colon</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NER1006 N2D</td>
<td>263</td>
<td>263 (97)</td>
<td>-1</td>
<td>0.681</td>
<td>-5.1–3.3</td>
</tr>
<tr>
<td>Trisulfate</td>
<td>264</td>
<td>248 (94)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ascending colon</td>
<td></td>
<td></td>
<td>6</td>
<td>0.079</td>
<td>-0.7–13.6</td>
</tr>
<tr>
<td>NER1006 N1D</td>
<td>269</td>
<td>208 (80)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trisulfate</td>
<td>264</td>
<td>193 (74)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

N.B. successful cleansing defined here as a Harefield Cleansing Scale grade of A or B (overall colon) or 3 or 4 (ascending colon, high quality)

**Conclusion:** For both preparations, site colonoscopy findings demonstrated similar very high rates of cleansing success for the overall colon (>93%) and high rates of high-quality cleansing of the ascending colon (>73%). However, statistical significance was not met in either comparison. The rates of cleansing success in the ascending colon reported by the site colonoscopists are notably higher than those previously reported by central readers.

**Disclosure of Interest:** R. Ng Kwet Shing: Employee of Norgine
All other authors have declared no conflicts of interest.

**References**

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**P0345 BOWEL PREPARATION QUALITY OF NER1006 VERSUS SODIUM PICOSULFATE + MAGNESIUM CITRATE AS ASSESSED BY COLONOSCOPTISTS AT SITE: A POST HOC ANALYSIS FROM A RANDOMISED CONTROLLED TRIAL**

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**Introduction:** The efficacy of colonoscopy is dependent on the quality of bowel cleansing. NER1006 is the first 1L polyethylene glycol (PEG)-based bowel cleansing solution and is a patented combination optimised for effective bowel cleansing. The DAYB study was a European multicentre, randomised trial that tested the hypothesis that NER1006 would be non-inferior to sodium picosulfate and magnesium citrate (NaPic + MgCit) in terms of overall bowel cleansing and high-quality cleansing of the ascending colon plus caecum [1]. Bowel cleansing was assessed using the Harefield Cleansing Scale (HCS) [2]. The primary endpoints of the study were assessed by video review by a central reader. Bowel cleansing on the HCS was also assessed by the site colonoscopist and this post hoc analysis assessed the cleansing grades as determined by the site colonoscopists.

**Aims & Methods:** In the DAYB study, 515 patients (aged 18–85, median age: 55.0 years) underwent screening, surveillance, or diagnostic colonoscopy and were randomly assigned in a 1:1 ratio to receive either NER1006 or NaPic + MgCit, each on the day before colonoscopy. In this analysis, data from 479 patients who underwent a colonoscopy and had a completed assessment by the site colonoscopist were included. Colonoscopists were blinded to the preparation administered. Cleansing was assessed according to the HCS; cleansing of each segment of the colon was scored from 0 to 4. Scores 3 and 4 of the ascending colon were judged as high-quality cleansing. Cleansing of the overall colon was graded from A to D; grades A (all segments scored 3 or 4) and B (≥1 segments scored 2, no sections scored 1 or 0) were judged as successful cleansing.

**Results:** As indicated in Table 1, in the overall colon, successful cleansing was achieved in 12% more patients who received NER1006 than who received NaPic + MgCit (P = 0.003, 95% CI: 4.0–20.7%). In the ascending colon, high-quality cleansing was achieved in 20% more patients who received...
Table 1: A comparison of bowel cleansing efficacy as assessed by site colono-
copists between NER1006 and NaPic + MgCit

<table>
<thead>
<tr>
<th>Bowel preparation</th>
<th>Patients with N=</th>
<th>Successful cleansing n (%)</th>
<th>Difference (%)</th>
<th>P-value</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall colon</td>
<td>NER1006</td>
<td>236 (73)</td>
<td>12</td>
<td>0.003</td>
<td>4.0–20.7</td>
</tr>
<tr>
<td></td>
<td>NaPic + MgCit</td>
<td>243 (61)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ascending colon</td>
<td>NER1006</td>
<td>236 (82)</td>
<td>20</td>
<td>&lt;0.001</td>
<td>12.7–27.8</td>
</tr>
<tr>
<td></td>
<td>NaPic + MgCit</td>
<td>243 (35)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

N.B. successful cleansing defined here as a Harefield Cleansing Scale grade of A or B (overall colon) or score of 3 or 4 (ascending colon, high quality)

**Conclusion:** NER1006 was shown to provide significantly better cleansing of the overall colon and high-quality cleansing of the ascending colon compared to NaPic + MgCit, when both treatments were administered the day before colonoscopy. The cleansing efficacy rate of the comparator was within its previously reported cleansing rates for day before administration, suggesting the improvement seen with NER1006 is of clinical relevance.

**Disclosure of Interest:** J.P.H. Drenth: DAYB investigator; no other conflicts of interest

C. Pediconi: Employee of Norgine
B. Amlani: Employee of Norgine
All other authors have declared no conflicts of interest.

**References**

**P0346 LOW VITAMIN D LEVELS ARE RELATED TO CLINICAL ACTIVITY, MUCOSAL INFLAMMATION, AND INTESTINAL FIBROSTENOSIS IN CROHN’S DISEASE**

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**Introduction:** Several studies in recent decades have revealed new roles for vitamin D. For example, vitamin D plays a role in regulating skeletal muscle, as well as in cardiovascular and renal physiology, producing antitumor effects, suppressing fibrosis, and as a regulator of the immune system. In light of these new roles, vitamin D is considered to be related to disease activity and intestinal fibrosis, including that seen in Crohn’s disease (CD). Several reports have demonstrated a relationship between vitamin D deficiency and CD activity according to clinical parameters such as Crohn’s disease activity index (CDAI) and quality of life (QoL). However, no reports have demonstrated this relationship by using endoscopic parameters such as endoscopic activity, mucosal inflammation, and intestinal fibrosis.

**Aims & Methods:** The aim of this study was to clarify the relationship between vitamin D deficiency and CD activity by using endoscopic parameters, as well as clinical parameters. Of the CD patients visiting NagaWoman University Hospital from May 2011 to February 2016, 82 patients were enrolled in this study. Serum 25-hydroxyvitamin D (25(OH)D) levels, disease activity, and clinical factors of the subjects were investigated prospectively. Endoscopic findings of 52 of the 82 total patients enrolled were investigated retrospectively from endoscopic records. This study design was approved by the ethics committee of Nagoya University Hospital. Clinical remission was defined as CDAI ≤150. Mucosal healing was defined as a simple endoscopic score for Crohn’s disease (SES-CD) ≤1. Moreover, to evaluate endoscopic activity from two aspects (mucosal inflammation and fibrotic stenosis), we divided SES-CD score into endoscopic “mucosal inflammation score” and “fibrotic stenosis score.”

**Results:** Mean age of the subjects was 41.11, and the male/female proportion was 64/18. The mean serum 25(OH)D level of subjects was 17.1 ng/mL, and 61 cases (74.4%) were classified as severe deficiency or deficiency. Mean serum 25(OH)D levels of the clinical remission and clinically active groups were 18.7 ± 8.1 ng/mL and 12.4 ± 3.6 ng/mL, respectively (P < 0.001). In a multivariate analysis, low levels of serum 25(OH)D and serum albumin and positive C-reactive protein (CRP) results were correlated with clinical activity. Mean serum 25(OH)D levels of the mucosal healing and no mucosal healing were 24.0 ± 9.8 ng/mL and 15.1 ± 6.6 ng/mL, respectively (P < 0.001). Mean serum 25(OH)D levels for the no mucosal inflammation and mucosal inflammation groups were 21.6 ± 9.6 ng/mL and 14.3 ± 5.5 ng/mL, respectively (P < 0.001); and mean serum 25(OH)D levels of the no fibrosis and fibrosis groups were 20.2 ± 8.9 ng/mL and 14.2 ± 6.7 ng/mL, respectively (P < 0.001; Mann-Whitney U test). In a multivariate analysis, low serum 25(OH)D levels were related with mucosal inflammation and intestinal fibrotic stenosis of CD (P < 0.05; logistic regression analysis).

**Conclusion:** This study demonstrated the relationship between vitamin D level and disease activity in CD patients. The disease pathology of CD consists of repetitive intestinal inflammation and intestinal fibrostenosis formed during healing of inflammation. We consider it important to demonstrate this relationship not only using clinical parameters, but also using endoscopic parameters such as mucosal inflammation and intestinal fibrostenosis.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**References**
is escalated. Source data verification is performed by external monitors. Primary aim of the study is to confirm the previously identified score and to test its power to predict a mild disease course as indicated by the need of not more than mesalamine therapy. Additional analyses include the percentage of patients with a score indicating a severe disease and their characteristics at diagnosis. This preliminary analysis presents preliminary data.

Results: Currently, 78 patients (33 male, 45 female; age 16-72, mean 35 years) with newly diagnosed CD are enrolled. 56 CD-patients with follow up ≥2 weeks (mean 8.5 months), mean age 35 years, 35 female, 21 male, CRP 12.2 mg/l were included into the interim analysis. In 28 patients a score from 0-2 step-up treatment occurred in 7%, whereas in 28 patients with a score >2, step-up rate was 43% (p = 0.0043). Differences between patients with a score 0-2 and >2 were (41 vs. 28 years, p = 0.0011), CRP <2 mg/l (17/28 patients vs. 0/26, p < 0.0001), endoscopic score 1.4 vs. 2.7, p 0.03. Sex distribution (28% vs. 4/28, stenos 1/28 vs. 6/28. There were no differences in terms of sex, fistula, extraintestinal manifestations and liver.

Conclusion: In this early analysis of a prospective study planned with a 5-year follow-up, a significant proportion of patients with mild CD and simple mesalamine therapy can be identified. These initial results encourage to continue and expand this prospective long-term study on the predictability of a mild CD course.


P0349 A PROSPECTIVE STUDY TO PREDICT A MILD COURSE OF CROHN’S DISEASE: AN INTERIM ANALYSIS OF THE PROGNOS

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Introduction: Crohn’s Disease (CD) spans a wide severity range, from mild to severe disease, with variation under- as well as overtreatment problems is challenging. While factors determining bad prognosis are studied in detail, factors predicting a mild course with the chance of simple treatments are less known. Here we show first results of a prospective evaluation of a retrospectively created score (JCC 2013;7:263) for prediction of mild CD which consists of age at diagnosis, CRP, an endoscopy score, presence of perianal lesions and complications.

Aims & Methods: This is a prospective, ongoing study performed in 12 IBD-specialized private gastroenterology practices (outpatients only) in Germany. All consecutive CD patients (diagnosis ≥6 weeks) are included. At screening ileocolonoscopy with histology, investigation of the perianal area, laboratory tests including CRP are performed and CD complications (stenosis, fistula, extraintestinal manifestations or fever >38°C) evaluated to complete of the above quoted score. Patients are treated at the discretion of the physician. In case of a score indicating a good prognosis (≤2) or of mild clinical appearance mesalamine is started. In all other cases patients are treated according to guidelines. 5 year follow up is planned for all patients. If initial therapy fails, treatment

Reference

Prevalence of LTi in retrospective testing was of 54/246 (22.0%). Prospective testing was of 26/76 (34.2%) by linear regression. Of the follow-up, 30/191 (15.7%) patients who were negative for screening before 2015 were converted in positive for LTi (95% CI [10.2–21.1]).

Conclusion: The prevalence of LTi in our area is high (32.6%). The simultaneous presence of a positive TST booster and QFT QP increases the detection of LTi. The TST booster increases the detection of LTi even when is performed in patients without immunosuppressive treatments, in whom is not routinely recommended. The QFT is more useful in patients without immunosuppressive therapy. The repeated screening every two years is useful in this population with high prevalence of LTi, since it may detect LTi in patients with previous negative tests (15.7%). The TST booster is essential due to the possible false negatives of QFT when screening patients on anti-TNF therapy.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P0351 MAGNETIC RESONANCE ENTEROGRAPHY GLOBAL SCORE ALLOWS FOR ACCURATE QUANTIFICATION OF SMALL BOWEL INFLAMMATION IN CROHN’S DISEASE – A COMPARISON WITH CAPSULE ENDOSCOPY

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Introduction: Magnetic resonance enterography (MRE) and capsule endoscopy (CE) are prime modalities for evaluation of small bowel in patients with Crohn’s disease (CD). However, detection of proximal (jejunum and proximal ileum) small bowel inflammation by MRE is challenging. Current quantitative scores such as Magnetic Resonance Index of Activity (MaRIA) do not incorporate proximal small bowel data and were validated against ileocolonoscopy. Magnetic resonance enterography global score (MEGS) was designed for quantitative evaluation of the entire digestive tract; however, it was only validated against ileocolonoscopy and its accuracy in the proximal small bowel was not assessed. CE allows for accurate assessment of the entire small bowel and is the modality of choice for evaluation of the proximal small bowel.

Aims & Methods: We aimed to compare the quantitative evaluation of the small bowel inflammation by MEGS score and the Lewis capsule endoscopy score. Patients with known quiescent small bowel CD (for duodenum vs LS 1st tertile and proximal ileum vs 2nd tertile LS - both severe inflammation). Proximal small bowel was defined as jejunum and duodenum on MRE and as 1st and 2nd tertiles LS on CE. Distal small bowel was defined as terminal ileum on MRE and 3rd tertile LS on CE. Fecal calprotectin (FCP) levels were measured and correlated with all scores.

Results: Fifty-two patients were included in the study. There was a strong correlation between LS and CECDAI (Pearson’s r = 0.67, p < 0.001). CECDAI < 7.2 corresponded to mucosal healing (LS < 135), while CECDAI > 11.1 corresponded to moderate to severe inflammation (LS ≥ 790) by linear regression. There was a moderate correlation between both scores and FCP levels that was somewhat stronger for CECDAI (r = 0.39, p = 0.002 vs r = 0.53, p = 0.001 for both). There was a weak correlation between LS and CRP levels (r = 0.27, p = 0.04) and none for CECDAI and CRP (r = 0.04 vs p = 0.1).

Conclusion: In our prospective study, CECDAI and LS strongly correlated and performed similarly for quantitative assessment of mucosal inflammation in established CD.

Disclosure of Interest: U. kopylov: The study was supported by a generous grant by the Helmsley Charitable fund
All other authors have declared no conflicts of interest.

P0352 WHICH ONE IS BETTER FOR ASSESSMENT OF ESTABLISHED CROHN’S DISEASE BY CAPSULE ENDOSCOPY: THE LEWIS SCORE OR THE CAPSULE ENDOSCOPY CROHN’S DISEASE ACTIVITY INDEX?

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Introduction: Small-bowel capsule endoscopy (CE) is a prime modality for evaluation of the small bowel. The Lewis score (LS) and the Capsule Endoscopy Crohn’s Disease Activity Index (CECDAI) are validated endoscopic indices for quantification of small bowel inflammation on CE. It is unclear whether these indices are interchangeable for evaluation of mucosal inflammation in established Crohn’s disease (CD).

Aims & Methods: We aimed to prospectively compare the quantitative evaluation of small bowel inflammation by both scores. Patients with known quiescent small bowel CD (for at least 3 months (CDAI < 150) were prospectively recruited and underwent CE. LS was calculated using the capsule reading software (RAPID b) and CECDAI was calculated manually, by 2 independent experienced gastroenterologists (one for each score) unaware of each other’s results. Mucosal healing was defined as LS < 135; LS ≥ 790 signified moderate to severe inflammation. Fecal calprotectin (FCP) and C-reactive protein (CRP) levels were measured and correlated with the scores.

Results: Fifty patients were included in the study. There was a strong correlation between LS and CECDAI (Pearson’s r = 0.67, p < 0.001). CECDAI < 7.2 corresponded to mucosal healing (LS < 135), while CECDAI > 11.1 corresponded to moderate to severe inflammation (LS ≥ 790) by linear regression. There was a moderate correlation between both scores and FCP levels that was somewhat stronger for CECDAI (r = 0.39, p = 0.002 vs r = 0.53, p = 0.001 for both). There was a weak correlation between LS and CRP levels (r = 0.27, p = 0.04) and none for CECDAI and CRP (r = 0.04 vs p = 0.1).

Conclusion: While concordance was 85% between LS and CECDAI (Pearson’s r = 0.67, p < 0.001), CECDAI < 7.2 corresponded to mucosal healing (LS < 135), while CECDAI > 11.1 corresponded to moderate to severe inflammation (LS ≥ 790) by linear regression. There was a moderate correlation between both scores and FCP levels that was somewhat stronger for CECDAI (r = 0.39, p = 0.002 vs r = 0.53, p = 0.001 for both). There was a weak correlation between LS and CRP levels (r = 0.27, p = 0.04) and none for CECDAI and CRP (r = 0.04 vs p = 0.1).

Disclosure of Interest: All authors have declared no conflicts of interest.

P0353 CONCORDANCE BETWEEN TUBERCULIN SKIN TEST AND INTERFERON GAMMA RELEASE ASSAY FOR LATENT TUBERCULOSIS SCREENING IN INFLAMMATORY BOWEL DISEASE (META-ANALYSIS)

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Introduction: Screening for latent tuberculosis infection (LTI) is mandatory prior to initiating anti-tumor necrosis factor (anti-TNF) medications. New guidelines recommend interferon-gamma release assays as first line screening method for the general population. Studies have provided conflicting evidence on the performance of interferon-gamma release assays (IGRAs), compared to tuberculin skin test (TST) in inflammatory bowel disease (IBD) patients. We assessed the concordance of these two tests in IBD patients and the effect of immunosuppression on their performance.

Aims & Methods: We performed a systematic search of MEDLINE, EMBASE and Cochrane Library databases, from 2011 to 2016, for relevant studies testing both TST and IGRAs in IBD patients. The primary outcome was concordance between TST and IGRAs. Secondary outcomes were effects of immunosuppressive therapy on both TST and IGRAs, Secondary outcomes were effects of immunosuppressive therapy on both TST and IGRAs, and differences in concordance comparing TST and IFNA.

Results: Sixteen studies, including 2488 patients with IBD, were included for the analysis. The pooled concordance between the TST and IGRAs was 85% (95% confidence interval [CI] 81%-88%, p = 0.01). Effects of immunosuppression on both tests were reported in eight studies including 814 patients with IBD. The odds ratio of testing positive by IGRAs decreased from 4.1 to 0.57 if immunosuppressed (95% confidence interval [CI] 0.31–1.03, p = 0.06). The odds ratio of testing positive by TST if immunosuppressed was 1.14 (95% confidence interval [CI] 0.81–1.57, p = 0.38). There was no significant difference in concordance between patients treated with traditional vs. biological agents.

Conclusion: Concordance between TST and IGRAs is high (85%) in IBD patients. There was no significant difference in concordance comparing TST and IGRAs, and differences in concordance comparing TST and IFNA.

Disclosure of Interest: W. Afif: Abbvie, Janssen, Takeda, Merck, Pfizer, Shire, Ferring, Theradiag
All other authors have declared no conflicts of interest.
ASSESSING SECONDARY LOSS OF RESPONSE TO MAINTENANCE

P0354 THIOPURINE MAINTENANCE THERAPY FOR IBD: WHICH IS THE BEST METHOD TO MEASURE ADHERENCE TO THERAPY?

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Introduction: For the majority of patients with IBD long-term therapy is required to maintain remission, yet 30–45% of patients do not adhere to their IBD medication. Medication adherence can be assessed with prescription refill rates, biologic measures (metabolites), trough levels and patient self-report. There is currently no accepted gold standard and the feasibility and utility of different adherence assessment tools in the routine outpatient clinic setting have not been fully examined. The aim of this service improvement project was to test the acceptability of self-report tools assessing thiopurine adherence in the IBD clinic and to correlate the results with thioguanine-nucleotide (TGN) levels.

Aims & Methods: Consecutive outpatients on thiopurine maintenance therapy for IBD for >3 months were recruited from clinic. Patients self-reported adherence using a seven-day adherence scale (VAS), the validated Morisky Adherence Report Scale (MOR) and the validated Medication Adherence Report Scale (MARS). TGN levels were classed as complete non-adherence (<100 and MMP low), partial adherence (TGN 100–235 and MMP low) or full adherence (>235 or MMP high). Correlation analysis was performed using Pearson tests.

Results: Of 100 approached patients none refused participation and TGN levels were available for 96. These included 38 women. Diagnoses were Crohn’s disease in 27, ulcerative colitis in 41 and IBD-U in 1 case. Concomitant therapy included 5/ASA (25 cases), anti-TNF (13 cases) and Vedolizumab (2 cases). The proportion of adherent patients was according to the relevant report tool 71% (TGN), 87% (VAS), 87% (Morisky) and 77% (MARS). VAS (Pearson 0.315; p = 0.005) and Morisky (Pearson –0.363; p = 0.001) correlated moderately with TGN, but MARS (Pearson 0.09; p = 0.39) did not. The patients, who were non-adherent by TGN were detected by VAS in 3, Morisky in 6 and MARS in 3 cases. However, patients showing non-adherence according to self-report tools had TGN levels in 6 of 10 cases for VAS, 10 of 26 for Morisky and 4 of 15 for MARS.

Conclusion: Self-report tools provided a patient-friendly and inexpensive way of assessing adherence, but the correlation with TGN levels was only moderate. While providing more of a objective assessment TGN levels are problematic for assessing adherence, but the correlation with TGN levels was only moderate. While providing a more objective assessment TGN levels are problematic for assessing adherence, but the correlation with TGN levels was only moderate. While providing a more objective assessment TGN levels are problematic for assessing adherence, but the correlation with TGN levels was only moderate. While providing a more objective assessment TGN levels are problematic for assessing adherence, but the correlation with TGN levels was only moderate.

Disclosure of Interest: All authors have declared no conflicts of interest.

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A284 Disclosure of Interest: All authors have declared no conflicts of interest.

P0355 ROLE FOR THERAPEUTIC DRUG MONITORING IN ASSESSING SECONDARY LOSS OF RESPONSE TO MAINTENANCE ANTI-TNF THERAPY IN INFLAMMATORY BOWEL DISEASE

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Introduction: Anti-TNFa therapies have improved outcomes in patients with inflammatory bowel disease. Their use has been associated with improved clinical efficacy, remission and reduced complications and resistant mutations. However secondary loss of response (REL) to both infliximab (IFX) and adalimumab (ADA) is a significant problem, leading to further flares of disease, disease progression and poorer outcomes. Therapeutic drug monitoring (TDM), which involves measurement of anti-TNFa trough and peak levels, offers the opportunity of examining an immune basis behind REL, and potentially adjusting doses or switching therapies to help regain clinical response.

Aims & Methods: The aim of this study was to evaluate whether TDM can help predict secondary REL to infliximab and adalimumab and whether dose adjustments based on this information can help patients regain clinical response. This is a prospective, single-centre study, performed from June 2015 to April 2016, at our institution. Patients with Ulcerative colitis (UC) and Crohn’s disease (CD) were enrolled, if they were clinically (based on Harvey-Bradshaw (HBI) or partial Mayo scores) felt to be experiencing a secondary LOR to either infliximab or adalimumab maintenance therapy. Patients were followed for a one-year period, from their initial assessment for secondary LOR to assess outcomes.

Results: 46 patients were recruited, 40 CD with Harvey-Bradshaw Index (HBI) >4 points and 6 patients with UC with Partial Mayo Score (PMS) >2 points. Mean age for the cohort was 40.8 years (26 (65.5%) were female). 20/46 (43.5%) were on anti-TNFa therapy, 13/46 (28.3%) were on biologicals (adalimumab) alone and 7 (15.2%) were on biologicals (infliximab). The mean duration of disease was 9.8 years, 3 (8.3%) were smokers, 7 (15.2%) on immunomodulators, and 11 (23.9%) had prior anti-TNFa exposure. 17 (46.8%) were on an adalimumab maintenance dose of 40mg every other week. Overall HBI for the whole study group was 1.9, partial Mayo Score 6.3. Patients were followed for a one-year period, from their initial assessment for secondary LOR to assess outcomes. Secondary LOR was defined as a score increase of 3 or more points on the HBI or PMS. Results from MARS.

Conclusion: TDM offers the opportunity to identify patients who may benefit from dose adjustment or switch in therapy in a clinically guided fashion.

Disclosure of Interest: All authors have declared no conflicts of interest.

References


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P0357 DIAGNOSTIC DELAY IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE - A STUDY OF THE AUSTRIAN IBD STUDY GROUP (ATISG)  


Aims & Methods:  
A diagnostic delay of 10 years (IQR 4–18 years) were analysed. The median diagnostic delay was 0.53 years (IQR 0.20–1.92 years) in CD and 0.28 years (IQR 0.61–0.95 years) in UC patients, respectively (p = 0.11–0.86 years) in UC, respectively (p = 0.001–0.0001) was found. Diagnostic delay did not differ significantly between patients with UC (3 months) and was associated with older age at diagnosis.  

Introduction:  
In an attempt to investigate the diagnostic delay in Austrian IBD patients and to identify associated risk factors for delayed diagnosis we sought to investigate the diagnostic delay in Austrian IBD patients and to identify associated risk factors for delayed diagnosis.  

Methods:  
Overall, 102 patients were enrolled in the study (Table 1).  

Results:  
A multivariable proportional hazards regression model was estimated using interval censored latency times as a dependent variable.  

Conclusions:  
In a multicentre cohort study adult patients with IBD (CD, UC) were included between September 2015 and September 2016. Clinical and endoscopic data were collected on the day of colonoscopy. Blood samples, stool samples and saliva samples (before bowel cleansing, saliva and ileal biopsies from healthy and naive patients) were also collected. CEACAM6 from ileal biopsies and saliva were measured (duplicates) using ELISA assays. AIEC attending 18 Austrian outpatient clinics were recruited between May 2014 and July 2015 to complete a multi-item questionnaire, which recorded medical and socioeconomic characteristics. Study outcome was the diagnostic delay defined as the time period from first symptom onset to diagnosis of IBD. A multivariable proportional hazards regression model based on interval censored latency times was calculated.  

Results:  
1217 patients (CD 779, UC 400, IBD 21, missing 17; females 615) with a median age of 40 years (interquartile range (IQR) 31–52 years) and a median disease duration of 10 years (IQR 4–18 years) were analysed. The median diagnostic delay was 0.53 years (IQR 0.20–1.92 years) in CD and 0.28 years (IQR 0.11–0.86 years) in UC, respectively (p < 0.001). In the multivariable regression analysis patients with CD had a significantly longer diagnostic delay than patients with UC (HR 1.56; 95% CI 1.34–1.82; p < 0.0001) and a quadratic effect of age leading to higher risk of delayed diagnosis in older patients (p < 0.001) was found.  

Conclusion:  
The median diagnostic delay was longer in CD (6 months) than in UC patients (3 months) and was associated with older age at diagnosis.  

Disclosure of Interest: All authors have declared no conflicts of interest.  

References  

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Introduction:  
Diagnostic delay seems to be common in inflammatory bowel disease (IBD), especially in Crohn’s disease (CD). We sought to investigate the diagnostic delay in Austrian IBD patients and to identify associated risk factors for delayed diagnosis as well as the impact of delayed diagnosis on the risk of intestinal surgery in CD.  

Aims & Methods:  
In a prospective multicentre study adult patients with IBD (CD, ulcerative colitis UC, inflammatory bowel disease uneclassified IBUD) attending 18 Austrian outpatient clinics were recruited between May 2014 and July 2015 to complete a multi-item questionnaire, which recorded medical and socioeconomic characteristics. Study outcome was the diagnostic delay defined as the time period from first symptom onset to diagnosis of IBD. A multivariable proportional hazards regression model based on interval censored latency times was calculated.  

Results:  
1217 patients (CD 779, UC 400, IBD 21, missing 17; females 615) with a median age of 40 years (interquartile range (IQR) 31–52 years) and a median disease duration of 10 years (IQR 4–18 years) were analysed. The median diagnostic delay was 0.53 years (IQR 0.20–1.92 years) in CD and 0.28 years (IQR 0.11–0.86 years) in UC, respectively (p < 0.001). In the multivariable regression analysis patients with CD had a significantly longer diagnostic delay than patients with UC (HR 1.56; 95% CI 1.34–1.82; p < 0.0001) and a quadratic effect of age leading to higher risk of delayed diagnosis in older patients (p < 0.001) was found.  

Conclusion:  
The median diagnostic delay was longer in CD (6 months) than in UC patients (3 months) and was associated with older age at diagnosis.  

Disclosure of Interest: All authors have declared no conflicts of interest.  

References  

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Introduction:  
Enterobacteria, especially adherent and invasive E. coli (AIEC), are suspected to play a key role in Crohn’s disease (CD). These bacteria are able to highly adhere to the ileal mucosa of CD patients through the CEACAM6 receptor (Carcinoembryonic antigen-related cell adhesion molecule 6). It has been shown that therapies targeting enterobacteria and/or AIEC could be more effective in mice overexpressing CEACAM6. In this line, the overexpression of CEACAM6 in the ileum as well as the presence of AIEC in the ileum could be potential biomarkers to select the patients who could benefit from drugs targeting the host-pathogen interaction. Unfortunately, the identification of these biomarkers is time-consuming and invasive highlighting the need for more convenient alternative.  

Aims & Methods:  
We aimed to assess the correlation between the level of CEACAM6 in the saliva and the level of CEACAM6 in the ileum in CD patients and to define the best threshold of CEACAM6 in the saliva to detect overexpression of ileal CEACAM6. In addition, we attempted to identify non-invasive biomarkers of AIEC infection. In this prospective multicentre study (8 centers), all the patients requiring ileoscopy, regardless the indication, were consecutively included between September 2015 and September 2016. Clinical and endoscopic data were collected on the day of colonoscopy. Blood samples, stool samples (before bowel cleansing), saliva and ileal biopsies from healthy and patients with complicated CD were also collected. CEACAM6 from ileal biopsies and saliva were measured (duplicates) using ELISA assays. AIEC attending 18 Austrian outpatient clinics were recruited between May 2014 and July 2015 to complete a multi-item questionnaire, which recorded medical and socioeconomic characteristics. Study outcome was the diagnostic delay defined as the time period from first symptom onset to diagnosis of IBD. A multivariable proportional hazards regression model based on interval censored latency times was calculated.  

Results:  
Overall, 102 patients were enrolled in the study (Table 1).  

Table 1: Baseline characteristics of the 102 CD patients included in the study.  

<table>
<thead>
<tr>
<th>Variable</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female gender n, %</td>
<td>56 (56.6%)</td>
</tr>
<tr>
<td>Active smokers n, %</td>
<td>34 (34.3%)</td>
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<td>Country of Europe</td>
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<tr>
<td>Montreal classification</td>
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<tr>
<td>Disease location</td>
<td></td>
</tr>
<tr>
<td>L1</td>
<td>27 (28.4%)</td>
</tr>
<tr>
<td>L2</td>
<td>12 (12.6%)</td>
</tr>
<tr>
<td>L3</td>
<td>58 (61.1%)</td>
</tr>
<tr>
<td>L4</td>
<td>7 (7.4%)</td>
</tr>
<tr>
<td>Disease behaviour</td>
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</tr>
<tr>
<td>B1</td>
<td>51 (53.4%)</td>
</tr>
<tr>
<td>B2</td>
<td>26 (27.7%)</td>
</tr>
</tbody>
</table>

Table 1: Baseline characteristics of the 102 CD patients included in the study.
Ileal CEACAM6 level did not depend on disease severity or the site of biopsies as the median level of ileal CEACAM6 was 8546 pg/ml (578.9–1646) and there was no difference in healthy or ulcerated tissue (756 pg/ml [487–1617] vs 947 pg/ml [604–1820], p = 0.86). The median level of CEACAM6 from salva was 3837 pg/ml [1889, 7338]. There was a positive correlation between the levels of CEACAM6 in saliva and CEACAM6 in the ileum (r = 0.47; p = 0.001) in both macroryscopically healthy areas (r = 0.53, p < 0.001) and ulcerated zone (r = 0.39, p = 0.002). Using a ROC curve, we determined the best threshold of CEACAM6 in saliva for detecting ileal CEACAM6 expression. Using a ROC curve (area under the curve (AUROC) = 0.73), the cut-off value of 3800 pg/ml demonstrated the best performances to detect ileal CEACAM6 overexpression with substantial specificity (76.0% [54.9–90.6]) and positive predictive value (67.5% [74.9–85.3]). The number of enterobacteria was increased in CD patients with prior intestinal resection (562 [20164] vs. 116 [0752] pg/ml, p = 0.03). Interestingly, the number of enterobacteria was also increased in AIEC-positive patients (640 [201729] vs. 610 [0298] pg/ml, p = 0.004). Using a ROC curve, we determined the best threshold of enterobacteria in the ileum to detect the presence of ileal AIEC bacteria. We found an area under the curve (AUROC) of 0.70 [0.61; 0.77]. The cut-off value of 60 cfu/biopsy demonstrated the best performances to detect the presence of ileal AIEC bacteria. The number of enterobacteria associated to ileal mucosa (cut-off value > 60 cfu/biopsy) strongly predicted the presence of AIEC and then is a reliable test for AIEC screening with very high negative predictive value (94.1% [80.3–99.3]) and high sensitivity (91.7% [73.0–99.0]).

Conclusion: CEACAM6 measurement in the saliva is feasible, non time-consuming and non-invasive. It could be a reliable test to detect the overexpression of CEACAM6 in the ileum from CD patients and could then be proposed as a non-invasive biomarker to select patients who might benefit from anti-adhesive therapies. In addition, we identify that the number of enterobacteria associated to the ileum is a convenient test to screen CD patients for AIEC bacteria.

Disclosure of Interest: The study was funded by LEOSSFFRE company. I declare lecture fees for Abbvie, Takeda, Hospira, MSD, Vifor Pharma, Sanoft-Aventis and Ferring. I declare consulting fees for Abbvie, Takeda, Hospira.

All authors have declared no conflicts of interest.

P0360 DOUBLE-BALLOON ENDOCOPIC EVALUATION OF Fecal CALPROTECTIN AS A BIOMARKER FOR SMALL INTESTINAL INFLAMMATION IN CROHN’S DISEASE

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Introduction: Crohn’s disease (CD) has a progressive course and often causes mucosal injury throughout the gastrointestinal tract. Mucosal healing (MH) has been proposed as a treatment goal for patients with CD. Endoscopy, computed tomography, magnetic resonance imaging, and other examinations are used to evaluate MH. However, repeated examinations require considerable effort and are highly invasive. Recently, fecal calprotectin (FC) has attracted attention as a new biomarker. The correlation between FC levels and CD activity is well established in ileocolonic or colonic CD, but few reports have described this correlation in ileal CD alone.

Aims & Methods: This study evaluated the correlation between FC levels and endoscopic activity in ileal CD. Fifteen patients with ileal CD who underwent double-balloon endoscopy (DBE) between May 2016 and February 2017 at our hospital were included in this study. The entire small intestine was examined with DBE and radiological enteroclysis. We evaluated the correlations of FC levels, C-reactive protein (CRP) levels, erythrocyte sedimentation rates (ESR), and CD activity index (CDAI) scores with the endoscopic activity. To evaluate the endoscopic activity of the small intestine, we used Double-Balloon Endoscopic Score for CD (DES-CD), which is a modified version of the Simple Endoscopic Score for CD (pDES-CD). To determine the DES-CD, the small intestine was divided into four segments (upper jejunum, lower jejunum, upper ileum, and lower ileum), and four variables were evaluated in each segment (allear size, extent of ulcerated surface, extent of affected surface, and stenosis) in accordance with the SES-CD. For the evaluation of mucosal injury, the partial DES-CD (pDES-CD) was calculated by excluding “stenosis” from the DES-CD. The DES-CD and pDES-CD ranges were 0–46 and 0–24, respectively.

Results: Fifteen patients (11 males and four females) with a median age of 42 (range, 27–71) were examined. No colitic lesions were observed in any of the patients. The DES-CD correlated with FC (r = 0.688, P = 0.005) and CRP (r = 0.765, P = 0.001) levels. In addition, the pDES-CD correlated with FC levels (r = 0.803, P = 0.001), CRP levels (r = 0.673, P = 0.006), and ESRs (r = 0.704, P = 0.003). The CDAI scores did not correlate with either of the endoscopic scores

Conclusion: In this study, the endoscopic activity in ileal CD correlated with FC both in DES-CD and in pDES-CD. In addition, the partial DES-CD (pDES-CD) exhibited a stronger correlation with FC levels than did DES-CD scores. This might be because FC levels reflect mucosal injury and not stenosis. Our findings suggest that FC can be used for monitoring mucosal injuries in the small intestine and as a biomarker for evaluating MH.

Disclosure of Interest: All authors have declared no conflicts of interest.

References:
Introduction: Increasingly, immunosuppressive medications such as azathioprine and mercaptopurine are used in order to prevent the induction or recurrence of inflammatory bowel disease (IBD) patients. It has been reported that such treatments increase the risk of developing all types of skin cancer. Education of these patients is key in order to promote their awareness of their increased risk and it is vital for gastroenterologists to counsel patients on sun protection strategies on initiating therapy. We recently performed a pilot study in this group which highlighted gaps in their knowledge of the increased risk and prevention strategies. We speculate clinician’s lack of knowledge was partly to blame.

Aims & Methods: Our aim was to determine Irish IBD clinicians’ knowledge of the skin cancer risk and advised photoprotective behaviours in this cohort. Cross-sectional descriptive study. We invited IBD clinicians via email to fill in an anonymous online survey designed to assess knowledge of skin cancer risk and preventative measures. We speculated clinician’s lack of knowledge was partly to blame. We recently performed a pilot study in this group which highlighted gaps in their knowledge of the increased risk and prevention strategies. We speculate clinician’s lack of knowledge was partly to blame.

Results: To date, 45 Irish Gastroenterology clinicians completed the online questionnaire. Of these, fifteen (33%) were consultants, fourteen (31%) gastroenterology trainees, four (9%) general medical trainees and twelve (27%) IBD nurse specialists. Overall, clinician’s knowledge of general factors associated with increased risk of skin cancer was reassuring; with all 45 (100%) knowing sun beds increased skin cancer risk and almost 100% (44, 98%) knew working outside doors incurred increased risk. 42 (93%) knew a personal history of skin cancer and previous blistering sunburn were risks; however, only 34 (79.1%) recognised family history as a risk. Regarding gender associated risk; only 67.4% (n = 29) knew men were greater risk than women of non-melanoma skin cancer (NMSC). Their knowledge of specific immunosuppressors risk was suboptimal; while many (37, 82%) recognized azathioprine was a risk factor for developing NMSC, only 7 (11%) knew anti-TNFα agents were strongly associated with an increased risk of malignant melanoma. Regards prevention strategies; the majority knew what changes to look for in a suspicious mole; 100% (n = 45) knew to be suspicious of changing color and 84% (n = 38) of an irregular border, but shockingly only five (11%) perform yearly skin checks on their patients on immunosuppressants. Their knowledge of preventative measures was also lacking; 37% (86%) knew patients should wear SpF 50 but almost half (47% n = 21) thought it should be applied twice daily rather than two hourly (51% n = 23) and only 47% (n = 20) knew patients should stay in the shade from 11am-3pm. Regards their own practice; 39 (87%) report they do emphasise the importance of sun protection in clinic (p < 0.0003), and of physicians, trainees had a more complete knowledge of all advised preventative measures (p < 0.03).

Conclusion: Our study highlights IBD clinicians’ suboptimal knowledge of immunosuppressors risk and their lack of emphasis on preventative measures and skin examination in clinics. A targeted educational and awareness programme may improve this deficiency.

Disclosure of Interest: All authors have declared no conflicts of interest.
Conclusion: Association of serum S100A4 protein with UC and CD was confirmed. In CD, disease behaviour did not have impact on serum concentration of S100A4 protein. In CD, higher levels of serum S100A4 were observed in patients with ileo-colonic and colonic involvement compared to those with isolated small bowel involvement.

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P0364 SEVERE VITAMIN D DEFICIT IN ACTIVE INFLAMMATORY BOWEL DISEASE
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Introduction: Hypovitaminosis D is common in Inflammatory Bowel Disease (IBD) patients. Some studies suggest that the finding may relate to severity of the disease.1,2

Aims & Methods: The aim of the study was to determine the VID status in an Italian IBD cohort in relation to disease activity. Serum VID levels were measured in 260 IBD outpatients, not supplemented with VID (110 Crohn’s Disease (CD) and 150 Ulcerative Colitis (UC); 145 males and 115 females, with median age 50.7 ± 15 years), and to compare VID levels of those to 205 healthy blood donors, matched by sex, age (+/– 2 years) and month in which the blood sample was collected. VID levels were correlated to C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), Harvey Bradshaw Index (HBI) and Crohn’s Disease Activity Index (CDAI) for CD and Mayo partial score for UC. Chi square, T test and linear correlation were used when appropriate.

Results: IBD patients were at higher risk of VID deficiency (defined as <20 ng/ml) than controls (OR 4.5, 95%CI 2.9–6.9, p < 0.0001). Of 260 IBD patients, 156 (60%) had VID deficiency, more often in CD than in UC (72.7% vs 48% respectively, p < 0.0001). Age <40 and ≥60 years, winter/spring season, CRP >2.5 mg/dL, ESR >20 mm/h, previous intestinal surgery and HBI ≥5 were significant risk factors for VID deficiency. No differences were observed in relation to sex, smoking status, BMI, age at diagnosis, localization and behavior of disease, and need of steroids. There was a weak negative correlation between CRP values, HBI scores and VID levels (R = –0.13, p = 0.037 and R = –0.26, p = 0.006 respectively).

Conclusion: VID deficiency is significantly more common in IBD patients than in controls, more so in CD. Patients with active disease are more likely to have VID deficiency than those in remission. The correlation with activity indexes should be confirmed in larger series.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P0365 MAGNETIC RESONANCE OF THE SMALL BOWEL WITH EARLY (70 MIN) AND LATE (7MLNS) PHASE POST GADOLINIUM IMAGING TO IDENTIFY FIBROSIS IN STRICING STRAIGHT BOWEL CROHN’S DISEASE
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Introduction: Extended small bowel (SB) Crohn’s disease (CD) strictures can comprise of both inflammatory and fibrotic elements. An accurate tool to discriminate fibrotic from inflammatory disease. Lesions with a dense fibrotic matrix exhibit means to assess activity, to date, no specific tool has been developed to identify both inflammatory and fibrotic elements. An accurate tool to discriminate fibro-inflammatory and strictures respectively. Neither parameter could differentiate between inflammatory and structuring disease. 26 MREs performed with ileal CD have been further assessed; median age =41yrs, male = 10(38%).

Conclusion: Unlike biochemical markers, MRE may be a useful means to differentiate between inflammatory and structuring disease. Further study is required to assess the long-term predictive value. MRE may be a useful adjunct to current MRE and help detect fibrosis in small bowel lesions and warrants further investigation.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0366 GASTRODUODENAL INVOLVEMENT IN PATIENTS WITH CROHN’S DISEASE – UPPER ENDOSCOPY ONLY IN SYMPTOMATIC PATIENTS?
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Introduction: The need for upper endoscopy in patients with Crohn’s disease (CD) with symptoms is controversial. The aim of this study was to establish any correlations with the prevalence of gastroduodenal involvement, regardless of symptoms, and its prognostic implications.

Aims & Methods: Patients from a single centre with established CD (n = 347) were retrospectively evaluated – inclusion criteria: upper endoscopy without treatment. Gastroduodenal involvement was defined by considering macroscopic (erosions, ulcers or stenosis) and microscopic criteria (focal gastritis, cryptic irregularity, erosion/ulceration and granuloma in the absence of Helicobacter pylori (HP) infection).

Results: We included 140 patients - phenotype: 50% inflammatory, 31% strictureing and 19% penetrating; Location: 42% ileal, 45% ileocolic and 13% colic. Upper endoscopy was performed in 19% for symptoms and in 81% for staging. Gastric macroscopic findings were detected in 49% (69/140); the most common were erosions (21%) and erythematous mucosa (18%). Biopsies were performed in 56% of patients: chronic gastritis 66%, normal 23%, granuloma 5%, focal gastritis 2% and cryptic microabcesses in 2%. HP was positive in 25% of patients. In the stomach, endoscopic assessment of the lesions was observed in 35% of the biopsies. Alimentary tract involvement due to CD that is associated with a worse prognosis.

Conclusion: The prevalence of gastroduodenal involvement by CD in this sample was 18%, and a larger percentage have macro/microscopic findings that are not disease specific. The presence of symptoms does not predict gastroduodenal involvement due to CD that is associated with a worse prognosis.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0367 INCIDENT Findings at CT Enterography in Patients with Crohn’s Disease: Clinical Significance and Impact on Targeted Therapy
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Introduction: CT enterography is one of the most accurate imaging methods for evaluating Crohn’s disease (CD) extent and intestinal involvement. Aims & Methods: The aim of this study was to determine the frequency and clinical impact of the incidental findings in CD patients who underwent CT enterography. This was a retrospective study that evaluated patients with CD who underwent CT enterography between January 2012 and December 2016. Incidental findings were defined as previously unknown extraintestinal lesions. The orientation of the patients after their detection was evaluated.
Results: A total of 520 patients who underwent CT enterography were identified, with 264 (50.7%) being male (CD: 178/35%) and 256 (49.3%) being female (CD: 150/53%). The median age was 43 (32–53) years and 53% were women. The main indication for CT enterography was CD staging (81%). A total of 531 incidental findings were detected (median of 2 [1–3] per patient). The main findings identified were hepatic nodules (n = 39), hepatic cysts (n = 55) and sarcoidosis (n = 46). The findings implicated orientations to another medical specialty in 80 patients (29%), the main ones being Urology (n = 14) and Gynecology (n = 11). The findings implied additional exams in 59 patients (21%). Five (2%) underwent subsequent surgical intervention. Clinically relevant findings were found in 38 patients (14%), including 2 renal tumors, 2 ovarian teratomas and 3 cases of primary sclerosing cholangitis. The detection of incidental findings implied a change in CD therapy in 9 patients (3%); one suspended biologic therapy, 2 suspended immunomodulator therapy and 6 initiated biologic therapy.

Conclusion: Incidental findings are relatively common in patients with CD who undergo CT enterography. A significant proportion is clinically relevant and may involve change CD therapy. A risk stratification may be important to avoid morbidity associated with unnecessary examinations to assess benign situations.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

P0368 CLINICAL SIGNIFICANCE OF ASYMPTOMATIC CLOSTRIDIUM DIFFICILE CARRIAGE IN PATIENTS ON IMMUNOMODULATOR FOR INFLAMMATORY BOWEL DISEASE
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Introduction: Clinical significance of asymptomatic Clostridium difficile (C. difficile) carriage in patients on immunomodulator for inflammatory bowel disease (IBD) is largely unknown. [1, 2]

Aims & Methods: The aim of this study was to investigate the clinical implication of asymptomatic carriage of C. diff in IBD patients. Consecutive IBD patients on immunomodulators in clinical remission for the past six months were prospectively recruited from the IBD clinic since 2013. Those cases were excluded if they had past history of total colectomy, the dosage of their immunomodulators were titrated according to their disease activity in the past six months or the types of their immunomodulators were other than azathioprine, mercaptopurine or methotrexate.

Stool specimen for C. difficile cytotoxin real-time polymerase chain reaction (RT-PCR) assay was obtained to all eligible patients at the time of enrollment and every follow-up during the study period. Patients were monitored for any IBD flare-up in which if happened, an additional stool specimen for C. difficile carriage was performed. The asymptomatic carriage group had a significant higher rate (33.33 vs. 7.45%, p 0.007) and earlier onset (18.78 vs. 34.42 months, log rank p 0.099) in Mann-Whitney U, p 0.037) in evolving into clinical C. difficile infection as compared with the non-carriage group.

No other serious complications, such as toxic megacolon, colonic perforation, sepsis, and death, were reported in the both groups during the study period.

Clinical characteristics of the IBD patients with and without asymptomatic carriage of C. difficile

<table>
<thead>
<tr>
<th>Non C. difficile carrier</th>
<th>C. difficile carrier</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (Yr)</td>
<td>43(26)</td>
</tr>
<tr>
<td>Sex (m/f)</td>
<td>128:60</td>
</tr>
<tr>
<td>Smoker (%)</td>
<td>24(12.77)</td>
</tr>
<tr>
<td>Year of Diagnosis (Yr)</td>
<td>7(9)</td>
</tr>
<tr>
<td>Crohn disease (%)</td>
<td>92(48.94)</td>
</tr>
<tr>
<td>Prior exposure of Anti-TNF (n, %)</td>
<td>4(2.13)</td>
</tr>
<tr>
<td>Flare up (n, %)</td>
<td>21(11.17)</td>
</tr>
<tr>
<td>mild/moderate/severe</td>
<td>16(5)</td>
</tr>
<tr>
<td>C. difficile infection (%)</td>
<td>14(7.45)</td>
</tr>
</tbody>
</table>

Data were expressed as median(interquartile range) *: all are UC cases and 3 for maintenance therapy with indications as follows: refractory colitis, spondyloarthropathy, rectovaginal fistula **: case of UC received 3 doses of anti-TNF for severe flare

Abbreviation: IBD, inflammatory bowel disease; C. difficile, Clostridiurn difficile; ulcerative colitis, UC; ns, non-significant

Conclusion: The incidence of asymptomatic carriage of C. difficile in the IBD patients on immunomodulators was not common. It did not associate with the disease flare-up but a significant portion of them could evolve subsequently into clinical infection.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P0369 BOWEL ULTRASOUND IS USEFUL IN DISEASE MONITORING OF ULCERATIVE COLITIS PATIENTS: FIRST ANALYSIS FROM THE TRUST&UC STUDY IN GERMANY
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Introduction: Due to the relapsing and highly variable nature of ulcerative colitis (UC), it would be desirable to have reliable tools for measuring parameters of disease activity in order to monitor response to therapy and to detect relapse. In recent years it has already been shown that ultrasound is a useful method to monitor the disease activity.1 The hypothesis of the TRUST&UC (TRansabdominal UltraSonography of the bowel To monitor disease activity in subjects with Ulcerative Colitis) study is that transabdominal US is an easy to use, easily repeatable, and accurate diagnostic tool in the assessment of UC activity, in monitoring the disease course, and response to therapy.

Aims & Methods: TRUST&UC is a German ongoing prospective, observational multi-center study in patients with active UC. The primary objective of this study is the prospective evaluation of bowel wall thickening in order to assess its value in monitoring UC patients in routine medical practice. Clinical parameters (e.g. CRP, fecal calprotectin) and the Simple Colitis Clinical Activity Index (SCCAI) were used for routine assessment of disease activity.

Results: 176 patients with active UC have been enrolled in 37 German IBT study group (GIGS) centres until February 2017. 47.2% of the patients were female, median age was 38.9 years (range 19–77) with median disease duration of 152.2 days (range 8–1057). Of all the patients with a clinical flare defined by SCCAI 90.3% showed a bowel wall thickening (BWT), and only 9.7% showed no US signals. At US examination, a BWT in the colonic sigmoids were present in 87.5% of the patients, in the colon descendens in 83.7%, in the colon transversum in 82.3% and in the colon ascendens in 83.3%. Loss of bowel wall
stratification was the case in 20.6% of the patients, mesenteric fibro-fatty prol- 
imination more than 50%, has an increased signal in the color Doppler US. At baseline systemic steroids were used in 62.1%, azathioprine in 36.2%, and TNF-α antagonists in 40.0% of patients (N = 174).

All follow-up patients (N = 104) displayed acute inflammatory symptoms at baseline, which require at least one medication. The number of patients recruited for an introduction or escalation of treatment. After 12 weeks, the study showed significant improvement of the following parameters: BWT in colon segmideum (87.5% vs 33.7%, p = 0.034) and colon transversum (42.3% vs 15.4%, p = 0.012), loss of haustration (58.8% vs 33.7%, p < 0.001), ulcers (9.7% vs 2.9%, p < 0.001), mesenteric lymphadenopathy (31.6% vs 14.3%, p = 0.005), mesenteric fibro-fatty proliferation (40.0% vs 10.0%, p = 0.041) and increased signal in color Doppler US (56.7% vs 23.1%, p = 0.039). A decrease of BWT was significantly accompanied by a decrease in SCCAI (8.0 to 1.5 points, p < 0.001).

Conclusion: In this real-life cohort almost 90% of the patients showed a BWT, a pivotal IBD symptom and within 12 weeks selected bowel US parameters improved significantly from treatment intensification. Therefore, US examination is a useful tool to monitor disease activity and response to therapy in UC patients.

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F. Petersen: F. Petersen has received lecture and consulting fees from AbbVie.

U. Heimga: U. Heimga has received lecture and consulting fees from AbbVie.

A. Rössler: A. Rössler is AbbVie employee and may own AbbVie stock or options.

D. Lang: D. Lang is AbbVie employee and may own AbbVie stock or options.

S. Rathi: S. Rathi is AbbVie employee and may own AbbVie stock or options.

T. Kucharzik: T. Kucharzik has received lecture and consulting fees from AbbVie.

All other authors have declared no conflicts of interest.

Reference

P0370 THE GUT MICROBIOME IN IBD IS CHARACTERIZED BY IMPAIRED METABOLIC COOPERATIVITY AND CAN BE RESTORED UPON ANTI-TNF THERAPY

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Introduction: Blocking TNFα is an important treatment option for inflammatory bowel disease (IBD). The etiology of the disorder comprises a permanent activation of immune cascades and imbalanced cytokine networks. Evidence has been put forward that alteration of the human gut microbiota may play a critical role in the pathogenesis of IBD. However, the impact of targeted cytokine blockade on dysbiosis of intestinal microbial communities is poorly understood. Here, we investigate the effect of anti-TNFα treatment on gut microbial community structures in a prospective, longitudinal study for 30 weeks. The study compares IBD as a disorder, which primarily affects the gut, with seropositive and -negative rheumatoid arthritis (RA) and gout, and therefore provides an option for individualized treatment for increasing number of IBD patients.

Results:naive patients suffering from IBD (n = 12) or RA (n = 17), subject to first-time anti-TNFα therapy were recruited for longitudinal stool sampling at baseline and 2, 6 and 30 weeks after therapy induction. Intestinal microbiota communities were studied by 16S rRNA gene (V4) sequencing. Changes in microbiota before and after therapeutic interventions were assessed by terms of alpha and beta diversity, indicator species and prediction of metabolic cooperative interactions. Samples from healthy controls (n = 19) were included as a benchmark of healthy microbial profiles.

Results: Intestinal microbial diversity and cooperativity are decreased in both disease entities, IBD and RA. In IBD, anti-TNFα therapy is able to restore microbial diversity and cooperativity. More over cooperative metabolic interaction is significantly increased only in anti-TNFα responders. In RA, anti-TNFα therapy did not significantly restore microbial community structures.

Conclusion: We show that anti-TNFα treatment increases the gut microbial diversity and coupling of cross feeding metabolic interactions towards the state of healthy individuals. Assessment of metabolic interactions of intestinal microbiota may serve as a marker for clinical response in IBD patients.

Disclosure of Interest: All authors have declared no conflicts of interest.

References:

P0371 SELF-MONITORING OF THE COLONIC INFLAMMATORY BOWEL DISEASE BY A RAPID HOME BASED FEACAL CALPROTECTIN TEST AND A SYMPTOM QUESTIONNAIRE

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Introduction: Fecal calprotectin (FC) is a most reliable noninvasive means to distinguish remission from active inflammation in inflammatory bowel disease (IBD). Commercially available FC tests are time-consuming, and consequently new rapid tests have been validated. As the incidence of IBD is increasing, self-monitoring and eHealth technologies have been evaluated in managing patients with this life-long disease.

Aims & Methods: The aim of this prospective study was to evaluate the feasibility and cost-effectiveness of a semi-quantitative rapid FC home test and a validated symptom questionnaire, in patients with colonic IBD. The influence of the self-monitoring to the course of the disease will also be evaluated. Between April 2015 and December 2016, 180 patients with colonic IBD (126 with UC, 47 with CD, and 7 with UC unclassified) were included in the study and randomized in a study group and control group. Patients in the study group were instructed to perform the FC home test and fill in a symptom questionnaire every other month and with increasing of the symptoms, and sent the results to the study/IBD nurse by e-mail. The control group patients filled in the symptom questionnaire at baseline and at 12 months and with the appointment to the outpatient clinic according to normal practice. Both groups were not reminded of performing the stool tests or filling in the questionnaires. The study period was 12 months, and it is still ongoing.

Results: By the end of February 2017, 134 of the 180 included patients had completed the 12 months’ follow-up. In the study group, 20/91 (22%) patients had performed the stool tests and filled in the symptom scores according to the study protocol for 6 months, and 14/91(15%) patients for 12 months. In the control group, 14/89 (16%) patients had filled in the symptom score at baseline and 0/22 at 12 kk. There was a significant difference of the adherence between patients stratified for IBD-diagnosis, age, sex. The satisfaction of the patients with the program as well as the reasons for the discontinuation of the study and influence of self-monitoring in the number of relapses, phone calls, e-mails, and appointments to the outpatient clinic were investigated in both groups and will be evaluated.

Conclusion: The self-monitoring of IBD activity with a rapid FC home test provides an option for individualized treatment for increasing amount of IBD patients. However, in this study the adherence to the self-monitoring program was low. The patients need to be reminded of performing the stool tests and filling in the questionnaires in time. Also, the selection and education of the patients, as well as the easy accessibility of the monitoring program are crucial and need further consideration.

Disclosure of Interest: All authors have declared no conflicts of interest.

References:

P0372 CLINICAL CHARACTERISTICS IN ULCERATIVE COLITIS PATIENTS WITH COLITIS ASSOCIATED DYSPLASIA/CANCER AND SPORADIC TUMOR

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Introduction: Although the incidence of ulcerative colitis (UC)-related colorectal cancer (CAC) is increased in cases with long duration of disease, it should also be recognized that sporadic tumors (ST) develop as older. Various studies have been conducted on CAC, but there are few clinical studies on ST merged with UC. In
P0373 CAN WE PREDICT THE LACK OF RESPONSE TO CYCLOSPORINE AS SECOND LINE THERAPY IN PATIENTS WITH ACUTE SEVERE COLITIS REFRACTORY TO CORTICOSTEROIDS?

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Introduction: Acute severe colitis (ASC) is a serious clinical condition that requires intensive intravenous (iv) corticosteroids treatment. Nevertheless, about 30-40% of patients fail to response. Intravenous cyclosporine is an effective rescue therapy in steroid-refractory patients.

Aims & Methods: The aim of our study was to identify the clinical and biological predictive factors of lack of response to cyclosporine as second-line therapy in patients with ASC refractory to iv corticosteroids.

Results: Our study included 52 females and 38 males, with a mean age of 35 years (14–70 years). There were 34 patients with Crohn's disease and 56 diagnosed with ulcerative colitis. Among the 90 enrolled, 68 patients (75.5%) had a good response to cyclosporine. Eleven patients were non responders and underwent corticosteroids withdrawal and corticosteroids rescue, while 6 patients continued corticosteroids. After the sporadic lesions were resected in remitting UC patients, regular surveillance colonoscopy is necessary because 8.5% (4/47) of patients was found CAC/dysplasia. Even in CAC group, prognosis is well in patients with IEN.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0374 CHANGES IN THERAPEUTIC STRATEGY AND OUTCOMES IN NEWLY DIAGNOSED PATIENT WITH CROHN'S DISEASE IN THE BIOLOGICAL ERA IN HUNGARY: A NATIONWIDE STUDY BASED ON THE NATIONAL HEALTH INSURANCE FUND DATABASE

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Introduction: Treatment of Crohn's disease (CD) in the past was based on mesalazine (5-ASA) alone or combined with corticosteroids. Nowadays the biological therapy is the first-line treatment option for the most severe cases. We aimed to analyze the changes in medical treatment of patients with CD in Hungary over a 10-year period.

Methods: We analyzed all newly diagnosed CD patients between 2004 and 2014 in Hungary, using a national database.

Results: In total, 745 patients were diagnosed during that time. The average age of diagnosis was 41.3 ± 16.8 years, and 43.7% of patients were male. The majority of patients received mesalazine only (68.3%), followed by combination of mesalazine and corticosteroids (21.5%). Biological therapy was used in 4 % of the cases. The use of biological therapy significantly increased over the years (p < 0.001).

Conclusion: The proportion of biological therapy increased in Hungary at the same time as the number of CD patients significantly increased. This may indicate an increase in the severity of the patients being diagnosed.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0375 RELATIVE FREQUENCY OF RELAPSES IN PATIENTS WITH ULCERATIVE COLITIS AND CROHN'S DISEASE TREATED WITH MESENCHYMAL STEM CELLS - 5 YEARS OF FOLLOW-UP

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Introduction: Mesenchymal stem cells (MSCs) have a potential for differentiation and immunosuppressive properties. Currently under phase I-II trials evaluated the autologous and safety of MSCs in the treatment of patients with inflammatory bowel disease - ulcerative colitis and Crohn's disease.

Aims & Methods: We aimed to compare the frequency of relapses and duration of remission for 5 years of follow up in patients with luminal Crohn's disease (CD) and the total defeat of ulcerative colitis (UC) receiving therapy with mesenchymal stem cells (MSCs), bone marrow. We compared the frequency of relapses in patients with luminal form of CD and luminal form of UC with UC (total lesion) receiving MSCs. A group of patients (CD) aged 22 to 56 years (Me=28) (n=24) received MSC culture scheme (0-1-2 weeks, then every 2 weeks). The second group of patients with UC (n=26) aged 20 to 62 years (Me=28) received the culture of MSCs in a similar way. Evaluation of the effectiveness of treatment for relapse frequency was carried out at 12, 24, 36, 48 and 60 months after initiation of therapy.

Results: Among the patients in 1st group relapse in the 12 months of observation was not found. In 2nd group, relapse occurred in 3/24 patients (12.5%) (OR=0.72; 95% CI 0.13–3.96, p = 0.92). After 24 months in the group of patients (group 1) receiving MSC, relapse occurred in 5/24 (20.8%) in group 2 patients with recurrent disease in 7/26 (26.9%) (OR = 0.97; 95% CI 0.13–3.96, p = 0.92).

Conclusion: MSCs transplantation longer contributes to clinical remission in patients with Crohn's disease luminal shape compared to a group of patients suffering from ulcerative colitis.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0376 CELL THERAPY FOR PERIANAL CROHN'S DISEASE

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Introduction: Local, perianal Crohn's disease (perianal CD) is a frequent complication of Crohn's disease, with a prevalence ranging from 3 to 47%. We aimed to assess the efficacy and safety of autologous bone marrow mononuclear cell transplantation in patients with perianal CD.

Methods: We performed a retrospective analysis of patients who underwent autologous bone marrow mononuclear cell transplantation for perianal CD between 2008 and 2016.

Results: Of the 24 patients included in the analysis, 18 (75%) had a complete remission at 6 months after transplantation. The remaining 6 patients had a partial remission. No complications related to the transplantation were observed.

Conclusion: Autologous bone marrow mononuclear cell transplantation is an effective and safe treatment for perianal CD.

Disclosure of Interest: All authors have declared no conflicts of interest.
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Introduction: Perianal fistulas are the most widespread and common types of fistulas in Crohn’s disease (CD). They are difficult to treat, worsen the quality of life of the patient and increase the risk of bowel resection. Despite the significant effect of anti-cytokine therapy fistulous forms of CD, treatment of these patients remains a difficult task with high risk of relapse of CD. Mesenchymal stem cells have immunomodulatory properties and a large regenerative potential, at present also used for treatment of fistulous CD and perianal fistulas of different etiologies.

Aims & Methods: We aimed to compare the efficacy of combined therapy (local and systemic) mesenchymal stem cell therapy (MSCs) of bone marrow, infliximab (IFX) and antibiotics/immunosuppression (IS) on the rate of healing of simple perianal fistulas in Crohn’s disease. 36 patients with Crohn’s disease with perianal lesions were divided into three groups depending on the method of therapy. The first group of patients aged from 19 to 58 years (Me-29) (n = 12) received culture of MSCs systematically via the scheme and locally; on the perimeter of the fistulas introduced 40 million MSCs - 4 point of injection and 1 ml of saline containing 10 million MSCs. After 4 months of therapy, 48 months of treatment 40 million MSCs in the area of the fistula. The second group of patients with CD (n = 10) aged 20 to 68 years (Me-36) were receiving anti-cytokine therapy of IFX. The 3rd group of patients with CD (n = 14) aged 20 to 62 years (Me-28) received antibiotics and is in the dynamics evaluated the closure of the fistula opening of the fistula. Ano-rectosigmoidoscopy carried out after 3, 6, 12 and 36 months from start of therapy.

Results: After 12 weeks among patients of the 1st group simple healing of fistulas was observed in 10/12 patients (83.3%), in the 2nd group healing simple fistulas have a 8/10 (80.0%) (OR-0.83; 95% CI 0.14–4.9; p = 0.04 in comparison with the 1st group). After 6 months in the 1st group of patients receiving MSCs, healing of simple fistulas persisted in 8/12 (66.7%) by the 2nd group - 7/9 (70.0%) (OR - 1.11; 95% CI 0.32–3.84; p = 0.76). In the 3rd group – patients 4/14 (28.6%) (OR - 0.47; 95% CI 0.2–1.1; p = 0.12 in comparison with the 1st group).

After 12 months in the 1st group receiving MSCs, healing of simple fistulas persisted in 9/12 (75.0%), in the 2nd group - in 6/10 (60.0%) (OR - 1.25, 95% CI 0.48–3.22; p = 0.69). In the 3rd group – 2/14 patients (14.3%) (OR-0.49; 95% CI 0.24 to about 0.98; p = 0.03 in comparison with the 1st group). After 36 months among the patients of the 1st group, the closure of the fistula was observed in 5/12 patients (41.6%), in the 2nd group - 5/10 (50.0%) (OR -1.17; 95% CI 0.53–2.55; p = 0.96). In the 3rd group – in 0/14 patients (0.0%) of (OR -0.58; 95% CI 0.36-0.94; p = 0.01 in comparison with the 1st group).

Conclusion: Combined stem cell and anti-cytokine therapy of CD with perianal lesions leads to more frequent closure of fistula, compared with antibiotics/immunosuppressant.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P0378 EFFICACY AND SAFETY OF RECTAL 5-AMINOSALICYLIC ACID VERSUS CORTICOSTEROIDS IN ACTIVE DISTAL ULCERATIVE COLITIS: A SYSTEMATIC REVIEW AND NETWORK META-ANALYSIS

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Introduction: Ulcerative colitis (UC) is characterized by diffuse and continuous inflammation of the colon. Currently, the etiology and pathogenesis remain unclear. According to a previous epidemiological study, approximately 75% of newly diagnosed UC patients have active distal UC. Topical 5-aminosalicylic acid (5-ASA) and corticosteroids are used frequently in the treatment of active distal UC.

Aims & Methods: Our study aimed to determine the efficacy and safety of different topical drugs used to treat active distal UC. A random-effects model within a Bayesian framework was utilized to compare treatment effects and safety as odds ratios (ORs) with corresponding 95% credible intervals (CrI). The surface under the cumulative ranking area (SUCRA) and median rank within a Bayesian framework was utilized to compare treatment effects and safety as odds ratios (ORs) with corresponding 95% credible intervals (CrI).

Disclosure of Interest: All authors have declared no conflicts of interest.

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Micromolar concentration of V565 in ileal fluid

| Hours post-dose | Subject | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 | 24 |
| 2h              | 31001   | – | 406| 306| 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 2h              | 31002   | – | 33 | 1130| 72 | 82 | 13 | 5(ave) | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 2h              | 31003   | – | 1060| 406| 7 | 0 | 38(ave) | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 2h              | 31004   | – | 126| 0.2 | 11 | 4 | 7 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

In addition to the V565 concentrations in ileal fluid, partially dissolved MTs were recovered from the ileostomy bags of all subjects. Each 1665 mg dose contained a total of 135 MTs. 50 MTs were recovered 2 h post dose from subject 31001; these were not analysed for V565 as this was a post hoc analysis and the MTs were not stored in a way to enable reliable analysis. 64MTs (containing 135 mg V565) were recovered 3h post dose from subject 31002; 78MTs (458 mg 3h post dose from subject 31003; 77MTs (485mg) 3h post dose from subject 31004). 66–82% of an administered dose was recovered from ileostomy bags when MT quantities were added to ileal fluid concentrations. V565 was not detected in any serum sample (LLOQ 62.5 ng/ml).

Conclusion: V565, an oral domain antibody (Vorabody) to TNF engineered to be resistant to intestinal proteases, resulted in high concentrations of active drug in ileal fluid and was not detected in serum following oral administration. In patients with no ileostomy the partially dissolved MTs seen in this study are expected to provide active V565 to lesions distal to the ileum. This profile may be beneficial for IBD and merits further investigation as a potential oral treatment.

Disclosure of Interest: J. Robinson: J Robinson is an employee of the Sponsor company. S. Crowe: S Crowe is an employee of the Sponsor company. G. Whale: G Whale is an employee of the Sponsor company. K. Roberts: K Roberts is an employee of the Sponsor company. M. Weis: M Weis is an employee of the Sponsor company. J. Ritter: J Ritter was a salaried employee of Quintiles at the time of the study; he has no other significant relationships.

S. Nurbhai: S Nurbhai is an employee of a Sponsor company.
Aims & Methods: The main objective was to assess the efficacy of electroacupuncture (EAc) vs. sham EAc and no treatment for treating fatigue in patients with quiescent IBD in a single-blind randomized study. Secondary objectives were to assess changes in quality of life, depression, anxiety and sleepiness after treatment with EAc.

Methods: Fifty-two patients with quiescent IBD and severe fatigue (FACIT-F < 40) (65.3% female, mean age 42 years) were randomized to EAc vs sham acupuncture group. Patients in each EAc group performed a total of 9 acupuncture sessions during eight weeks (2 sessions/first week and one session per week during 7 weeks). Fatigue was evaluated with IBV validated Functional Assessment of Chronic Illness Therapy-Fatigue Scale (FACIT-F). Patients also validated questionnaires to assess quality of life in IBD, depression, anxiety and sleepiness during and after the treatment periods.

Results: Both EAc and Sham group improved the FACIT-F score post-treatment (EAP = -9.53 points, 95% CI [12.3 to -6.75, Basal Vs 9th session p < 0.001]; Sham = -11.97 to -2.06, Basal Vs 9th session p = 0.003). No significant differences were observed in control group (p = 0.339). We found a trend for better response in the EAP than in the sham group although the difference in FACIT-F score was not significant (p = 0.09). EAc also improved quality of life (5.17 points, 95% CI [-8.2 to -2.06, Basal Vs 9th session p = 0.003]; depression (8.9 points, 95% CI [4.3 to 13.8, Basal Vs 9th session p = 0.002); anxiety (10.6 points, 95% CI [3.6 to 17.6, Basal Vs 9th session p = 0.006) and sleepiness scale (1.46 points, 95% CI [0.096 to 2.83, Basal Vs 9th session p = 0.038). However, the differences in between EAc and sham and control groups were not significant (p > 0.05).

Conclusion: Both targeted and sham electroacupuncture are effective in managing fatigue in patients with quiescent IBD.

Disclosure of Interest: All authors have declared no conflicts of interest.

References


P0382 EFFICACY AND SAFETY OF GOLIMUMAB IN CROHN’S DISEASE: A FRENCH NATIONAL RETROSPECTIVE STUDY

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Introduction: Anti-TNF, such as adalimumab (ADA) and infliximab (IFX), have improved the therapeutic care of Crohn’s disease (CD). However their use may be associated with loss of efficacy, adverse events and sometimes primary failure. Among the possible reasons for discontinuation, it is possible to switch to another anti-TNF. In France, three anti-TNF are available in ulcerative colitis (IFX, ADA and golimumab), but only the first two are approved in CD, because golimumab has not been studied in this indication. The aim of this study was to report golimumab efficacy and safety in CD.

Aims & Methods: This national multicenter retrospective study included patients with CD from 12 French tertiary centers who received golimumab and analyzed: clinical response, duration of treatment, tolerance, reasons for discontinuation of treatment, concomitant phenotype, and treatments preceding and associated with golimumab. The main endpoint was the efficacy of golimumab defined by the duration of treatment before failure (need for therapeutic optimization or cessation). Predictive factors of therapeutic response were determined (log rank and Cox model), and the tolerance was evaluated.

Results: One hundred and fifteen patients with a median duration of the disease of 13.5 years received on average golimumab in 3, 6th line of biotherapy. The overall clinical response assessed by the physician was 55.8% at the time of the re-evaluation (on average, at 3.8 months [0.6-24] after initiation of therapy). The median duration of treatment was 12 months (0.55-44). Sixty-seven percent of patients received treatment for more than 6 months and 48.7% of patients were still treated with golimumab at the end of the follow-up. At 12 months, 34.9% of patients still received golimumab without optimization. At 24 months, this figure was 18.1%. In univariate analysis, the factors associated with a longer golimumab treatment duration without stopping or optimizing were the active smoking status (p = 0.043), the absence of anorectal lesions (p = 0.012), the presence of extra-intestinal symptoms (p = 0.035), the presence of a co-immunosuppression of more than 6 months were independently associated with golimumab efficacy (OR 2.16, 95% CI [2.5-36.3], p = 0.005 and OR 3.9895% CI [2.3-7.1], p < 0.001, respectively). Side effects led to discontinuation in treatment of 6% of patients. These were paradoxical psoriasis in three patients, paresthesia (n = 1), lower extremity edema (n = 1), injection site reaction (n = 1) and not reported reason for one patient.

Conclusion: After failure of the other anti-TNF agents, golimumab is well tolerated and results in sustained clinical response in one in two patients with Crohn’s disease, particularly when associated with a co-immunosuppression, and if the reason for discontinuation of the first anti-TNF was an intolerance.

Disclosure of Interest: H. Sokol: consulting fee; Tillotts, Abbvie, MSD, Enterome, Maat.

All other authors have declared no conflicts of interest.

P0383 BIOLOGICS AND BIOSIMILARS: WHAT MATTERS TO PHYSICIANS?

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Aims & Methods: The purpose of this survey was to determine physicians’ familiarity and comfort level with prescribing biosimilars to patients. The survey was sent to physicians residing in the European Union and specializing in the following clinical fields: dermatology, endocrinology, gastroenterology, neurology, oncology, and rheumatology.

Introduction: Biologic medicines and their biosimilar counterparts are effective therapies for many conditions, including inflammatory bowel disease, Crohn’s disease, and ulcerative colitis. The European Medicines Agency (EMA) has approved twenty-two biosimilar medicines, which are derivatives of eight original biologics, and four more biosimilars are scheduled to be reviewed this year. As the number of approved biosimilars rises, regulatory agencies must closely monitor their safety and efficacy.

Results: The majority of survey respondents specialized in endocrinology (19%) and gastroenterology (19%). Respondents were recruited almost equally from the five countries, with France being the most represented country (22%) and the UK being the least represented (18%). The majority of respondents (55%) indicated that safety and efficacy is the most important factor in determining whether a patient should be switched from a prescribed biologic therapy to its approved biosimilar. Thirty percent of respondents indicated that clinical trials related to the biosimilar or current condition being treated was the most important factor in switching. Only 12% of respondents indicated that cost to the government or insurance companies is a primary concern, and only 3% were primarily concerned with improved safety.

Conclusion: This survey suggests that the safety and efficacy of biosimilar medicines is of paramount concern to switching clinicians and patients; physicians highly value clinical trial data for biosimilars. Given that biosimilars are structurally distinct from their original innovator biologics, regulatory agencies and the EMA should consider requiring more stringent clinical trials for biosimilars seeking approval. Specifically, the EMA should require clinical trials for each proposed indication and should provide physicians with this data so that physicians can make informed prescribing choices for the safety of their patients.

Disclosure of Interest: D. Charles: David Charles receives income from Medtronic, Allergan, Ipsen, and the Alliance for Patient Access for education or consulting services.

This data was generated from a SERMO Poll. SERMO is the largest global social network exclusively for doctors. All other authors have declared no conflicts of interest.

P0384 ARE STERREOIDS STILL USEFUL IN THOSE INFAMMATORY BOWEL DISEASE PATIENTS UNDER IMMUNOSUPPRESSION? A RETROSPECTIVE POPULATION-BASED STUDY

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Introduction: Oral steroids are effective in inducing remission of moderate flares of patients with either ulcerative colitis (UC) or Crohn’s disease (CD). However, we know little about their efficacy in immunosuppressed patients or their possible role in reducing biologics and/or surgical needs in these patients.
**Abstract No: P0385**

**ADALIMUMAB LONG-TERM EFFECTIVENESS IN ADALIMUMAB-NAIVE PATIENTS WITH CROHN’S DISEASE: FINAL DATA FROM PYRAMID REGISTRY**


**Aims & Methods:** We aimed to determine the efficacy of systemic or low bioavailability (LB) biologic treatment for moderate flares of patients with at least 6 months of immunosuppressive treatment, and describe long-term follow-up. Inflammatory bowel disease (IBD) immunosuppressed patients (thiopurines or methotrexate) from our population-data registry were analyzed. For statistical analysis, Chi-square test, U Mann-Whitney test and Kaplan Meier survival analysis were used.

**Results:** 392 IBD patients with a median of 82 (6-271) months of immunosuppressive (IMM) treatment were identified (table 1). 89 patients (23%) (33% UC and 67% CD) needed at least one steroid treatment during follow-up (63% systemic steroid and 37% low bioavailability oral steroid) with a median time of steroid treatment of 4 (1-168) months. Average time from IMM to steroid treatment was 26 (6-207) months. In IMM patients there were no differences regarding sex, age, disease, location, perianal disease, extra intestinal manifestations, appendectomy, smoke habit, need for steroids at diagnosis and previous abdominal surgery between patients with no need of steroids and patients with steroid treatment during follow-up. In CD patients, biological treatment for perianal disease before IMM (p=0.00199) and fistulizing (B3) or fistulizing (B3) behavior (p=0.005; OR: 2.284) were risk factors for using steroids after IMM treatment. In UC patients, no statistically significant variables were identified. 49 of these 89 steroid treatment patients (55%) needed biological treatment or surgery after a median of 13 months (0-178); 19 (21%) needed more than one steroid treatment (2-5) and just 31 patients (35%) did not need any other treatment. CD patients had higher risk (p=0.007; OR: 3.529) to receive biological treatment or surgery versus UC patients. Otherwise, the more months using steroids in UC patients, the greater risk for biological or surgery treatment (p=0.009). During follow-up, though it’s not statistically significant (p=0.078), we observe that 75% probability of rescue treatment for UC patients is to be maintained for up to 36 months for CD patients.

**Conclusion:** 23% of IMM immunosuppressed patients needed at least one steroid treatment after 6 months of IMM. Previous biological treatment and B2-B3 behavior predicted steroid treatment in CD patients, who had 3.5 times more risk to receive biological treatment or surgery after steroid treatment using it earlier than UC patients. Just 1/3 of patients who needed steroid treatment after IMM did not need any other rescue treatment.

**Disclosure of Interest:** All authors have declared no conflicts of interest.
**P0386 EFFECT OF ADA LUMABAB IN CLINICAL AND HEALTH-RELATED QUALITY OF LIFE OUTCOMES BY DISEASE SEVERITY AND PRIOR TUMOUR NECROSIS FACTOR INHIBITOR USE IN PATIENTS WITH ULCERATIVE COLITIS IN A CLINICAL PRACTICE SETTING: SUBGROUP ANALYSES FROM INSPIRADA**


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**Introduction:** Adalimumab (ADA) has been shown to improve clinical outcomes and health-related quality of life (HRQoL) significantly in patients (pts) with ulcerative colitis (UC) in a clinical practice setting. Evidence is limited about the benefits of ADA among UC pts with different characteristics.

**Aims & Methods:** The aim was to examine clinical and HRQoL effects of ADA in pts with UC based on disease severity and prior use of tumour necrosis factor inhibitor (TNFI). InspiraDA details have been presented. Pts received ADA 160 mg at week (wk) 0/2 followed by ADA 40 mg at wk 4 through wk 26. Pts who did not respond to ADA by wk 8 were to discontinue. Pts who lost response at or after wk 8 could escalate to ADA 40 mg weekly. UC pts were categorized into subgroups based on physician global assessment (PGA) of disease severity (moderate [baseline PGA = 2] vs severe [baseline PGA = 3]) and previous TNFI use (naïve vs experienced). Proportions of pts with Simple Clinical Colitis Activity Index (SCCAI) response (defined as a decrease of ≥ 2 points vs baseline) and remission (defined as an SCCAI ≤ 2) were calculated for each cohort at wk 2, 8, 26, and 52. Change from baseline in HRQoL outcomes was calculated, including Short Inflammatory Bowel Disease Questionnaire (SIBDQ), European Quality of Life-5 Dimensions-5 Level (EQ-5D-5L), Treatment Satisfaction Questionnaire for Medication (TSQM) and Work Productivity and Activity Impairment (WPAI).

**Results:** Among pts with moderate UC (n = 386) and severe UC (n = 74), SCCAI response rates were 74.6% vs 74.3%, 80.1% vs 71.6%, and 67.1% vs 64.9% at wk 2, 8, 26, respectively. Although remission rates were similar between moderate and severe pts at wk 26 (49.5% vs 40.5%, p = 0.16), ADA provided greater disease control for moderate pts at wk 2 (29.8% vs 9.5%, odds ratio [OR] 4.195, confidence interval [CI] 1.8-9.1, p < 0.0001) and wk 8 (52.3% vs 31.1%, OR 2.4, 95% CI 1.4-4.4, p = 0.01) compared to severe pts (table 1). The rate of dose escalation (ADA 40 mg weekly) was 28.0% in moderate and 28.4% in severe UC pts. HRQoL outcomes were similar between the moderate and severe cohorts. Among pts who were naïve (n = 389) and those experienced to TNFI (n = 72), response rates were 74.0% vs 76.4%, 79.2% vs 75.0%, and 66.3% vs 68.1% at wk 2, 8, 26, respectively. No significant difference was observed in remission rates for naïve vs experienced pts at wk 2 (28.0% vs 19.4%, p = 0.43) and wk 26 (49.4% vs 41.7%, p = 0.39), but naïve pts showed a significantly higher remission rate than experienced to TNFIs at wk 8 (52.2% vs 31.9%, OR 2.1, 95% CI 1.2-3.7; p < 0.0001). The rate of dose escalation was 26.5% in naïve pts vs 36.1% in experienced pts (p = 0.09). In general, HRQoL outcomes were similar between naïve and experienced TNFI pts.

**Conclusion:** ADA treatment achieved clinically relevant rates of SCCAI response and remission even in pts who had severe UC and those who were more treatment-refractory (experienced to TNFIs), in clinical practice. In addition, ADA was associated with greater disease control in the induction period for pts with moderate than severe UC and for naïve pts than those experienced to TNFIs. Insufficient data were available to make meaningful comparisons between groups by prior TNFI use. Future studies are needed to further evaluate these findings.

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P0387 SUBCUTANEOUS ADMINISTRATION OF A NOVEL FORMULA OF CT-P13 (INFLIXIMAB BIOSIMILAR) IS SAFE AND ACHIEVES PROJECTED THERAPEUTIC DRUG LEVELS: A PHASE I STUDY IN HEALTHY SUBJECTS


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Introduction: Treatment with intravenous (IV) CT-P13, a biosimilar infliximab (INX) licensed for use in 80 countries, is highly effective and well tolerated. To increase treatment modalities with CT-P13 for patients, a new subcutaneous (SC) formulation was developed.

Aims & Methods: This phase I and open label study, conducted at a single site in Korea, was designed to evaluate safety and pharmacokinetics (PK) of SC administration of CT-P13 in healthy subjects. In a single dose escalation study, 38 subjects received either SC injection or IV infusion of CT-P13 on Day 0 and were followed for 12 weeks (20 subjects in 3 different dosages of SC; 18 subjects in 2 different dosages of IV). After reviewing safety data observed for 48 hours, the study cohort was conducted subsequently from low dose to high dose. The PK profile of SC and IV formulation was evaluated by measuring the AUC0-last, Cmax, Tmax and T1/2.

Results: A total of 38 male subjects with median age of 23 years (range 19, 30 years) were included. No treatment-emergent serious adverse events or systemic hypersensitivity reaction. In SC cohort, two subjects experienced mild injection site reactions, and both have resolved without any treatment. Mean AUC0-last and Cmax ranged from 5016.4 to 14253.6 h*ug/mL and 10.0 to 23.1 ug/mL, respectively, after a single SC injection of CT-P13. SC CT-P13 formulation was absorbed slower into the systemic circulation (median Tmax ranging from 7.0 to 7.1 days) in comparison with IV formulation (median Tmax ranging from 2.2 to 3.2 hours) but the drug elimination measured by half-life (T1/2) was similar (mean range 13.2 to 13.7 days vs. 11.7 to 12.2 days) between SC and IV formulations, respectively. Bioavailability of CT-P13 SC was approximately 60.6%, when comparing across all CT-P13 SC cohorts to CT-P13 IV cohorts.

Conclusion: PK profiles after a single SC injection were linear by dose levels. SC administration of CT-P13 is feasible in terms of bioavailability and safety profiles.

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All other authors have declared no conflicts of interest.

Reference

P0388 REAL-WORLD HEALTHCARE UTILISATION IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE NEWLY TREATED WITH VEDOLIZUMAB AND ANTI-TUMOUR NECROSIS FACTOR AGENTS

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Introduction: Biological therapy has been highly effective for inflammatory bowel disease (IBD). In addition to anti-tumour necrosis factor (anti-TNF) drugs, a gut-selective anti-integrin biologic, vedolizumab (VDZ), has been approved since 2014. However, the real-world comparative effectiveness of VDZ and anti-TNF has not been fully investigated.

Aims & Methods: This study aimed to evaluate all-cause and IBD-related healthcare utilisation in IBD patients (pts) newly treated with VDZ and anti-TNFs. Cohrs’s disease (CD) and ulcerative colitis (UC) pts ≥18 years old with ≥2 claims for VDZ or ≥2 claims for anti-TNF from 20/5/2014 to 31/12/2016 were identified from a large, de-identified administrative claims database in the US (Truven MarketScan® Commercial and Medicare Supplemental Databases). The first date of the first VDZ/anti-TNF claim was defined as index date. New VDZ/anti-TNF treatment was defined as no claims for these agents in the 1 year before index date. All pts had ≥12 months of continuous enrollment prior to and ≥6-months of continuous enrollment following the index date. All-cause and IBD-related healthcare utilisation including hospitalisation, emergency department (ED) visits and outpatient visits during 6 months post-index were examined for the IBD cohort overall, as well as in CD and UC cohorts. Multivariable logistic regression was employed to estimate the odds ratio (OR) for hospitalisation and ED visits, while Poisson regression was used to examine the rate ratio (RR) for outpatient visits with VDZ compared to anti-TNF use, controlling for demographic characteristics, index year, baseline Charlson comorbidity index (CCI) and baseline hospitalisation and ED visits 1 year prior to index date. In sensitivity analyses, outpatient visits related to infusion administration for VDZ or anti-TNF were excluded to examine the RR associated with outpatient visits that were not related to the visits for infusion procedure.

Results: A total of 652 and 6974 IBD pts newly treated with VDZ and anti-TNF were identified, respectively (mean age [year]: 45 VDZ vs 42 anti-TNF: male: 47% vs 48%). VDZ pts had a higher CCI than anti-TNF pts (0.7 vs 0.5). During the 6 month follow-up, compared to anti-TNF, use of VDZ had significantly higher rates of all-cause hospitalisation (16.3% vs 13.1%, OR 1.30, 95% confidence interval [CI] 1.03–1.64), all-cause outpatient visits (mean visits 45.1 vs 31.0, RR 1.39, 95%CI 1.32–1.37) and IBD-related outpatient visits (mean visits 28.1 vs 17.5, RR 1.60, 95%CI 1.51–1.69). A sensitivity analysis excluding outpatient visits related to infusion administration showed similar results for IBD-related outpatient visits (RR 1.53, 95%CI 1.44–1.62). In pts with CD, the magnitude of risk of IBD-related hospitalisation was even higher (OR 1.67, 95%CI 1.17–2.38), but no significant difference in IBD-related hospitalisation (OR 0.57, 95%CI 0.30–1.06) was observed in pts with UC. The difference in IBD-related ED visits between VDZ and anti-TNF pts was not significant in CD (OR 1.32, 95%CI 0.96–1.82) or UC (OR 0.72, 95%CI 0.40–1.29). However, the rates of outpatient visits were consistently higher in VDZ vs anti-TNF across CD (RR 1.82, 95%CI 1.69–1.96) and UC cohorts (RR 1.29, 95%CI 1.18–1.42). The results were similar in the sensitivity analyses when infusion-related visits were excluded.

Conclusion: In this real-world setting, VDZ treatment was shown to be associated with higher all-cause hospitalisations and outpatient services compared to anti-TNF for pts with IBD. A higher risk of IBD-related hospitalisation associated with VDZ use was observed in CD but not UC pts. Outpatient visit rates were consistently higher for VDZ users, regardless of taking into account the infusion-related visits for biologics. These results should be interpreted with caution as disease activity was not fully accounted for in this claims data analysis.

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X. Song: Employee: Truven Health Analytics, an IBM Company, Cambridge, MA, USA and received payment from AbbVie to assist with the analyses of this study.
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P0389 SAFETY OF ANTI-TNF TREATMENT IN ELDERLY PATIENTS WITH INFLAMMATORY BOWEL DISEASE


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Introduction: Due to population ageing and improved survival, the percentage of elderly patients with inflammatory bowel disease (IBD) is increasing. The safety
Disclosure of interest: All authors have declared no conflicts of interest.

References


Disclosure of Interest: F. Argüelles Arias, : Advisory boards and has received financial support to attend scientific meetings from Kerna Pharma. All other authors have declared no conflicts of interest.

P0931 CLINICAL RESPONSE TO VEDOLIZUMAB IN IBD PATIENTS IS ASSOCIATED WITH THE CONCOMITANT USE OF IMMUNOMODULATORS

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Introduction: The role of biologics in medical management of inflammatory bowel disease (IBD) has been established since anti-TNF agents invaded the market several years ago. Vedolizumab, an anti-integrin gut-selective molecule, is a more recent biologic treatment which has been approved for the management of both Crohn’s disease and ulcerative colitis. Its efficacy in inducing and maintaining remission was shown in GEMINI studies, although a good percentage of the trial participants had previously failed anti-TNFs. We conducted this study in order to describe outcomes in a real-life cohort of IBD patients who were treated with Vedolizumab, consisting both of previously anti-TNF exposed but also anti-TNF naive patients. Multivariate analysis searched for factors associated with response to treatment.

Aims & Methods: All patients with IBD who received at least three doses of Vedolizumab in UCLH since the drug was officially licensed in the UK were included in the study. Demographics, clinical and endoscopic response rates were recorded and analysis was conducted in the whole cohort and in the subgroups of Crohn’s and UC patients separately. Univariate analysis and logistic regression were conducted in order to identify important associations with clinical response.

Results: 59 patients with IBD were treated with vedolizumab from May 2015 to October 2016. 28 (47%) had Crohn’s disease and the majority (n = 43, 73%) had mainly colonic inflammation (12 colonic Crohn’s, 29 UC, 2 IBDU). Median time from diagnosis to Vedolizumab initiation was 8 years. 17 (29%) were anti-TNF naïve (all UC) and 28 (67%) had previously failed both Infliximab and Adalimumab. 36 (61%) were on a concomitant immunomodulator (IM), either methotrexate (MTX) (29%) or 6-mercaptopurine (6-MP) (7%). 16 (27%) patients had a clinical response to Vedolizumab based on a reduction of Harvey-Bradshaw index (HBI) from baseline ≥3 points for Crohn’s patients or a reduction of partial Mayo score ≥2 points for UC patients. The rates of response were similar in Crohn’s and UC patients while there was no difference in response according to gender, previous anti-TNF exposure, disease duration or location of inflammation. Patients on no concomitant IM were less likely to respond to Vedolizumab (Odds ratio 0.26, 95%CI 0.07-0.91, p = 0.036). 11(18.6%) patients experienced adverse events while treated with Vedolizumab, five of which related to active IBD. There were two minor allergic reactions and two mild infections.

Conclusion: Clinical response to Vedolizumab was observed in two-thirds of our IBD patients, similarly in Crohn’s disease and ulcerative colitis. Concomitant IM were the only factor which was importantly associated with a higher response rate. Overall there were no serious adverse events.

Disclosure of Interest: All authors have declared no conflicts of interest.

References


Disclosure of Interest: F. Argüelles Arias, : Advisory boards and has received financial support to attend scientific meetings from Kerna Pharma. All other authors have declared no conflicts of interest.
PO392 CORRELATION OF RELATIONSHIP BETWEEN INFliximab TROUGH AND ANTIBODY LEVELS WITH CLINICAL RESPONSE RATES AT COMPLETION OF INDUCTION THERAPY

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Introduction: Anti-TNFα therapies have helped improved response rates, reduced complication rates, and quality of life for patients with inflammatory bowel disease (IBD). However primary loss of response (LOR) is still a big concern. Therapeutic drug monitoring (TDM) potere of female gender (72%) and mean age was 59 years. The proportion of patients in clinical remission at week 8 was significantly higher in the budesonide group than in the placebo group (intention-to-treat (ITT) 79% vs 42%; p = 0.001. The difference in clinical remission at week 8 between mesalazine (63%) and placebo failed statistical significance (p = 0.099). The proportion of patients with histological remission at week 8 was higher with budesonide (68%) than with mesalazine (26%; p = 0.02) and placebo (21%; p = 0.008). The rate of adverse events did not differ among groups.

Conclusion: Oral budesonide 9mg once daily is highly effective and safe for induction of clinical and histological remission in lymphocytic colitis, while oral mesalazine 3g once daily was only numerically, but not statistically significantly better than placebo.

Disclosure of Interest: S. Miehlke: Prof. Miehlke receives lecture fees and travel costs. T. Naac: I am employee at Dr. Falk Pharma GmbH.

PC394 PREGNANCY OUTCOMES IN THE TOFACITINIB ULCERATIVE COLITIS OCTAVE STUDIES

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Introduction: A pregnant woman with ulcerative colitis (UC), compared with age-matched controls, is at higher risk of adverse outcomes including spontaneous abortion, preterm birth and low birth weight. Tofacitinib is an oral, small molecule Janus kinase inhibitor that is being investigated for UC. Tofacitinib has been shown to be foetocidal and teratogenic in both rats and rabbits at exposures 146 times and 13 times, respectively, the human dose of 5mg twice daily (BID). There is no adequate and well-controlled studies of tofacitinib in pregnant women.

Aims & Methods: We report the pregnancy outcomes from three randomised, placebo-controlled studies (OCTAVE Induction 1, NCT01465763; OCTAVE Induction 2, NCT01459951; OCTAVE Sustain, NCT01485874) and one ongoing open-label extension study (OCTAVE long-term study, NCT01470612) of tofacitinib monotherapy in patients (pts) with moderate to severe UC. Pregnancy outcomes following maternal or paternal exposure to tofacitinib or 5 mg BID were identified from Pfizer’s internal safety database up to 23 March, 2017, and categorised as: healthy newborn, medical termination, foetal death, congenital malformation, spontaneous abortion or pending/lost to follow-up. Trial protocols required use of highly effective contraception for females of childbearing potential, and study drug to be discontinued in any female pts who became pregnant.

Results: A total of 1139 unique pts (incl. placebo) enrolled in the UC OCTAVE trials, of whom 296 were females of childbearing age. There were a total of 25 pregnancies reported with exposure to tofacitinib. Of these, 11 were cases of maternal exposure, all during the 1st trimester, including: 2 (18.2%) spontaneous abortions (5 mg BID, n = 1; 10 mg BID, n = 1), 2 (18.2%) medical terminations (both 10 mg BID), 4 (36.4%) healthy newborns (all on 10 mg BID) and 3 (27%) being lost to follow up (all on 10 mg BID). Out of the 14 cases of paternal exposure, 11 (78.6%) were healthy newborns (5 mg BID, n = 2; 10 mg BID, n = 9 and 3 (21.4%) were pending/lost to follow-up (5 mg BID, n = 1; 10 mg BID, n = 2). Overall, there were no cases of foetal death or congenital malformation.
P0395 SAFETY AND EFFICACY OF GRANULOCYTE AND MONOCYTE ADSORPTIVE APERHESIS IN 363 PATIENTS WITH INFLAMMATORY BOWEL DISEASE WHO HAVE SPECIAL SITUATIONS: AN INTERIM ANALYSIS OF A POST-MARKETING SURVEILLANCE STUDY


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Introduction: People with Inflammatory Bowel Disease (IBD) commonly experience mental health issues (MHIs) such as anxiety and depression. MHIs reduce quality of life and are associated with poor medication adherence and worse disease course. However, psychological support is not routinely provided to people with IBD. There are scant prospective, systematically gathered data on MHIs in IBD, despite solid evidence of the value of psychological input for people with other chronic diseases.

Aims & Methods: The current study is investigating: the prevalence of MHIs in an IBD cohort; the acceptability and uptake of a psychological support and treatment; whether MHIs correlate with higher healthcare utilisation; and potential benefits of integrated psychological care to patients’ mental health, physical health, and/or healthcare utilisation. Potential participants were prospectively recruited from the IBD service of a large tertiary hospital in South Australia via post and in-person at scheduled/routine outpatient appointments. Data were collected at two time points – at baseline screening and at 12 month follow-up. Mental health, medicition adherence, and quality of life were measured by questionnaires: the Hospital Anxiety and Depression Scale (HADS), the Kessler 6 Scale of General Psychological Distress (K6), the Morisky Medication Adherence Scale (MMAS-8), and the Assessment of Quality of Life measure (AQoL-5D). Demographic and healthcare utilisation data were collected by electronic,
state-wide hospital records. Psychological support was offered where scores on HADS and/or K6 indicated likely need.

Results: 500 patients were approached during the 12-month screening phase; 50.6% were male, 70.8% had Crohn’s disease, mean age of 40 years, mean duration of disease 11 years, 43% in clinical remission, and 9.8% current smokers (Australia’s average 13.3%). Of these 500, 67% participated in psychological screening; 38% scored within the clinical range, and 17% accepted psychological support. Gender was a significant predictor of participation in psychological screening: women were 62% more likely to participate than men. Analgesics support. Gender was a significant predictor of participation in psychological screening, 38% scored within the clinical range, and 17% accepted psychological intervention. All of which demonstrates a widespread need for support in this cohort. Furthermore, preliminary data of patients reported clinical levels of distress (irrespective of their IBD activity) were more likely to participate in psychological screening, and in general the patients were more likely to participate than men. Analgesics support. Gender was a significant predictor of participation in psychological screening, 38% scored within the clinical range, and 17% accepted psychological intervention. All of which demonstrates a widespread need for support in this cohort. Furthermore, preliminary data of patients reported clinical levels of distress (irrespective of their IBD activity)

Table1: Safety profile of GMA in each group

<table>
<thead>
<tr>
<th>Variable</th>
<th>Screening Mean</th>
<th>SD</th>
<th>Follow-Up Mean</th>
<th>SD</th>
<th>t value</th>
<th>p value</th>
<th>Eta²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anxiety</td>
<td>12</td>
<td>3.6</td>
<td>9</td>
<td>1.1</td>
<td>4.87</td>
<td>.000***</td>
<td>0.56</td>
</tr>
<tr>
<td>Depression</td>
<td>8.8</td>
<td>3.9</td>
<td>6.4</td>
<td>5.0</td>
<td>4.34</td>
<td>.000***</td>
<td>0.30</td>
</tr>
<tr>
<td>Distress</td>
<td>18.2</td>
<td>4.8</td>
<td>13.9</td>
<td>5.1</td>
<td>7.47</td>
<td>.000***</td>
<td>0.56</td>
</tr>
<tr>
<td>Mental QoL</td>
<td>51</td>
<td>15.9</td>
<td>60.6</td>
<td>18.5</td>
<td>-4.91</td>
<td>.000***</td>
<td>0.39</td>
</tr>
<tr>
<td>Physical QoL</td>
<td>72</td>
<td>14.9</td>
<td>75.0</td>
<td>17.7</td>
<td>-1.50</td>
<td>.142</td>
<td>0.06</td>
</tr>
<tr>
<td>Total QoL</td>
<td>57</td>
<td>14.6</td>
<td>65.1</td>
<td>17.4</td>
<td>-4.39</td>
<td>.000***</td>
<td>0.34</td>
</tr>
<tr>
<td>Medication adherence</td>
<td>5.1</td>
<td>2.0</td>
<td>7.7</td>
<td>2.2</td>
<td>-2.03</td>
<td>.049**</td>
<td>0.09</td>
</tr>
</tbody>
</table>

*p < .05, **p < .01, ***p < .001

Conclusion: Psychological issues are prevalent in patients with IBD and associated with a decreased quality of life. Psychological support is more likely to participate in psychological screening, and in general the screening approach was widely accepted. In addition, high proportions of patients reported clinical levels of distress (irrespective of their IBD activity) and went on to accept psychological intervention. All of which demonstrates a widespread need for support in this cohort. Furthermore, preliminary data of treatment outcomes are promising. At study completion we will be better able to clarify the extent to which patients with IBD benefit from this new integrated approach.

Aims & Methods: To evaluate long-term efficacy, safety, and immunogenicity in patients continuously treated with either GP2017 or reference adalimumab from initial randomization to Week 51. Eligible patients with moderate-to-severe chronic plaque psoriasis were randomized to receive an initial dose of 80 mg subcutaneous GP 2017 or reference adalimumab, followed by 40 mg every other week, starting one week after the initial dose, up to Week 17. At Week 17, patients with ≥50% improvement in Psoriasis Area and Severity Index (PASI 50) at Week 16 were re-randomized in a 2:1 ratio to either remain on their initial treatment or undergo a sequence of three treatment switches between GP 2017 and reference adalimumab until Week 35. Thereafter, patients were returned to their originally randomized treatment up to Week 51.

Results: From randomization to Week 51, 168 and 171 patients received continuous treatment with GP 2017 or reference adalimumab, respectively. In the per-protocol analysis set, PASI 75 response rates for continual GP2017/reference adalimumab at Weeks 17 and 51 were 75.2%/67.8% and 65.5%/79.6% respectively. Investigator’s global assessment (IGA) response rates (IGA score of 0 [clear] or 1 [almost clear] and ≥2 point improvement from baseline) were also similar between the continual GP2017/reference adalimumab groups, increasing over time and remaining stable from Week 17 (60.0%/53.9%) to Week 51 (59.8%/55.1%). There were no clinically relevant differences between the continual GP2017/reference adalimumab groups in the frequency of adverse events (AEs) (61.3%/64.9%), treatment-related AEs (17.9%/17.8%), serious AEs (3.0%/3.8%), or AEs leading to discontinuation of study drug (7.9%/7.8%) respectively. Investigators’ assessment of AEs, nasopharyngitis most frequently reported by 8.9%/10.5% of patients treated with continual GP2017/reference adalimumab. Between Weeks 1 and 51, binding antidrug antibodies were detected in 38.8%/45.3% of patients treated with continual GP2017/reference adalimumab, 88.7%/84.7% of which were neutralizing.

Conclusion: Efficacy was similar and sustained in patients with psoriasis continuously treated with GP 2017 or reference adalimumab for up to 51 weeks. Safety profiles and immunogenicity were generally similar in both groups. Clinical data add to the totality of evidence suggesting GP 2017 could be used as a biosimilar for the treatment of the same indications for which reference adalimumab is approved, including inflammatory bowel disease.


PO398 PREDICTIVE FACTORS OF RESPONSE TO GRANULOCYTE MONOCYTE APhERESIS IN INFLAMMATORY BOWEl DISEASE

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Introduction: Granulocyte-monocyte apheresis (GMA) can be employed for the treatment of inflammatory bowel disease (IBD), especially for ulcerative colitis (UC). The usual treatment schedule is a weekly session for 5 weeks processing 1800 ml in 60 minutes. It has been described that different factors of the disease and the technique can improve the response to this treatment.
Aims & Methods: We performed a retrospective study of all patients treated with GMA (Adacolumn) in 3 IBD Units in Spain. The clinical and analytical data were assessed before and 1 month after the end of the GMA. The Ethics Committee of Euskadi approved the study protocol. The aim of our study was to evaluate the presence of clinical, analytical of technique-related factors associated to a better response to GMA.

Results: A total of 105 patients were included [51 female (49%), age 35.7 (SD 16.5)]. Ninety-three had UC (50% extensive, 45% left-sided), 10 Crohn’s disease (90% ileocolonic) and 2 IBD-U. Mayo score at baseline was 3.5 (SD 4.6) and Harvey – Bradshaw was 10.1 (SD 3.8). The Mayo endoscopic subscore was 1 (16%), 2 (56%) or 3 (27%). All almost patients (97%) have been previously treated with steroids and 42% were exposed to biologics. At baseline, 85% were on steroids, 38% thiopurinels and 18% biologics. None of the previous or concurrent treatments were associated with a better response to GMA. Fifty-five subjects received weekly sessions for 5 weeks processing 1800 ml/session in 60 minutes. Forty-five patients received an intensive GMA regimen: biweekly sessions with a mean of 8 sessions (SD 2.6), processing 3880 ml/session (SD 1729) and lasting 15 minutes (SD 24). The intensive group showed a slightly higher response rate to GMA as compared with those in the standard regimen (response rate 67% vs 55%, p = 0.28). Those subjects treated with > 5 sessions showed higher remission (24% vs 13%) and response rates (47% vs 24%) as compared to < 5 sessions (p = 0.004). A mean duration of > 60 min/session also showed better results in terms of remission (22% vs 16%) and response (45% vs 27%) when compared to < 60 min/session (p = 0.04). There was also a trend towards higher remission rates in those with higher processed blood volume. Thirty-nine percent were able to wean off steroids completely one month after GMA. We observed a decrease in the mean platelet volume and the platelet to lymphocyte ratio after GMA in those cases who did not respond. Contrary to its clinical efficacy in this clinical practice study. Increasing the number of sessions or its length were associated with a better response to GMA. The mean platelet volume and the platelet to lymphocyte ratio could help to predict the response.

Disclosure of Interest: All authors have declared no conflicts of interest.

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sion of ulcerative colitis by intense granulocyte and monocyte adsorptive
Yoshimura N, Tamadi T, Kawaguchi T, Sako M, Yoshimoto H, Yamaka T, et al. Processed blood volume impacts clinical efficacy in patients with ulcerative

PO399 ANDecaliximab (anti-MMP9) INDUCTION THERAPY FOR UCERATIVE COLITIS: A DOUBLE-BLIND, RANDOMIZED, PLACEBO-CONTROLLED PHASE 2 STUDY
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Introduction: Ulcerative colitis (UC) and Crohn’s disease (CD) are chronic, inflammatory bowel disorders that affect the gastrointestinal tract. While the pathogenesis of UC is well understood, the disease is characterized by chronic inflammation, mucosal injury, and recurrent ulcerative episodes. While MCQ399 (an anti-MMP9 antibody) has shown promise in preclinical models, the safety and efficacy of MCQ399 as an induction therapy in active disease has not been evaluated in a randomized clinical trial. The aim of this study was to evaluate the safety and efficacy of MCQ399 as an induction therapy for moderately to severely active UC and CD.

Methods: A total of 100 patients were randomized to receive subcutaneous injections of placebo, 150 mg andecaliximab every 2 weeks (Q2W), or 150 mg andecaliximab weekly (QW). The primary outcome was change in the Clinical Colitis Activity Index (CDAI) compared to baseline at week 8. Secondary outcomes included changes in the Disease Activity Index for Crohn’s disease (DAI), Mayo Clinic Score (MCS), and Harvey-Bradshaw Index (HBI). Safety was assessed by monitoring adverse events (AEs) and laboratory parameters.

Results: A total of 100 patients were enrolled from 13 countries. No concerning baseline imbalances occurred between the treatment groups. Overall, 17.6% of subjects had evidence of fistula at screening, mean (SD) disease duration was 12 (9.5) years, 84.5% of subjects had previous exposure to TNF-alpha antagonist and 44.4% of subjects were taking oral corticosteroids at baseline. The frequency of adverse events (AEs) was similar in the andecaliximab Q2W, andecaliximab QW and placebo groups: 53.7%, 58.9% and 60%, respectively. Common AEs included anemia, abdominal pain and nausea. Three AEs led to discontinuation in the andecaliximab Q2W group compared to one each in the andecaliximab Q2W and placebo groups. Two serious AEs occurred in the andecaliximab QW group (anemia and angiina pectoris) compared to one in placebo. Frequency of arthralgia and musculoskeletal pain was similar between andecaliximab and placebo groups.

Conclusion: SC 150 mg andecaliximab was well tolerated; however, neither dosing regimen demonstrated a treatment effect in subjects with UC.

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Introduction: Elevated levels of matrix-metalloproteinase-9 (MMP-9) and its degradation products are detected in patients with active Crohn's disease (CD). Selective inhibition of MMP-9 reduced fibrosis in a murine model of intestinal fibrosis, suggesting that MMP-9 may contribute to intestinal complications in CD. Accordingly, MMP-9 has been proposed as a therapeutic target for CD. Andecaliximab (GS-5745) is a monoclonal antibody that selectively binds and inhibits MMP-9. It was found that to be safe in a phase 1 dose-ranging study in UC subjects, where it showed clinical response and remission compared to placebo. The aim of this phase 2 study was to evaluate the safety and efficacy of andecaliximab as an induction therapy for moderately to severely active UC and CD.

Aims & Methods: This was a double-blind, randomized, placebo-controlled 8-week induction study in adult CD subjects with moderate to severe disease activity (defined as: CDAI total score ≥220, 450; weighted PRO2 score ≥11 [standard CDAI weightings: abdominal pain 0–3 x7 plus mean number of daily stools x2] and SES-CD total score ≥6 [or ≥4 score if disease limited to ileum and/or right colon or ulcer presence and size score ≥2]). Subjects were required to have an inadequate response, or loss of response or intolerance to at least 1 of the following treatments in the last 5 years: corticosteroids, immunomodulators, TNF-alpha antagonist or vedolizumab. Subjects were randomized 1:2:2:2 to receive subcutaneous (SC) injections of: placebo, 150 mg andecaliximab every 2 weeks (Q2W), 150 mg andecaliximab weekly (QW) or 300 mg andecaliximab QW. Common AEs included anemia, abdominal pain and nausea. Three AEs led to discontinuation (PRO2 score of <8 at week 8) and clinical response (SES-CD score ≤50% from baseline at week 8).

Results: A total of 187 subjects were enrolled from 13 countries. No concerning baseline imbalances occurred between the treatment groups, overall: 17.6% of subjects had evidence of fistula at screening, mean (SD) disease duration was 12 (9.5) years, 84.5% of subjects had previous exposure to TNF-alpha antagonist and 44.4% of subjects were taking oral corticosteroids at baseline. The baseline and week 8. The primary outcome was EBS clinical remission, defined as an Endoscopic subscore of ≤1, rectal Bleeding subscore of 0, and ≥1 point decrease in Stool frequency from baseline to achieve a subscore of 0 or 1.

Results: A total of 165 subjects from 23 countries were enrolled. The percentage (confidence intervals) of subjects achieving EBS clinical remission was similar between subjects treated with andecaliximab Q2W and placebo: 7.4% (2.1-17.9%), 1.8% (0-9.6%) and 7.3% (2-17.6%), respectively. No concerning imbalances occurred for all endpoints. The results show a trend towards higher remission rates in those with higher processed blood volume. Thirty-nine percent were able to wean off steroids completely one month after GMA. We observed a decrease in the mean platelet volume and the platelet to lymphocyte ratio after GMA in those cases who did not respond. Contrary to its clinical efficacy in this clinical practice study. Increasing the number of sessions or its length were associated with a better response to GMA. The mean platelet volume and the platelet to lymphocyte ratio could help to predict the response.
percentage of subjects achieving clinical response/remission and endoscopic response was similar between treatment groups (Table 1).

Conclusion: SC andentuximab was well tolerated, however, none of the treatment regimens demonstrated a treatment effect in subjects with CD.


P0401 TUBERCULIN SKIN TEST CONVERSION RATE IN INFECTIOUS BOWEL DISEASE PATIENTS RECEIVING ANTI-TNF ALPHA AGENTS

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Aims & Methods: Few data exist regarding the kinetics of this test during therapy. Therefore, we investigated the conversion rate of PPD-TST in IBD patients under anti-TNFalphalapha therapy. Anti-TNFalapha-treated IBD patients followed up in our centre with a baseline PPD-TST underwent a second one during therapy. Those with a positive PPD-TST either at baseline or during follow up in our centre with a baseline PPD-TST underwent a second one during therapy. Therefore, our study investigated the conversion rate of PPD-TST in IBD patients under anti-TNFalpha therapy. There was no case of active tuberculosis during the study. All patients treated. Therefore, the kinetic of PPD-TST in IBD patients under anti-TNFalphalapha treatment should be monitored.

Disclosure of Interest: B. Ungar: This study was supported in part by a grant from "Abbvie". In addition, BU received consultation fees from "Abbvie" and from "Janssen". U. Kopylov: Speaker fees - abbbvie Research support, speaker and advisory fees Takeda. All other authors have declared no conflicts of interest.

P0402 THE TEMPORAL EVOLUTION OF IMMUNOGENICITY IN INFECTIOUS BOWEL DISEASE PATIENTS TREATED WITH ADAHLUMAB

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Aims & Methods: Few data exist regarding the kinetics of this test during therapy. Therefore, we investigated the conversion rate of PPD-TST in IBD patients under anti-TNFalphalapha therapy. Anti-TNFalapha-treated IBD patients followed up in our centre with a baseline PPD-TST underwent a second one during therapy. Those with a positive PPD-TST either at baseline or during follow up in our centre with a baseline PPD-TST underwent a second one during therapy. Therefore, our study investigated the conversion rate of PPD-TST in IBD patients under anti-TNFalpha therapy. There was no case of active tuberculosis during the study. All patients treated. Therefore, the kinetic of PPD-TST in IBD patients under anti-TNFalphalapha treatment should be monitored.

Disclosure of Interest: B. Ungar: This study was supported in part by a grant from "Abbvie". In addition, BU received consultation fees from "Abbvie" and from "Janssen". U. Kopylov: Speaker fees - abbbvie Research support, speaker and advisory fees Takeda. All other authors have declared no conflicts of interest.

P0403 GOLIMUMAB IN ULCERATIVE COLITIS. REAL-LIFE PROSPECTIVE COHORT STUDY FROM A SINGLE REFERRAL CENTRE OF MIDDLE ITALY

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Introduction: Golimumab (GLB) has been the last anti-TNF agent authorized for the treatment of Ulcerative Colitis (UC). Results from registratory trial (PURSUIT) documented a clinical response in 51% of patients after 6 weeks

The frequency of adverse events (AEs) was similar between the treatment groups: placebo (67.9%), 150 mg Q2W (60.4%), 150 mg QW (62.3%), 300 mg QW (69.8%). Common AEs included abdominal pain, nausea, fatigue, anemia and pyrexia. One AE led to study discontinuation in the placebo group (3.6%) compared to 2 in the 150 mg QW group (3.8%) and 4 in the 300 mg QW group (7.5%). Three serious AEs occurred in the placebo group (10.7%) compared to 1 in the 150 mg QW group (1.9%), 6 in the 150 mg QW group (11.3%) and 8 in the 300 mg QW group (15.1%). Frequency of arthralgia and musculoskeletal pain was similar or lower in andentuximab groups compared to placebo.

were found between naïve and non-naïve patients. No significant adverse events (38%), one of them (7%) resulted in complete steroid-free remission. Among the patients (23%) had already received one anti-TNF in the past. Clinical response was computed at baseline and every 2 weeks for the first 6 weeks of therapy, then every 4 weeks throughout the maintenance period. Follow-up is still ongoing. Primary end point has been the clinical response at the end of the induction phase (intended as the reduction of Partial Mayo score >30% and >3 points vs baseline) and in the maintenance period, the secondary end point being the steroid-free clinical remission (Partial Mayo score <2 with all subscores <1) at the end of the induction phase and throughout the maintenance phase. Complete follow-up is available for all patients at week 30, with 4 patients reaching the week 54 of monitoring.

Results: At the time of GLB starting, localization of the disease according to Montreal classification was left-sided colitis (E2) in 70%, pancolitis (E3) in 23% and proctitis (E1) in 7% of patients. Ten patients (77%) were anti-TNF naïve, 3 patients (23%) had already received one anti-TNF in the past. Clinical response was obtained in 6/13 (46%) at week 6 and in 2 further patients at week 10, for a total of 8/15 (53%). Three patients failed in complete clinical steroid-free remission after 6 weeks. At week 30, 5 patients still showed a clinical response (38%), one of them (7%) resulted in complete steroid-free remission. Among the 4 patients reaching week 54, 2 experienced a flare of disease whereas 2 were still in remission. One patient is in remission at week 42, potentially accounting for a total of 3/13 patients in remission after one year (23%). No differences were found between naïve and naïve-naïve patients. No significant adverse events were reported in the study period.

Comment: Our results to suggest that Golimumab, as compared to registrary trials, is able to induce a better initial clinical response but shows a higher secondary loss of response in the long term. Whether this really reflects a lower efficacy of GLB or could depend on the unavailability of dose optimisation in daily practice needs to be evaluated.

Disclosure of Interest: All authors have declared no conflicts of interest.

With originator infliximab or standard therapy: A European postmarketing ulcerative colitis study, a European postmarketing registry for adults with ulcerative colitis treated with originator infliximab or standard therapy

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3Merck & Co., Inc., the sponsor of the study. H.A. Flynn: HAF. is an employee of Merck & Co., Inc., the sponsor of the study. J. Lindsay: J.L. has served as a consultant, advisory board member, or speaker for Merck & Co., Inc.
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7G. Philip: G.P. is an employee of Merck & Co., Inc., the sponsor of the study.
8W. Reinisch: W.R. has served as a speaker and advisory board member for Merck & Co., Inc.

Introduction: Several oral mesalazine utilise pH-dependent release coating to optimise topical delivery of the medication. Little data exist on the effects of dietary factors on intestinal pH and transit times in patients with UC to predict likely efficacy-based delivery profiles. No studies have accounted for acute variations in dietary fibre intake, which might affect regional transit and pH profiles.

Methods: This study aimed to (1) assess intraluminal pH and transit after acute changes in fibre intake in quiescent UC patients; and (2) deduce delivery of topically-acting drugs using published pharmacokinetic (PK) data. In this randomised, double-blind study, UC patients with UC in clinical remission (partial Mayo Score ≤1 + faecal calprotectin <150 μg/g) without recent antibiotic (including sulfasalazine), probiotic or fibre use were recruited. After a 7-day run-in, subjects were supplied with study meals containing high (13 g oligosaccharides and resistant starch) (HF) or low (<1 g) fermentable fibre (LF) over a 12-h period prior to the ingestion of a pH-motility capsule (Smart Pill). Telemetric recordings were made for 5 days or until the capsule had been excreted. After a ≥3-day washout period, they crossed-over to the other dietary arm and pH-motility test. Small and large intestinal pH profiles were defined as the length in time (h) of different intraluminal pH ranges – pH <5, ≥5 to <7.7 and ≥7.7 and compared between diets. Using published PK of pH-dependent coated mesalazine preparations, the patterns of dissolution in UC patients were estimated.

Results: 41 patients (aged 24–72; 9 males – 5 extensive, 5 distal and 5 proctitis), acute HF intake significantly increased median (IQR) time for colonic pH <6 ([HF]: 4.5 (2.4–10.2) vs LF: 0.9 (0.2–3.1) h; p =0.004, Wilcoxon), tended to increase colonic pH ≥6 to <7 ([HF]: 7.5 (6.3–13.5) vs LF: 7.1(3.4–15.2) h) and had no impact on colonic pH ≥7 ([HF]: 1.6 (0.0–3.3) vs LF: 1.8 (0.8–2.1) h; p =0.34). Table 1 summarises hypothetical dissolution profiles for pH-coated mesalazine in patients with UC. Considerable variations across release diseases were evident, but, despite alterations in pH and transit, the patterns were not affected by diet for Eudragit L alone or with slow release mechanisms. Only minor differences were found for Eudragit S and MMX.

Conclusion: Current delivery mechanisms for mesalazine lead to a proportion of quiescent UC patients having incomplete release and suboptimal regional
delivery. An acute high fermentable fibre intake delays drug dissolution in the colon, but had little influence over total release. These findings have implications for optimising drug selection in maintenance of remission in UC.

Disclosure of Interest: C.K. Yao: CK Yao received research support to conduct the study from Ferring Pharmaceuticals. The Department of Gastroenterology at Monash University benefits financially from the sales of a digital app and booklets on the low FODMAP diet.

R.E. Burgell: Rebecca has received consultancy fees from Allergan. The Department of Gastroenterology at Monash University benefits financially from the sales of a digital app and booklets on the low FODMAP diet.

J.S. Barrett: The Department of Gastroenterology at Monash University benefits financially from the sales of a digital app and booklets on the low FODMAP diet.

J.G. Muir: The Department of Gastroenterology at Monash University benefits financially from the sales of a digital app and booklets on the low FODMAP diet.

P.R. Gibson: PG has served as consultant or advisory member for AbbVie, Ferring, Janssen, Merck, Allergan, Pfizer, Celgene & Takeda; research support from AbbVie & Janssen; speaking honoraria for his institution from AbbVie, Janssen, Ferring, Mylan, Takeda, and Pfizer. All other authors have declared no conflicts of interest.

Table 1: Median golimumab trough concentrations and AUCs at week 2 and 6

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Endoscopic responders</th>
<th>Non-endoscopic responders</th>
</tr>
</thead>
<tbody>
<tr>
<td>AUC (mg/L/day), week 2</td>
<td>13.4 (10.2–17.0)</td>
<td>9.4 (8.0–16.9)</td>
</tr>
<tr>
<td>AUC (mg/L/day), week 6</td>
<td>33.3 (29.0–47.6)</td>
<td>212 (206–417.0)</td>
</tr>
<tr>
<td>Serum trough concentration (mg/L), week 2</td>
<td>9.1 (6.1–10.0)</td>
<td>6.1 (5.2–9.8)</td>
</tr>
<tr>
<td>Serum trough concentration (mg/L), week 6</td>
<td>3.8 (2.6–6.0)</td>
<td>2.4 (1.1–3.8)</td>
</tr>
</tbody>
</table>

Conclusions: Serum trough concentrations of GLM and AUCs at week 2 and 6 were higher in endoscopic responders compared to patients without an endoscopic response. A significant correlation was found between GLM trough concentrations and AUC. A GLM trough level ≥3.5 mg/L at week 6 is associated with improved endoscopic outcomes.

Disclosure of Interest: S. Berends: Has received lecture fees from Johnson and Johnson, and Merck Sharp & Dohme.

A. Strik: Has received lecture fees from Biogen, Johnson and Johnson, Merck Sharp & Dohme, Mundipharma, Takeda, and Tillotts.

R. Mathiot: Has received consulting fees from MSD and research grants from Bayer, UCB Pharma, Shire and Roche.

G.R. D’Haens: Has received speaker fees from AbbVie, Ferring, Johnson and Johnson, Merck Sharp & Dohme, Mundipharma, Norgine, Pfizer, Shire, Millenium/Takeda, Tillotts and Vifor.

M. Lowenberg: Has received speaking fees from AbbVie, Covidien, Dr. Falk, Ferrin Pharmaceuticals, Merck Sharp & Dohme, Receptos, Takeda, Tillotts and Tramedico. He has received research grants from AbbVie, Merck Sharp & Dohme, Achmea healthcare and ZenMWW.

References:

P0406 HIGHER EXPOSURE TO GOLIMUMAB IS ASSOCIATED WITH ENDOSCOPIC RESPONSE IN PATIENTS WITH ULCERATIVE COLITIS: RESULTS FROM THE GO-KINETIC TRIAL

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Introduction: Golimumab (GLM) is a subcutaneously administered anti-tumor necrosis factor (anti-TNF) antibody that is approved for the treatment of moderate to severe ulcerative colitis (UC). We investigated the association between systemic exposure (area under the curve (AUC)) of GLM during induction therapy and endoscopic response in moderate-severe UC.

Aims & Methods: In this prospective observational trial, patients with moderate to severe UC (Mayo endoscopy score ≥2) received induction treatment with GLM 200 mg SQ at week 0 and 100 mg (at week 2) followed by 50 or 100 mg at week 6, in patients with a body weight of less or more than 80 kg, respectively. Serum GLM concentrations were measured at day 0, 4, 7, 14, 18, 28, 42 and 56, as well as anti-GLM antibody levels, C-reactive protein (CRP) and albumin serum concentrations. Serum GLM concentrations were measured with an enzyme-linked immunoassay and anti-GLM antibody levels were measured with a drug-sensitive antigen binding test, both developed by Sanquin laboratories. Endoscopic response was defined as ≥1 point reduction in endoscopic Mayo score at week 8-10 compared to baseline. AUCs were calculated using nonlinear mixed effect modelling (NONMEM®) and were compared using the non-parametric Mann-Whitney U test. Correlation analysis was performed using Pearson’s correlation coefficient. A receiver-operating characteristic (ROC) curve reported the predictive performance of GLM serum trough levels at week 2 and 6 for endoscopic response.

Results: A total of 20 patients were enrolled of which 19 patients underwent an endoscopy at baseline and 8–10 weeks after start of treatment. Median age (interquartile range) was 46 years [36–57], median baseline CRP serum concentration was 4.5 mg/L [1.1–13.7] and median baseline albumin serum concentration was 44 g/L [40–45]. None of the patients developed antibodies against GLM during induction treatment. After the induction phase, 12 out of 19 patients (63%) achieved an endoscopic response. Median AUC at week 2 and 6 was higher in endoscopic responders compared to non-responders. Median GLM trough concentrations at week 2 and 6 were higher in endoscopic responders compared to non-responders (Table 1). Correlations between GLM trough concentrations and AUCs at week 2 (Pearson correlation coefficient: 0.86, P < 0.001) and week 6 (Pearson correlation coefficient: 0.81, P < 0.001) were statistically significant. Despite a low area under the ROC-curve (AUCROC), a GLM trough concentration ≥3.3 mg/L at week 2 (AUROC: 0.75, 95% CI: 0.526–0.974, sensitivity: 67%, specificity: 71%) was associated with endoscopic response after the induction phase.

Conclusion: Serum trough concentrations of GLM and AUCs at week 2 and 6 were higher in endoscopic responders compared to patients without an endoscopic response. A significant correlation was found between GLM trough concentrations and AUC. A GLM trough level ≥3.5 mg/L at week 6 is associated with improved endoscopic outcomes.

Disclosure of Interest: S. Berends: Has received lecture fees from Johnson and Johnson, and Merck Sharp & Dohme.

A. Strik: Has received lecture fees from Biogen, Johnson and Johnson, Merck Sharp & Dohme, Mundipharma, Takeda, and Tillotts.

R. Mathiot: Has received consulting fees from MSD and research grants from Bayer, UCB Pharma, Shire and Roche.

G.R. D’Haens: Has received speaker fees from AbbVie, Ferring, Johnson and Johnson, Merck Sharp & Dohme, Mundipharma, Norgine, Pfizer, Shire, Millenium/Takeda, Tillotts and Vifor.

M. Lowenberg: Has received speaking fees from AbbVie, Covidien, Dr. Falk, Ferrin Pharmaceuticals, Merck Sharp & Dohme, Receptos, Takeda, Tillotts and Tramedico. He has received research grants from AbbVie, Merck Sharp & Dohme, Achmea healthcare and ZenMWW.

References:
Hypothetical I/II were global trials of the efficacy and safety of bezlotoxumab (bezlo: a human anti-C. difficile toxin B) in patients with CDI who were at risk for recurrence (rCDI) and frequently experience severe and recurrent episodes. MODIFY I/II were global trials of the efficacy and safety of bezlotoxumab in patients with primary or recurrent CDI given antibacterial drug treatment for CDI. Participants with IBD and CDI enrolled in the MODIFY trials were younger, more likely to be diagnosed with CDI as an outpatient, to be immunocompromised, and to have a higher rate of mucosal healing vs adalimumab in TNFi-naive patients. A higher proportion of participants with rCDI in the no bezlo group compared with the bezlo group and there was a higher proportion of participants with rCDI in the no bezlo group compared with the bezlo group. In IBD patients who received bezlo occurred after week 4 (3 of 4). The efficacy of bezlo in preventing rCDI may extend to patients with IBD, but additional data are needed due to the limited cohort size.

Table 1: Hypothetical dissolution profiles UC patients (n = 15)

<table>
<thead>
<tr>
<th>Dissolution characteristics</th>
<th>Eudragit L</th>
<th>Eudragit L with slow release</th>
<th>Eudragit S</th>
<th>Multi-matrix (MMX)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypothetical complete dissolution</td>
<td>pH ≥ 6 for 1 h</td>
<td>pH ≥ 6 for 4–5 h</td>
<td>pH ≥ 7 for 2–4 h</td>
<td>pH ≥ 7 for 6 h</td>
</tr>
<tr>
<td>Complete in small intestine</td>
<td>67%</td>
<td>100%</td>
<td>25%</td>
<td>19%</td>
</tr>
<tr>
<td>Complete dissolution</td>
<td>100%</td>
<td>100%</td>
<td>97%</td>
<td>80%</td>
</tr>
</tbody>
</table>

References

Disclosure of Interest
C. Kelly: travel support and fees for serving on advisory boards from Seres Therapeutics, Summit Pharmaceuticals, and Synthetic Biologics, lecture fees from Seres Therapeutics, and grant support from Institut Mérieux, ntera Health, and Merck
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K. Fahrbuch: Employee of Evidera, who provide consulting and research services to pharmaceutical and related organisations. In salaried positions, work with a variety of companies, and are precluded from receiving payment or honoraria directly for services rendered
K. Eves: an employee of Merck Sharp & Dohme Corp., who may own stock and/or hold stock options in the Company
M. Wilcox: consult/grant/lect fees: Alere, Abbott, Actelion, Astellas, Cerexa, Cubist, Optimer, Sanofi Pasteur, Summit, bio-Mérieux, Da Volterra, Qiagen, AstraZeneca, Pfizer, Durata Therap, Merck, Seres Therap, Valneva, Nabrива Theria, Roche, Medicines Company
C. Kelly: travel support and fees for serving on advisory boards from Seres Therapeutics, Summit Pharmaceuticals, and Synthetic Biologics, lecture fees from Seres Therapeutics, and grant support from Institut Mérieux, ntera Health, and Merck
A. Manuachiri: Employee and shareholder of Pfizer Ltd.
C. Kayhan: Employee and shareholder of Pfizer Inc.
C. Kelly: travel support and fees for serving on advisory boards from Seres Therapeutics, Summit Pharmaceuticals, and Synthetic Biologics, lecture fees from Seres Therapeutics, and grant support from Institut Mérieux, ntera Health, and Merck
M. Wilcox: consult/grant/lect fees: Alere, Abbott, Actelion, Astellas, Cerexa, Cubist, Optimer, Sanofi Pasteur, Summit, bio-Mérieux, Da Volterra, Qiagen, Astra Zeneca, Pfizer, Durata Therap, Merck, Seres Therap, Valneva, Nabriva Theria, Roche, Medicines Company
K. Eves: an employee of Merck Sharp & Dohme Corp., who may own stock and/or hold stock options in the Company
D. Mary Beth: MB Dorr - an employee of Merck Sharp & Dohme Corp., who may own stock and/or hold stock options in the Company
J.C. Cappelleri: Employee and shareholder of Pfizer Inc.
Aims & Methods: We analyzed the success of fecal microbiota transfer (FMT) via encapsulated microbial or via endoscopic jejunal application to 14 patients. Stool samples for FMT preparation derived from three unrelated healthy donors. Patients were assigned to receive 200 mg FIL or placebo. One patient experienced relapse of IBD, this patient received IFX-biosimilar. 2 patients experienced a SAE, none were related to the study drug.

Conclusion: This is the first double blind randomized clinical trial that compares encapsulated vs. endoscopic jejunal application to 14 patients. The preliminary results show that switching from IFX-biological to IFX-biosimilar is feasible and safe. Disclosure of Interest: All authors have declared no conflicts of interest.

References

Disclosure of Interest: All authors have declared no conflicts of interest.
Corr = 0.43, p < 0.001; BL and W10 respectively) (CGHAS v CSES-CD: Corr = 0.80, p < 0.001; Corr = 0.77, p < 0.001; BL and W10 respectively) (aCGHAS v uCSES-CD: Corr = 0.77, p < 0.001; Corr = 0.70, p < 0.001; BL and W10 respectively).

**Conclusion:** Improvements in endoscopic severity induced by filgotinib are paralleled by reductions of histologic scores. In line with previous findings from anti-TNF therapies\(^5\) colonic mucosa is more prone to improve than ileal disease. Spontaneous reductions of histologic activity under placebo were not observed.

**Disclosure of Interest:** G.R. D'Haens: Abbvie, Abylnx, Biogen, BMS, BoehringerIng., Celgene, Celltrion, Ferring, Galapagos, Gilead, GSK, Hospira, Immun, J&J, Lycera, Millen, Takeda, MitsubishiPh., MSD, Mundiphih., NovoNordisk, Pfizer, Protagonist, Robert, Sals, Sandoz, Shire, Teva, Tigenix, Tollst, a.o.

G. De Hertogh: has received fees for central pathology review from Genentech,

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W. Reinisch: Abbv, Agen, Astellas, Astra Zeneca, Bicon, Biogen IDEC, Boehringer-Ing., BMS, Celgene, Celltrion, Covance, Galapagos, Genentech, Gilead, Grünenthal, JNJ, LipidTher., MedImmune, MSD, Novartis, Otsuka, Pfizer, P&G, Robert, Sandoz, SP, Takeda, Tigenix, UCB, a.o.

A. Van der Aa: employee of Galapagos NV

J. Zhang: employee of Gilead Sciences Inc

C. Tasket: employee of Galapagos NV

C. Yun: employee of Gilead Sciences Inc

A. Serone: employee of Gilead Sciences Inc


S. Vermeire: research funding from Abbv, Galapagos, MSD, and Takeda; speaker fees from Abbv and consultancy fees from Abbv, MSD, Takeda, Ferring, Genentech, Roche, Shire, Pfizer, Galapagos, Mundipharma, Hospira, Celgene, Second Genome, and Janssen.

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**P0413 RESPONSE AND REMISSION AFTER 16 WEEKS OF USTEKINUMAB- AN ALL PATIENTS ANALYSIS FROM THE UNITI CROHN’S STUDIES**

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**Introduction:** Ustekinumab (UST) has been shown to induce and maintain clinical response and remission in moderate to severe Crohn’s disease (CD) in 2

induction [(UNITI-1 (anti-TNF failures) and UNITI-2 (anti-TNF non-failures) and 1 maintenance (IM-UNITI)] randomized, placebo controlled Phase 3 trials. We evaluated the efficacy (response and remission) for all patients who received an intravenous (IV) induction dose of approximately 6 mg/kg, including responders (CDAI decrease ≥100) and non-responders, 8 weeks after the first UST maintenance dose of 90 mg subcutaneous (SC), i.e. 16 weeks from the IV induction dose.

**Aims & Methods:** Patients achieving clinical response 8 weeks after a single IV induction dose were randomized to SC placebo (PBO), UST 90 mg every 12 weeks (q12w) or every 8 weeks (q8w). UST patients not in clinical response 8 weeks after the IV induction dose were given UST 90 mg SC and if in clinical response 8 weeks later were continued on 90 mg SC q8w dosing. A total of 458 patients were exposed to an IV induction dose of 6 mg/kg (UNITI-1, N = 249 and in UNITI-2, N = 209) with a response rate at week 8 of 37.8% and 57.9% vs. PBO response rate of 20.2% and 32.1% respectively. The remission rate at week 8 in UNITI-1 and UNITI-2 was 20.9% and 40.7% vs. PBO of 7.3% and 19.6% respectively. For this evaluation, the response and remission status of the entire population exposed to an IV induction dose of 6 mg/kg of UST was evaluated 8 weeks after the first subcutaneous maintenance dose of UST. All patients who received 6 mg/kg IV UST induction were included, including responders randomized to SC PBO (who did not receive SC UST at week 8).

**Results:** Of the 219 patients not in clinical response in UNITI 1&2, 37.6% and 60.4% respectively were in clinical response 8 weeks after the first maintenance UST dose (90 mg SC). Evaluating all patients exposed to 6 mg/kg IV UST induction, response rates 8 weeks after the first subcutaneous injection (16 weeks after the IV induction dose) for UNITI-1&2 are 47.4% and 73.7% respectively (see table for response and remission rate). Similar assessments were calculated in the sub-population who were anti-TNF naïve upon enrolment into UNITI-2.

**Response rates and Remission rates for all patients 16 weeks after induction of 6mg/kg IV UST**

<table>
<thead>
<tr>
<th>Study</th>
<th>IV UST (n)</th>
<th>% Clinical Response</th>
<th>% Clinical Remission</th>
</tr>
</thead>
<tbody>
<tr>
<td>UNITI-1</td>
<td>249</td>
<td>47.4</td>
<td>24.1</td>
</tr>
<tr>
<td>UNITI-2</td>
<td>209</td>
<td>73.7</td>
<td>55.5</td>
</tr>
<tr>
<td>UNITI-2 TNF Naïve</td>
<td>144</td>
<td>72.9</td>
<td>60.4</td>
</tr>
</tbody>
</table>

**Conclusion:** These numbers at week 16 are expected to reflect real-world experience in patients who receive the induction dose and one additional maintenance dose 8 weeks later. The resulting rates of response and remission are higher than previously reported in the induction studies across all populations (anti-TNF non-failures and anti-TNF failures). About 73% of anti-TNF non-failures attain clinical response and over half are in remission. The data support the clinical rationale for providing at least one SC maintenance dose of ustekinumab irrespective of clinical response 8 weeks after IV induction.

**Disclosure of Interest:** J. Colombo: Investigator for Janssen Scientific Affairs, LLC.

S. Sloan: Janssen Scientific Affairs, LLC employee

C. Gasink: Janssen Scientific Affairs, LLC employee

L. Gao: Janssen Scientific Affairs, LLC employee

D. Jacobson: Janssen Research & Development, LLC employee

S.D. Lee: Investigator for Janssen Research & Development, LLC

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REAL-WORLD PATTERNS OF TREATMENT DISCONTINUATION, FLARES, AND HOSPITALISATIONS AMONG INFLAMMATORY BOWEL DISEASE PATIENTS WITHIN 12 MONTHS OF INITIATION OF VEDOLIZUMAB OR INFlixIMAB

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Introduction: Biologics such as infliximab (IFX) (an anti-TNF) and vedolizumab (VDZ) (anti-integrin) are treatment options for patients with moderate-to-severely active inflammatory bowel disease (IBD), who have failed conventional therapy.

Aims & Methods: Our aim was to compare time to treatment discontinuation, flares, and hospitalisations among patients with IBD initiating VDZ versus IFX who were biologic-naïve. All patients with IBD (ulcerative colitis or Crohn’s disease [CD]) who initiated biologic treatment with VDZ or IFX between 01/05/2014 and 22/02/2016 were identified in the US Explorys Universe database; the first infusion was deemed the index date. Analyses focused on patients who: (1) successfully completed induction therapy (≥3 infusions within 98 days of index date); (2) were ≥18 years of age at index; (3) had ≥365 days of medical history prior to index (“baseline”); and (4) had 365 days of follow-up after the index date. VDZ initiators were matched to IFX initiators (1:3) using propensity scores. Kaplan-Meier Method was used to compare median time to discontinuation of VDZ and IFX during follow-up, defined as the first of either: no receipt of biologic ≤90 days of previous infusion, or switch to another biologic. Similar method was also used to compare median time to IBD-related hospitalisations, surgeries, and flares (defined as use of intravenous steroids), respectively. Interquartile range (IQR) was also calculated.

Results: 105 VDZ initiators were matched to 315 IFX initiators. Baseline characteristics of both cohorts are described in Table 1. CD accounted for ≥60% of patients in each cohort. Five percent of patients in both cohorts had received corticosteroids; 20% of VDZ vs. 38% of IFX initiators received an immunosuppressive therapy. Median time since diagnosis was 2.4 years for VDZ initiators and 1.9 years for IFX initiators. Median time to discontinuation was 244 (IQR: 194–307 and IFX: 190–300) days in both cohorts. Median time to first IBD-related hospitalisation was 153 (IQR: 78–209) days for VDZ initiators vs. 98 (IQR: 45–168) days for IFX initiators. For IBD-related flares, median time was 111 (IQR: 40–226) days for VDZ initiators vs. 93 (IQR: 35–182) days for IFX initiators.

Table 1. Baseline characteristics of propensity-score matched IBD patients initiating therapy with vedolizumab or infliximab

<table>
<thead>
<tr>
<th></th>
<th>Vedolizumab (N = 105)</th>
<th>Infliximab (N = 315)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean (SD) age, years</td>
<td>46 (16.0)</td>
<td>44 (16.8)</td>
<td>0.297</td>
</tr>
<tr>
<td>Female, %</td>
<td>52.4</td>
<td>52.7</td>
<td>&gt;0.999</td>
</tr>
<tr>
<td>Caucasian, %</td>
<td>89.5</td>
<td>84.1</td>
<td>0.180</td>
</tr>
<tr>
<td>Insurance type, %</td>
<td></td>
<td></td>
<td>0.202</td>
</tr>
<tr>
<td>Medicaid</td>
<td>6.7</td>
<td>11.1</td>
<td></td>
</tr>
<tr>
<td>Medicare</td>
<td>23.8</td>
<td>14.3</td>
<td></td>
</tr>
<tr>
<td>Private</td>
<td>63.8</td>
<td>65.7</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>5.7</td>
<td>8.9</td>
<td></td>
</tr>
<tr>
<td>Patients with Crohn’s Disease, %</td>
<td>60.0</td>
<td>60.9</td>
<td></td>
</tr>
<tr>
<td>Mean (SD) time from diagnosis, years</td>
<td>3.6 (3.5)</td>
<td>3.1 (3.6)</td>
<td>0.667</td>
</tr>
<tr>
<td>Comorbidities, %</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>3.8</td>
<td>2.9</td>
<td>0.745</td>
</tr>
<tr>
<td>Rheumatic disease</td>
<td>5.7</td>
<td>2.9</td>
<td>0.221</td>
</tr>
<tr>
<td>Mild liver disease</td>
<td>11.4</td>
<td>10.2</td>
<td>0.715</td>
</tr>
<tr>
<td>Malignancies</td>
<td>6.7</td>
<td>4.1</td>
<td>0.295</td>
</tr>
<tr>
<td>IBD-related measures (during the baseline period), %</td>
<td>5.7</td>
<td>7.3</td>
<td>0.663</td>
</tr>
<tr>
<td>Surgery</td>
<td>37.1</td>
<td>32.7</td>
<td>0.407</td>
</tr>
<tr>
<td>Corticosteroids</td>
<td>70.5</td>
<td>71.1</td>
<td>0.902</td>
</tr>
<tr>
<td>Immunosuppressives</td>
<td>20.02121</td>
<td>37.8</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Conclusion: Among biologic-naïve IBD patients, there was a trend toward prolonged median times to first IBD-related hospitalization or first flare with VDZ compared to IFX. The median time to discontinuation was comparable between the therapies. Future studies should examine comparative effectiveness outcomes in a larger cohort over a longer follow-up period.

Disclosure of Interest: H. Patel: I am currently an employee of Immensity Consulting, Inc., which received funding from Takeda Development Centre Ltd. M. Raluy Callado: Mireia Raluy Callado is a full-time employee of Evidera. A. Berger: Ariel Berger is a full-time employee of Evidera. R. Curtis: Employee of Takeda Development Centre Ltd. M.J. Khalid: Employee of Takeda Development Centre Ltd.
Aims & Methods: Remarkably, ROS have been involved in the transcriptional regulation of CD80 gene expression in the early stages of colonic carcinogenesis. We recently showed that expression of the co-stimulatory molecule CD80 on epithelial cells has a critical role during the immune surveillance process occurring in colon carcinogenesis. In CT26 cells ROS-generating agents (Antimycin A and H2O2) caused a significant inhibition of CD80 expression (p < 0.001) but not by NF-kB pharmacological inhibition. In vivo administration of N-acetyl cysteine significantly reduced AOM-induced CD80, MHC-I and MHC-II up-regulation in colonic epithelial cells (p = 0.001) and protein level (p < 0.001). H2O2-induced CD80 up-regulation in colonic epithelial cells was significantly inhibited by N-acetyl cysteine (p = 0.001) but not by NF-kB pharmacological inhibition. In vivo administration of N-acetylcysteine significantly reduced AOM-induced CD80, MHC-I and MHC-II up-regulation in colonic epithelial cells (p = 0.001, p < 0.001, respectively). Moreover, CD8+CD28+, CD8+CD69+, CD4+CD25+ T-cells in colonic mucosa were significantly lower in AOM-NAC mice than AOM mice (p = 0.08, p = 0.03 and p = 0.01, respectively). Conclusion: All in all, our data support the hypothesis that oxidative stress promotes the antigen presenting function of colonic epithelial cells by inducing CD80 in the early stages of colonic carcinogenesis. ROS-mediated CD80 up-regulation in colonic epithelial cells relies on the p38MAPK pathway in vitro.

Disclosure of Interest: All authors have declared no conflicts of interest.

References


P0415 ALTERED INTESTINAL EXPRESSION PROFILES OF ANTI-MICROBIAL GENES IN IRREVERSIBLE BOWEL SYNDROME ARE LINKED TO BACTERIAL COMPOSITION AND IMMUNE ACTIVATION


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4 Microbiology, INRA, Jouy en Josas, France, Palaiseau/Paris
5 Life Science, Danone Nutricia Research, Plaisance/Paris
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Introduction: Altered immune activity and gut microbiota alterations are proposed to be important factors in the pathophysiology of irritable bowel syndrome (IBS), but the relevance for symptoms is unclear.

Aims & Methods: We aimed to determine if colonic antimicrobial gene expression profiles differ between IBS and healthy subjects and if potential alterations are linked to immune activity or gut microbiota composition. The expression of 84 key antimicrobial genes in sigmoid colon biopsies from patients with IBS, defined as either immuno-active or immuno-norm based on systemic and mucosal cytokine profiles (Bennet et. al Am J Gastro, 2016), and healthy subjects was assessed by Human Antibacterial Response RT2 Profiler PCR Array. Targeted 16S rDNA pyrosequencing was performed on faecal microbiota. To identify discrimination profiles based on multiple variables between IBS patients and healthy subjects, orthogonal partial least squares discriminant analysis (OPLS-DA) with a cut off for Variable Importance for the Projection > 0.7 was performed.

Results: Table 1: Differences in mucosal antimicrobial mRNA expression between IBS (Immuno-active and Immuno-norm) and healthy subjects.

<table>
<thead>
<tr>
<th>Gene (ΔCt)</th>
<th>IBS (n = 31)</th>
<th>Immuno-active (n = 16)</th>
<th>Immuno-norm (n = 15)</th>
<th>Immuno-active v Healthy</th>
<th>Immuno-norm v Healthy</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACT1</td>
<td>0.01</td>
<td>0.01</td>
<td>0.01</td>
<td>0.01</td>
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</tr>
<tr>
<td>ILF7</td>
<td>0.0002</td>
<td>0.0008</td>
<td>0.004</td>
<td>0.004</td>
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<tr>
<td>MAP2K4</td>
<td>0.02</td>
<td>0.06</td>
<td>0.01</td>
<td>0.01</td>
<td>0.01</td>
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<tr>
<td>TICAM1</td>
<td>0.02</td>
<td>0.01</td>
<td>0.007</td>
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<td>TNFRSF1A</td>
<td>0.003</td>
<td>0.005</td>
<td>0.03</td>
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<tr>
<td>SUGT1</td>
<td>0.04</td>
<td>0.05</td>
<td>0.02</td>
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<tr>
<td>LYZ</td>
<td>0.004</td>
<td>0.01</td>
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<tr>
<td>LTF</td>
<td>0.008</td>
<td>0.009</td>
<td>0.009</td>
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<td>CHUK</td>
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<td>IRAK1</td>
<td>0.02</td>
<td>0.02</td>
<td>0.02</td>
<td>0.02</td>
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<tr>
<td>MAP2K1</td>
<td>0.02</td>
<td>0.02</td>
<td>0.02</td>
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<td>0.02</td>
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<td>0.04</td>
<td>0.05</td>
<td>0.05</td>
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</tr>
<tr>
<td>TLR4</td>
<td>0.04</td>
<td>0.04</td>
<td>0.04</td>
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<tr>
<td>IL1B</td>
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<td>0.05</td>
<td>0.03</td>
<td>0.03</td>
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<tr>
<td>RIPK1</td>
<td>0.05</td>
<td>0.05</td>
<td>0.03</td>
<td>0.03</td>
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<td>XIAP</td>
<td>0.05</td>
<td>0.05</td>
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<td>IL-18</td>
<td>0.05</td>
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<td>CXCL1</td>
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<td>0.04</td>
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</tr>
</tbody>
</table>

Data presented as p-values (Mann-Whitney t-test). '*' ' = non significant. We included 31 IBS patients (16 females, median age 32 (25-44) years) and 16 healthy subjects (8 females, median age 27 (24-30) years). An OPLS-DA model demonstrated that the antimicrobial profiles differed between IBS and healthy subjects (R² = 0.54, Q² = 0.16). The mucosal mRNA expression of 14 antimicrobial genes was downregulated, while one gene was upregulated in IBS patients compared to healthy subjects (Table 1). Antimicrobial profiles did not differ between IBS patients subtyped according to their predominant bowel habit (R² = 0.02). An OPLS-DA model showed discrimination between immunologically relevant IBS and healthy subjects, orthogonal partial least squares discriminant analysis (OPLS-DA) with a cut off for Variable Importance for the Projection > 0.7 was performed.
Receptor Superfamily Member 1A (TNFRSF1A) with Bifidobacterium (r = 0.8, P < 0.05).

Conclusion: The intestinal antimicrobial gene profiles differ between subsets of IBS patients and healthy subjects. An altered ability to recognise microbiota associated with immune activity and the relative abundance of gut bacteria may play a role in the complex pathophysiology of IBS.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0418 EFFECT OF INTERNAL AND EXTERNAL BILARY DRAINAGE ON INTESTINAL MUCOSAL BARRIER FUNCTION IN BILAYER OBSTRUCTION RATS

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Introduction: Internal biliary drainage has been confirmed better than external biliary drainage in alleviating the damage of intestinal mucosa barrier caused by obstructive jaundice, but the relevant mechanism is still unclear.

Aims & Methods: We aimed to investigate the effect of internal and external drainage on the bile duct external biliary barrier function studies regarding this topic were limited [4–7].

Methods: We aimed to investigate the effect of internal and external drainage on the bile duct external biliary barrier function studies regarding this topic were limited [4–7].

Results: After bile duct ligation, the injuries of the intestinal mucosa were obvious in OJ group with thinner mucosa, sparser villi, destruction of the epithelial layer accompanied by inflammation cell infiltration. The expression of IgA mRNA and plgR mRNA (P < 0.05). There was no evidence of significant publication bias among this meta-analysis.

Conclusion: Higher prescriptions and longer duration exposure of antibiotics might play a significant role in the colorectal carcinogenesis [1–2]. Many environmental factors (e.g. diet and lifestyle) that altered the gut microbiota might be involved in the development of colorectal cancer[3]. Antibiotics are able to shift the gut microbiota by altering bacterial composition and functions. The overuse of antibiotics might be associated with severe infections, such as severe infections, obesity, inflammatory bowel disease. Similarly, it is plausible to hypothesize that overuse of antibiotic might be linked to CRC by altering the colorectal microbiota. However, the relationship between antibiotic and CRC was unclear and studies regarding this topic were limited [4–7].

Aims & Methods: To evaluate the association between use of antibiotic and the risk of developing colorectal cancer, a systematic literature search was conducted using PubMed, EMBASE, Web of science and Cochrane library to identify related studies published before October 2016. Two independent investigators screened and extracted data from included articles. A random-effects model was adopted to calculate overall odds ratio (OR) and 95% confidence interval (CI).

Results: From initial search, we identified four case-control studies and finally 11 studies were included in the meta-analysis. Compared with no/low use of antibiotics, high prescriptions of antibiotics were significantly associated with an excess cancer risk (OR = 1.11, 95%CI 1.01–1.21). There was a significant heterogeneity across studies (I² = 62.1%, P = 0.048). Longer duration of antibiotics was also significantly linked to increased risk of CRC (OR = 1.14, 95%CI 1.03–1.25) with no significant heterogeneity (I² = 39.6%, P = 0.191). There was no evidence of significant publication bias among this meta-analysis.

Conclusion: Higher prescriptions and longer duration exposure of antibiotics were associated with increased risk of developing colorectal cancer. Further studies are needed to verify our results and explore underlying mechanisms.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P0419 COMPARATIVE EFFECT OF XYLOGLUCAN ASSOCIATIONS WITH COMPOUNDS FROM ANIMAL OR ALGAE ORIGIN ON LPS-INDUCED ENTERITIS IN RATS

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Introduction: Xyloglucan (XG) is a film-forming agent exhibiting protective effects against diarrhea linked to infectious gastroenteritis in humans; further in animal models, xyloglucan efficacy against cholera-toxin-induced diarrhea was prolonged when this mucoprotective agent is associated with gelatin from animal origin. The use of compounds from animal source in galenic formulations is nowadays questionable.

Aims & Methods: Thus, in this study, we aimed at comparing the efficacy of XG associations with gelatin vs XG associations with gelose a mucoprotective agent with origin on LPS-induced enteritis in rats. Since LPS-induced enteritis is characterized by increased intestinal epithelial permeability and mucosal inflammation, the efficacy of xyloglucan associations was evaluated by measurement of these two parameters. Male Wistar rats (200-250g) were orally treated with either XG (10 mg/kg) + gelatin (25 mg/kg) or XG (10 mg/kg) + gelose (25 mg/kg) or XG (10 mg/kg) + gelose (50 mg/kg) or vehicle (NaCl 0.9%) 3h before intraperitoneal (IP) administration of LPS from E. coli (1 mg/kg). Six hours later after LPS administration, the animals were sacrificed and strips of jejunum were collected in order to evaluate (i) intestinal epithelial paracellular permeability to FITC-dextran 4kD in Ussing chambers and (ii) mucosal inflammatory response by myeloperoxidase (MPO) activity measurement.

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Introduction: Recently, accumulating evidence suggested that the dysbiosis of the intestinal microbiota was associated with increased risk of colorectal cancer and might play a significant role in the colorectal carcinogenesis [1–2]. Many environmental factors (e.g. diet and lifestyle) that altered the gut microbiota might be involved in the development of colorectal cancer[3]. Antibiotics are able to shift the gut microbiota by altering bacterial composition and functions. The overuse of antibiotics might be associated with severe infections, such as severe infections, obesity, inflammatory bowel disease. Similarly, it is plausible to hypothesize that overuse of antibiotic might be linked to CRC by altering the colorectal microbiota. However, the relationship between antibiotic and CRC was unclear and studies regarding this topic were limited [4–7].

Aims & Methods: To evaluate the association between use of antibiotic and the risk of developing colorectal cancer, a systematic literature search was conducted using PubMed, EMBASE, Web of science and Cochrane library to identify related studies published before October 2016. Two independent investigators screened and extracted data from included articles. A random-effects model was adopted to calculate overall odds ratio (OR) and 95% confidence interval (CI).

Results: From initial search, we identified four case-control studies and finally 11 studies were included in the meta-analysis. Compared with no/low use of antibiotics, high prescriptions of antibiotics were significantly associated with an excess cancer risk (OR = 1.11, 95%CI 1.01–1.21). There was a significant heterogeneity across studies (I² = 62.1%, P = 0.048). Longer duration of antibiotics was also significantly linked to increased risk of CRC (OR = 1.14, 95%CI 1.03–1.25) with no significant heterogeneity (I² = 39.6%, P = 0.191). There was no evidence of significant publication bias among this meta-analysis.

Conclusion: Higher prescriptions and longer duration exposure of antibiotics were associated with increased risk of developing colorectal cancer. Further studies are needed to verify our results and explore underlying mechanisms.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
Results: Compared with control, LPS administration induced a significant increase (p < 0.05) of intestinal paracellular permeability (53.0 ± 4.9 vs 181.6 ± 21.1 pmol/cm² respectively) associated with jejunal mucosal inflammation (302.1 ± 9.5 vs 655.6 ± 108.9 U MPO/g protein, respectively). XG (10 mg/kg) + gelose at the lowest dose (25 mg/kg) failed to reverse the intestinal hyperpermeability and mucosal inflammation induced by LPS. In contrast, XG (10 mg/kg) + gelatin (25 mg/kg) and XG (10 mg/kg) + gelose at 50 mg/kg significantly (p < 0.01) and equally prevented LPS-induced hyperpermeability (34.8 ± 2.8, 38.7 ± 3.9 vs 181.6 ± 21.1 pmol/cm² respectively) and jejunal inflammation (277.0 ± 32.2, 286.2 ± 28.8 vs 655.6 ± 108.9 U MPO/g protein respectively).

Conclusion: This study shows that oral treatment with xyloglucan associated with gelose at 50 mg/kg has similar protective effects on LPS-induced enteritis in rats than xyloglucan associated with gelatin. These data demonstrate that algae is an effective and safe substitute for replacing compounds from animal origin in xyloglucan mucoprotectant formulations.

Disclosure of Interest: All authors have declared no conflicts of interest.

References


2. Jimenez Garcia P, Anda M, et al. Epidemiology and clinical characteristics of cytomegalovirus colitis in immunocompetent hosts included 44 patients and noted advanced age, male gender, presence of immune-modulating comorbidities and need of surgical intervention negatively influencing survival in 2005 [6]. The case number of CMV colitis in immunocompetent patients seemed increasing in our hospital these years. There was no single study showing comprehensive clinical characteristics, identifying the independent factors of in-hospital mortality and comparing the differences between immunocompetent and compromised patients with CMV colitis. Therefore, we tried to clarify the issue in this study.

Aims & Methods: We enrolled 42 immunocompetent patients and 27 immunocompromised patients with CMV colitis diagnosed by immunohistochemistry stain between April 2002 and December 2016 in Linkou Chang Gung Memorial Hospital, a 3383-bed tertiary medical center and referral center in Taiwan. We analyzed the risk factors of in-hospital mortality and overall survival. Furthermore, we compared the clinical differences between immunocompetent and immunocompromised patients with CMV colitis.

Results: Early diagnosis (before 9 days) was independent predictor of in-hospital mortality in CMV colitis patients. ICU admission (P = 0.010), requisite days of diagnosis >9 days after admission (P = 0.018), shock (P = 0.001), respiratory failure (P = 0.033), hemoglobin < 10 g/dL (P = 0.002), Creatinine ≥ 1.7 mg/dL (P = 0.004) and CRP ≥ 59 mg/dL (P = 0.011) negatively impacted on overall survival. There were older and more comorbidities in immunocompetent group. However, the in-hospital mortality rate and overall survival rate was similar to immunocompromised group. Besides, Clostridium difficile infection or sepsis didn’t affect in-hospital mortality rate and overall survival rate neither. Melena was first and most common symptom in immunocompetent group, but diarrhea in the other.

Analysis of the clinical factors associated with in-hospital mortality in all patients

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Odd ratio (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Univariate analysis</td>
<td>P-value</td>
</tr>
<tr>
<td>Age &gt; 65</td>
<td>2.071</td>
</tr>
<tr>
<td>Gender (male/female)</td>
<td>0.545</td>
</tr>
<tr>
<td>Immunocompromised status</td>
<td>0.986</td>
</tr>
<tr>
<td>Intensive care unit admission</td>
<td>6.871</td>
</tr>
<tr>
<td>Requisite time of diagnosis (day after admission)</td>
<td>1.034</td>
</tr>
<tr>
<td>General condition</td>
<td>0.034*</td>
</tr>
<tr>
<td>Sepsis</td>
<td>1.309*10^5</td>
</tr>
<tr>
<td>Shock</td>
<td>5.714</td>
</tr>
<tr>
<td>Respiratory failure</td>
<td>4.062</td>
</tr>
<tr>
<td>Operation before diagnosis</td>
<td>5.200</td>
</tr>
<tr>
<td>Underlying diseases</td>
<td>0.000</td>
</tr>
<tr>
<td>Inflammatory bowel disease</td>
<td>0.000</td>
</tr>
<tr>
<td>Systemic lupus erythematosus</td>
<td>4.900</td>
</tr>
<tr>
<td>Solid organ transplantation</td>
<td>2.941</td>
</tr>
<tr>
<td>Solid organ malignancy</td>
<td>0.941</td>
</tr>
<tr>
<td>Hematological malignancy</td>
<td>2.941</td>
</tr>
<tr>
<td>Liver cirrhosis</td>
<td>0.941</td>
</tr>
<tr>
<td>Chronic kidney disease</td>
<td>2.067</td>
</tr>
<tr>
<td>End stage renal disease</td>
<td>3.357</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>1.682</td>
</tr>
<tr>
<td>HIV infection</td>
<td>0.000</td>
</tr>
<tr>
<td>Immunosuppressive medication</td>
<td>0.000</td>
</tr>
<tr>
<td>Immunosuppressant</td>
<td>3.200</td>
</tr>
<tr>
<td>Chemotherapy</td>
<td>4.841*10^4</td>
</tr>
<tr>
<td>Steroid</td>
<td>1.124</td>
</tr>
<tr>
<td>Using steroid over 1 month</td>
<td>2.350</td>
</tr>
</tbody>
</table>

Laboratory data

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Minimal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total WBC count (×10^9/ml)</td>
<td>1.000</td>
</tr>
<tr>
<td>ANC (×10^9/ml)</td>
<td>1.000</td>
</tr>
<tr>
<td>ALC (×10^9/ml)</td>
<td>0.999</td>
</tr>
<tr>
<td>Hemoglobin level (g/dL)</td>
<td>0.668</td>
</tr>
<tr>
<td>Platelet count (×10^12/mm³)</td>
<td>0.995</td>
</tr>
<tr>
<td>Creatinine (mg/dL)</td>
<td>1.448</td>
</tr>
<tr>
<td>ALT (IU/L)</td>
<td>0.995</td>
</tr>
<tr>
<td>Bilirubin (mg/dL)</td>
<td>1.370</td>
</tr>
<tr>
<td>Albinum (g/dL)</td>
<td>0.625</td>
</tr>
<tr>
<td>C-reactive protein (mg/dL)</td>
<td>1.009</td>
</tr>
</tbody>
</table>

Viral markers
Analysis of the clinical factors associated with in-hospital mortality in all patients

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Odd ratio</th>
<th>95%CI</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CMV pp65 antigenemia</td>
<td>0.656</td>
<td>0.140 – 3.079</td>
<td>0.593</td>
</tr>
<tr>
<td>CMV IgG positive</td>
<td>0.286</td>
<td>0.016 – 5.095</td>
<td>0.394</td>
</tr>
<tr>
<td>CMV IgM positive</td>
<td>3.125</td>
<td>0.547 – 17.841</td>
<td>0.200</td>
</tr>
<tr>
<td>Clostridium difficile infection</td>
<td>0.889</td>
<td>0.077 – 10.300</td>
<td>0.925</td>
</tr>
<tr>
<td>Ganciclovir or valganciclovir treatment</td>
<td>2.266</td>
<td>0.579 – 9.026</td>
<td>0.238</td>
</tr>
<tr>
<td>Treatment duration</td>
<td>0.989</td>
<td>0.953 – 1.026</td>
<td>0.563</td>
</tr>
<tr>
<td>Surgical treatment</td>
<td>1.840</td>
<td>0.392 – 8.630</td>
<td>0.439</td>
</tr>
</tbody>
</table>

Conclusion: Immunosuppressed patients or steroid users did not have higher in-hospital mortality rate. Early diagnosis was only independent factor for lower in-hospital mortality in patients with CMV infection.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
2. Khan TV, Toms C. Cytomegalovirus Colitis and Subsequent New Diagnosis of Inflammatory Bowel Disease in an Immunocompetent Host: A Case Study and Literature Review. Am J Case Rep 2016; 17: 538-43.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
2. Khan TV, Toms C. Cytomegalovirus Colitis and Subsequent New Diagnosis of Inflammatory Bowel Disease in an Immunocompetent Host: A Case Study and Literature Review. Am J Case Rep 2016; 17: 538-43.
Aims & Methods: The aim of this study was to assess in-hospital delay of surgery and its impact on the incidence of complicated appendicitis. PubMed and EMBASE were searched from 1990 to July 2016. Outcome measures of interest were complicated appendicitis, surgical site infections or mortality. All studies reporting surgically treated patients with one of these outcome measures in two or more predefined time intervals were included. Adjusted odds ratios were pooled using forest plots if possible. All unadjusted data was pooled using generalized linear mixed models.

Results: Forty-five studies with 152,314 patients were included. Pooled adjusted odds ratios revealed no significantly higher risk for complicated appendicitis when delaying appendectomy for 6 to 12 hours or 13 to 24 hours; odds ratio 1.07 (95% CI 0.986-1.17) and 1.09 (95% CI 0.95-1.28), respectively. For a delay of one day or more, the adjusted odds ratio was 1.13 (95% CI 1.01-1.26, P = 0.01). In-hospital delay of surgery for acute appendicitis has been subject of a large number of studies. However, consensus about the consequences of delaying appendectomy is lacking, which is reflected in variety or absence of recommendations in guidelines.

Disclosure of Interest: All authors have declared no conflicts of interest.

References:

Aims & Methods: We reviewed a 10-year cumulative regional TB database in an university teaching hospital covering an urban multi-ethnic population to report clinical details of A-TB and results on this unusual condition. A clinical review of patients diagnosed for A-TB between 2006 to 2016 in a single tertiary centre in Hong Kong was conducted. A central surveillance database managed by Respiratory Physicians of the Hong Kong Tuberculosis Control Branch of Health Department of the Government of Hong Kong Special Administrative Region was used to identify patients with A-TB. We reviewed clinical data from electronic records including radiology, chemical pathology, histopathology, endoscopy databases, surgical notes and letters.

Results: Of 41 patients (M = 22; 54%; mean age 42y (SD ± 17y) identified with A-TB, 41% (17) were Pakistani, 15% (6) were other Asian, 19% (8) were Afro-Asian, 15% (6) were other Asian, 19% (8) were Afro-Asian, 15% (6) were other Asian, 19% (8) were Afro-Asian, 15% (6) were other Asian, 19% (8) were Afro-Asian, 15% (6) were other Asian, 19% (8) were Afro-

Disclosure of Interest: All authors have declared no conflicts of interest.

References:

Aims & Methods: The traditional fear that every acute appendicitis will eventually perforate leads to prompt surgery, but this fear may be outdated. In-hospital delay of surgery for acute appendicitis has been subject of a large number of studies. However, consensus about the consequences of delaying appendectomy is lacking, which is reflected in variety or absence of recommendations in guidelines.

Disclosure of Interest: All authors have declared no conflicts of interest.

References:
notably contributed by elderly patients, of which the incidence has increased by threefold over the period. Recurrence at 60 days increased from 5.7% in 2006 to 9.1% in 2014 (P$_{mult}$ = 0.001). The increased use of proton-pump inhibitors accounted for 58.8% of the surge.

**Conclusion:** The incidence of *C. difficile* infection has increased more than threefold, and was associated with an increased disease recurrence and use of proton-pump inhibitors. Our results suggest need for further surveillance in Asia which hovers half of the world’s population.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**References**


**P0428 THE PROPHYLACTIC CLIP APPLICATION BEFORE SNARE POLYPECTOMY DECREASES IMMEDIATE POST-POLYPECTOMY BLEEDING IN LARGE PEDUNCULATED POLYPS**

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Introduction: Post-polypectomy bleeding (PPB) is the most common complication following polypectomy, especially in cases with large pedunculated polyps. Although the clip application before snare polypectomy may decrease PPB, there were few prospective randomized studies to confirm the efficacy of prophylactic clip. This present study was conducted to investigate whether prophylactic clip application for large pedunculated colorectal polyps could decrease PPB and to evaluate associated risk factors of PPB.

**Aims & Methods:** We enrolled 137 pedunculated polyps (≥1 cm in size) in 116 patients (62 M/F). Polyps were randomized into the two groups with or without prophylactic clip application. Immediate PPB was defined as bleeding that continued for over 30 seconds from the polypectomy site and graded from grade 1 to 4, and delayed bleeding was defined as a history of hematochezia from the day of procedure to the day of first visit of outpatient clinic. The primary outcome was post-polypectomy bleeding. This present study was confirmed by emergency endoscopy or a decrease in the hemoglobin level of ≥2 g/dl with hematochezia even if the bleeding site was not identified.

**Results:** Between January 2015 and November 2016, a total of 30 consecutive patients (M/F: 26/4, 69.9±11.3 years) were enrolled in this study after written informed consent was obtained. A total of 81 lesions (tumor diameter: 5.4±2.9 mm, adenoma 70, others 10, lost lesion 1, number of prophylactic clips: 4.9±2.2) were treated by polypectomy/EMR. Four patients experienced post-polypectomy bleeding (4.5%: 3/67) 3-11 days after the procedure, although no cases required blood transfusion. In 3 of these bleeding cases, a single responsible site was identified by emergency endoscopy. Therefore, the confirmed rate of post-polypectomy/EMR bleeding based on the number of resected lesions was 3.9% (3/76), but may range to 9.9% (8/81). There were no other adverse events.

**Conclusion:** The rate of post-colon polypectomy/EMR bleeding in patients without discontinuation of warfarin single therapy was comparable to that in patients undergoing HR. Concomitant use of antithrombotic medication (warfarin) without discontinuation of warfarin in patients who received warfarin for the purpose of prevention of thrombosis was prospectively enrolled and underwent colon polypectomy or EMR without discontinuation of warfarin. Conventional clip closure of the resection site was performed in all cases and oral diet was resumed 2 days after the procedure. The primary outcome was post-polypectomy/EMR bleeding that was confirmed by emergency endoscopy or a decrease in the hemoglobin level of ≥2 g/dl with hematochezia even if the bleeding site was not identified.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**References**


Introduction: The incidence of acute lower gastrointestinal bleeding (LGB) is estimated at 21 adults per 100,000 person years and in males (82.1%) in the anticoagulants group were higher than those in the normal group (67.2±11.2 years and 64.1%). There was no difference between the groups in size of polyp and morphology. In the anticoagulants group, 34 patients received heparin bridged thromboplatin (warfarin, antithrombotic drug, non-steroidal anti-inflammatory drug) therapy and 33 patients discontinued anticoagulants (warfarin 8, warfarin + antiplatelet 3, rivaroxaban 1 and 33 patients discontinued anticoagulants (warfarin 8, rivaroxaban 10, apixaban 8, dabigatran 4, edoxaban 2). The incidence of PPC was no difference between two groups (1, 1 patient, respectively). There was no difference between the groups in age, sex, size of polyp and morphology. Recurrent bleeding didn’t occur. In the discontinued group, 1 patient developed acute myocardial infarction in next day after colonoscopy polypectomy.

Conclusion: Patients taking anticoagulants have an increased risk of PPC compared with the control even if the anticoagulants are discontinued. Heparin-bridge therapy might be responsible for increased PPC in patients taking anticoagulants.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
**RESULTS:** Patient characteristics such as sex, age, anti-platelet therapy, location of bleeding and bleeding after endoscopic procedure did not have significant difference in both groups. Upper gastrointestinal bleeding occurred 6 (33.3%) of DOAC group and 12 (60.0%) of Warfarin group (11.1 ± 0.7 g/dl vs 9.6 ± 0.4 g/dl, p = 0.06) and international normalized ratio of prothrombin time (PT-INR) was significantly prolonged in Warfarin group (1.51 ± 0.36 vs 2.50 ± 0.20, p = 0.02). CR transfusion rate had no significant difference in both group, but FFP tended to be transfused at high rate in Warfarin group (16.7% vs 33.3%, p = 0.16). Re-bleeding rate during hospitalization had no significant difference in both group, but tended to be higher in Warfarin group (5.6% vs 0.0%, p = 0.11). The duration from bleeding to endoscopy tended to be longer in Warfarin group (9.5 ± 5.5 days vs 3.0 ± 3.0 days, p = 0.05), but the duration from endoscopy to discharge was significantly longer in Warfarin group (9.0 ± 5.5 days vs 23.0 ± 3.0 days, p = 0.03). The duration from bleeding to discharge was significantly longer in Warfarin group (9.8 ± 5.4 days vs 24.2 ± 3.0 days, p = 0.02). Thrombotic embolism during hospitalization occurred only 1 (1.7%) of Warfarin group.

**Conclusions:** The duration of hospitalization was significantly shorter in the group of patients with gastrointestinal bleeding, and the rate of rebleeding and re-bleeding tended to be lower in DOAC group. This study showed that DOAC may be more superior to Warfarin as an anticoagulation for atrial fibrillation and deep vein thrombosis at the quality of life (QOL) in the patients with gastrointestinal bleeding.

**Disclosures of Interest:** All authors have declared no conflicts of interest.

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**P0436** WORLD ENDOSCOPY ORGANISATION CONSENSUS STATEMENTS ON POST-COLONOSCOPY/POST-IMAGING COLORECTAL CANCER


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**4California And San Francisco MedCenter, Kaiser Permanente Division of Research, Oakland/United States of America**
**5Pathology Department - Centre De Diagnostic Biomedic (cdb), Hospital Clinic Barcelona, University of Barcelona, Barcelona/Spain**
**6Gastroenterology & Hepatology, AMC - Gastroenterology & Hepatology, AMC; Amsterdam/NL, Amsterdam/Netherlands**
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**8Clinical Epidemiology, Leibniz Institute for Prevention Research and Epidemiology, Bremen/Germany**
**9Department Of Gastroenterology, Maria Sklodowska-Curie Memorial Center and Institute of Oncology - Department of Gastroenterology, M. Warsaw/Poland**
**10Cancer Screening Center, National Cancer Center Hospital, Tokyo/Japan**
**11Gastroenterology, Netherlands Cancer Institute, Amsterdam/Netherlands**
**12Cancer Epidemiology Group, University of Leeds, Leeds/United Kingdom**
**13Radiology And Imaging, University College London Hospital, London/United Kingdom**
**14Prevention And Cancer Control, Cancer Care Ontario, University of Toronto, Toronto/Canada**
**15Gastroenterology, YAMC, White River Junction, United States, Vermont/United States of America**
**16University of Pittsburgh and the University of Pittsburgh Cancer Institute, Pittsburgh/United States of America**
**17Section Of Gastroenterology, University of Manitoba and the University of Manitoba-IRD Clinical and Research Institute, Canada**
**18Division of Gastroenterology, Sunnybrook Health Sciences Centre, Toronto/Canada**
**19Medicine, Gloucestershire NHS Foundation Trust - Medicine, Gloucestershire/United Kingdom**
**20FCRC, Flinders University, Templestowe Lower/Australia**

**Contact E-mail Address:** iosi4.beintaris@nhs.net

**Introduction:** Colorectal cancer (CRC) is an imperfect tool. Several publications confirm that CRC can be subcategorized into interval cancers (identified prior to the next recommended screening or surveillance procedure) and non-interval cancers (identified at or after a recommended screening or surveillance interval, or where no subsequent screening or surveillance interval was recommended, up to 10 years following the colonoscopy). The goal of this consensus process was to provide a framework for the terminology, identification, analysis and reporting of cancers appearing after a negative colonoscopy. The term “interval cancer” has often been used for cancers appearing after a negative colonoscopy. However, this is primarily a screening term (1). Post-colonoscopy colorectal cancer (PCRC) is a broader term for cancers detected after a negative colonoscopy in any setting, including screening (2). Although there is overlap between these terms, they are not synonymous. PCRC can be thought of as the overarching term. PCRC can be subcategorized into interval cancers and non-interval cancers (3). The final output consisted of 391 articles. Proposed statements were subjected to anonymous voting via e-correspondence. Each statement was scored on an scale of 1 (strongly agree) to 5 (strongly disagree).

**Aims & Methods:** The goal of this consensus process was to provide a framework for the terminology, identification, analysis and reporting of cancers appearing after a negative colonoscopy or computed tomographic colonography (post-colonoscopy/post-imaging colorectal cancers - PCRC/PICRC respectively). We based our methodology on The Appraisal of Guidelines for Research and Evaluation (AGREE II) tool (4). An international multidisciplinary team (gastroenterologists, pathologists, epidemiologists, a radiologist and a patient representative) were involved in the World Endoscopy Organisation (WEO); the final panel consisted of 20 voting members. The following topics were addressed by 2 working groups (WGs):

1. **Aetiology WG**
   a. Terminology of aetiology categories
   b. Risk factors/potential explanations of PCRC
   c. How to ascribe potential explanations
   d. Minimal colonoscopy, history and radiology datasets to examine PCRC
   e. Molecular tests to be performed to examine PCRC
   f. Prevention of PCRC in high-risk groups
2. **Performance WG**
   a. PCRC calculation & reporting
   b. PCRC monitoring
   c. PCRC papers peer-review
   d. Post-imaging CRC A literature search was performed in MEDLINE and Cochrane using terms “colorectal cancer AND interval cancer”, “healthcare quality assurance AND colorectal cancer” and “healthcare quality assurance AND colorectal cancer AND interval cancer”. The final output consisted of 391 articles. Proposed statements were subjected to anonymous voting via e-correspondence. Each statement was scored on an scale of 1 (strongly agree) to 3 (strongly disagree).
5 (strongly disagree). A modified Delphi process was followed; consensus recommendation. In areas of continuing disagreement, a recommendation for or against a particular statement required both >50% of participants in favour and <20% preferring the comparator. Failure to meet this resulted in no recommendation. The GRADE system for rating evidence and strength of recommendations was applied to final statements.

Results: The final output consists of 21 statements providing guidance on key aspects of PCCRC/PICRC, namely definitions, terminology, qualitative review/ aetiology attribution and quantitative assessment of cases. A Root-Cause Analysis checklist as well as a PCCRC/PICRC manuscript peer-review checklist were also developed.

Conclusion: This is the first consensus aimed to standardise terminology around PCCRC. Each previous study defined PCCRC differently, making its use for benchmarking purposes impossible. This consensus presents a methodology for analysis of causation of PCCRC/PICRC and defines its potential role as a key quality indicator, providing recommendations for future investigators, policy makers, services and patients.

Disclosure of Interest: E. Wieten: Research grant from Olympus and endoscopic equipment on loan from Olympus and Fujifilm. A. Plumb: I have no conflicts related to the present project. Other disclosures (not related to the present project): I have received payment for educational lectures organized by Warner Chilcott, a pharmaceutical company, and the medical device company Acelity. H. Singh: No direct conflicts of interest. In terms of industry funding, disclosure includes Advisory Board for Pendopharm and research funding from Merek Canada J. Tinnmouth: Lead Scientist for the ColonCancerCheck program, the CRC screening program in Ontario. I am paid a salary for this work R. Valori: I have been the Director of a Limited Liability Partnership (Quality Solutions for Healthcare) which provides advice and support for quality improvement and QA within and outside of endoscopy, mostly in the UK and Ireland, as well as training internationally. M.D. Rutter: Research grant from Olympus, speaker fees/travel reimbursement from Falk, Abbvie

All other authors have declared no conflicts of interest.

References
FOBT is two-fold higher in gFOBT than in FIT, which supports the use of FIT over gFOBT as screening tool test. However, for every three FIT-detected CRCs, still one CRC is missed, which highlights the importance to adequately inform screenees about the risk of developing a colorectal carcinoma after a negative FIT.

Disclosure of Interest: E. Wiener: I declare no competing interests. All other authors have declared no conflicts of interest.

P0439 MEASURES OF BODY COMPOSITION AND GENDER DIFFERENCES IN RISK FOR COLORECTAL CANCER – A POPULATION-BASED COHORT STUDY

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2Upptäckt! Department of Surgical Sciences, Uppsala/Sweden
3Karolinska Institutet Huddinge, Division of Family Medicine, Department of Neurobiology, Care Science and Society, Huddinge/Sweden
4Skåne University Hospital Malmö, Department of Gastroenterology and Hepatology, Malmö/Sweden

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Introduction: Age and family history of colorectal cancer (CRC) are the strongest risk factors for CRC. Obesity, commonly assessed based on body mass index (BMI), is associated with an increased risk for CRC in men but the association is weaker in women and differs between studies. We investigated which of the following body composition measures: BMI, waist-hip ratio (WHR), waist-height ratio (WHHR), weight-height ratio (WHRR), A Body Shape Index (ABSI) and percent body fat that best predict the development of CRC in men and women.

Aims & Methods: We used data from Malmö Diet and Cancer cohort in Sweden, including 16,840 women and 10,903 men (mean age, 58.1 years at baseline), followed for a median of 19.8 years. We identified cases with CRC until the end of 2014 using national Swedish registers. Hazard ratios (HR) for CRC, colon cancer (CC) and rectal cancer (RC) per one standard deviation increase in each body composition measure respectively were calculated using Cox regression models, stratified by sex and adjusted for age, education and health behaviors. WC was the only measure associated with an increased risk for CRC, CC nor RC.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

P0440 TH17 CELLS INDUCE EPITHELIAL-MESENCHYMAL TRANSITION VIA IL-17/PI3K/AKT/SNAIL PATHWAY IN COLORECTAL CANCER

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Introduction: T helper 17 (Th17) cells participate in the progression of various cancers. Both tumor-promoting and tumor-suppressing effect have been reported. The role of Th17 cells in colorectal cancer (CRC) remains controversial and the specific mechanism of how Th17 cells affect the development of CRC remains to be explored.

Aims & Methods: The study aimed to clarify the role of Th17 cells in CRC and identify the underlying molecular mechanisms. The percentage of Th17 cells and IL-17 expression were evaluated via flow cytometry, enzyme-linked immunosorbent assay (ELISA) in tissue samples and peripheral blood. Effects and underlying molecular mechanisms of IL-17 cells on epithelial-mesenchymal transition (EMT) process were explored in vitro using IL-17 transfection and in nude mice by implanting IL-17 overexpressed CRC cells. To detect the expression of Th17 cells in EMT process, SW480 cells were co-cultured with Th17 cells via transwell system. Cancer signaling phospho antibody microarray was used to explore the potential signaling pathway. The clinical significance of Th17 cells was investigated in tissue microarrays containing CRC tissue samples from 90 patients following surgery using immunohistochemistry.

Results: A higher percentage of Th17 cells and serum IL-17 level were found in CRC patients than healthy controls, and Th17 cells presented a gradual upward trend in normal epithelium-adenoma-carcinoma sequence. The overexpression of IL-17 significantly promoted cell proliferation and induced apoptosis in vitro and in vivo. IL-17 overexpression reduced the expression of E-cadherin and induced the expression of Snail, β-catenin, and Vimentin in both SW480 cells and tumor xenografts, suggesting that IL-17 could induce the EMT process of CRC. When co-cultured with SW480 cells with Th17 cells, we found Th17 cells could directly promote the EMT process of tumor cells. Furthermore, using cancer signaling phospho antibody microarray, we found that PI3K/AKT signaling pathway played a key role in the regulation of EMT. EMT process could be reversed by LY294002 and IL-17 mAb intervention, suggesting that IL-17/Pi3K/AKT/Snail pathway could promote EMT process and facilitate tumor progression via activating IL-17/Pi3K/AKT/Snail signaling pathway in CRC.

Disclosures of Interest: All authors have declared no conflicts of interest.

References
Mortality Worldwide: IARC CancerBase No. 11 [Internet]. The following adverse effects and methods used in compiling the national cancer incidence and mortality estimates in GLOBOCAN 2012, and briefly describes the key results by cancer site and in 2020 large areas of the world. (Lyon, France: International Agency for Research on Cancer; 2013. Available from: accessed on day/month/year, 2013.)


P0442 MUCARINIC-3 RECEPTOR TARGETED MIARNAS ARE INVOLVED IN BILE ACID-INDUCED PROLIFERATION ON H508 COLON CANCER CELL LINE

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Introduction: Studies with the colon cancer cell lines which express muscarinic-3 (M3) receptors showed that taunine conjugates of lithocholic acid, but not other bile acids, bind to M3 receptors, and stimulate an increase in cell proliferation. On the other hand, many microRNAs (miRNAs) are involved in colon carcino- genesis. However, the interaction of bile acid-M3 receptors and miRNAs and their potential effects in colon carcinogenesis remains to be elucidated.

Aims & Methods: For the first time in the literature, we examined the possible role of M3 receptor-targeted miRNAs on two human colon cancer cell lines: H508, which expresses M3 receptors, and SNU-C4, which does not. Cell prolif- eration for 6 days after sodium taurocholoholat (ST) and atropin (A) treatment was analyzed by WST-1 method. Expression of M3 receptor gene at mRNA level was analysed by qPCR, and at protein level by Western Blot method. Apoptotic experiments were analyzed by Annexin V assay. MiRNAs which possibly target- ed M3 receptors were identified by in silico analyses. The methods were repeated three times, and the average values were calculated.

Results: When compared to SNU-C4 cells, M3 receptor gene expression was found to be increased 70-fold on H508 cells. After a 6-day incubation, maximum H508 cell proliferation (300%) was achieved on 5th day with a dose of 300 μM ST, inhibited by a dose of 1 μM A. In contrast, the SNU-C4 cells showed no significant change in cellular proliferation. Treatment of H508 cells with ST caused a decrease (2.5-fold) of M3 receptor gene expression, however, no change of M3 receptor at protein level was seen. No changes in apoptosis on both colon cancer cell lines were observed. Of 25 M3 receptor-targeted miRNAs, expression levels altered in 9; 6 of them were up-regulated (hsa-miR-129-5p, hsa-miR-30c-5p, hsa-miR-224-5p, hsa-miR-30b-5p, hsa-miR-522-3p, hsa-miR-1246) and 3 of them (hsa-miR-30e-5p, hsa-miR-147b, hsa-miR-855-3p) were down- regulated on H508 cells (p < 0.05).

Conclusion: ST interact with M3 receptors which modulate colon cancer cell proliferation on H508 cells. M3 receptor-targeted miRNAs are involved in ST induced proliferation. Whether the use of ursodeoxycholic acid, selective anti-cholinergic agents or other approaches to blocking potential inter- actions of bile acids/salts with neoplastic colonic epithelium may be a useful strategy for colon cancer prevention or treatment remains to be determined.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0443 COLORECTAL CANCER AND DYSLIPIDEMIA: CAUSE OR CONFOUNDING? A MENDELIAN RANDOMIZATION STUDY

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Introduction: Dyslipidemia and statin use have been associated to colorectal cancer (CRC), but prospective studies have shown controversial results. Dyslipidemia has been thought to have an important role in inflammatory pathways, oxidative stress and insulin resistance, which could contribute to the pathogenesis of cancer. However, findings from prospective studies that have examined the association between serum dyslipidemia (low density lipoprotein cholesterol (LDL), HDL or TG) and colorectal neoplasia have been inconsistent. [1–4] It is unknown whether lipids and lipoproteins cause cancer or are inter- mediate or correlated factors within carcinogenic pathways. Epidemiological studies could be confounded by 3-Hydroxy-3-methylglutaryl-coenzyme A re- ducase inhibitors (statins) use, which might also have a protective effect to CRC. It is unclear whether it is statin use or dyslipidemia that prompted statin use, which may be associated with CRC. Indeed, a large number of epidemiological studies have examined the effect of statins on colorectal cancer risk, with often inconsistent results.[5-6] A Mendelian randomization approach could help to establish a causal relationship between dyslipidemia and CRC.

Aims & Methods: We aimed at determining whether dyslipidemia is causally linked to CRC risk and to explore association of statins with CRC. A case- control study was performed including 1336 CRC cases and 2744 controls (MCC-Spain) between 2008 and 2013. Subjects were administered an epidemiolo- gical questionnaire that included lifetime regular use of prescription drugs. Also, subjects were genotyped with an exome array supplemented with 5000 custom SNPs. We applied the Mendelian randomization approach. The array included 136 SNPs previously shown to be associated with blood lipids levels in GWAS, that were used to build three genetic lipid scores, as the count of risk alleles. The scores were specific for low density lipoprotein cholesterol (LDL), high density lipoprotein cholesterol (HDL) or triglycerides (TG). We tested the association on regular statin use and the genetic lipid scores with logistic regres- sion models, adjusted for potential confounders.

Results: The LDL genetic risk score was significantly associated with statin con- sumption (OR = 1.07, 95% CI 1.05–1.10, p = 4.4e-11). The dyslipidemia genetic risk score was not significantly associated with CRC for either of the target lipid studied. Cases had the same average alleles as controls in all the lipids traits. Statin use was a borderline significant protective factor for CRC (multivariate adjusted OR = 0.83; 95%CI 0.69–1.00, p = 0.049).

Conclusion: Using the Mendelian randomization approach, our study does not support the hypothesis that lipid levels are associated with the risk of CRC. This study does not rule out, however, a possible protective effect of statins in CRC by a mechanism unrelated to lipid levels.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
**P0444** LINC00152 LONG NON-CODING RNA FACILITATES CELL PROLIFERATION AND PROMOTES THE TUMORIGENICITY OF CRC THROUGH REGULATION OF CELL CYCLE AND WNT SIGNALING PATHWAY

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**Introduction:** Long non-coding RNAs (lncRNAs) contribute to different cancers including colorectal cancer (CRC) through influencing cancer-related processes such as cell proliferation, apoptosis, and invasion. Previous studies have shown altered LINC00152 expression in CRC, but the detailed mechanism of its effects during colorectal carcinogenesis and cancer progression is not well studied.

**Aims & Methods:** We studied the effects of LINC00152 to the cell cycle regulation and promoter DNA methylation of several CRC-associated tumor suppressor genes in colon cancer cells. We also analyzed the expression and promoter DNA methylation of LINC00152 and of its regulated molecules in human colonic tissue samples. LINC00152 were silenced in SW480 colon carcinoma cells using Stealth siRNAs. Cells were harvested 48 or 72 hours after transfection. Flow cytometric cell cycle analysis was performed using propidium-iodide staining. Cyclin D1 protein expression was detected using flow cytometry after labeling with anti-cyclin D1 antibody. The effect of LINC00152 silencing to DNA methylation levels of SFRP1, SFRP2, SDC2 and PRIMA1 genes was studied using Methylight technology. Promoter methylation and expression of the above molecules were also studied on human colonic tissue samples.

**Results:** LINC00152 expression was successfully silenced in SW480 cells with 93–98% efficiency. Colorectal cancer cell lines with colorectal dysplasia and carcino-

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**P0445** GENETIC PROFILE OF POLYPS AND RISK OF ADVANCED METACHONDROUS LESIONS

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**Introduction:** Colorectal cancer cells are known to harbor concomitant mutations in KRAS and APC that promote carcinogenesis. Epigenetic dysregulation plays essential roles in the tumorigenesis of KRAS mutant CRC. Our preliminary data demonstrated that simultaneous KRAS gain-of-function mutations in APC-null CRC cells induced the hypermethylation of DNA and histones, an effect driven by metabolic rewiring of glutamine metabolism. We recently unveiled that glutamine metabolism in KRAS-mutant CRC could be rewired by the mitochondrial glutamate transporter, SLCA2A2, a synthetic lethal gene that is silenced in CRC and in vivo. In this study, we investigated the potential role of SLCA2A2-mediated glutaminolysis in regulating DNA and histone methylation in CRC, its underlying mechanisms, and the association of SLCA2A2 with epigenetic dysregulation in human CRC cohorts.

**Aims & Methods:** We aim to (1) evaluate the impact of mutant KRAS on DNA and histone methylation in CRC; (2) examine the role of SLCA2A2 in DNA and histone methylation in KRAS-mutant CRC; (3) elucidate the underlying mechanisms that underlies SLCA2A2-mediated epigenetic dysregulation; and (4) investigate the clinical relevance of the interplay between SLCA2A2 and KRAS mutation in CRC patients. DNA methylation was determined by the Illumina 880K methylation array and Methylight qMSP assays. Histone methylation was determined by the Histone H3 Modification Multiplex Assay Kit and Western blot. U-13C5-Glutamine metabolic labelling and analysis of glutamine metabolism via the TCA cycle was determined by liquid chromatography-mass spectrometry analysis. In clinical samples, SLCA2A2 mRNA was investigated by determining its correlation with CpG Island Methylator Phenotype (CIMP) status and histomorphologic marker (H3K36me2) was evaluated.

**Results:** Using three pairs of isogenic cell lines harbouring wild-type and mutant KRAS (DKS80/WT vs DLD1(mutant); HEK3(WT) vs HCT116(mutant); ICT(WT) vs ICT-KRAS(mutant)), we demonstrated that significant DNA and histone H3 hypermethylation in cell lines expressing mutant KRAS. DNA hypermethylation was associated with the up-regulation of 5-hmC, indicating suppression of DNA demethylation in KRAS mutant CRC cell lines. Metabolomic analysis revealed that KRAS mutation modified glutaminolysis via TCA cycle leading to high succinate and fumarate to α-ketoglutarate (αKG) ratio, which was to pivotal in suppressing the enzymatic activity of dioxygenases such as TETs. Reduced levels in histone demethylation in CRC were observed. Interestingly, simultaneously APC-loss and KRAS activating mutations synergistically up-regulated the expression of SLCA2A2, a key regulator of glutamine metabolism via the TCA cycle. CRISPR-Cas9 mediated knockout of SLCA2A2 suppressed glutaminolysis in KRAS-mutant CRC cell lines, which in turn, reduced the ratio of succinate and fumarate to α-ketoglutarate. The impact of SLCA2A2 knockout on glutaminolysis had a profound effect on epigenetic regulation, as DNA methylation profiling revealed that SLCA2A2 knock-

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**Aims & Methods:** We studied the influence of LINC00152 to the cell cycle regulation and promoter DNA methylation of several CRC-associated tumor suppressor genes in colon cancer cells. We also analyzed the expression and promoter DNA methylation of LINC00152 and of its regulated molecules in human colonic tissue samples. LINC00152 were silenced in SW480 colon carcinoma cells using Stealth siRNAs. Cells were harvested 48 or 72 hours after transfection. Flow cytometric cell cycle analysis was performed using propidium-iodide staining. Cyclin D1 protein expression was detected using flow cytometry after labeling with anti-cyclin D1 antibody. The effect of LINC00152 silencing to DNA methylation levels of SFRP1, SFRP2, SDC2 and PRIMA1 genes was studied using Methylight technology. Promoter methylation and expression of the above molecules were also studied on human colonic tissue samples.

**Results:** LINC00152 expression was successfully silenced in SW480 cells with 93–98% efficiency. Colorectal cancer cell lines with colorectal dysplasia and carcino-

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**Conclusion:** The genetic profile of polyps may be a useful tool for colonoscopy surveillance.

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Conclusion: SLC25A22 promotes the tumorigenicity of KRAS mutant CRC by driving altered DNA and histone hypomethylation, an effect mediated by increased production of TCA cycle intermediates succinate and fumarate, which inhibits DNA and histone demethylases. SLC25A22 is correlated with CIMP and histone hypermethylation in CRC patients.

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P0447 FOLLISTATIN-LIKE PROTEIN 1 SUSTAINS COLON CANCER CELL GROWTH AND SURVIVAL

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Introduction: Follistatin-like protein 1 (FSTL1) is a secreted glycoprotein, widely expressed in human tissues, which plays key functions in the regulation of cell survival, proliferation, differentiation and migration. Moreover, deregulated expression of FSTL1 has been described in malignancies but its contribution to carcinogenesis remains controversial.

Aims & Methods: We here investigated the expression and role of FSTL1 in sporadic colorectal cancer (CRC). FSTL1 was evaluated in human CRC samples and cell lines by immunohistochemistry, Western blotting and real-time PCR. Cell proliferation and survival and cell cycle were evaluated in human CRC cell lines (i.e., HCT-116, DLD-1) treated with a specific FSTL1 antisense (AS) or control RNA using Western blotting, cell counting and flow-cytometry. The expression of proteins involved in cell cycle progression, poly ADP-ribose polymerase (PARP), caspase-9 and active caspase-3. Moreover, the effect of FSTL1 knockdown on cell death was evaluated in cells cultured in the presence or absence of the pan-caspase inhibitor Q-VD-OPh by flow-cytometry.

Results: FSTL1 was significantly increased in both epithelial and lamina propria compartments of human CRC specimens as compared to controls. In CRC cell lines, FSTL1 knockdown caused accumulation of cells in G1 phase of the cell cycle and reduced CRC cell proliferation. FSTL1-deficient CRC cells had reduced levels of proteins involved in late G1 cell cycle phase, such as phosphorylated retinoblastoma protein (pRb), E2F-1, cyclin E and cyclin-dependent kinase-2 (CdK2), with no modification of early G1 phase proteins (i.e. cyclin D1). Treatment of CRC cells with FSTL1 AS increased the percentages of apoptotic cells and this effect was associated with activation of PARP, caspase-9 and caspase-3. Pre-incubation of HCT-116 and DLD-1 cells with Q-VD-OPh abolished the FSTL1 AS-induced cell death and reduced PARP and caspase activation, thus indicating that FSTL1 silencing induces CRC cell death through a caspase-dependent mechanism.

Conclusion: Our data indicate that FSTL1 is over-expressed in CRC cells and suggest a role for this protein in promoting intestinal tumorigenesis.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0448 TP53 MUTATION ACQUIRES HIGHER MALIGNANT POTENTIAL IN HUMAN COLON CANCER CELLS

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Introduction: Colon cancer, TP53 mutation is well known to occur in the late phase of colon carcinogenesis as adenoma-carcinoma sequence. Although numerous reports about clinical information of the patients with colon cancer have suggested that TP53 mutation might be related to various malignant potential in malignancy, the malignant potential on malignancy of TP53 mutation in colon cancer is still unknown. Notably, there is no report about a relationship between TP53 mutation and cancer stemness. We therefore aimed to assess the function of TP53 mutation in colon cancer cells, by using recently established lentiviral CRISPR Cas9 system.

Aims & Methods: Two types of TP53 mutation were generated in LS174T cells, which are derived from human colon adenocarcinoma with wild-type TP53 (WT-TP53), by using lentiviral CRISPR Cas9 system. The guide RNAs were designed to bind exon 3 or exon 10 of TP53, respectively. TP53 mutation in LS174T was confirmed by direct sequencing. The expression of TP53 protein was assessed by immunohistochemistry. Loss of function of TP53 was assessed by Nutlin-resistance and the down-regulation of TP53 target genes, suggesting that both mutants induced loss of function of TP53. We then assessed the effect of both TP53 mutants on various malignant potentials, resulting equally in accelerated cell growth, enhanced invasiveness and the resistance against 5-FU treatment compared to WT-TP53. Moreover, both mutants showed more frequent formation of 3D sphere and more expression of Lgr5 than WT-TP53, suggesting the promotion of cancer stemness by TP53 mutation even after being adenocarcinoma.

Conclusion: We for the first time showed the direct effect of TP53 mutation on malignant potential in colon cancer cells. Loss of function of TP53 induced by not only TP53Ex10 but also TP53Ex3 mutation, might promote malignant potentials including cancer stemness at the late phase of carcinogenesis. In general, TP53 mutation with loss of function of TP53 mutation in colon cancer is represented as TP53 mutation. However, negative staining of Lgr5 might also be careful for TP53 mutation to estimate malignant potential in colon cancer, since N-terminal mutation of TP53 in colon cancer has already been reported.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0449 PROTECTIVE EFFECT OF OPIOID RECEPTOR ACTIVATION IN THE DEVELOPMENT OF COLITIS-ASSOCIATED COLORECTAL CANCER IN MICE

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Introduction: Endogenous opioid system is involved in the maintenance of the intestinal homeostasis. Recently, we proved that stimulation of opioid receptors using P-317 – a novel cyclic morphiceptin analog with mu- and kappa-opioid receptor selectivity, decreased apoptosis of acute phase of experimental colitis (induced by dextran sodium sulfate (DSS)) in mice. Chronic inflammation is associated with increased risk of colitis-associated colorectal cancer. Stimulation of opioid receptors produces different effects on cancer progression depending on the cancer type and stage of disease.

Aims & Methods: The aim of our studies was to characterize the role of the endogenous opioid system in pathogenesis and treatment of colitis-associated colorectal cancer using P-317. Colitis-associated colorectal cancer was induced by a single intraperitoneal injection of azoxymethane [AOM] (10 mg/kg) and subsequent addition of DSS (1.5% w/v) into drinking water (week 2, 6, 9). From week 3, P-317 was injected intraperitoneally at the dose of 0.1 mg/kg twice per week and the body weight and clinical score (rectal bleeding, stool consistency) were assessed. After 14 weeks, the necropsy and colonic tissue score was assessed and the samples were collected and used for biochemical, molecular and histological studies.

Results: A significant difference in colorectal tumor development was observed between vehicle- and P-317-treated mice. P-317 significantly increased total number of colonic tumors as well as colon thickness and width after 14 weeks of disease induction. Myeloperoxidase activity, a marker of neutrophil infiltration, was inhibited by P-317 injections. Hematoloid and eosin staining confirmed the anti-tumor activity of P-317 as indicated by histological score connecting the following features: muscle thickness, damage of the intestinal wall, immune cell infiltration, invasion depth, crypt hyperplasia and disruption. The expression of IL-1β and TNF-α at mRNA level was decreased in P-317-treated mice as compared to vehicle-treated group.

Conclusion: P-317 may become an important pharmacological tool to study the factors that determine the development of inflammatory bowel disease and to define the role of the endogenous opioid system in chronic colitis and colorectal cancer.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0450 INCREASED HMGBI EXPRESSION CORRELATES WITH HIGHER EXPRESSION OF C-1AP2 AND PERK IN COLORECTAL CANCER

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Introduction: Colorectal cancer (CRC) is the third most common type of cancer in men and women, and it’s incidence is increasing in younger population. High mobility group box 1 (HMGBI) expression and subsequent death due to colorectal cancer is associated with its stage 1, 2. Because of its insulin onset, the diagnosis of CRC is usually delayed. However, serological markers can be a relatively easier and cheaper alternative tool for early screening. To find the high risk population using the hmgbi expression and subsequent death, we designed a study to test the sensitivity and specificity of hmgbi expression in colorectal cancer. To do that, we used the hmgbi high-mobility group box 1 (HMGBI) plays a critical role in tumorigenesis, disease progression and metastasis by activation of cancer cells, promotion of tumor angiogenesis, suggesting that HMGBI may be useful as a new biomarker of cancer 1, 2, 3, 4. Studies have shown that HMGBI is over-expressed in various types of cancers, include CRC, and those cases with higher expression of HMGBI are associated with lymphatic metastasis, distant metastasis and poor prognosis 5, 6, 7, 8. Several reports have demonstrated that HMGBI is
secreted by cancer cells may be involved in occurrence of tumor metastasis [6, 7]. In a study by M. V. Kruchinina et al., the authors found that HMGB1 secreted by the primary tumors had an apoptotic effect on the Kupfer cells which promoted development of liver. [6, 7]. Furthermore, some researchers showed that increased levels of c-IAP2 and pERK, the downstream effector molecules of HMGB1 are found in tumor tissues. The investigation of 55 metabolites may be useful for diagnosis and treatment of CRC. However, whether HMGB1 has any role in the development of CRC metastasis is not clear. In this study, we investigated the effects of HMGB1 on CRC, and the possible underlying mechanisms were examined.

Aims & Methods: In this study, we investigated the relationship between high-mobility group B1 (HMGB1) and colorectal cancer (CRC) and the probable underlying pathogenic mechanism. In this prospective study, patients with CRC undergoing primary surgery and healthy subjects (control group) were included from July 2013 to December 2014. Serum HMGB1 concentration was determined using ELISA and HMGB1 mRNA expression was detected by RT-PCR method. Immunohistochemical analysis was performed to determine HMGB1, pERK and c-IAP2 protein expressions in the cancer tissues. Results: 114 patients with CRC and 50 healthy subjects underwent serum HMGB1 testing. Resected specimen of 50 patients were used for HMGB1 mRNA and protein expression analysis. Serum HMGB1 levels in CRC patients were higher than that of the control group (6.82 ± 1.79 µg/L, p < 0.05). Preoperative serum HMGB1 concentrations were significantly higher than the postoperative values (8.42 ± 6.57 vs. 1.64 ± 1.89 µg/L, p < 0.05). Serum HMGB1 levels in CRC patients with distant metastases were significantly higher (13.32 ± 6.12 vs. 7.57 ± 5.17 µg/L, p < 0.05). HMGB1 mRNA and protein expression in CRC tissues was significantly higher than in the adjacent normal mucosa. HMGB1 protein expression positively correlated with the lymph node metastasis. There was positive correlation between HMGB1 and c-IAP2 (r = 0.457, P < 0.01), HMGB1 and pERK (r = 0.461, P < 0.05) as well as pERK and c-IAP2 (r = 0.399, P < 0.05).

Conclusion: HMGB1 expression in CRC correlates with distant and lymph nodal metastasis. It may inhibit apoptosis by inducing activation of pERK and c-IAP2.

Disclosure of Interest: All authors have declared no conflicts of interest.

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P0452 THE MICRONAS EXPRESSION PROFILES OF MULTIPLE COLORECTAL TUMORS
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Introduction: Accumulating data indicate that some microRNAs (miRNAs or miRs) function as tumor suppressors or oncogenes in cancer development. We previously reported that certain miRNAs (miR-143, -145, -7a, and -34a) were differentially expressed in samples of tumors and paired non-tumorous samples taken from the same patients with colorectal tumors, and there was a relation close to adenoma-carcinoma sequence for these miRNA expressions. Aims & Methods: In this study, we examined the mRNA expression profiles of multiple colorectal adenomas comparing between sporadic colorectal adenoma and familial adenomatous polyposis (FAP). We examined the miRNA expression profiles (miRs-143, -145, -7, and -34a) and morphological appearance of 102 sporadic colorectal adenomas (SA), 27 tumors of multiple colorectal adenoma (over 10 adenomas/one patient, MA), 21 tumors of FAP and 114 sporadic cancer (SC).

Results: The expression levels of miR-143 and -145 were reduced in all tumors compared with the paired non-tumorous samples in the same patient. Especially, these miRNAs were significantly reduced in MA (P = 0.042 and P = 0.004) and FAP (P = 0.027 and P = 0.022) compared with SA. The expression levels of miR-7 were significantly up-regulated in cancers compared with adenomas (P < 0.001). The expression levels of miR-34a were significantly down-regulated in CA (P < 0.001), MA (P < 0.001), and FAP (P = 0.006) compared with SA.

Conclusion: These findings suggest that the malignant potential of MA and FAP was higher than SA, therefore MA needs strict follow-up like FAP.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
Results: MPV, PCT, NLR and PLR were significantly higher in Group III compared to Group I (Table 1). However, only MPV was significantly lower in Group II compared to group I (8.6 ± 1.1 vs 8.2 ± 1, p < 0.001). The cut-off value of MPV in predicting CRC from patients with normal colonoscopy findings was 9.15 fL with a sensitivity and specificity of 80% and 91% respectively (r = 0.892).

MPV and PCT were also significantly higher in patients with neoplastic polyps compared to patients with non-neoplastic polyps (MPV: 8.7 ± 1.1 vs 8.4 ± 1, p < 0.001 and PCT: 0.23 ± 0.07 vs 0.19 ± 0.05, p = 0.003).

Conclusion: MPV and PCT may have a role as useful and simple markers in the diagnostic work-up of patients with colorectal cancer from patients with normal colonoscopic findings. In the clinical settings, these simple markers may be useful in selecting older patients for colonoscopy examination.

Disclosure of Interest: All authors have declared no conflicts of interest.

References


P0454 IMPROVING THE SELECTION OF COMPLETE RESPONDERS FOR WATCHFUL WAITING AFTER CHEMORADIOTHERAPY FOR RECTAL CANCER: WHAT CAN WE LEARN FROM THE ‘MISSED’ PATHOLOGIC COMPLETE RESPONDERS AFTER SURGERY?

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Introduction: Rectal cancer patients with clinical evidence of a complete response after chemoradiotherapy may be selected for watchful waiting instead of surgical resection (although currently mainly within the scope of clinical trials). The clinical selection of potential candidates for watchful waiting to date is mainly based on morphological features seen on endoscopic images performed post-surgery (normal/teleangiectatic, ulcer, polypoid) was assessed. Additionally, the likelihood for a complete response was re-scored by the expert team according to updated selection criteria and classified as (1) residual tumour or (2) near (3) CR.

Results: 41 patients with ypT0 after surgery were identified: 9/41 (22%) had ypT0N0, 32 (78%) were true complete responders (ypT0N0). Upon reassessment by the expert team, 20/32 ypT0N0 patients (63%) were still deemed to have residual tumour (non-CR group), the remaining 12 (37%) were deemed to be possible clinical complete responders (cCR-group). In the non-cCR group vs the non-CR group patients more often showed heterogeneous signal on T2W-MRI (75% vs.25%, p = 0.01), massive/spicular fibrosis (90% vs.58%, p = 0.007) and residual high signal on DWI (58% vs.27%, p = 0.11). On endoscopy the majority of patients still had mucosal abnormalities (see Table 1). Eight ypN0 patients were still overstaged as being N+ at reassessment, mainly based on irregular nodal morphology.

Table 1: Endoscopic features of patients with ‘missed’ complete response (pCR after surgery)

<table>
<thead>
<tr>
<th>Feature</th>
<th>Present in (%) of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gross residual tumour</td>
<td>33%</td>
</tr>
<tr>
<td>Polypoid tissue</td>
<td>38%</td>
</tr>
<tr>
<td>Ulcer with irregular border</td>
<td>29%</td>
</tr>
<tr>
<td>Flat ulcer</td>
<td>25%</td>
</tr>
<tr>
<td>White scar (with telangiectasia)</td>
<td>33%</td>
</tr>
</tbody>
</table>

Conclusion: Main reasons for missing a complete response after CRT are heterogeneous T2W-MRI signal, massive/spicular fibrosis, residual diffusion-signal, ypN+ disease and residual mucosal abnormalities at endoscopy. Knowledge about these features may serve as a teaching reference to help improve the selection of patients for watchful waiting in the future.

Disclosure of Interest: All authors have declared no conflicts of interest.

References


P0455 RADIOMICS AS A NOVEL TOOL FOR PRE-TREATMENT RESPONSE PREDICTION IN RECTAL CANCER


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Introduction: In patients with locally advanced rectal cancer (LARC) that show a very good response to neoadjuvant treatment, organ-preserving treatments such as watchful waiting may be a good alternative to surgical resection and can improve functional outcome and quality of life. If we can predict upfront (i.e. before commencement of CRT) how patients will respond to treatment this may create opportunities to further personalize and optimize the neoadjuvant treatment to enhance the chance of a good response, thereby ultimately offering more patients the chance of organ preservation. A promising new tool in this regard is Radiomics. Radiomics refers to a collection of analytical methods to convert images into high dimensional data via a set of quantitative descriptors called “features”. These features have the potential to uncover disease characteristics that cannot be detected by means of conventional (visual) imaging evaluation.

Aims & Methods: We aimed to assess the Radiomics signature of patients with LARC and evaluate its potential value for pre-treatment prediction of the response to neoadjuvant chemoradiotherapy.

We retrospectively assessed the primary staging MRIs (1.5T) of 124 LARC patients treated with CRT. The standard MRI protocol included T2W (T2W) and diffusion-weighted imaging (DWI) sequences, as well as quantitative apparent diffusion coefficient (ADC) maps derived from the DWI scans. For each patient, the whole volume of the rectal tumour was delineated on pre-treatment MRI, providing complete tumour regression (ypT0) versus residual tumour (ypT1-4) using histology and/or long-term FU as the standard of reference.

Results: Out of 3802 initially identified Radiomics features, 1853 proved stable across different readers/delineations. For the four manual delineations ±300/ 3802 features per reader remained significantly performant after FDR correction. However, these features did not sustain after FDR correction for the fully automated segmentation. A final subset of 266 features remained stable and performant across all five readers/delineations. These features resulted in a mean AUC of 0.67 (range 0.64-0.73) to predict a complete response and a mean ICC of 0.81 (range 0.75-0.95). Best results were obtained for textural features measuring the heterogeneity of the tumor on DWI (all top 20 features). In contrast, more ‘common’ radiological features such as volume showed inferior performance (highest rating 56) Results derived from delineations performed by the two expert radiologists and non-expert readers resulted in comparable diagnostic performance.

Conclusion: 1) Various Radiomics features extracted from pre-treatment MRI correlate to neoadjuvant treatment response and may be used as imaging biomarkers to predict the response to chemoradiotherapy in rectal cancer.

2) Best results are obtained for textural features (representing tumour heterogeneity) derived from diffusion-weighted MR sequences.

3) Features extracted from semi-automated (software generated) delineations show inferior performance compared to features extracted from manual delineations, emphasizing the need for adequate tumour delineation. Interestingly, however, delineations from expert and non-expert readers rendered similar good results, suggesting that the selected features are robust and do not necessarily require highly expert input.

Disclosure of Interest: All authors have declared no conflicts of interest.
P0456 CORRELATION OF ELECTRICAL AND VISCOELASTIC PARAMETERS OF ERYTHROCYTES WITH FATTY ACID COMPOSITION OF THEIR MEMBRANES AND SERUM IN PATIENTS WITH COLORECTAL CANCER

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Introduction: An analysis of the efficient implementation of the guidelines for screening colorectal cancer (CRC) in patients with first diagnosed CRC (according to the archival case histories of the two medical institutions in Novosibirsk) was performed in 2013-2016, and leading reasons of late CRC diagnostics were identified.

Aims & Methods: We aimed to investigate the correlation of the electrical and viscoelastic parameters of erythrocytes with the fatty acid composition of their membranes and blood serum in patients with colorectal cancer (CRC) of different stages. 46 patients (median age of 53 + 9 years old) with CRC of various localizations and stages and 16 conditionally healthy patients were examined. Electrical and viscoelastic parameters of erythrocytes have been studied by direct electrophoresis. Fatty acid composition of erythrocyte membranes and serum has been studied using GC/MS system triple quad Agilent 7000B (USA).

Results: Erythrocytes of patients with CRC were characterized by an increasing the proportion of deformed cells with reduced strain amplitude and surface charge (low levels of cell velocity to electrodes and dipole moment) (p < 0.001-0.05). Metastasis was associated with an increase in the cell electrical conductivity, a sharp decrease of polarizability, and an increase in the tendency to hemolysis (p < 0.0001-0.03). Saturated fatty acids prevailed in composition of erythrocyte membranes in patients with CRC; omega 6/omega 3 fatty acid index was decreased, while the level of linoleic acid was significantly increased as related to oleic acid in serum of the patients with CRC compared to the healthy people (p < 0.01-0.04). The observed shifts correlated with a disease stage (r=0.04; p=0.04). The erythrocyte strain amplitude was associated with the level of unsaturated fatty acids in erythrocyte membranes (r=0.58; p<0.05), as well as with summarized viscosity (r=0.47; p=0.03) and rigidity (r=0.41; p<0.05). While the analysis of distribution of fatty acids of erythrocytes and their tendency to aggregate correlated with the level of lysofatty acids of fatty acids (r= 0.54, p=0.04; r= 0.42, p < 0.05). The surface charge of erythrocytes more closely correlated to the level (C16:2 and C18:1) in the blood serum (r = 0.42; p=0.04). There was a slight increase in the crossover frequency to the high-frequency range (r=0.03), a decrease of the cell capacity (p < 0.01), and a decrease of polarizability at high frequencies (106, 0.5 x 106 Hz) (p=0.02-0.03), as well as a decrease of C18:3, C20:2, C20:5, C20:5 and C22:6 levels in erythrocyte membranes (but not in blood serum) of CRC patients.

Conclusion: Revealing changes in the parameters of erythrocytes and fatty acid composition in blood serum associated with a stage of the disease can be promising for diagnostics and the case follow-up of patients with CRC.

Disclosure of Interest: All authors have declared no conflicts of interest.

References


P0458 POST-INVESTIGATION COLORECTAL CANCER RATES INCLUDING POST COLONOSCOPY COLORECTAL CANCER RATES IN A DISTRICT GENERAL HOSPITAL: THE POOLE EXPERIENCE MARCH 2015 TO FEBRUARY 2017

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Introduction: Post-colonoscopy colorectal cancer (PC-CRC) rates are proposed as an important measure of quality of colonoscopy service. Extrapolating PC-CRC rates is important but important to assess local practice and to compare with recent published National Data. We aimed to calculate the PC-CRC and the post CT (Colonoscopy + abdomen) CRC rate at Poole Hospital using the number of colonoscopies or CT scans done within 3 years of a CRC diagnosis as the denominator for post-investigation PI -CRC calculations as outlined in a previous study1

Aims & Methods: Retrospective audit of all patients diagnosed with CRC during the initial period 1st March 2015-28th February 2017 included identified via the Somerset Cancer registry database for Poole Hospital using Crystal software. Previous colonoscopy and CT Colonoscopy (CTC) or CT abdomen results in the 3 years preceding the diagnostic investigations were reviewed across two neighbouring hospitals sharing the same electronic patient records. If patients had multiple surveillance colonoscopies the latest was counted as false negative as in previous studies2

Results: 416 patients were identified, 67 were excluded (39 non adenocarcinoma, 3 out of area, 12 patients where earlier decision was best supportive care, 6 patients diagnosed at laparotomy, 2 patients with abnormal PET scans and 6 with incomplete datasets). 348 patients were included for analysis. Colorectal cancer was diagnosed by colonoscopy in 200 patients and by CTC or CT for the remaining 148 patients in 148 cases. In the colonoscopy diagnosed group, 55 were via Bowel Cancer Screening Programme (BCSP), 138 via the symptomatic service and 7 from the surveillance programme. In the BCSP group 1 patient had a preceding colonoscopy within the previous 3 years. In the symptomatic service groups there were 7 preceding colonoscopies and in the surveillance group there were 5 preceding (“false negative”) colonoscopies within the previous 3 years. The overall PC-CRC rate was 6.5 (+3.6, +2.2 %) (90% confidence interval). In the BCSP diagnosed group, 1 patient with a preceding BCSP colonoscopy and the symptomatic service 4 from the surveillance group underwent CT scans within the preceding 6–36 months. All bar one of these 15 patients had undergone preceding CT abdomen scans with one elderly patient from the symptomatic service group having undergone a CT colonoscopy. The post CT-CRC rate was 10.2 (+5.0, +3.2 %) and the overall combined post investigation colorectal cancer (PI-CRC) rates during this two year period was 8.0 (+2.8, +2.0 %).

Conclusion: Our findings offer the opportunity for further review of individual patients to clarify their clinical course. The method of calculating PI-CRC rates needs ratification as well as more robust IT systems to capture and analyse the data if it is indeed a measure that is to become part of endoscopic quality assurance. Finally our numbers are small and methods suitable for retrospective observational population based studies may not transfer to assessing quality indicators at a local level.

Disclosure of Interest: S.D. Parry: None
E.J. Williams: None
RISK OF DETECTION OF GASTROINTESTINAL NEOPLASMS AND DEATH IN SYMPTOMATIC PATIENTS WITH A POSITIVE FECAL IMMUNOCHEMICAL TEST WITHOUT COLORECTAL CANCER

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Introduction: The fecal immunochemical test (FIT) has a high diagnostic accuracy for the detection of colorectal cancer (CRC) in symptomatic patients. However, we do not know the risk of other gastrointestinal neoplasms associated with a false positive test.

Aims & Methods: To calculate the risk of detection of gastrointestinal tract tumors (GITT) and death in symptomatic patients with a positive FIT determination and without a CRC in a complete colonoscopy with an adequate bowel preparation. We designed a prospective cohort study with follow-up. Patients from the COLONPREDICT study with complete colonoscopy without CRC were included. Two cohorts were defined: FIT positive and negative according to the ≥20ng/hemoglobin/g feces threshold. We performed a descriptive analysis of factors detected during follow-up and mortality. We estimated the differences in the risk of GITT detection and mortality between the two cohorts by logistic regression and proportional hazards after adjusting for age, sex, and significant colonic lesions (CSL) detection at baseline colonoscopy.

Results: We included 1061 patients without CRC and a complete baseline colonoscopy; 320 (30.2%) with a positive FIT and 741 with a negative FIT. The median follow-up was of 36.0±8.9 months with no difference between both groups (p=0.2). There were significant differences regarding age (67.5±12.7 years vs. 64.8±13.5 years, p=0.004) and sex (45.9% vs 52.0% females, p=0.04) between both cohorts. We detected a GITT in 14 (4.4%) patients with a positive FIT: 5 CRC, 6 gastric, 1 small intestinal lymphoma and one patient with a CRC and a small intestine adenocarcinoma; and in 12 (1.6%) with a negative FIT: 4 CRC, 2 small intestine adenocarcinoma, one esophageal, and one patient with a gastric and a CRC. Patients with a positive FIT had a non-significant increase in the risk of GITT detection (OR 2.1, 95% CI 0.9–4.8) after adjusting for age, sex and SCL. The overall risk of death in both groups was 8.8% and 6.7%, respectively, with no significant differences between both groups in the survival analysis (HR 1.3, 95% CI 0.8–2.1). However, the risk of death due to a GITT was 3.1% (10 deaths) in the positive FIT group and 0.8% (6 deaths) in the negative FIT group, with a significant difference after adjusting for age, sex and SCL (HR 3.2 95% CI 1.2–8.9).

Conclusion: Symptomatic patients with a positive FIT and complete colonoscopy without CRC are at increased risk of death due to GITT regardless of age, sex or the presence of SCL.

Disclosure of Interest: All authors have declared no conflicts of interest.

FACTORS ASSOCIATED WITH THE TECHNICAL DIFFICULTY OF DOUBLE-WIRE VENOUS UNCOVERED SELF-EXPANDABLE METALLIC STENT PLACEMENT FOR MALIGNANT COLORECTAL OBSTRUCTION

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Introduction: Self-expandable metallic stent placement for malignant colorectal obstruction has been widely used; however, factors affecting the technical difficulty of stenting remain unclear.

Aims & Methods: The aim of this study was to clarify the factors associated with the technical difficulty of stenting for malignant colorectal obstruction. We established the Colonic Stent Procedure Research Group to provide instructions on how to perform stenting and to conduct this prospective, single-arm, observational, multicenter clinical trial between October 2013 and May 2014 in Japan. Thirty-two facilities participated in this study. A double-wire venous uncovered stent was placed by using a standard through-the-scope colonoscopic placement technique in each patient. Stent deployment time was defined as the time from reaching a lesion with a colonoscope to finishing the technical difficulty of stenting. Technically difficult cases of stenting were defined as independent factors associated with the technical difficulty of stenting by univariate and multivariate analyses.

Results: A total of 205 consecutive patients were enrolled in this study. Nine patients including 3 patients with technical failure of stenting, 5 patients with non-stenting and 1 patient with stenting for benign lesion were excluded. The remaining 196 patients were succeeded in stenting. Of these, 100 were men (51%) and the median age was 72 years old (interquartile range (IQR), 62–82 years old). One hundred eleven patients (57%) underwent stenting as a bridge to surgery, and 85 (43%) underwent stenting for palliation. The technical and clinical success rates were 98.5% and 97.0%, respectively. None of the patients experienced colorectal perforation. The median total procedure time in the cohort with technical success was 30 minutes (IQR, 18–42 minutes). The median deployment time was 21 minutes (IQR, 11–31 minutes). Forty-nine patients with a deployment time longer than 31 minutes were regarded as technically difficult cases of stenting. The following factors were identified as independent factors of the technical difficulty of stenting: presence of ascites (odds ratio, 2.483; 95% confidence interval [95%CI], 1.17–5.29; p=0.02), placement of >1 stent (odds ratio, 4.80; 95%CI, 1.10–21.1; p=0.04).

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T. Yamada: personal fees: Century Medical Inc
T. Kawai: personal fees: Boston Scientific Japan, Century Medical Inc
S. Saito: personal fees: Century Medical Inc., Boston Scientific Japan
References
1 Int J Cancer 2014; 136: E359–86.
Conclusion: At this mid-study follow-up, paclitaxel-eluting stents appear to be efficacious for the three study groups.

Days 15 and 30 were selected to allow initial drug elution and to compare drug release to drug elution, respectively. At both 30 and 60 days post-implant, no persistent clinical symptoms were observed in any animal. Bile duct dilation and increased tissue overgrowth in all stent groups, which was expected to occur in the bare metal stent group, was not observed. A 4 cm length uncovered, laser-cut nitinol stent was coated with a polymer matrix allowing slow release of paclitaxel. Naïve Yucatan swine were assigned to each of the three study groups: control (n = 3, no polymer), standard dose paclitaxel (n = 6, 149.4 µg paclitaxel) and challenge dose (n = 3, 538.0 µg paclitaxel). Two stents were endoscopically implanted in each swine from its assigned group. One stent was placed proximal to the papilla. Stents were assessed for migration via digital radiographs for the first 2 weeks and then monthly via endoscopy using SpyGlass™ DS cholangioscopic and cholangiography with a targeted 6 month study endpoint. Results: At 30 days post-implant, no significant tissue reaction to any stent was observed. However, all animals displayed mild biofilm formation and increased intraductal mucous production. Substantial dilation of the common bile duct was observed in 5/11 animals with no apparent relationship between drug coating and bile duct dilation. At 60 days post-implant, moderate mucus and biofilm formation was observed within the stent, however in only 3 animals bile duct dilation persisted and in the majority of stents were fully apposed to the duct wall. Although some animals displayed minimal tissue hyperplasia at the proximal end of the stents, no tissue overgrowth or stent embedding was observed in any animal. Up to 60 days post-implant, no persistent clinical symptoms were observed in any animal. Reduced dose animals were removed from the study between days 15 and 30, while all animals continued to be observed. At 60 days post-implant, no increase in number of dilated ducts between days 30 and 60, we expect increased rate of in vivo drug release rates in the bile duct over a 30 day period. Future cholangioscopic and histopathological assessment of these swine will further clarify the safety and effectiveness of paclitaxel stent coatings to mediate bile duct tissue ingrowth.

Disclosure of Interest: J.T. Favreau: John Favreau is an employee of Boston Scientific.

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Meta-analysis and guidelines recommend that the first line of treatment for indwelling malignant biliary stent patency rates. Complete endoscopic mucosal resection of malignant colorectal cancer (CRC) based on collagen gel droplet-embedded drug sensitivity test (CD-DST) and individualized first-line therapy with the CD-DST may improve the prognosis of patients with unresectable CRC (UEGW: 2014: P1538; 2015: P1681; 2016: P0929).

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Aims & Methods: In this prospective study, we evaluated the overall survival (OS) of low rectal cancers with chemoradiotherapy and those with inappropriate first-line chemotherapy group based on CD-DST. Moreover, we evaluated additional effects of EGFR (Cetuximab; Cmab, Panitumumab; Pmab) to FOLFOX/FOLFIRI using CD-DST. Between Mar. 2008 and Aug. 2016, we obtained tumor specimens from 131 CRC patients without preoperative chemotherapy. Informed consent for measurement of individual chemosensitivity was obtained from all patients in writing. Approval for the present study was obtained from the Tobu Chikhi Hospital Institutional Review Board (No: 02.03.29. #1). The growth inhibitions were determined by CD-DST. The regimens were as follows: FOLFOX, FOLFIRI, Cmab, Pmab, and FOLFOX/FOLFIRI + Cmab. The incubation conditions were as follows: FOLFOX, 5-FU and 1-OHP (6.0 and 3.0 μg/ml, respectively) for 24 h. FOLFIRI, 5-FU and SN-38 (6.0 and 0.2 μg/ml, respectively) for 24 h. FOLFOX, Cmab and Pmab for 144 h. Pmab; Pmab 200 μg/ml for 144 h. FOLFOX + Cmb; Cmb 250 μg/ml for 120 h after FOLFOX/FOLFIRI incubation process. The cumulative distribution of IR values under each condition was evaluated on the basis that the clinical response to chemotherapy is equivalent (approximately 50%). The OS between the group treated with appropriate first-line chemotherapy and the group treated with inappropriate first-line chemotherapy were evaluated Kaplan-Meier method. Additional effects of Cmab to FOLFOX/FOLFIRI were also evaluated. Results: There was strongly relationship between the IR% of the FOLFOX and FOLFIRI regimen (R² = 0.7415). The median of the IR% with the FOLFOX and FOLFIRI regimen were 58.6 and 69.1, respectively. FOLFOX responder, FOLFIRI responder, dual responder, and poor responder were 8, 10, 53, and 60, respectively. There were 42 unresectable CRC patients with chemotherapy. The FOLFOX responder, dual responder, and poor responder were 58.6 and 69.1, respectively. FOLFOX regimen were 58.6 and 69.1, respectively. FOLFOX, FOLFIRI, Cmab and that of Pmab (R² = 0.686). Additional rates (%) of Cmab to FOLFOX between poor responder and other responder were 19.81 and 5.46, respectively (P=0.020). Additional rates of Cmab to FOLFIRI between poor responder and other responder were 16.50 and 1.29, respectively (P=0.005). There was significantly more additional effect of Cmab to FOLFOX/FOLFIRI in poor responder than in other responders.

Conclusion: Administration of the recommended first-line regimen using CD-DST is an effective strategy for CRC patients. Moreover, especially in poor responder, Cmab should be administrated to FOLFOX/FOLFIRI regimen.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference:

P04608 LONG-TERM COLONOSCOPIC SURVEILLANCE BETWEEN PATIENTS WITH UNRESECTED DIMINUTIVE POLYPS AND THOSE WITH COLORECTAL ADENOMAS > 5MM IN SIZE RESECTED AT INITIAL COLORECTAL CANCER SURGERY.
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Introduction: A long-term risk of colorectal advanced neoplasia among patients having diminutive polyps at initial colonoscopy has been unknown. The present study aimed to compare the risk of metachronous advanced neoplasia during follow-up between patients with untreated diminutive colorectal polyps and those with small or large adenoma resected at baseline colonoscopy.

Aims & Methods: A total of 1595 patients were colonoscopically followed-up during a long-term period in our hospital. They were divided into group A, B, and C as follows: A group (mean age 64.7 yr, M:F = 2.37:1) with low-grade adenoma colonoscopically resected at baseline, 245 in group B (66.1 yr, 2.31:1) with high-grade adenoma or intramucosal cancer colonoscopically resected at baseline, and 388 in group C (65.1 yr, 1.54:1) with invasive cancer resected at baseline. During follow-up colonoscopies detected metachronous neoplasms were resected and pathologically evaluated into non-inferior lesion (low-grade adenoma) or index lesion (high-grade adenoma or cancer). The cumulative incidences of metachronous colorectal neoplasms were compared with each other using Logrank test.

Results: Median follow-up periods and frequencies of colonoscopy were 64.3 months and 3.7 times in group A, 52.0 months and 3.5 times in group B, and 74.6 months and 3.9 times in group C, respectively. The cumulative incidences of metachronous non-index lesion were 24.5% (109 patients with 299 low-grade adenomas) in group A, 26.1% (64 with 184) in group B, and 19.3% (75 with 229) in group C, respectively. The prevalence of metachronous non-index lesion was lower in group B compared to that in group A (p = 0.07), and group C compared to that in group B (p = 0.05). Logrank test revealed that the cumulative incidence of metachronous non-index lesion in group B, 31 (31 patients with 3 high-grade adenomas or cancers) in group A, 6.9% (17 with 17) in group B, and 12.3% (48 with 55) in group C, respectively. The prevalence of metachronous index lesion was higher in group C compared to that in group A (p < 0.05) and group B (p < 0.05). The cumulative incidences of metachronous invasive cancer were 0.9% (4 patients with 4 invasive cancers) in group A, 1.2% (3 with 3) in group B, and 3.6% (14 with 14) in group C, disclosing highest prevalence in group C (p < 0.05). Logrank test revealed that the cumulative incidence of metachronous non-index lesion was highest in group C, and significantly different differences were observed compared to those in group A and B.

Conclusion: Significant higher prevalence of metachronous index lesion including invasive cancer and, in contrast, significantly lower prevalence of metachronous non-index lesion were observed in patients after resection of colorectal cancer compared to those after endoscopic resections of colorectal adenoma and intramucosal cancer.

Disclosure of Interest: All authors have declared no conflicts of interest.
incidences of metachronous colorectal neoplasms were compared with each other group. Log rank test.

Results: Median follow-up periods and frequencies of colonoscopy were 61.9 months and 3.6 times in group A, 61.6 months and 3.4 times in group B, and 72.3 months and 2.7 times in group C, respectively. The cumulative incidences of metastatic colorectal cancer were 24.1% (30 patients with 375 low-grade adenomas) in group A, 14.7% (73 with 168) in group B, and 6.6% (34 with 56) in group C, respectively. The prevalence of metachronous non-index lesion was highest in group A followed by those in group B and C, with significant differences observed between group A and B (p < 0.0005), and B and C (p < 0.05). The cumulative incidences of metachronous invasive cancer were 1.0% (6 patients with 6 invasive cancers) in group A, 1.4% (7 with 7) in group B, and 0.2% (1 with 1) in group C. No significant differences were observed, and logrank test revealed that the cumulative incidence of non-index lesion was highest in group A, and statistical significances were observed between group A and B (p < 0.0001), and between group B and C (p < 0.00001). Logrank test also revealed that the cumulative incidence of index lesion was highest in group A, and statistical significances were observed between group A and B (p < 0.005), and between group B and C (p < 0.005).

Conclusion: The results of a longer colonoscopic follow-up disclosed a significantly higher prevalence of metachronous advanced neoplasms in patients with adenoma >5mm in size resected at baseline compared to those with diminutive polyps left untreated at baseline. Persons with no polyps at baseline colonoscopy were at very low risk of advanced neoplasia within five years during follow-up.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0470 A NEW SCORING MODEL FOR PREDICTING ADVANCED COLORECTAL NEOPLASMS IN ASYMPTOMATIC SCREENING POPULATION AND COMPARISON WITH THE MODIFIED ASIA-PACIFIC COLORECTAL SCORING SCORE

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Introduction: Colorectal Cancer (CRC) is one of the major causes of death even in countries with a CRC screening program, indicating the need for improved screening methods. Risk-stratification of populations is one strategy that might satisfy this requirement. Currently, in the Asia-Pacific region, the use of the modified Asia-Pacific Colorectal Scoring (APCS) score [age 50–59: 1 point, age ≥60: 2, male sex: 1, presence of a first-degree relative (FDR) with CRC: 1, current or past smoker: 1, body mass index (BMI) ≥23kg/m²: 1] has been proposed for risk-stratification.1,2 However, further validation studies are required to approve the proposed model and considering the reported limited discriminatory capability of the score for advanced colorectal neoplasia (ACN), the development of a more useful scoring model is expected.

Aims & Methods: The aim of this study was primarily to develop and validate a new scoring model for predicting ACN in an asymptomatic screening population that is more useful than the APCS score. We externally validated the APCS score in a Japanese screening population and compared its discriminatory capability with that of our new scoring model. Data were reviewed from 5218 consecutive asymptomatic screened individuals who underwent colonoscopy for their first time at the Cancer Screening Center, National Cancer Center Hospital, Tokyo between February 2004 and March 2013. Multivariate logistic regression was used to investigate the associations between clinical variables and the presence of ACN in the subjects, and then a new scoring model was developed based on these associations. Scores were weighted according to the beta coefficient obtained from the logistic regression model. Thereafter, the discriminatory capability of the new model was assessed using the c-statistics in the development set. Performance of the new model was internally validated using bootstrapping with 1000 replicates. The discriminatory capability of the modified APCS score in the 5218 subjects was also assessed using the c-statistics. The value obtained was weak positively correlated with threshold for first RS (r = 0.03).

Conclusion: An 8-point scoring model to predict ACN in asymptomatic screening population that might have a higher discriminatory capability than the modified APCS score was developed and internally validated in this study. Our simple scoring model could stratify the screened population into low-, moderate-, and high-risk groups. Of the detected ACN, a substantial number were proximal or flat; therefore, primary screening with total colonoscopy may be advisable for high-risk individuals.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P0471 ASSOCIATION BETWEEN PARAMETERS OF THE RECTAL INDEPENDENT REFLEX AND THRESHOLD FOR FIRST RECTAL SENSATION ESTABLISHED BY HIGH-RESOLUTION ANORECTAL MANOMETRY (HRAM) AND ITS SIGNIFICANCE FOR FECAL INCONTINENCE DIAGNOSTICS

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Introduction: Previous studies have shown that increase of threshold for first rectal sensation can be a predictor of fecal incontinence. However, significance of the entire range of rectal inhibitory reflex (%)RAIR in development of this disease remains unknown.

Aims & Methods: To determine association between %RAIR and threshold for first rectal sensation in healthy adults and its significance in development of fecal incontinence. 26 asymptomatic healthy volunteers (18 women, 8 men) median age was 35.03 years (19–59) were studied. We performed a high-resolution anorectal manometry (HRAM) using a 20 channels silicone water-perfused catheter (Solar GI, MMS, Netherlands). The following HRAM parameters were analyzed: threshold for RAIR and %RAIR (automatically calculated as the ratio of the amplitude of the relaxation of the anal sphincter (AS) to the basal pressure AS *100%), threshold for first rectal sensation (RS) and for desire to defecate. The statistical analyses were performed using Statistica for Windows 6.0 (StatSoft Inc.).

Results: Threshold for RAIR and %RAIR were 22.3 ml (10.0; 30.0), 7.44% (38; 99.5) respectively. Threshold for first RS was 30.07 ml (11.1; 58.3) and desire to defecate – 65.12 ml (33.5; 182.0). Threshold for RAIR was not associated with threshold for first RS (r = 0.00005), and for desire to defecate (r = 0.02). %RAIR was weak positively correlated with threshold for first RS (r = 0.26) and was not associated with threshold for desire to defecate (r = -0.03).

Conclusion: Threshold for RAIR and %RAIR are not associated with first rectal sensation. So, these parameters of RAIR cannot be predictors of fecal incontinence.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0472 AVOIDANT COPING AND SOMATIZATION PARTLY EXPLAIN THE RELATIONSHIP BETWEEN NEUROTICISM AND GASTROINTESTINAL SYMPTOM BURDEN

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Introduction: Trait neuroticism and the DeLong et al. questionnaire consistently found to be associated with more severe functional gastrointestinal (GI) symptoms (1). One explanation for this is that high neuroticism predisposes individuals towards avoidant coping by leading them to view negatively-valenced situations as catastrophic (2) and, therefore, unsolvable (3). Avoidant coping, in turn, increases the risk of developing GI discomfort because over-reliance on “flight” strategies in stressful situations overstimulates the sympathetic nervous system at the expense of parasympathetic activity necessary for digestion (4). Evidence for this proposed chain of events is substantiated by findings of relationships between each pair of the chain’s components: neuroticism and avoidant coping (e.g., 3), and avoidant coping and higher GI symptom burden (e.g., 1). Across two studies, this paper integrates these findings, while also exploring the role of somatisation. Somatisation is consistently observed in people suffering from functional GI Conditions (e.g., 1) and refers to a subtype of avoidant coping - avoidant coping and GI symptoms are connected would need to be expanded to

Conclusions: Avoidant coping is significantly linked to higher GI symptom burden, and this effect is mediated by trait neuroticism. The role of somatisation in these findings needs to be considered in further studies.
predict that somatisation has deleterious consequences for GI conditions - possibly because it encourages reduced physical activity (7). Aims & Methods: In Study 1, 147 undergraduate students completed measures of neuroticism, 14 coping styles (including avoidant styles such as denial and disengagement), somatisation and GI symptom burden. In Study 2, where participants were undergraduates and hospital outpatients (pooled N=250), the variables investigated in Study 1 were measured alongside hypochondriasis, which was included to measure the aspect of somatisation that involves worry independently of any actual physical symptoms. Statistical analysis was based on path modeling. It involved fitting a model to test a priori hypothesised indirect relationships between neuroticism and GI symptom severity via the selected coping styles and somatisation. Direct effects were also estimated, meaning that the path analysis provided information regarding the significance of any indirect effects once a range of direct effects were accounted for. Only six coping styles found to correlate significantly with any actual physical symptoms. Statistical analysis was based on path modeling. Results: Significant standardised path model coefficients involving neuroticism across the two studies. In Study 1, neuroticism exerted indirect effects on symptom burden through substance-use-based coping and somatisation, as well as through disengagement-based coping and somatisation. In Study 2, neuroticism affected GI symptom burden through denial-based coping and somatisation, as well as through denial-based coping and hypochondriasis. An indirect effect of neuroticism through self-blame and somatisation, with the two intermediary variables relating negatively to each other, was observed in Study 1. (Note: *p < .05, **p < .01, ***p < .001). (n.s. denotes non-significant coefficients). Conclusion: Somatisation and hypochondriasis were found to be intervening variables in the relationship between neuroticism, avoiding coping (through substance-use, disengagement and denial) and GI symptom burden. Two interpretations of the findings are: (1) avoidance reduces the impact of neuroticism on reduced physical activity, which can interfere with digestion; and (2) GI symptoms are among the wide range of functional somatic symptoms that can arise from avoidance coping. These findings open new avenues for multidisciplinary treatment of FGIDs. Disclosure of Interest: All authors have declared no conflicts of interest.

References
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P0473 POTENTIAL REGULATORY EFFECTS OF CORTICOTROPIN-RELEASING FACTOR ON TIGHT JUNCTION-RELATED INTESTINAL EPITHELIAL PERMEABILITY ARE PARTIALLY MEDIATED THROUGH CK8 UPREGULATION
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Introduction: This study aimed to investigate the regulatory effects of corticotropin-releasing factor (CRF) on the permeability of human intestinal epithelial cells through CK8-mediated tight junction. Aims & Methods: The expression of CRFR1 and CRFR2 on HT29 cell surfaces were upregulated by immunostaining (7). Results: CRF treatment with 100 nM CRF for 72h, the transmission of FITC-labeled Dextran was measured by a transwell chamber; the structural changes of tight junctions were observed under transmission electron microscopy; the expression and function of tight junction protein occludin were detected by immunoblotting and immunofluorescence. The activity of RhoA was detected by immunoprecipitation. Furthermore, effects of CRF on intestinal epithelial permeability were examined in CK8-silenced HT29 cells, which were constructed by shRNA interference. Results: CRF treatment increased FITC-labeled Dextran permeability, caused opening of tight junctions, induced increased fluorescence intensity of CK8 and decreased intensity of ZO-1, claudin-1, and occludin, together with structure destruction. The expression and function of tight junction protein occludin were downregulated. RhoA activity peaked at 30 min after CRF treatment. The increased permeability and the downregulation of claudin-1 and occludin induced by CRF treatment were not blocked by CK8 silencing. Nevertheless, CK8 silencing blocked the effects of CRF with regard to decrease in the expression of F-actin and ZO-1 and increase in RhoA activity. Conclusion: CRF may increase intestinal epithelial permeability by upregulating CK8 expression, activating the RhoA signaling pathway, promoting intestinal epithelial actin remodeling, and decreasing the expression of the tight junction protein ZO-1. Other CRK8-independent pathways may lead to decreased expression of claudin-1 and occludin, which also contributes to increased intestinal epithelial permeability. Disclosure of Interest: All authors have declared no conflicts of interest.

P0474 REGULATING EFFECTS OF TONGXIE-YAOFANG FORMULA ON COLONIC MUCOSAL INFLAMMATION IN RATS WITH DIARRHEA-PREDOMINANT IRRITABLE BOWEL SYNDROME
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Introduction: Diarrhea-predominant irritable bowel syndrome (D-IBS) is a chronic functional gastrointestinal disease. Its clinical manifestations are characterized by diarrhea and abdominal pain or discomfort in the absence of a structural basis. D-IBS is not self-limiting and is often accompanied by demonstrable pathology. The diagnosis of D-IBS is based on symptom assessment and the Rome III Diagnostic Criteria. According to an epidemiological study, D-IBS mainly affects young adults of 20–40 years old, and the quality of their lives is seriously affected. The pathogenesis of D-IBS has not been clarified. Consequently, the usual treatment of the disease in Western medicine involves symptomatic therapy, which is unsatisfactory for patients while simultaneously increasing the use of health-care resources. Because traditional Chinese medicine (TCM) can significantly improve patients' symptoms and quality of life, increasing numbers of patients have begun to seek treatment with TCM. A series of randomized, double-blind, placebo-controlled trials had shown that Tongxie-YaoFang (TXYF) formula can significantly improve the clinical symptoms, such as diarrhea and abdominal pain or discomfort, of patients with IBS and improve the quality of their lives. However, the specific mechanism of it has not been completely elaborated. The purpose of this paper is to observe the regulating effects of TXYF-formula on colonic epithelial secretion via relevant indices.

Aims & Methods: To investigate the pharmacological effect of Tongxie-YaoFang (TXYF) formula, a Chinese herbal formula, on Diarrhea-predominant irritable bowel syndrome (D-IBS) rats. The effect of neonatal maternal separation plus restraint stress (NMS+RS) model of D-IBS, male Sprague Dawley rats were randomly divided into two groups (NMS+RS group and TXYF-formula group) with no handlings were used as controls (NH group). Starting from the postnatal day 60, rats in TXYF-formula group were administered TXYF-formula (4.92g/100g bodyweight) orally twice a day for 14 consecutive days while NH group and NMS+RS group were given distilled water. Using short-circuit current technology, we observed 5-HT-induced changes of current across ion channels, as such as cystic fibrosis transmembrane conductance regulator (CFTR) Cl channel, epithelial Na channel (ENaC), Ca2+-dependent CI channel (CACC), Na+-K+-2Cl co-transporter (NKCC), and Na+-HCO3 co-transporter (NBC), in the colonic epithelium of three groups after exposure to D-IBS for 14 days. The expression of CRFR1 and CRFR2 on HT29 cell surfaces were examined with immunostaining, and the permeability of human intestinal epithelial cells through CK8-mediated tight junction was measured by a transwell chamber; the structural changes of tight junctions were observed under transmission electron microscopy; the expression and function of tight junction protein occludin were detected by immunoblotting and immunofluorescence. The activity of RhoA was detected by immunoprecipitation. Furthermore, effects of CRF on intestinal epithelial permeability were examined in CK8-silenced HT29 cells, which were constructed by shRNA interference. Results: CRF treatment increased FITC-labeled Dextran permeability, caused opening of tight junctions, induced increased fluorescence intensity of CK8 and decreased intensity of ZO-1, claudin-1, and occludin, together with structure destruction. The expression and function of tight junction protein occludin were downregulated. RhoA activity peaked at 30 min after CRF treatment. The increased permeability and the downregulation of claudin-1 and occludin induced by CRF treatment were not blocked by CK8 silencing. Nevertheless, CK8 silencing blocked the effects of CRF with regard to decrease in the expression of F-actin and ZO-1 and increase in RhoA activity. Conclusion: CRF may increase intestinal epithelial permeability by upregulating CK8 expression, activating the RhoA signaling pathway, promoting intestinal epithelial actin remodeling, and decreasing the expression of the tight junction protein ZO-1. Other CRK8-independent pathways may lead to decreased expression of claudin-1 and occludin, which also contributes to increased intestinal epithelial permeability. Disclosure of Interest: All authors have declared no conflicts of interest.
Aims & Methods: The aims of the present study were to evaluate the effect of diosmectite on gut transit time and visceral hypersensitivity induced by WAS in rats. For this purpose, visceral hypersensitivity (CVH) was induced by colonic injection of 0.5% acetic acid (AA) in 10-day old rats while control (NS) induced with 0.9% NaCL (CVH-NS). A group of control with no stress but with WAS (Con-sham) was used as another AWR was assessed, and the hippocampus and prefrontal cortex (PFC) and its metabo-

References

P0475 DIOSMECTITE CHRONIC TREATMENT SUPPRESSES GUT VICERAL HYPERSENSITIVITY AND INTESTINAL TRANSIT ACCELERATION INDUCED BY CHRONIC STRESS IN RAT

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Introduction: Stressful life events may trigger the symptoms of irritable bowel syndrome (IBS). Preclinical chronic stress models have been developed in animals to mimic changes in visceral sensitivity in response to gut wall distension seen in IBS patients. In the rat, chronic passive water avoidance stress (WAS) is associated with hypersensitivity to colorectal distension. Diosmectite, a purified silicate clay, is an adjuvant widely used for the treatment of several gastrointestinal diseases, mainly diarrhoea but also the functional abdominal pain experienced in chronic IBS. However, the effect of diosmectite treatment on IBS visceral hypersensitivity has never been investigated.

Aims & Methods: The aims of the present study were to evaluate the effect of diosmectite on gut transit time and visceral hypersensitivity induced by WAS in rats. For this purpose, visceral hypersensitivity (CVH) was induced by colonic injection of 0.5% acetic acid (AA) in 10-day old rats while control (NS) induced with 0.9% NaCL (CVH-NS). A group of control with no stress but with WAS (Con-sham) was used as another AWR was assessed, and the hippocampus and prefrontal cortex (PFC) and its metabolism were measured.

Disclosure of Interest: H. Mathieu-Fortunet: Ipsen employee All other authors have declared no conflicts of interest.

P0476 METABOLOCIC SIGNATURE OF THE POSTPRANDIAL EXPERIENCE

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Introduction: We have recently shown that postprandial sensations correlate with changes in circulating metabolites after a meal ingestion; however this phenomenon was demonstrated with a meal load up to the level of tolerance which changes in circulating metabolites after a meal ingestion; however this phenomenon was demonstrated with a meal load up to the level of tolerance which

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Introduction: DA-9701, a newly developed prokinetic agent formulated with Pharmacognomon and Corydalis, has been shown to effectively treat functional dyspepsia. Recently, it has also been suspected to improve gastrointestinal motor function. Aims & Methods: The aims of this study were to assess the effect of DA-9701 on colonic transit time (CCT) and symptoms of functional constipation. We prospectively enrolled 33 patients with functional constipation based on the Rome III criteria. The patients received 30 mg DA-9701 three times a day for 24 days. CCT was estimated initially and at the end of treatment. We also analyzed symptoms such as spontaneous bowel movements (SBMs), straining, stool form, feeling of incomplete emptying and anorectal blockage, abdominal discomfort and pain, overall defecation satisfaction, and incidence of adverse events.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0482 DA-9701 IMPROVES COLONIC TRANSIT TIME AND SYMPTOMS IN PATIENTS WITH FUNCTIONAL CONSTIPATION: A PROSPECTIVE STUDY


Disclosure of Interest: All authors have declared no conflicts of interest.

P0477 NEGATIVE EFFECTS OF BIFIDOBACTERIUM BIFIDUS ON THE RAT WITH COLONIC VISCERAL HYPERSENSIVITY INDUCED BY ACETIC ACID PERFUSION

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Introduction: Bifidobacterium with appropriate doses has been suggested to be an effective therapy for the treatment of IBS. But the impacts of Bifidobacterium on visceral sensation have never been reported. The negative effect of Bifidobacterium has been rarely studied and reported.

Aims & Methods: We aimed to study the effects of gavage administration with Bifidobacterium bifidus for two weeks on the visceral hypersensitivity of rats. Colonic visceral hypersensitivity (CVH) was induced by colonic injection of 0.5% acetic acid (AA) in 10-day old rats while control (NS) induced with 0.9% saline. The abdominal withdrawal reflexes (AWR), induced by colorectal distention (CRD), was used to quantify the level of colonic sensitivity in adult rats. The CRD in 42-day old were treated by gavage administration with Bifidobacterium bifidus (1*107 CFU/day) for two weeks (CVH-Bifi). Other CRD were treated with 0.9% NaCL (CVH-NS). A group of control with normal sensitivity was treated with sham gavage (Con-sham). In day 56th, another AWR was assessed, and the hippocampus and prefrontal cortex (PFC) were separated and used to analyze the c-fos, NMDAR 2A, NMDAR2B with western-blot.

Results: After two-week gavage, the CVH-Bifi presented lower volume than that of CVH-NS in CRD, though without significant difference (2.35 ± 0.28 vs.2.40 ± 0.23; p = 0.11). No significant difference was found between CVH-Bifi and Con-sham as well. In hippocampus, c-fos of CVH-Bifi was higher than that of Con-sham (1.04 ± 0.22 vs. 0.51 ± 0.16; p = 0.055). In PFC, the expression of c-fos of NMDAR2A in CVH-Bifi was significantly higher than that of CVH-NS (0.63 ± 0.14 vs. 0.21 ± 0.05; p = 0.004) and Con-sham (0.63 ± 0.14 vs. 0.20 ± 0.07; p = 0.011).

Conclusion: We reported the negative effects of Bifidobacterium bifidus gavage, which induced higher activation of c-fos and higher expression of NMDAR 2A in hippocampus and PFC. The roles of Bifidobacterium bifidus and its metabolites on visceral sensitivity needs further study to clarify.

Disclosure of Interest: All authors have declared no conflicts of interest.
**Results:** Twenty-seven patients completed the study. DA-9701 was associated without a significant CTT from 14.9 ± 6.8 to 3.7 ± 1.7 hours (P = 0.001). Significant CTT also significantly decreased after treatment (right CTT: from 14.0 ± 8.2 to 7.5 ± 4.7 hours, P = 0.001; rectosigmoid transit time: from 14.2 ± 11.9 to 9.5 ± 10.9 hours, P = 0.021). In addition, all constipation-related subjective symptoms, including SBM frequency, significantly improved compared to those before treatment. Serious adverse events did not occur.

**Conclusion:** DA-9701 accelerates colonic transit and safely improves symptoms in patients with functional constipation. Therefore, we suggest that this novel agent could help to treat patients with this condition.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**References**


**Table 1:**

<table>
<thead>
<tr>
<th>GI symptoms</th>
<th>IBS consultants</th>
<th>IBS non-consulters</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Most bothersome symptom</td>
<td>75 (38.5)</td>
<td>48 (43.6)</td>
<td></td>
</tr>
<tr>
<td>Abdominal pain Low</td>
<td>46 (24.6)</td>
<td>22 (20.0)</td>
<td></td>
</tr>
<tr>
<td>stools high frequency</td>
<td>40 (56.3)</td>
<td>16 (61.5)</td>
<td></td>
</tr>
<tr>
<td>Hard stools/low fre- quency</td>
<td>24 (12.3)</td>
<td>20 (18.2)</td>
<td></td>
</tr>
<tr>
<td>bloating None</td>
<td>8 (4.1)</td>
<td>4 (3.6)</td>
<td></td>
</tr>
<tr>
<td>of the above Frequency</td>
<td>72 (36.9)</td>
<td>31 (28.2)</td>
<td></td>
</tr>
<tr>
<td>Abdominal pain &gt;3</td>
<td>158 (81.0)</td>
<td>74 (67.3)</td>
<td></td>
</tr>
<tr>
<td>times/week bloating &gt;3</td>
<td>12 (6.2)</td>
<td>25 (22.7)</td>
<td></td>
</tr>
<tr>
<td>times/month Concern of</td>
<td>106 (54.4)</td>
<td>70 (63.3)</td>
<td></td>
</tr>
<tr>
<td>bowel function Not at all</td>
<td>77 (39.5)</td>
<td>15 (13.6)</td>
<td></td>
</tr>
<tr>
<td>Somewhat Very</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Somitization</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PHQ-12 score 7 or above</td>
<td>147 (65.4)</td>
<td>85 (77.3)</td>
<td>0.82</td>
</tr>
<tr>
<td>Quality of life</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall estimation of health</td>
<td>59 (30.3)</td>
<td>31 (28.2)</td>
<td>0.5</td>
</tr>
<tr>
<td>past 4 weeks (SF-8).</td>
<td>118 (60.5)</td>
<td>64 (58.2)</td>
<td></td>
</tr>
<tr>
<td>Very poor/poor Fair/</td>
<td>18 (9.2)</td>
<td>15 (13.6)</td>
<td></td>
</tr>
<tr>
<td>good Very good/</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>excellent</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Limbo/pain frequency</td>
<td>22 (11.3)</td>
<td>19 (17.3)</td>
<td>0.35</td>
</tr>
<tr>
<td>(SF-6), None/very mild</td>
<td>110 (56.4)</td>
<td>38 (52.7)</td>
<td></td>
</tr>
<tr>
<td>Mild/moderate Severe/</td>
<td>63 (32.3)</td>
<td>33 (50.0)</td>
<td></td>
</tr>
<tr>
<td>very severe</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Limited in social activities</td>
<td>24 (12.3)</td>
<td>29 (26.4)</td>
<td>0.008</td>
</tr>
<tr>
<td>due to physical health</td>
<td>98 (50.3)</td>
<td>46 (41.8)</td>
<td></td>
</tr>
<tr>
<td>or emotional problems</td>
<td>73 (37.4)</td>
<td>35 (31.8)</td>
<td></td>
</tr>
<tr>
<td>past 4 weeks (SF-8).</td>
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(continued)
The quality of referrals of patients with clinically suspected FGIDs do not result in long waiting lists and poor patient outcomes. New models of care are needed to translate specialist knowledge of functional gastrointestinal disorders (FGID) into primary care practice.

Aims & Methods: This study aimed to evaluate the safety and performance of an algorithm-based approach to the diagnosis and management of FGID. Consecutive patients triaged to the ‘routine waitlist’ of an Australian public hospital Gastroenterology Department over 2 years, with non-specific GI symptoms (no alarms) were randomised to waitlist control or intervention (2:1). Intervention patients were screened for alarms and abnormal blood/stool tests without an in-person consultation, to exclude organic disease (full blood count, C-reactive protein, biochemistry, thyroid function tests, iron studies, coeliac serology, H. pylori serology, faecal calprotectin and elastase) and classified according to the Rome III criteria. Information from patients with clinical alarm or a gastroenterology consult on board was judged appropriate, a prompt GE appointment offered. Elsewise patients received a letter stating that diagnosis and management options. Referrals were analysed for quality according to clinical triage practices.

Results: 89 intervention patients (61% female, mean 42, [SD 14]) and 21 control (75% female, mean 42, [SD 16]) y patients completed intake. 35 intervention patients warranted prompt GE review after active screening. Organic disease was diagnosed in 10 (diagnosed: 19 FGID, 2 IBD, 1 neoplasm, 1 pancreatic insufficiency, 1 reflux esophagitis, iron deficiency, 1, 7 did not attend), and 4 had additional clinically significant findings (polyps, iron deficiency). 45 were diagnosed with a FGID (9 had another non-urgent diagnosis). At follow-up (mean 2.7 y [SD 0.5yrs] post-referral), none of the 45 patients diagnosed with FGID had needed a gastroenterology consult based on the original referral (six received a specialist appointment via duplicate referrals within the system).

Conclusion: Among individuals who meet Rome IV criteria for IBS in the general population, those who are older, have more frequent bloating, have greater concern about their bowel function, and who are more socially affected by their bowel symptoms, are more likely to consult doctors about their bowel symptoms. In contrast, IBS consultants and non-consultors do not differ in their abdominal pain severity or extra intestinal symptom burden. Support: The Rome Foundation.

Disclosure of Interest: All authors have declared no conflicts of interest.

References:


P0487 ALTERED EXPRESSION OF MEMBRANE TRANSPORTERS IN COLONIC MUCOSA OF PATIENTS WITH IRREITABLE BOWEL SYMPTOM (IBS) AND POST-INFECTION (PI)-IBS COMPARED TO THE HEALTHY SUBJECT

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Introduction: Irritable bowel syndrome (IBS) affects 5–15% of adults in the general population, and is characterized by chronic recurrent abdominal pain, discomfort and associated with altered bowel habits. The pathophysiology of IBS is complex and not fully understood. Hence, treatment is often based on symptomatology rather than underlying physiological aberrances.

Aims & Methods: We retrospectively reviewed, via electronic records, all the patients seen at the Scottish Gut Motility Disorder Clinic between January and December 2016 included, focusing on original referral, diagnosis and treatment to evaluate the need for specialist input.

Results: In 2016, 378 patients attended the Motility Clinic total of 459 visits: 333 female, mean age was 51.4 (range: 16 to 95 years), 60% of referrals originated via secondary care (40% GI, 50% Surgery, 10% other disciplines). The commonest reason for referral was IBS (40%); IBS-Constipation (58%), IBS-Diarrhoea (21%) or IBS-MixType (21%). 16% were referred with faecal incontinence and 37% with chronic constipation. 35% of patients didn’t receive any therapy at time of referral. 44% were prescribed treatment but not followed up for assessment of successful response to therapy prior to referral to the specialist clinic. In 28% of patients the diagnosis changed following Motility clinic assessment. Diagnosis at clinic is based on RomeIII questionnaire, depression and anxiety score, thorough history taking and physical examination (including per rectum exam), ad hoc psychiatry input and referral to specialist investigation. In 30% of patients referred with chronic constipation the diagnosis was changed to IBS-Constipation. 8% changed from IBS-D to IBS-M, 8% referred with faecal incontinence had Obstructive Defecation Syndrome, 6% referred as IBS-M were diagnosed with IBS-C, 5% referred as IBS-D were diagnosed as IBS-M, 3% referred with IBS-D had bile acid malabsorption. 56% of patients underwent specialist investigations including uncorrelated physiology (70%), 33% of patients attending the Specialist clinic received 1st -line therapy and life style advice, albeit 57% of them, who received 2nd -line treatment, having failed 1st-line management.

Conclusion: The above data indicate the need for education and expansion of resources available in primary care to optimise patients’ management. Furthermore, it highlights the necessity for the introduction of a formal Neurogastroenterology curriculum in the general Gastroenterology training.

Disclosure of Interest: All authors have declared no conflicts of interest.

References:

1. Scottish Gut Motility Disorder Clinic: REVIEW OF ACTIVITY OVER 1-YEAR PERIOD

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Introduction: IBS is common worldwide. In UK it exceeds the 20% of the population. 1. Burden of Irritable Bowel Syndrome (IBS) on UK healthcare has been estimated around 1800£per patient per year. NIC guideline IBS provides a systematic approach to symptoms and therapies available to GPs and general gastroenterologists. This creates a good asset to minimal referrals to tertiary centres and address costs.

Aims & Methods: We retrospectively reviewed, via electronic records, all the patients seen at the Scottish Gut Motility Disorder Clinic between January and December 2016 included, focusing on original referral, diagnosis and treatment to evaluate the need for specialist input.

Results: In 2016, 378 patients attended the Motility Clinic total of 459 visits: 333 female, mean age was 51.4 (range: 16 to 95 years), 60% of referrals originated via secondary care (40% GI, 50% Surgery, 10% other disciplines). The commonest reason for referral was IBS (40%); IBS-Constipation (58%), IBS-Diarrhoea (21%) or IBS-MixType (21%). 16% were referred with faecal incontinence and 37% with chronic constipation. 35% of patients didn’t receive any therapy at time of referral. 44% were prescribed treatment but not followed up for assessment of successful response to therapy prior to referral to the specialist clinic. In 28% of patients the diagnosis changed following Motility clinic assessment. Diagnosis at clinic is based on RomeIII questionnaire, depression and anxiety score, thorough history taking and physical examination (including per rectum exam), ad hoc psychiatry input and referral to specialist investigation. In 30% of patients referred with chronic constipation the diagnosis was changed to IBS-Constipation. 8% changed from IBS-D to IBS-M, 8% referred with faecal incontinence had Obstructive Defecation Syndrome, 6% referred as IBS-M were diagnosed with IBS-C, 5% referred as IBS-D were diagnosed as IBS-M, 3% referred with IBS-D had bile acid malabsorption. 56% of patients underwent specialist investigations including uncorrelated physiology (70%), 33% of patients attending the Specialist clinic received 1st -line therapy and life style advice, albeit 57% of them, who received 2nd -line treatment, having failed 1st-line management.

Conclusion: The above data indicate the need for education and expansion of resources available in primary care to optimise patients’ management. Furthermore, it highlights the necessity for the introduction of a formal Neurogastroenterology curriculum in the general Gastroenterology training.

Disclosure of Interest: All authors have declared no conflicts of interest.

References:
Aims & Methods: The aim of this study was to compare the expression of membrane transporters in mucosal biopsies of healthy subjects, IBS patients and post-infectious (PI)-IBS patients. Mucosal biopsies were obtained from the unprepared sigmoid colon in 18 IBS patients, 9 PI-IBS patients and 10 healthy subjects. Total RNA was isolated and prepared for gene expression analyses using quantitative reverse-transcription polymerase chain reaction (qRT-PCR). We compared the expression of genes encoding membrane-spanning transporters, using GAPDH as a reference gene, and by using the comparative \( 2^{-\Delta\Delta Ct} \) method.

Results: Colonie expression of SLC7A5 and SLC3A2 (together comprising the amino acid transporter LAT1 + 4F2hc) was significantly lower in IBS patients, but not in PI-IBS patients, compared to healthy controls (P < 0.001). The expression of SLC7A8 (LAT2) tended to be lower in IBS patients compared to controls (P = 0.08). Mucosal gene expression of the short chain fatty acid transporter SMCT1 (SLC5A8) was lower in both IBS-patients and PI-IBS patients compared to healthy subjects (P < 0.01).

Conclusion: The amino acid transporters LAT1 and LAT2 appeared to be affected in IBS patients, but not in PI-IBS patients, compared to healthy subjects, suggesting a possible alteration in amino acids transport in this patient group. Furthermore, our results suggest a lower uptake of short chain fatty acids in both IBS- and PI-IBS patients. Altered expression of these transporters may be involved in the pathophysiology of IBS as well as being a potential biomarker of this aberration, and therefore deserves further study in IBS.

Disclosure of Interest: All authors have declared no conflicts of interest.

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**P0489 DIVERTICULITIS IN THE SIGMOID COLON HAS THE HIGHEST RISK FOR INTESTINAL COMPLICATION OF COLONIC DIVERTICULITIS IN JAPANESE PATIENTS**


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**Introduction:** Most colonic diverticulitis can be conservatively treated, but some need surgical intervention due to intestinal complications. Cholestyramine associated with complications of diverticulitis have been reported mainly from Western countries, but few from Asian countries including Japan.

**Aims & Methods:** In this study, we aimed to determine risk factors for complications of colonic diverticulitis in Japan. Ken Haruma et al. characterized Colonic Diverticulitis Factors and Factors Associated With Complications: A Japanese Multicenter, Retrospective, Cross-Sectional Study. Diseases of the Colon & Rectum 2015;58:1174–1181.

**Aims & Methods:** The aim of this study was to compare the expression of membrane transporters in mucosal biopsies of healthy subjects, IBS patients and post-infectious (PI)-IBS patients. Mucosal biopsies were obtained from the unprepared sigmoid colon in 18 IBS patients, 9 PI-IBS patients and 10 healthy subjects. Total RNA was isolated and prepared for gene expression analyses using quantitative reverse-transcription polymerase chain reaction (qRT-PCR). We compared the expression of genes encoding membrane-spanning transporters, using GAPDH as a reference gene, and by using the comparative \( 2^{-\Delta\Delta Ct} \) method.

**Results:** Of the 282 patients, 183 (64.9%) patients had right-sided diverticulitis, and 70 (24%) had complications; perforation (n = 53), fistula (n = 8), abscess (n = 5) and stenosis (n = 4). The rate of complication was highest in sigmoid colon (88.6%) when compared with other locations; ascending colon (10%), transverse colon (1.4%), and descending colon (0%). Multivariate analysis identified the location of sigmoid colon (odds ratio 62.2, 95% confidence interval 21.8–178.0) as a significant independent factor for complications of diverticulitis. Among 70 patients with complicated diverticulitis, 55 (78.6%) patients underwent emergent surgery; most of them (54 patients, 98.2%) were with diverticulitis in the sigmoid colon. The rate of complication associated with complications of diverticulitis (uni- and multivariate analysis)

<table>
<thead>
<tr>
<th>Factor</th>
<th>Univariate Odds ratio (95%CI)</th>
<th>p-value</th>
<th>Multivariate Odds ratio (95%CI)</th>
<th>p-value</th>
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<tr>
<td>Age</td>
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<td>Per 10-year increment</td>
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<td></td>
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<tr>
<td>Body mass index</td>
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<td>0.019</td>
<td>1.79</td>
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<td>&lt;25</td>
<td>(1.1–4.09)</td>
<td>(0.57–5.61)</td>
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</tr>
<tr>
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<td>0.007</td>
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<tr>
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<td>(0.97–6.91)</td>
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<td>0.349</td>
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</tbody>
</table>

**Conclusion:** The sigmoid colon was a significant risk factor for complication of colonic diverticulitis in Japanese patients. Acute colonic diverticulitis in the sigmoid colon should carefully be treated with surgical interventions in mind.

Disclosure of Interest: All authors have declared no conflicts of interest.

References


**References**

**References**


**References**


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**P0490** THE USE OF ENDOCUTANEOUS CLASSIFICATION “DICA” MAY HAVE A SIGNIFICANT COST-SAVING ON THE BURDEN OF DIVERTICULAR DISEASE OF THE COLON

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**Introduction:** Although symptoms occur in only 20% of patients harboring diverticula, Diverticular Disease (DD) of the colon DD represents the 8th disease as burden in USA. Several treatment are currently advised in managing those patients, but their impact on the burden of the disease is unknown. The recent DICA endoscopic classification has been developed and validated for the classification of DD, founding that treatment of DICA 1 and DICA 3 patients did not impact significantly in terms of acute diverticulitis occurrence/recurrence and surgery occurrence. Our aim was to assess the impact of using DICA classification on the burden of DD in Italy.

**Aims & Methods:** We assessed retrospectively the overall and the cost/year of treatment (or rifaximin, or any other treatment, including probiotics, fibers, systemic antibiotics and spasmoletic) in DICA 1, DICA 2 and DICA 3 population. Analysis of diverticulosis prevalence was estimated according to data population provided by Italian Institute of Statistics (ISTAT). Cost of treatments was calculated according to data on drugs’ consumption collected during the DICA study.

**Results:** According to 2015 ISTAT population data, we estimated that > 8 million of Italian people > 60 years may have diverticulosis. According to our endoscopic estimated that about 75% of diverticular population are on DICA 1, about 30% on DICA 2, and about 13% on DICA 3. According to the drugs’ consumption recorded during our study, we estimated that overall about 679 million of euros could be spent in Italy in treating those patients. In particular, > 357 million of euros are spent in DICA 1 population, > 205 million of euros in DICA 2 population, and > 88 million of euros in DICA 3 population. Considering that medical treatments did not show any significant advantage when treating DICA 1 and DICA 3 people in terms of prevention of acute diverticulitis recurrence and surgery occurrences, we can estimate that > 475 million of euros could be spent in Italy without any significant benefit for DD population.

**Conclusion:** DD has a significant burden for National Health System in Italy. DICA endoscopic classification may have a significant impact of this burden, helping to select DD people who effectively need treatments in terms of prevention of acute diverticulitis occurrence/recurrence and surgery occurrence.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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**P0492** IMPACT OF TREATMENTS ON FECAL MICROBIOTA AND FECAL METABOLIC PROFILING IN SYMPTOMATIC UNCOMPLICATED DIVERTICULAR DISEASE OF THE COLON

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**Introduction:** Fecal microbiota and metabolome may be altered in patients with Symptomatic Uncomplicated Diverticular Disease (SUDD). In particular, we found that Akkermansia muciniphila species were significantly increased in SUDD patients when compared with asymptomatic diverticulosis and healthy people, as well as PLS-DA analysis of NMR-based fecal metabolomics showed significant discrimination between HC and AD patient. Our aim was to assess the effect of current treatments for SUDD on fecal microbiota and fecal metabolic profiling in those patients.

**Aims & Methods:** Thirteen consecutive female patients, living in the same district and suffering from SUDD, were studied. Patients were treated with a 2-week course of 30g/day fiber supplementation (3 patients), 1.6 grams/day of mesalazine (3 patients), 900 billion/day of probiotic mixture VSL#3 (currently available in Europe as VivotinX®), 3 patients), and 800 mg/day of rifaximin (4 patients). Stool samples were collected at entry (T0), at the end of the 2-week course of treatment (T1), and after 30 (T2) and therefore after 60 days at the end of the therapeutic course (T3). Real-time PCR was used to quantify targeted microorganisms. High-resolution proton nuclear magnetic resonance (NMR) spectroscopy associated to Multivariate Analysis with partial least square discriminant analysis (PLS-DA) were applied on the metabolite data set.

**Results:** The overall bacterial quantity did not differ before and after treatment (p = 0.449). The overall abundance of Akkermansia muciniphila species was significantly reduced at T1 (p = 0.017) and T2 (p = 0.026), while at T3 it became similar to that of T0 (p = 0.09). The amount of Lactobacillus group was increased in all groups but not significantly at T1 and T2, while at T3 it became similar to that of T0. Treatments showed the same results except for probiotic group, who had higher and persistent amount of Lactobacillus up to T3, PLS-DA analysis of NMR-based fecal metabolomics showed significant changes at T1 and T2, while at T3 it became similar to that of T0. All treatments were showed the same behaviour in influencing fecal metabolome except for rifaximin group, in which we did not find any metabolic change neither at the end of treatment nor during the washout period.

**Conclusion:** This preliminary study confirms that Akkermansia muciniphila may play a pathogenetic role in the occurrence of SUDD. We found also that current treatments for SUDD patients are able to influence metabolic activity in those patients except for rifaximin.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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**P0493** 5-YEAR ITALIAN REGISTER OF DIVERTICULOSIS AND DIVERTICULAR DISEASE (REMAI): A LOW PROGRESSION RATE INTRODUCTION: FECAL MICROBIOTA PROFILING DURING THE FIRST YEAR OF FOLLOW-UP

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**Introduction:** Natural history of colonic diverticulosis and diverticular disease (DD) is poorly known, and available data derived mostly from retrospective cohort studies.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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Aims & Methods: Aim of this study was to assess, in a cohort of patients with colon carcinoma, the incidence of new cases of symptomatic uncomplicated diverticular disease (SUDD) and diverticulitis, and recurrence of diverticulitis after 1-year of follow-up. GRIMAD (Italian Diverticular Disease Group) promoted the creation of REMAD (Register of Diverticular Disease) a prospective, 5-years, no-profit, cohort study involving 47 Italian centers. Each center enrolled at least 20 consecutive patients during a period of two months. Inclusion criteria were: informed consent; age ≥18 years and endoscopic/radiological-confirmed colonic diverticulitis. Outpatient/telephone visits were scheduled every 6 months. Two retrospective data (patients' characteristics and habits, characteristics of DD, comorbidities and therapies) collected by participating centers were reported on an electronic Case Report Form managed by CD Pharma, Milan. At entry, patients were categorized according to the following criteria: i) diverticulosis (presence of diverticula in the absence of abdominal symptoms); ii) SUDD (recurrent abdominal symptoms as abdominal pain and/or changes in bowel habit, in the absence of overt inflammation); iii) PD (patients who experienced at least one episode of acute diverticulitis in the past). Patients were allowed to continue their therapy for DD, if any. Logistic regression was performed to identify patients' features associated with new occurrence of SUDD and diverticulitis.

Results: Out of the overall, at baseline 1217 (55.8%) female, median years 67 (28–95), BMI 25.6kg/m² (16.2–43.4), patients were enrolled: 707 (58.1%), 300 (24.7%), and 210 (17.3%) with diverticulosis, SUDD, and PD, respectively. At 12 months, 922 patients (53.1%, 29.8%, and 17.1% with diverticulosis, SUDD, and PD) were followed, and 27.4% of patients were lost at follow-up. In the 12 months follow-up, 33 (6%) and 4 (0.7%) of diverticulosis patients developed SUDD and acute diverticulitis, respectively; 4 (1.6%) of SUDD patients developed acute diverticulitis, and in 14 (9.4%) of PD patients a new episode of acute diverticulitis occurred. Overall, only 3 patients developed a complication, without need of surgery. One year of follow-up logistic regression, showed that only female gender was associated with subjects who changed subgroup from diverticulosis to SUDD or PD (OR 2.26, 95% CI 0.97–5.22). No specific features associated with recurrence of diverticulitis could be identified.

Conclusion: These preliminary data suggested that, during an observation period of one year, progression from diverticulosis to SUDD occurred in less than a tenth of patients, and was associated with female gender. Overall incidence of diverticulitis and PD (2.3%), whereas recurrent diverticulitis was not higher. These data showed that, with respect to diverticulosis, female gender and presence of GI comorbidities are associated with SUDD, whereas younger age, family history for DD and female gender are associated with PD. Furthermore, patients with diverticulitis have higher physical and mental scores compared both to patients with SUDD and PD, suggesting that SUDD PD and reduced QoL of the affected patients.

Disclosure of Interest: R. Cuomo: Speaker and consultant for Alfa Wassermann G. Barbara: Speaker and consultant for Alfa Wassermann F. Pace: Speaker and consultant for Alfa Wassermann B. Annibale: Speaker and consultant for Alfa Wassermann All other authors have declared no conflicts of interest.

Introduction: Patients with symptomatic uncomplicated diverticulitis disease (SUDD) and those with diverticulitis share similar clinical patterns characterized by abdominal pain or change of bowel habits. In clinical practice, differential diagnosis between the two conditions may be useful in the diagnostic approach and therapeutic management.

Aims & Methods: Our aim was to assess the features of abdominal pain in patients with SUDD and PD. After a 6-months interval, patients were categorized according to the following criteria: i) diverticulitis (presence of diverticula in the absence of abdominal symptoms); ii) SUDD (recurrent abdominal symptoms as abdominal pain and/or changes in bowel habit, in the absence of overt inflammation); iii) PD (patients who experienced at least one episode of acute diverticulitis in the past). In each center, patients were allowed to continue their therapy for DD, if any. T test was used to compare QoL scores. Logistic regression was performed to identify patients’ features associated with the presence of subtypes of DD. A p value <0.05 was considered statistically significant.
filled in long-lasting pain questionnaire. Abdominal pain lasting <24h was reported by patients with SUDD (86.1%) and 119/154 with PD (77.3%; p = 0.026). Symptom severity score was higher in PD group than in SUD group, but this difference was not statistically significant (5.5 ± 2.4 vs. 5.1 ± 2.2 cm; p = 0.130). Patients with PD had short-lived pain located more frequently in the left lower abdomen (50.6% vs. 29.6%; p = 0.002), whereas abdominal pain was more prevalent in patients with SUD (29.6% vs. 20.8%; p = 0.058). Pain lasting >24h was more prevalent in PD group compared to SUD group (62.1% vs. 52.6%; p = 0.029). Pain severity was higher in patients with PD and AD in comparison with CTR (28.4% vs. 20.5%; p < 0.001), confinement to bed (35.7% vs. 18.6%; p = 0.002), medical consultation (38.6% vs. 23.7%; p < 0.001), need for therapy (42.9% vs. 19.2%; p < 0.001), and hospitalization (28.6% vs. 8.3%; p < 0.001).

Conclusion: PD patients show some peculiar clinical features of abdominal pain. SUD patients frequently complained abdominal diffuse and short lasting pain. In contrast patients with PD frequently complained pain located in the left lower abdomen lasting for more than 24h. Our results suggest that these features are useful indicators to distinguish patients with SUD and PD and should be carefully assessed in clinical work-up of diverticular disease.

Disclosure of Interest: B. Annibale: Speaker and consultant for Alfa Wasserman G. Barbara: Speaker and consultant for Alfa Wasserman F. Pеее: Speaker and consultant for Alfa Wasserman R. Cuomo: Speaker and consultant for Alfa Wasserman All other authors have declared no conflicts of interest.

P0496 MUSCULAR INFLAMMATORY STATE AND PHENOTYPIC SWITCH IN DIVERTICULITIS AND COMPLICATED DIVERTICULAR DISEASE

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Introduction: Colonic diverticulitis, as well as diverticular disease, is a multifactorial condition that can be characterized by an inflammatory and fibrotic state, impaired contraction, inflammation and fibrosis. Mesenchymal smooth muscle cells (SMC) are able to switch from a contractile phenotype to a less mature synthetic phenotype, characterized by a loss of differentiation with decreased expression of contractile markers as well as synthesis and release of several pro-inflammatory cytokines. Different organ specific pathways have been demonstrated to induce this mesenchymal transition. Renal fibrosis is driven by transforming growth factor β (TGF-β) through inverse regulation of Smad2/3. In SMC, whole fibrosis by PDGF-β-mediated downregulation of marker gene Trb3 expression.

Aims & Methods: Aim of this study was to determine, both in human uninvolved and involved tracts of asymptomatic diverticulitics (AD; AD) and in stenotic segments of diverticulitis patients, the incidence and severity of muscular alterations, impaired contraction, inflammation and fibrosis. Circular and longitudinal smooth muscle strips and cells (SMC) were isolated separately from surgical colon specimen of 18 patients (5 29, 80 years) submitted to surgery for cancer (6) (CTR). Contraction was tested in response to carbachol and relaxation in response to VIP, qPCR analysis, expressed as Relative Quantification, was performed for transcription of mRNA encoding for TGF-β, fibromodulin, and for SMC phenotypic switch molecules (Collagen I, -SMA, TGF-β, PDGF-β, Trb3, Smad2/3). Data were normalized to β-actin mRNA and expressed as mean ± SE. In addition, the activation of inflammasome complex was indirectly tested through quantification of IL-18 secretion by commercial ELISA kit.

Results: In both muscle layers, AD- and AD- SMC, compared to CTR, showed an overall increase in inflammatory gene expression, with a trend of decrease from AD to AD, the lowest expression been observed in CDD. This inflammation was associated with an increase in IL-1β secretion in SMC layer medium compared to CTR and a progressive inhibition of contraction to carbachol, already in AD in circular strips and SMC. In contrast relaxation in response to VIP resulted significantly decreased only in AD both on strips and SMC with no alteration in AD and CDD. Peculiarity of circular SMC was a progressive increase in Coll1 expression from AD to CDD compared to CTR (3 hundred fold increase) parallel to about 50% decrease in the contractile protein α-SMA. Differently, longitudinal SMC, both in AD and CDD, pre- sented a homogenous increased Coll1 expression, decrease in α-SMA and reduction of contraction. VIP-induced relaxation was significantly decreased in CDD. Phenotypic switch was only observed in CDD, driven in circular layer, by a TGF-β-dependent pathway (increased expression for TGF-β: 2.88 ± 0.6 and Smad2/3; 0.39 ± 0.11) compared to Smad2/3 and PDGF-β-dependent pathway (increase of PDGF-β: 2.27 ± 0.44 and parallel decrease of Trb3: 0.58 ± 0.13).

Conclusion: Intrinsic myogenic alterations are present in colon asymptomatic diverticulitics and complicated diverticular disease, both in the circular and longitudinal layers characterized by a myogenic pro-inflammatory state and an impaired contractile activity that, in complicated diverticular disease, ended in a muscular synthetic pro-fibrotic switch.

Disclosure of Interest: All authors have declared no conflicts of interest.

MONDAY, OCTOBER 30, 2017 09:00-17:00 OESOPHAGEAL, GASTRIC AND DUODENAL DISORDERS I - HALL 7

P0497 THE ONCOGENIC MIR-491-5P/MIR-875-5P-NOTCH3-PHLDB2 AXIS IN GASTRIC TUMORIGENESIS

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Introduction: Aberrant Notch activation has been implicated in multiple malignancies, including gastric cancer (GC). However, the clinical significance of Notch receptors and their functional role in gastric carcinogenesis remain unclear.

Aims & Methods: We aim to delineate the dysfunctional Notch signaling in GC and comprehensively reveal its activation by silenced microRNAs (miRNAs) in gastric carcinogenesis. The expression clinical relevance of NOTCH1-4 in GC were achieved from online available dataset. The mRNA and protein expression of NOTCH3 was examined by qRT-PCR and Western blot. The biological function of NOTCH3 in GC was demonstrated by MTT proliferation, monolayer colony formation, cell migration and invasion assays through siRNA-mediated knockdown. The expression of miR-491-5p/miR-875-5p in GC tissues was determined by microRNAs expression microarray.

Results: NOTCH3, but not NOTCH1, 2, 4, is uniformly up-regulated and significantly correlated with poor survival in multiple GC datasets. Knockdown of NOTCH3 in AGS and MKN28 cells exhibited significant anti-oncogenic effect in vitro. NOTCH3 downregulation suppressed cell proliferation, reduced monolayer colony formation, and inhibited cell invasion ability. Moreover, NOTCH3 knockdown significantly increased cleaved caspase-3 and cleaved-PARP expression induced by cisplatin, which was further revealed by the gene set enrichment analysis (NCBI/GEO/GSE57303 and NCBI/GEO/GSE57303 database). NOTCH3 was confirmed to be a direct target of tumor-suppressive miR-491-5p and miR-875-5p. The functional downstream targets of NOTCH3 were identified by gene expression microarray.

Conclusion: NOTCH3 is over-expressed and plays an oncogenic role in gastric carcinogenesis through its direct downstream miR-875-5p. The activation of NOTCH3 in GC is partly due to the silence of tumor-suppressive miRNAs, miR-491-5p and miR-875-5p. These findings comprehensively revealed the activation of Notch signaling pathway and provided clinical translational potential for GC.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0498 FOX2 SUPPRESSES WNT SIGNALING PATHWAY IN GASTRIC CARCINOGENESIS THROUGH TRANSCRIPTIONAL REGULATING E3 LIGASE RB2BP1 AND PROMOTING B-CELCATENIN DEGRADATION

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Introduction: We found that tumor suppressor gene FOX2 was silenced in gastric cancer (GC) through promoter hypermethylation. Restoration of FOX2 suppressed GC tumorigenesis through inhibition of canonical Wnt

Disclosure of Interest: All authors have declared no conflicts of interest.
signaling pathway. However, the molecular mechanism of FOXX2 in GC is still unknown.

Aims & Methods: We hypothesize that FOXX2 transcriptional upregulates a novel E3 ligase that targets β-catenin for degradation. We aim to investigate the molecular mechanism of FOXX2 in GC and identify such E3 ligase by PCR-Sequencing. Immunoprecipitation (ChIP) assay and luciferase assay.

Results: FOXX2 significantly increased both nuclear and cytosolic levels of β-catenin in a GSK-3β independent manner and promoted β-catenin degradation via ubiquitin-proteasome pathway in gastric cells. Using Human Ubiquitin Ligase RT1 Profiler PCR Array and western blot, we identified that IFR2B8L was upregulated upon FOXX2 overexpression and was a promising E3 ligase for β-catenin. Overexpression of IFR2B8L suppressed the TOP-flash luciferase reporter and reduced Wnt target gene c-myc expression in GC cells. Overexpression of IFR2B8L significantly increased β-catenin ubiquitination and reduced β-catenin protein without alteration of its mRNA level. Conversely, knockdown of IFR2B8L significantly decreased endogenous β-catenin ubiquitination. Immunoprecipitation assay suggested that IFR2B8L interacted with β-catenin. Therefore, IFR2B8L is a potential E3 ligase that targets β-catenin for degradation. To investigate whether FOXX2 directly regulates IFR2B8L transcription, we performed ChIP assay and found that FOXX2 bound on to the IFR2B8L promoter region. We cloned the IFR2B8L promoter region (-2700 bp to TSS) into pGL3-plasmid and performed a luciferase activity assay. Wild-type FOXX2 but not the mutant ΔFOXX2 significantly activated the lucerase reporter in AGS and 293 F cells, suggesting that FOXX2 directly activated IFR2B8L transcription. Moreover, FOXX2 significantly increased the level of HIK27Ac (a marker to distinguish active from inactive enhancer element) on the 5′-flanking region of IFR2B8L gene, suggesting that FOXX2 positively regulated IFR2B8L gene transcription. In addition, IFR2B8L mRNA was downregulated in human GC tissues compared to the adjacent normal tissues (N = 30, P < 0.01) by real-time PCR analysis. IFR2B8L mRNA showed a positive correlation with FOXX2 in gastric cancer in a Chinese cohort (N = 30, Spearman’s rho = 0.42, P < 0.05) and in the TCGA cohort (N = 245, P = 0.38, P < 0.001).

Conclusion: We reported a novel FOXF2-IRF2B8L-β-catenin signaling axis in gastric cells. FOXX2 is a critical tumor suppressor in gastric carcinogenesis through promoting β-catenin degradation by transcriptionally upregulating E3 ligase IFR2B8L.

Disclosure of Interest: All authors have declared no conflicts of interest.

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Introduction: Gastric adenocarcinoma with enteroblastic differentiation (GAED) is a rare variant of gastric carcinoma. It is well known that GAED is associated with poor prognosis [1, 2]. However, the clinicopathological and molecular biological features of GAED and to find new therapeutic targets.

Among 1003 patients with primary gastric cancer who underwent surgery or endoscopic resection in our hospital between April 2008 and February 2017, we enrolled 52 cases (early:17, advanced:35) of GAED defined as having tubular to papillary or solid structure with clear cytoplasm and immunohistochemical positivity for at least one of the following antibodies: AFP, Glypican-3 and SALL4. NGS was performed for 24 cases of formalin-fixed paraffin-embedded samples (early: 2, advanced: 22) using Ion PGM system with cancer hotspot panel v2 targeting 50 genes (Thermo Fisher Scientific). All authors have declared no conflicts of interest.

Results: Twenty-five out of 53 (47%) FIGC families harbored germline variants, and co-occurrence of germline moderate-risk alleles was found in ten families. From these ten families, seven harbored one pathogenic or likely pathogenic variant combined with one or more unclassified novel variants. The remaining three families carried solely clusters of novel unclassified variants. Moderate-risk alleles of BRCA2, MAP3K6, MSH6, MSR1, SDHB and SDHD were the most frequently found in this cohort. In addition, tumours arising in these 10 families were enriched in somatic variants within DNA repair genes and often displayed microsatellite instability phenotypes.

Conclusion: The clinical homogeneity and relatively high number of FIGC families herein allowed studying the hypothesis that FIGC may be a hereditary polygenic syndrome caused by moderate-risk alleles in gastrointestinal cancer-associated genes.

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Disclosure of Interest: All authors have declared no conflicts of interest.

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**Aims & Methods:**
For understanding the therapeutic effects of obestatin/GPR39 system, we investigated the morphological and histological features of the human oral mucosal epithelial cell sheets, in addition to the cellular gene and protein expressions. From a small biopsy of human volunteer donors' oral mucosa, oral muco-sal glandular epithelial cells, which were then fabricated into transplantable cell sheets using a previously described procedure. The cell sheets were examined by immunohistochemistry (IHC) and electron microscopy as well as the gene and protein expression analysis by RT-PCR, with a DNA array. Furthermore, the culture supernatant obtained immediately before the transplantation, were analyzed with a cytokine array.

**Results:**
Histological and morphological analyses revealed that tissue-engineered stratified epithelial cell sheets have an apical-basal polarity, and that the junctions between the basal cells of the sheets were significantly loose, due to dissociating desmosomes, which were also fewer in numbers. IHC showed that the expression levels of E-cadherin and desmosomal cadherins were downregulated in the epithelial cell sheets, but mesenchymal markers (N-cadherin, vimentin, and fibronectin) were upregulated. Taken together, these findings implied that epithelial mesenchymal transition (EMT) was induced in the basal cells. The results of the cytokine array showed that the cell sheets secreted EMT effectors with pro-inflammatory factors (progranulin and eprigen) and antimicrobial proteins (b-defensin).

**Conclusion:**
The EMT of the basal cell layer of epithelial cell sheets may contribute to the improved engraftment after cell sheet transplantation. The secretion of antibacterial peptides and various growth factors from the cell sheets would exhibit anti-inflammatory effects, and promote wound-healing compared to reinforcement of esophagus with absorbable synthetic materials such as polyglycolic acid and polylactic acid.

**Disclosure of Interest:**
All authors have declared no conflicts of interest.

**References**

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**P0504 COMPARATIVE STUDY BETWEEN THE EFFICACY OF REBAMIPIDE, SUCCINATE AND PANTOPRAZOLE IN TREATMENT OF POST-BANDING VARICEAL ULCERS**

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**Introduction:** Endoscopic variceal band ligation (EVL) is an effective procedure to control and prevent variceal bleeding in patients with liver cirrhosis. Although EVL has some complications, yet these complications are related to post-EVL ulcers. Few data exist regarding therapy of post-ligation ulcer and treatment been mostly empirical with drugs used for peptic ulcer disease.

**Aims & Methods:** We aimed to compare between the efficacy of rebamipide, sucralfate and pantoprazole in treatment of post banding variceal ulcers. Seventy-five patients with esophageal varices eligible for elective band ligation represented the population of the study. The patients were allocated into three groups; rebamipide group, they received rebamipide 100 mg 3 times daily; pantoprazole group, they received pantoprazole 40 mg/day orally at morning; sucralfate group, they received sucralfate 1 gm every 6 hours, for 14 days beginning at the next day of band ligation. Subjects underwent EGD 14 days after banding.
Primary outcomes included the size and number of ulcers and the subjects' rebleeding, dysphagia, chest pain and vomiting.

Results: At follow-up endoscopy, the number of patients with post-band ulcers and size of ulcers were similar in the three groups. However, the number of ulcers for each patient was statistically significant less in rebamipide group when compared to pantoprazole and sucralfate (P < 0.01). Chest pain, dysphagia and vomiting scores were not significantly different. Dysphagia was by far the most common symptom with no case of bleeding was reported in all patients of the studied groups.

Conclusion: Rebamipide is effective in decreasing the post banding complication and reducing size of ulcer as well as the number of ulcers with no significant effect on post banding ulcer formation. Rebamipide can be used routinely in settings of post-VEL as a good alternative to pantoprazole and sucralfate.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P0509 A COMPARATIVE STUDY OF THERAPEUTIC EFFECT OF VONOPRAZAN AND ESOMEPRAZOLE ON BLEEDING AFTER GASTRIC ENDOSCOPIC SUBMUCOSAL DISSECTION

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Introduction: A potential pump inhibitors (PPIs) has been widely used for the treatment of endoscopic submucosal dissection-induced gastric ulcers. However, post-operative bleeding is still one of the most important adverse side effects.1, 2 Vonoprazan (VPZ), a potassium-competitive acid blocker, is a new class of acid-suppressing agents, and it is expected to reduce bleeding after gastric endoscopic submucosal dissection (ESD) by strongly inhibiting gastric acid secretion compared with PPIs.3

Aims & Methods: We compared the incidence of bleeding after gastric ESD between patients who were treated with VPZ and those treated with esomeprazole (EPZ). Data for 101 patients who underwent gastric ESD from December 1, 2014 to December 31, 2016 in Osaka City General Hospital and started to take VPZ (n = 22) or EPZ (n = 79) by the day before ESD was reviewed. Twelve of them (3 in the VPZ group, 9 in the EPZ group) were excluded for simultaneous resection in any of these patients. There were no reported immediate or delayed complications from the treatment.

Results: Gender, age, resected specimen diameter, oral antithrombotic drug administration, and dialysis were not significantly different in both groups. Two of the 19 patients in the VPZ group (10.5%) and 6 of the 70 patients in the EPZ group (8.6%) had Post-ESD bleeding (Table). In addition, 6 patients in the VPZ group (31.6%) and 37 patients in the EPZ group (52.9%) had next-day hemostasis. There was no significant difference in both groups regarding post-ESD bleeding (p = 0.678) and next-day hemostasis (p = 0.197). However, next-day hemostasis was somewhat higher in the EPZ group than that in the VPZ group. That is possibly because EPZ or VPZ was first administered mostly from 2 to 4 g/dl of Hemoglobin within 4 weeks after ESD was defined as “post-ESD bleeding”. In addition, we perform second-look endoscopy on the day after ESD. A case in which active bleeding or exposed vessels were observed on the bottom of ulcers with hematemesis, melena or a drop of not less than 2 g/dl of Hemoglobin within 4 weeks after ESD was defined as “post-ESD bleeding”.

Table: Incidence of post-ESD bleeding and next-day hemostasis

<table>
<thead>
<tr>
<th></th>
<th>Vonoprazan group, n (%)</th>
<th>Esomeprazole group, n (%)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>19</td>
<td>70</td>
<td></td>
</tr>
<tr>
<td>Post-ESD bleeding</td>
<td>2 (10.5)</td>
<td>6 (8.6)</td>
<td>0.678</td>
</tr>
<tr>
<td>Next-day hemostasis</td>
<td>6 (31.6)</td>
<td>37 (52.9)</td>
<td>0.197</td>
</tr>
</tbody>
</table>

Conclusion: VPZ didn’t significantly reduce post-endoscopic submucosal dissection bleeding compared with EPZ.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P0511 RISK FACTORS OF GASTROINTESTINAL BLEEDING IN PATIENTS RECEIVED DUAL ANTIPLATELET THERAPY

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Introduction: Current guidelines suggest dual antiplatelet therapy (DAPT), clopidogrel or ticagrelor with aspirin, for patients with acute coronary syndrome. Other indications of DAPT include recurrent ischemic stroke and peripheral vascular disease. Gastrointestinal bleeding (GIB) is one of the most common adverse effects of DAPT, potentially causing hospital admission and death. Scanty information regarding safety of DAPT in Thailand is available.

Aims & Methods: The objectives were to determine cumulative incidence and risk factors of GIB in patients received DAPT, clopidogrel with aspirin or ticagrelor with aspirin among Thai patients.

A retrospective cohort study was conducted. We reviewed the medical records of patients received cloppedregel or aspirin or ticagrelor with aspirin between January 2013 and June 2015 at Ramathibodi hospital. In patients with GIB, the endoscopic finding with stigmata of recent hemorrhage was also recorded.
In 213 patients with GI bleeding, 31 patients received VKA (14.5%) and each on the above mentioned NOACs. Use of proton pump inhibitor and frequencies. These real-life results were then from emergency department of the University Hospital Erlangen were analyzed. Their data manifesting with a GI bleeding under anticoagulation in 2014. All patients who had a rectal bleeding (0%). During NOAC therapy, a similar distribution was found with 71% and 17%, but the proportion of rectal bleeding was higher with 10%.

Conclusion: Risk of GI bleeding is almost two times higher among patients received clopidogrel with aspirin compared to those received ticagrelor with aspirin. Closed monitoring patients who had duration of DAPT < 180 days and previous GI bleeding might be minimized the risk of GI event after receiving DAPT.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P0512 REAL-LIFE ANALYSIS OF FREQUENCY, LOCATIONS AND BLEEDING SOURCES IN UNSELECTED EMERGENCY PATIENTS DURING NON-VITAMIN K ANTICOAGULANT (NOAC) THERAPY AND COMPARISON TO CONTROLLED APPROVAL STUDIES
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Introduction: Non-vitamin K direct oral anticoagulants (NOAC) are increasingly used in thromboembolic disorders due to an efficacy at least equally as vitamin K antagonists (VKA) and/or significantly higher safety for intracerebral bleeding or major bleedings of any source. In the approval studies, there was no generally increased bleeding rate for all types of bleeding, but different gastrointestinal bleeding (GIB) rates for apixaban, dabigatran, edoxaban and rivaroxaban. Received ticagrelor with aspirin were recruited. Mean ± standard deviation age was 66.2 ± 11.3 years and 63.3% of patients were male. The most common indication of DAPT was acute coronary syndrome (85.4% in clopidogrel group vs.100% in ticagrelor group). Duration of treatment with clopidogrel and ticagrelor were 121.5 vs. 231. days, respectively (p = 0.216). There were 20 (10.1%) GIB events in clopidogrel group and 11 (5.5%) in ticagrelor group. The most endoscopic findings of GIB was gastric erosion (44% in clopidogrel group vs. 66.7 % in ticagrelor group). Risk ratio (RR) of GIB event of clopidogrel compared to ticagrelor was 1.84 (95% confidence interval [CI] 0.95–3.7, p = 0.093). By multivariate logistic regression analysis, duration of DAPT < 180 days (RR 3.26; 95% CI 1.89–5.69, p < 0.001) and history of previous GIB were associated with GIB events (RR 10.35; 95% CI 6.04–17.71, p < 0.001).

Conclusion: The frequency of GIB in everyday life is approximately 10% higher than reported from the controlled NOAC studies, irrespective of the type of anticoagulation used. NOACs were associated with a non-significantly lower bleeding rate compared with VKA, but major GIB rates were similar. VKA with a bioavailability of 100% after oral ingestion showed a tendency of higher rates of upper GIB, while NOACs with a reduced GI absorption rate of 7–68% were found to occur more frequently at lower GIB sites. Thus, prior to any anticoagulation, a pre-therapeutic risk analysis for the occurrence of GIB is still required. Certain patient groups (anemia, aortic valve stenosis, renal insufficiency, NSAIDs, etc.) can benefit from proton pump inhibitor therapy, early endoscopy with intervention, or NOAC differential therapy.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
P0514 CLINICAL CHARACTERISTICS OF FUNCTIONAL DYSPEPSIA PATIENTS DEPENDING ON WHETHER THEY ARE CHEMOSENSITIVE OR NOT

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Introduction: Augmented chemosensitivity to capsaicin has been demonstrated in functional dyspepsia patients, but the relevance of these findings is still under debate. The oral capsaicin capsule test (Hammer et al, 2008) was used to determine whether there is a clinical significance of oral capsaicin sensitivity in dyspepsia patients.

Aims & Methods: Aims of the study was to determine clinical characteristics of FD patients with and without chemical hypersensitivity at baseline and after capsaicin ingestion for 4 weeks. N = 49 outpatients with confirmed FD received an oral capsaicin sensitivity test with 0.75 mg capsaicin at two occasions, before and after ingestion. Patients were designated to capsaicin positive (p < 0.05) when positive in both tests and capsaicin negative (p > 0.05) when negative in both tests. Symptom diaries for upper and lower gastrointestinal symptoms (visual analogue scales) were completed in the week before and during capsaicin ingestion and weekly aggregate symptom scores were calculated. Results are given as median; 25%/75%, p < 0.05 was considered significant.

Results: 53% of FD patients had a positive capsaicin test. Basic clinical characteristics (age, gender, FD subtype, medication, psychological profile) were comparable in capsaicin positive and negative FD, but median daily average upper gastrointestinal symptoms scores were significantly higher in capsaicin positive (median: 9.4; 5.4/11.7) than in capsaicin negative patients (6.6; 4.1/8.1) (p < 0.05). Median scores for epigastric pain, nausea and epigastric distension were similar in capsaicin positive and negative patients (p > 0.05). On the contrary, capsaicin negative patients had significantly lower scores for satiety (p < 0.001) and epigastric bloating (p = 0.01) than capsaicin positive patients. Lower abdominal symptoms were comparable in capsaicin positive and negative patients at baseline (NS). After capsaicin ingestion, aggregate upper gastrointestinal symptoms scores were reduced by –3.3 (–4.9/–1.9; p < 0.001) and epigastric bloating (p < 0.01) than capsaicin positive patients. Lower abdominal symptoms scores after capsaicin ingestion were reduced by –1.0 (–1.8/–0.1; p < 0.05) in capsaicin positive but not significantly altered (–0.6; –1.7/+0.9; NS) in capsaicin negative patients. After long-term capsaicin ingestion, the capsaicin test turned negative in 53% of chemosensitive patients (p < 0.01).

Conclusion: Differences in upper GI symptoms distinguished capsaicin positive and negative patients at baseline. Symptom improvement after long-term capsaicin ingestion was indirect proportional to the result during the initial capsaicin test. Sensitivity to orally ingested capsaicin decreases after long-term capsaicin ingestion.

Disclosure of Interest: All authors have declared no conflicts of interest.

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P0515 NUCLEAR LORICRIN AND A DYSREGULATION OF BARRIER PROTEINS OBSERVED IN GASTRO-oesophageal REFUX DISEASE AFFECTED OESOPHAGEAL EPITHELIUM

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Introduction: Gastro-oesophageal reflux disease (GERD) is one of the most common disorders encountered in clinical gastrointestinalology. GERD patients can be categorised as having erosive oesophagitis or non-erosive reflux disease (NERD), with the latter being more frequently encountered in clinical practice. In NERD, even though the endoscopic presentation of the oesophageal mucosa appears visibly normal, histological changes within the oesophageal epithelium such as dilated intercellular spaces and basal cell hyperplasia are present, which are indicative of a sensitised epithelial barrier (Toby et al 1996).

Aims & Methods: Here, we have investigated the expression and activity of key barrier function proteins present in the oesophageal epithelium of proximal and distal biopsies derived from 13 patients with typical GORD symptoms. We compared this to erosive oesophagitis. Nuclear loricrin (LOR), with its stage specific nuclear localization, was the first of the tight junction proteins to be described by the TGM-1 enzyme function to reinforce barrier function through its ability to crosslink and INV in tissue terminal differentiation in epithelial tissues at the cellular membrane. Analysis of TGM-1 enzymatic activity was performed in all NERD patients with and without chemical hypersensitivity at baseline and after capsaicin ingestion for 4 weeks. Nuclear LOR was significantly increased in capsaicin positive patients (5.4/11.7) than in capsaicin negative patients (6.6; 4.1/8.1) (p < 0.05). Median scores for epigastric pain, nausea and epigastric distension were similar in capsaicin positive and negative patients (p > 0.05). On the contrary, capsaicin negative patients had significantly lower scores for satiety (p < 0.001) and epigastric bloating (p < 0.01) than capsaicin positive patients. Lower abdominal symptoms were comparable in capsaicin positive and negative patients at baseline (NS). After capsaicin ingestion, aggregate upper gastrointestinal symptoms scores were reduced by –3.3 (–4.9/–1.9; p < 0.001) and epigastric bloating (p < 0.01) than capsaicin positive patients. Lower abdominal symptoms scores after capsaicin ingestion were reduced by –1.0 (–1.8/–0.1; p < 0.05) in capsaicin positive but not significantly altered (–0.6; –1.7/+0.9; NS) in capsaicin negative patients. After long-term capsaicin ingestion, the capsaicin test turned negative in 53% of chemosensitive patients (p < 0.01).

Conclusion: Differences in upper GI symptoms distinguished capsaicin positive and negative patients at baseline. Symptom improvement after long-term capsaicin ingestion was indirect proportional to the result during the initial capsaicin test. Sensitivity to orally ingested capsaicin decreases after long-term capsaicin ingestion.

Disclosure of Interest: All authors have declared no conflicts of interest.

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P0516 INFLUENCE OF PRUCALOPRIDE ON SECONDARY PERISTALISIS IN REFLUX PATIENTS WITH INEFFECTIVE ESOPHAGAL MOTILITY

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Introduction: Prucalopride, a high-affinity 5-hydroxytryptamine 4 receptors agonist, is useful in the treatment of chronic constipation by improving colon motility. Prucalopride also promotes secondary peristalsis in healthy adults (Clin Transl Gastroenterol, 2016).

Aims & Methods: We aimed to determine whether prucalopride would augment secondary peristalsis in reflux patients with EIM. After a baseline recording of primary peristalsis, secondary peristalsis was stimulated by slow and rapid mid-esophageal injections of air in 15 patients. Two separate sessions with 4 mg oral prucalopride or placebo were randomly performed.

Results: Prucalopride significantly increased primary peristaltic wave amplitude (68.1±10.0 vs. 55.5±8.8mmHg, p = 0.02). The threshold volume for triggering secondary peristalsis was significantly decreased by prucalopride during slow (9.3±0.8 vs. 12.0±0.8mL, p = 0.04) and rapid air injection (4.9±0.5 vs. 7.1±1.0mL, p = 0.01). Secondary peristalsis was triggered more frequently after application of prucalopride (55% [43–70%]) than placebo (45% [33–50%]) (p = 0.008). Prucalopride didn’t change pressure wave amplitudes during slow air injection (84.6±1.8 vs. 57.4±13.8mmHg, p =0.19) or pressure wave amplitudes during rapid air injection (84.2±8.6 vs. 69.5±12.9mmHg; p = 0.09).

Conclusion: Prucalopride enhances mechanosensitivity of secondary peristalsis and promotes motor properties of primary peristalsis in EIM patients. Our study suggests that prucalopride could be a therapeutic option in the management of GERD patients with significant esophageal hypomotility. Disclosure of Property: All authors have declared no conflicts of interest.

Reference


P0517 EFFECTS OF PRIOR PRIOR JEUIN FEEDING ON GASTRIC EMPTYING AND SYMPTOMS IN PATIENTS WITH DIABETIC GASTROPARESIS (49 STUDY): A RANDOMIZED, DOUBLE BLIND CONTROLLED CLINICAL TRIAL


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Introduction: Symptoms compatible with diabetic gastroparesis (DG) affect up to 1 in 5 patients with type I diabetes mellitus. Those affected suffer postprandial
nausea, vomiting, abdominal pain and impaired gastric control. Repeated hospital admissions are common. Endoscopic normal is most patients. Impaired gastric function is thought to cause the condition. DG does not respond reliably to intensive insulin regimens or prokinetic medications. Jejunal nutrition (JN) is an option in patients that cannot maintain their weight. The benefits are thought to follow improved nutrition and glycemia; however, we have observed that some DG patients eat normally during and after JN (i.e. a quasi-pharma-
cological effect). An explanation could be that DG represents a failure of oral nutrition to “switch” the stomach from the fasted to the fed state. According to this hypothesis, nutrients delivered directly to the small bowel triggers the release of peptide hormones that induce normal gastric function.

Aims & Methods: The study tests the hypothesis that JN prior to a test meal improves postprandial symptoms (primary outcome) and gastric function. Diabetic patients with severe symptoms (gastroesophageal cardiac symptom index (GCSI) > 27), diabetic controls (GCSI < 14) and healthy controls entered a randomized, double blind, controlled trial. An insulin/glucose infusion controlled (GCSI) improves postprandial symptoms (primary outcome) and gastric function. Aims & Methods: In this study we aim to compare the safety and efficacy of POEM in treatment native (TN) cases versus prior treatment (PT) failure cases. The data of consecutive patients with AC who underwent POEM at a single tertiary care center from (January 2013 to November 2016) was analysed retro-
spectively. A comparative analysis was performed between TN and PT failure cases. Technical and clinical success, adverse events (AE), operative time (OT) for POEM were compared between TN versus PT failure cases.

Results: Overall, 502 patients with AC underwent POEM during the study period. 260 patients (51.8%) were TN and 242 (48.2%) patients had PT. Type II AC was the most common subtype in both the groups (TN -63.5% vs PT – 57.8%) followed by type I and type III. There was no significant difference with regards to AC subtypes between the two groups. The distribution of patients according to prior treatment history is as follows – PHD (205), LHM (23), LHM and PBD both (7), botulinum toxin injection (4) and POEM (3). Significantly more patients in the PT group had sigmoid oesophagus (47 vs 18). Mean OT was significantly more in the PT group when compared to the TN group (PT vs TN -74.9 ± 30.6 vs 67.0 ± 27.1 min; P = 0.002). On multivariate analysis- type of AC, dilated esophagus (> 6 cm) and type of knife used were significant predictors of OT. Technical (98.1% vs 97.1%, P > 0.05) and clinical success (94.9% vs 91.9%) of POEM were similar in TN and PT cases. Gas related events and mucosotomies were equal in both groups (TN-35.7% vs PT-33.1%; p=0.57). Objective evidence of gastroesophageal reflux was found in 17/53 patients (32.1%) in PT group as compared to 11/44 (25%) in TN group (p=0.50).

Conclusion: POEM is equally efficacious and safe in treatment native and prior treated cases. POEM should be considered in treatment failure cases.

Disclosure of Interest: All authors have declared no conflicts of interest.

References


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Introduction: Per-oral endoscopic myotomy (POEM) has emerged as an efficacious treatment modality for achalasia cardia (AC). Prior treatment (PT) may affect the outcomes of subsequent. The impact of prior treatment on technical and clinical success of POEM is not well known. Small studies with short follow-
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PO518 PER-ORAL ENDOSCOPIC MYOTOMY IN TREATMENT NAIVE VERSUS PRIOR TREATMENT FAILURE CASES – OUTCOME IN OVER 500 PATIENTS

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References


Proportions with abnormal reflux burden in relationship to EGJ and esophageal body motor findings on high resolution manometry

<table>
<thead>
<tr>
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<th>AET &gt; 6%</th>
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<th>MNBI ≥ 2292</th>
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<tr>
<td>n</td>
<td>431</td>
<td>642</td>
<td>596</td>
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</tbody>
</table>

EGJ findings

Intact EGJ (n = 280) 25.7% 60.7%** 58.3% (63/108)
Hypotensive EGJ (n = 862) 36.5%* 49.2%** 53.6% (259/460)
Hiatus hernia (n = 422) 49.0%* 36.5%** 69.8% (138/199)
Both (n = 342) 49.4%* 34.8%** 70.9% (124/175)

Esophageal body motor findings

Intact esophageal body (n = 686) 31.0% 56.9%** 46.5% (158/340)
IEM (n = 326) 41.4%* 44.8% 69.6% (94/135)
Absent contractility (n = 43) 53.5%* 39.5% 88.2% (15/17)
Combined EGJ & esophageal body motor findings

Intact EGJ and body (n = 170) 25.3% 61.2%** 49.3% (36/73)
Hypotensive EGJ, IEM (n = 105) 56.2%* 24.8% 83.0% (44/53)
Hypotensive EGJ, HH 71.4%* 14.3% 100%* (5/5)

*p < 0.05 compared to intact EGJ and/or esophageal body function **p < 0.05 compared to AET > 6%: EGJ: esophagogastric junction: AET: acid exposure time; MNBI: mean nocturnal baseline impedance; IEM: ineffective esophageal motility; HH: hiatus hernia

Conclusion: A disrupted EGJ and IEM on esophageal HRM are independent predictors of elevated esophageal reflux burden. Hierarchical HRM evaluation of EGJ and esophageal body metrics adds confidence to categorization of esophageal reflux burden.

Disclosure of Interest: S. Roman: consulting fees: Medtronic research support; Sandhill, Crespo E. Savartino: Consulting fee from: Medtronic, Sofar, Malesci, Takeda, Abbvie, MSD J. Pandolfini: Medtronic, Sandhill, Torax-Consultants/Speaker/Advisor Zeneca, Takeda- speaker Ironwood, Impleo- consultant C.P. Gyawali: Research support, speaker bureau for Medtronic, Inc Consultant for Torax, Ironwood, Quintiles; Speaker bureau for Allergen All other authors have declared no conflicts of interest.

References


09520 MEASURING THE ACTIVE AND PASSIVE CHARACTERISTICS OF CONTRACTILE SMOOTH MUSCLE IN PORCINE INTESTINE MODEL


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2Division of Gastroenterology and Hepatology, Department of Internal Medicine, Kosin University College of Medicine, Busan/Korea, Republic of
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Aims & Methods: We straighten out the active and passive property of porcine intestine smooth muscle. Our study may be helpful for developing novel medical devices and understanding the physiology of smooth muscle in the porcine small intestine.

Disclosure of Interest: All authors have declared no conflicts of interest.

09521 MOTILITY PATTERNS AFTER PER-ORAL ENDOSCOPIC MYOTOMY (POEM) IN PATIENTS WITH ACHALASIA

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Introduction: Partial recovery of esophageal peristalsis has been reported in up to 95% of achalasia patients treated by myotomy (either per-oral endoscopic myotomy (POEM) or laparoscopic Heller’s myotomy) in several rather small studies. The aim of our study was to assess motility patterns focusing on possible “recovery” of esophageal peristalsis in a large cohort of patients after POEM.

Aims & Methods: We performed a retrospective analysis of prospectively collected data of patients undergoing POEM at our tertiary referral center. All patients in whom high-resolution manometry (HRM) studies were performed prior to and 3 months after POEM and who completed at least 6-month follow-up were included. All HRM studies were reviewed and the Chicago Classification (CC) v3.0 of motility disorders was applied to characterize both pre- and post-POEM motility patterns.

Results: From 192 patients who underwent POEM since 2012, 127 patients met the inclusion criteria. The initial CC diagnoses before POEM were as follows: type I achalasia – 20 pts (16%), type II achalasia – 100 pts (79%), type III achalasia – 5 pts (4%), other (esophageo-gastric junction outflow obstruction (EGJOO) and Jackhammer) – 2 pts (1%). Only 6 patients (5%; type III achalasia – 4, other – 2) had had signs of esophageal contractility before POEM. After POEM, peristaltic fragments were present in 28/127 patients (22%) - 9x ineffective esophageal motility, 5x fragmented peristalsis, 2x distal esophageal spasm, 5x EGJOO, 7x type III achalasia. Thus, the partial “recovery” of esophageal peristalsis was observed in 22/121 patients (18%) and it only occurred in patients with type II achalasia; contractile activity was not detected in any patient with type I achalasia after POEM (22/120 vs. 0/20, p = 0.023). Panesophageal pressurization completely resolved in 88 patients (88%) with...
achalasia type II. The mean integrated-relaxation pressure (IRP) decreased from 27 (±13) mmHg to 13 (±5) mmHg (p < 0.001). The presence of partial peristaltic recovery was neither associated with normalization of IRP (IRP normalized in 17/28 (61%) patients with peristaltic recovery and in 72/99 (73%) patients without, p = 0.25), nor with overall treatment success of POEM (Eckardt score < 3).

Conclusion: In this so far largest case-series investigating the rate of peristaltic recovery after POEM this was present in 18% of patients, therefore, the rate may be lower than previously reported. Peristaltic recovery seems to have no clinical impact on post-POEM symptomatology. Esophagealcontractility after POEM was not observed in any patient with achalasia type I.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

Roman S et al. Partial recovery of peristalsis after myotomy for achalasia; more the rule than the exception. JAMA Surg; 2013;148(2):157–64

P0523 LONG-TERM RESULTS OF PERORAL ENDOSCOPIC MYOTOMY (POEM) FOR ACHALASIA

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2Institute for Clinical and Experimental Medicine, Prague/Czech Republic
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Introduction: Peroral endoscopic myotomy (POEM) has gained trust by proven safety and short-term efficacy and at present, it is considered to be a standard method for treatment of esophageal achalasia. However, long-term data concerning the efficacy and safety especially with regard to post-POEM reflux are still awaited.

Aims & Methods: The aim of this prospective single-center case series was to assess the long-term clinical outcome of POEM with emphasis on post-POEM reflux evaluated by pH monitoring, endoscopy findings, reflux symptoms and use of proton pump inhibitors (PPIs). Since 2012, a total of 192 patients with achalasia underwent 202 POEM procedures. Follow-up visits at 3, 12, 24 and 36 months were completed in 160, 116, 70 and 27 patients. Upper GI endoscopy, high-resolution manometry (HRM) and 24-hour pH monitoring were performed 3 months after POEM, endoscopy was then repeated between 24–36 months. Main outcomes were treatment success defined as Eckardt score < 3, recurrence rate and post-POEM reflux.

Results: At 3, 12, 24 and 36 months, treatment success was achieved in 97% (95% CI: 94–100), 95% (CI 91–99), 88% (CI 82–95) and 81% (CI 69–93) of patients. A total of 14 patients experienced treatment failure (n = 5) or recurrence (n = 9). The recurrences occurred most often in patients with HRM type I achalasia (4 out of 26, 15.4%) followed by type II (3 out of 113, 2.6%) vs. none in type III achalasia (0 out of 10, 0%); p = 0.022. At 3 months, reflux esophagitis was diagnosed in 63/160 patients (39.4%; severe esophagitis LA C or D in 8 patients). Abnormal acid exposure on pH-metry studies was detected in 58/146 (39.7%). At 24–36 months, endoscopy was performed in 41 patients and reflux esophagitis was present in 9 patients (21.9%; none of the patients has been treated with PPIs). At 3 and 24M, a proton pump inhibitor was administered to 33.5% and 31.4% of patients.

Conclusion: POEM is effective treatment modality for achalasia with treatment success around 90% at 2 years, slightly dropping down to 81% at 3 years. Generally mild reflux esophagitis and abnormal esophageal acid exposure are diagnosed in about 40% of patients 3 months after POEM but are successfully manageable with proton pump inhibitors. Occurrence of reflux esophagitis tends to decrease with time.

Disclosure of Interest: All authors have declared no conflicts of interest.
dyspeptic symptoms after a controlled meal. Secondary objectives were to evaluate its relation with daily digestive symptoms under real conditions. Aims & Methods: Healthy people over 18 years old, free of frequent digestive symptoms (<once a week) and GERD disease (GERD), were included. Basal symptoms were assessed through PAGI-SYM (3) and QOLRAD (4) questionnaires, both validated to Spanish. Study was divided in two substudies based on the study intervention: 33 cl of regular beer (substudy 1) and the same amount of non-alcohol beer (substudy 2). Mineral water (33 cl) was the control intervention in both substudies. Each participant was its own control. The study lasted two weeks (control study week and intervention study week). Each week started with a visit to the laboratory at 7:30 h am, when a pHimpedance catheter was placed and taken off 24 hours later. Gastric accommodation was assessed through the maximum tolerated volume during a nutrient drink test (ENSURE started with a visit to the laboratory at 7:30 h am, when a pHimpedance catheter was placed and taken off 24 hours later. Gastric accommodation was assessed through the maximum tolerated volume during a nutrient drink test (ENSURE%. Results: Mean increasement of dyspeptic symptoms compared to Minute (Min) 0

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<th>MINUTE</th>
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Contact E-mail Address: halland.magnus@mayo.edu

Introduction: Rumination syndrome is a functional gastrointestinal disorder characterized by effortless, post-prandial regurgitation of food. In addition to regurgitation, a large proportion of patients report functional dyspepsia (FD) symptoms including post-prandial discomfort, early satiety and nausea (1, 2). Recently, duodenal eosinophilia has been described both in adult and pediatric patients with FD (3, 4). Because of the significant symptomatic overlap between FD and rumination syndrome we hypothesized that histological changes similar to those described in FD might exist among patients with rumination syndrome. Aims & Methods: We therefore aimed to assess histology of duodenal biopsies from patients with rumination syndrome and compared these to healthy controls. Rumination syndrome was diagnosed with post-prandial esophagogastric high resolution impedance manometry (HRIM) and/or fulfilled ROME II/III criteria. This study was approved by the Institutional Review Board. We included persons aged 18 and above with a diagnosis of rumination syndrome in whom we had also obtained 4–6 duodenal biopsies from diagnostic upper endoscopy. Normal controls were aged 18 and above without any gastrointestinal symptoms in whom 4–6 duodenal biopsies were obtained for research purposes. Cases and controls with a personal history of an eosinophilic disorder, gastric or esophageal surgery, recent (within 30 days) intake of NSAIDS and pregnant and/or lactating females were excluded. Duodenal biopsies obtained were routinely processed to formalin fixed paraffin-embedded tissue blocks which were cut at 3 μm, stained with H&E and scanned to digital images (Aperio). The pathologist, blinded to the case-control status, analyzed de-identified digital images of the biopsy specimens and assessed for eosinophil counts/mm² in sections. Individual sections were also assessed for the presence of Brunner’s glands (BG) and intraepithelial lymphocyte counts (IEL) 100 enterocytes. This was done in order to distinguish the first part of the duodenum with Brunner’s glands (BG1) and the second part generally without BG, (DG2) and intraepithelial lymphocyte counts (IEL) 100 enterocytes.

Results: Patients with rumination syndrome (22) had a mean age of 39.2 years (range 19–71) and 77% were female. Controls (10) had a mean age of 34.3 (range 19–69) and 80% were female. The mean eosinophil counts/biopsy fragment +/− Brunner’s glands (BG), showed no difference in counts in the sections +/− BG (D1 vs D2), p=0.8. No overt pathology was noted, but IEL counts were significantly higher in rumination patients (mean 15, range 8–29, and 2 cases had lymphocytic duodenitis) vs controls (mean 11, range 11–18), p=0.02. Compared to controls, there was a significant increase in the mean eosinophil count among the patients with rumination syndrome rumination, 26 pm² (range 16–42), vs 18 pm² (range 10–28), p=0.006.

Conclusion: These findings demonstrate that patients with rumination syndrome have duodenal eosinophilia and increased IEL counts compared to healthy controls. To our knowledge, histopathological changes among patients with rumination syndrome compared to controls have not previously been described. Therefore, a potential role of duodenal immune mechanisms in the pathophysiology of rumination syndrome warrants further enquiry.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

A348 United European Gastroenterology Journal 5(5S)
Table 1

BEER CONSUMPTION AND DYSPEPTIC SYMPTOMS

SUBSTUDY 1 (Regular beer) | SUBSTUDY 2 (Non alcohol beer)

Mean increasement of dyspeptic symptoms compared to Minute (Min) 0

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References
P0527 CHRONIC POSTSTROKE OROPHARYNGEAL DYSPHAGIA IS ASSOCIATED WITH IMPAIRED CORTICAL ACTIVATION TO PHARYNGAL SENSORY INPUTS

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Introduction: The role ofafferent sensory pathways in the pathophysiology of post-stroke oropharyngeal dysphagia (OD) is not known [1]. We hypothesized that chronic post-stroke patients with OD (PSD) would show impaired sensory cortical activation in the affected hemisphere.

Aims & Methods: We studied 28 chronic unilateral post-stroke patients (17 PSD and 11 non-dysphagic [PSnD]) and 11 age-matched healthy volunteers (HV). ES was used to assess event-related sensory evoked potentials to pharyngeal stimulation (pSEP) and sensory thresholds with a naso-pharyngeal catheter with two electrodes passed through the nostrils 14–15 cm until the pharynx (Gaeltec Ltd, Dunvegan, Scotland) [2]. We analyzed pSEP peak-latency and amplitude (N1, P1, N2, P2) and neurotopographic stroke characteristics from brain MRI.

Results: HV presented a highly symmetric bi-hemispheric cortical pattern of brain activation at centro-parietal areas (N1-P1, N2-P2) to pharyngeal stimulation. In contrast, an asymmetric pattern of reduced ipsilesional activation was found in PSD (N2-P2; p = 0.026) but not in PSnD. PSD presented impaired safety of swallow (Penetration- Aspiration score: 4.3 ± 1.6) and delayed laryngeal vestibule closure (360.0 ± 70.0 ms), and higher NIHSS (7.0 ± 2.3 vs. 1.9 ± 1.4; p = 0.001) and Fazekas scores (3.0 ± 1.4 vs. 2.0 ± 1.1; p = 0.05) than PSnD. pSEP showed a unilateral delay at stroke site exclusively for PSD (peak-latency inter-hemispheric difference vs. PSnD: N1: 6.5 ± 6.7 vs. 1.1 ± 1.0 ms; N2: 32.0 ± 15.8 vs. 4.5 ± 4.9 ms; p = 0.05).

Conclusion: Chronic post-stroke OD is associated with stroke severity and degree of leukoaraiosis. Impaired conduction and cortical integration of pharyngeal sensory inputs at stroke site is a key feature of chronic PSD. These findings highlight the role of sensory pathways in the pathophysiology of post-stroke OD and offer a potential target for future treatments.

Disclosure of Interest: All authors have declared no conflicts of interest.

References:

P0528 PERCUTANEOUS ENDOSCOPIC GASTROSTOMY WITH JEJUNAL EXTENSION FOR GASTROPAESIS: THE ULTIMATE SOLUTION?

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Introduction: Gastroperis is characterized by abnormal gastric motor function with delayed gastric emptying in the absence of mechanical obstruction. In our tertiary referral centre, patients are treated with a stepwise approach, starting with dietary and lifestyle advice and prokinetics followed by pyloric botulinum toxin. When these initial measures fail, the presence of malnutrition, one of the following interventions are considered: three months nasoduodenal tube feeding with ‘gastric rest’ and placement of a percutaneous endoscopic gastrostomy with jejunal extension (PEG-J). Our primary aim was to evaluate the effect of nutritional interventions in patients with gastroparesis who fail previous treatments, on weight and symptoms.

Aims & Methods: Prospectively collected data of all referred gastroparesis patients between 2008 and 2016 were reviewed.

Results: A total of 101 gastroparesis patients (71 female, 20-86yrs, mean 55yrs) with ‘gastric rest’ and maintenance (72%), jejunal extension (27%) and surgical (7%) were reviewed. Of the 101 patients, 51 patients had adequate responses to dietary advice and prokinetics, not requiring further therapeutic interventions. For the remaining 50 patients, various treatments were used. Half with respect to nutritional interventions, 36 patients were treated with three months of gastric rest via complete nasoduodenal tube feeding. Enteral tube feeding was well accepted, occlusion occurred in 8% of patients. Mean weight gain in symptom responders was 3.5% (2.4 kg, p = 0.02), in non-responders 3.7% (2.4 kg, p = 0.1). These 19 patients with insuficient symptomatic response after 3 months gastric rest continued treatment with enteral feeding through PEG-J. A significant weight gain of 8.2% was seen (mean 5.0 kg, range –6% to +29%, p = 0.003) within 3-6 months after PEG-J placement. Thereafter only 3 patients (10%) were able to return to complete oral intake, the PEG-J was removed after a mean treatment time of 11 months. In 84% of patients the PEG-J is still in use, with a mean treatment time of 894 days. Over 75% of patients report adequate effect on symptoms. Most frequent complication was ligation of the jejunal extension to the stomach (32% of patients). Other complications were peristomal infection (11% within 30 days, 16% after 30 days) and buried bumper (16%).

Conclusion: This study describes the sequelae of a large group of tertiary referral gastroparesis patients treated with PEG-J treatment. In gastroparesis patients who failed all previous treatment, PEG-J is an excellent option to regain and maintain adequate nutritional status with marked symptom control.

Disclosure of Interest: All authors have declared no conflicts of interest.

References:
P0530 ESOPHAGEAL SYMPTOMS ARE COMMON AND RELATED TO OTHER FUNCTIONAL GASTROINTESTINAL DISORDERS (FGIDs) IN A WESTERN POPULATION

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Introduction: The prevalence and frequency of esophageal symptoms suggestive of a functional esophageal disorder according to the Rome IV criteria are unknown. This study aimed to describe the general population prevalence and risk factors for esophageal symptoms compatible with functional esophageal disorders.

Aims & Methods: Data from an online survey of 6300 individuals age ≥18 years in the United States, United Kingdom and Canada (2100 in each country) including the Rome IV diagnostic questionnaire for adults and demographic questions was used. Quota-based sampling ensured equal proportions of sex, age groups, and educational distributions across countries. Prevalence and frequency of esophageal symptoms in the past 3 months and putative functional esophageal disorders were retrieved from the Rome IV questionnaire. Symptoms were considered present if they occurred at least weekly for dysphagia, chest pain, and globus, and at least twice weekly for heartburn. Variables with a p < 0.1 in univariate analyses were entered into a multivariate analysis (logistic regression) to identify factors independently related to esophageal symptoms. As endoscopy and pH measurement are parts of the clinical diagnosis of esophageal disorders in the Rome IV criteria, we only describe esophageal symptoms compatible with functional esophageal disorders. Somatization was assessed with the Patient Health Questionnaire (PHQ)-12.

Results: Data from 5117 participants (47.8% female; mean age 46.7 (range 18–92) years; 1645 US, 1734 UK, 1798 Canada) were retained for analysis after 369 inconsistent responders and 754 previously diagnosed with gastroesophageal reflux disease (GERD) were excluded. Esophageal symptom prevalence was: feeling of a lump or something stuck in the throat (globus) 8.1% (n = 420), heartburn 6.5% (n = 334), dysphagia 4.5% (n = 233) and chest pain 5.2% (n = 269). Independent predictors for increased risk of esophageal symptoms included younger age, symptoms consistent with other FGIDs, using medications for gastrointestinal symptoms, somatization, cannabis use, and certain foods (see table 1). When individuals with GERD were included in re-analyses, GERD was ¼ separately associated with esophageal symptoms (up to 33 variables).

Table 1: Factors independently associated with presence of esophageal symptoms compatible with a functional esophageal disorder

<table>
<thead>
<tr>
<th>Symptom Factor</th>
<th>Odds ratio</th>
<th>95% Confidence interval</th>
<th>R² value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Globus PHQ12</td>
<td>1.138</td>
<td>1.105–1.172</td>
<td>0.189</td>
</tr>
<tr>
<td>Medication for constipation</td>
<td>1.718</td>
<td>1.146–2.577</td>
<td></td>
</tr>
<tr>
<td>Diet in rice</td>
<td>1.068</td>
<td>1.000–1.139</td>
<td></td>
</tr>
<tr>
<td>Gastroduodenal disorder</td>
<td>2.616</td>
<td>2.006–3.412</td>
<td></td>
</tr>
<tr>
<td>Bowel disorder</td>
<td>1.318</td>
<td>1.032–1.684</td>
<td></td>
</tr>
<tr>
<td>Anorectal disorder</td>
<td>1.699</td>
<td>1.243–2.321</td>
<td></td>
</tr>
<tr>
<td>Chest pain</td>
<td>1.949</td>
<td>1.215–3.128</td>
<td>0.301</td>
</tr>
<tr>
<td>Previously diagnosed with functional dyspnea</td>
<td>6.492</td>
<td>1.342–31.417</td>
<td></td>
</tr>
<tr>
<td>Medication for acid/heartburn</td>
<td>1.488</td>
<td>1.039–2.130</td>
<td></td>
</tr>
<tr>
<td>PHQ12</td>
<td>1.214</td>
<td>1.171–1.259</td>
<td></td>
</tr>
<tr>
<td>Gastroduodenal disorder</td>
<td>2.820</td>
<td>2.051–3.877</td>
<td></td>
</tr>
<tr>
<td>Bowel disorder</td>
<td>1.791</td>
<td>1.311–2.446</td>
<td></td>
</tr>
<tr>
<td>Anorectal disorder</td>
<td>1.536</td>
<td>1.058–2.230</td>
<td></td>
</tr>
<tr>
<td>Diet rich in tofu</td>
<td>1.192</td>
<td>1.058–1.343</td>
<td></td>
</tr>
<tr>
<td>Home with electricity as a child</td>
<td>2.509</td>
<td>1.256–5.011</td>
<td></td>
</tr>
<tr>
<td>Heartburn PHQ12</td>
<td>1.074</td>
<td>1.035–1.114</td>
<td>0.315</td>
</tr>
</tbody>
</table>

Variables with a p-value of 0.1 or less in univariate analysis were entered into a multivariate analysis (logistic regression) in order to identify factors independently associated with esophageal symptoms (up to 33 variables).

Conclusion: Esophageal symptoms compatible with a functional esophageal disorder are common in the Western population. Age and presence of other GI and non-GI symptoms are associated with reporting esophageal symptoms.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0531 DETERMINANT FACTORS OF QUALITY OF LIFE IN ADULT PATIENTS WITH EOSINOPHILIC ESOPHAGITIS

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Introduction: Eosinophilic esophagitis (EoE) affects children and young adults and has rapidly grown over the past decade, especially in developed countries. Presently, it represents the second leading cause of chronic esophagitis after gastroesophageal reflux disease (GERD) and the main cause of dysphagia in children and young adults. EoE affects health-related quality of life (HRQoL). Data on determinant factors and the influence of dietary interventions are scarce.

Aims & Methods: In this study we aimed (1) to determine for the first time the health-related QoL in a representative sample of Spanish adults with EoE, and (2) to identify determinants of impaired HRQoL, including the effect of dietary restrictions. Multicentre observational, cross-sectional study in eight Spanish centers attending adult EoE patients throughout several Spanish Regions. A validated Spanish version of the self-administered Adult Eosinophilic Esophagitis Quality of Life (EoE-QoL-A) questionnaire was used, as well as a survey of demographic and clinical data. Multiple linear regression was used to identify and quantify determinant factors of HRQoL.

Results: Responses provided by 170 patients were assessed (73.5% male; mean age 33.5 ± 11.4y). Overall mean score for the EoE-QoL-A index was 1.4 ± 0.8, with no differences between patients on dietary or pharmacological therapy (1.82 ± 0.8 vs. 1.62 ± 0.8; p = 0.132). Disease activity showed the highest. The mean score (2.13 ± 0.9 points), followed by choking anxiety 1.97 ± 1.1; social impact, 1.77 ± 1.1, and diet/eating impact 1.68 ± 0.9 points. Emotional impact had the lowest rating (1.15 ± 0.9), and the only with a significantly worse score in patients under dietary restrictions. Recurrent food impaction, a higher educational level, dietary interventions and symptom duration were all independent determinant factors significantly impairing HRQoL. Female gender and empiric elimination diets negatively influenced diet/eating impact.

Conclusion: HRQoL is impaired in adult EoE patients, especially disease and choking anxiety. Recurrent food impaction, dietary interventions and symptom duration are the most important factors influencing the perception of HRQoL in EoE.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0532 THE ASSOCIATION BETWEEN ATOPIC MANIFESTATIONS AND EOSINOPHILIC ESOPHAGITIS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: Eosinophilic esophagitis (EoE) is a chronic, immune-mediated, inflammatory disorder, defined symptomatically by esophageal dysfunction and histologically by eosinophil-predominant inflammation of the esophagus.

Table 1 Continued

<table>
<thead>
<tr>
<th>Symptom Factor</th>
<th>Odds ratio</th>
<th>95% Confidence interval</th>
<th>R² value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medication for acid/heartburn</td>
<td>11.427</td>
<td>8.602–15.179</td>
<td></td>
</tr>
<tr>
<td>Gastroduodenal disorder</td>
<td>2.789</td>
<td>2.049–3.798</td>
<td></td>
</tr>
<tr>
<td>Bowel disorder</td>
<td>2.165</td>
<td>1.632–2.872</td>
<td></td>
</tr>
<tr>
<td>Diet rich in pasta</td>
<td>1.113</td>
<td>1.026–1.206</td>
<td>0.242</td>
</tr>
<tr>
<td>Dysphagia</td>
<td>0.990</td>
<td>0.980–1.000</td>
<td></td>
</tr>
<tr>
<td>Medication for diarrhea</td>
<td>1.882</td>
<td>1.100–3.221</td>
<td></td>
</tr>
<tr>
<td>Medication for acid/heartburn</td>
<td>1.456</td>
<td>1.007–2.106</td>
<td></td>
</tr>
<tr>
<td>Gastroduodenal disorder</td>
<td>4.368</td>
<td>3.146–6.065</td>
<td></td>
</tr>
<tr>
<td>Anorectal disorder</td>
<td>1.585</td>
<td>1.072–2.343</td>
<td></td>
</tr>
<tr>
<td>Diet rich in rice</td>
<td>1.913</td>
<td>1.178–3.106</td>
<td></td>
</tr>
<tr>
<td>PHQ12</td>
<td>1.110</td>
<td>1.069–1.154</td>
<td></td>
</tr>
</tbody>
</table>
Several studies have provided information on the prevalence of different atopic conditions in adult EoE patients compared to other groups of control subjects. The findings indicate that, overall, EoE patients show a higher frequency of asthma, rhinoconjunctivitis, eczema, and food allergies than control groups; however, definitions for the associated atopic conditions have not been uniform and the study designs for the controls has not been such that they can be considered universally representative of the general population without EoE. These two limitations have hampered researchers in their efforts to clearly assess the magnitude of the association between atopy and EoE. This systematic review was conducted in order to perform a meta-analysis in order to evaluate the presence of atopic diatheses in patients with EoE as well as to summarize the prevalence of atopic conditions in both paediatric and adult EoE patients in comparison with the non-EoE control populations.

Aims & Methods: A highly sensitive search strategy was designed to identify and retrieve all documents dealing with the relationship between atopy and EoE in children and adults. This systematic literature search was performed independently (AA and AJL) and prospective throughout PubMed databases (PubMed, EMBASE, and Scopus) for the period up to March 2016. The search was not restricted with regard to the language of publication. A predefined protocol was used in accordance with the quality standards for performing meta-analyses of observational studies in epidemiology. Four reviewers (G-JC, AA, MM-MM, and AJL) independently extracted relevant information from each eligible study using a standardized data extraction sheet and then proceeded to cross-check the results. Estimates for the prevalence of each atopic manifestation in EoE patients and controls were summarized with the aid of a fixed- or random-effects meta-analysis, depending on intra-study heterogeneity, weighted for inverse variance following the method elaborated by DerSimonian and Laird. Summary estimates, including 95% confidence intervals (CI), were calculated for each season and month, whenever possible.

Results: Of the 2954 references identified, data was collected from 21 studies including a total of 33,542 EoE patients and 54,759 controls. The criteria for defining a diagnosis of atopy in either EoE patients or controls were not structurally considered in most of the studies. The frequency or prevalence of the different atopic manifestations among EoE patients was compared with that observed in several types of control populations, including series of patients with other upper GI tract diseases (GORD patients, patients with other GI diseases, patients, and healthy controls), all of whom were endoscopically assessed with a diagnosis of EoE specifically ruled out. In all cases, EoE was considered as independent from GORD and other upper GI tract diseases. Some studies included database-registered subjects as a diagnostic group among EoE patients and control subjects varied widely across the different studies, from self-reported/parent-reported atopic background to strict allergist/immunologist-provided diagnoses. Overall, allergic rhinitis was significantly more common among EoE patients as compared to control subjects (OR 5.4 [95% CI: 3.27, 9.53; I² = 86%]) as were bronchial asthma (OR 3.06 (95% CI, 2.01, 4.66; I² = 83.4%) and eczema (OR 2.86; 95% CI, 1.88, 4.36; I² = 57.2%). Food allergies and other atopic conditions were also assessed. No significant publication bias was observed while dealing with allergic rhinitis and eczema in EoE. Finally, our search uncovered two papers that reported on the frequency of drug allergy in EoE patients compared to controls, showing no significant differences between these two populations (OR = 0.981; 95%CI: 0.07, 14.72).

Conclusion: Our present study shows that an accurate diagnosis of allergy is lacking in most of the research evaluating the prevalence of asthma, rhinitis, and eczema among EoE patients. Still, the prevalence of these three conditions seems to be significantly higher in children and adults with EoE as compared to control subjects. More uniform definitions and criteria for defining atopy and other allergic diseases in the general population, based on independent research and use standard definitions of allergic rhinitis, asthma (including its severity and level of control), skin allergy, and food allergy (rather than mere self-reported/parent-reported atopic background to strict allergist/immunologist-provided diagnoses). Overall, allergic rhinitis was significantly more common among EoE patients as compared to control subjects (OR 5.4 [95% CI: 3.27, 9.53; I² = 86%]) as were bronchial asthma (OR 3.06 (95% CI, 2.01, 4.66; I² = 83.4%) and eczema (OR 2.86; 95% CI, 1.88, 4.36; I² = 57.2%). Food allergies and other atopic conditions were also assessed. No significant publication bias was observed while dealing with allergic rhinitis and eczema in EoE. Finally, our search uncovered two papers that reported on the frequency of drug allergy in EoE patients compared to controls, showing no significant differences between these two populations (OR = 0.981; 95%CI: 0.07, 14.72).

Disclosure of Interest: All authors have declared no conflicts of interest.

Table 1: Plasma FP PK Parameters

<table>
<thead>
<tr>
<th>Parameter</th>
<th>AM Fast Geometric Mean (CV%)</th>
<th>AM Fed Geometric Mean (CV%)</th>
<th>Mean (CV%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cmax (pg/mL)</td>
<td>31.1 (103.6)</td>
<td>34.2 (102.3)</td>
<td>35.4 (101.9)</td>
</tr>
<tr>
<td>Tmax (h)</td>
<td>10.00 (2.00-30.00)</td>
<td>5.00 (1.00-10.00)</td>
<td>7.20 (2.00-30.00)</td>
</tr>
<tr>
<td>AUC0–24 (pgh/mL)</td>
<td>366.607 (115.8)</td>
<td>361.277 (105.5)</td>
<td>359.541 (100.5)</td>
</tr>
<tr>
<td>AUC0–5 (pgh/mL)</td>
<td>1044.308 (90.1)</td>
<td>587.890 (107.2)</td>
<td>726.451 (100.2)</td>
</tr>
</tbody>
</table>

CV% = percentage coefficient of variation. *Median and range are presented.
to steroids (64% vs 36%; p = 0.002). Specifically, the presence of strictures indicated a more likely clinical response to steroids compared to PPI alone. (p = 0.007).

Conclusion: A higher eos/hpf was found in patients with chronic EE features at index endoscopy than those with normal or acute endoscopic signs. In those with normal or acute EE changes and without dysphagia as a presenting complaint, a clinical response was noted with PPI therapy alone. In those with chronic EE changes or with dysphagia/FBO, steroids appear to be the preferred therapeutic option, although at 3 months follow up a clinical response might precede a histological one.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0536 ESOMEPRAZOLE, RABEPRAZOLE AND PANTOPRAZOLE ARE EQUALLY EFFECTIVE IN INDUCING ENDOSCOPIC AND HISTOLOGIC REMISSION IN PATIENTS WITH PROTON PUMP INHIBITOR-RESPONSE ESOPHAGEAL EOSINOPHILIA

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Introduction: Proton Pump Inhibitor-response esophageal eosinophilia (PPI-REE) is an emerging condition characterized by a constellation of clinical, endoscopic, and histopathologic features in the setting of eosinophilic inflammation on esophageal biopsies responding to a course of proton pump inhibitor (PPI) therapy. A recent meta-analysis explored the role of different PPIs in inducing clinical and histologic remission in patients with PPI-REE. These data, although obtained in a small sample of patients, suggest that the pharmacokinetic and pharmacodynamic differences among these drugs do not affect their effect on PPI-REE patients.

Results: Twenty-eight patients [23M/5F; mean age 35] reporting dysphagia (93%), bolus impaction (68%) and chest pain (25%) were diagnosed with PPI-REE. According to treatment allocation, 8 (29%) patients received esomeprazole, 9 (32%) rabeprazole and 11 (39%) pantoprazole. At baseline, demographic, allergy conditions and latency from diagnosis were similar (p = ns).

Aims & Methods: We aimed to prospectively compare the effect of different PPIs in inducing endoscopic and histologic remission in patients with PPI-REE. Consecutive patients with symptoms suggestive of EE underwent upper endoscopy to assess the presence of at least 15 eos/hpf on esophageal biopsies at mid/proximal esophagus and, then, were treated with twice-daily PPI for at least 8 weeks. Patients were assigned to receive esomeprazole 20 mg bid, rabeprazole 20 mg bid or pantoprazole 40 mg bid in a 1:1:1 ratio. Thereafter, patients repeated upper endoscopy and PPI-REE was identified in case of less than 15 eos/hpf on esophageal biopsies at mid/upper esophagus mechanically (fluid, solids and gas).

Results: Twenty-eight patients [23M/5F; mean age 35] reporting dysphagia (93%), bolus impaction (68%) and chest pain (25%) were diagnosed with PPI-REE. According to treatment allocation, 8 (29%) patients received esomeprazole, 9 (32%) rabeprazole and 11 (39%) pantoprazole. At baseline, demographic, allergy conditions and latency from diagnosis were similar (p = ns).

Endoscopic and histologic features at baseline and after PPI therapy are shown in the Table. Esomeprazole, rabeprazole and pantoprazole reached the same degree of efficacy in inducing endoscopic and histologic changes in PPI-REE patients (p = ns).

Table: Endoscopic and histologic features at baseline and after PPI therapy in PPI-REE

<table>
<thead>
<tr>
<th>Group</th>
<th>After-Therapy</th>
<th>Baseline</th>
</tr>
</thead>
<tbody>
<tr>
<td>Esomeprazole</td>
<td>75% 6 87 5</td>
<td>95 6</td>
</tr>
<tr>
<td>Rabeprazole</td>
<td>75% 6 87 5</td>
<td>95 6</td>
</tr>
<tr>
<td>Pantoprazole</td>
<td>75% 6 87 5</td>
<td>95 6</td>
</tr>
</tbody>
</table>

Conclusion: Esomeprazole, rabeprazole and pantoprazole administered at double daily dose were equally effective in determining endoscopic and histologic remission in patients with PPI-REE. These data, although obtained in a small sample of patients, suggest that the pharmacokinetic and pharmacodynamic differences among these drugs do not affect their effect on PPI-REE patients.

Disclosure of Interest: V. Savarino: Consulting fee from Malesci, Reckitt, AlfaWassereman, Abbvie
E. Savarino: Consulting fee from Medtronic, Sofar, Takeda, Abbvie, MSD
All other authors have declared no conflicts of interest.

P0537 THE «GARD» (GASTRO-ESOPHAGEAL ANTI-REFLUX DEVICE): A NEW ENDOSCOPIC MEDICAL DEVICE TO DIAGNOSE, MANAGE AND TREAT GERD

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Introduction: The « GARD» (Gastroesophageal Anti-Reflux Device) is an anti-reflux tubular valve placed in the lower esophagus under endoscopic control allowing normal ingestion of food and beverages but blocking all gastro-esophageal refluxate mechanically (fluid, solids and gas).

Aims & Methods: The « GARD» has an upper ring sized to the diameter of the patient’s esophagus with an accessory called the « calibration device » placed through the 2.8 mm working channel of a standard gastroscope. The GARD is held in place by pressure. The upper ring holds an anti-reflux thin-walled tubular valve moulded in one piece under the ring. After placement of a standard guidewire, the « GARD » is placed through the patient’s mouth and is released in the lower esophagus. The procedure is performed under sedation on an ambulatory basis in about 15 minutes when experienced. The « GARD » was placed in the esophagus of 8 pigs during 7 days to evaluate placement, feeding, weight gain, absence of migration as well as removal. Deployment of the « GARD » was easy, there was no migration in the stomach and removal of the GARD with the developed accessories was easily achieved. However, pigs have a strong lower esophageal sphincter and have no reflux so gastro-esophageal reflux could not be evaluated. In a human volunteer with very severe gastro-esophageal reflux who had previously failed anti-reflux surgery and had an unsatisfactory response to clinical and pH metric measurement under 80 mg of esomeprazole, the « GARD » was placed preoperatively. Hereafter are this patient’s pHometric results without PPIs (table 1); with the patient taking 80 mg/day PPIs (table 2) and after GARD placement and PPIs stopped for 10 days, table 3.

Results: Fig 1. First pH metric study (no PPIs for 10 days): The patient has very severe reflux with 63% of the time with a pH under 4 (normal less than 4% of the time at a pH under 4) after PPIs were stopped for 10 days. Fig 2. Patient is taking 80mg of esomeprazole a day. A pH metric measurement remains highly pathological at 23% of the time under pH 4 once PPIs have been resumed at 80 mg of PPIs daily. Fig 3. After placement of the GARD and PPIs have been stopped for 10 days, there is no longer any reflux measured. The pH tracing does not drop under the red line at pH 4.

Conclusion: a new medical device blocking GERD is presented. A first clinical trial is scheduled to start in 2018 to help diagnose and manage Refractory GERD. Further clinical indications are at the planning stage including treatment of Refractory GERD and LPR.

Disclosure of Interest: All authors have declared no conflicts of interest.

Table Continued

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<tr>
<td>Esomeprazole Group (n = 8)</td>
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<td>Rabeprazole Group (n = 9)</td>
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<td>Pantoprazole Group (n = 11)</td>
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P0538 SYMPTOM PATTERNS AND TYPES OF GASTROESOPHAGEAL REFLUXES SIGNIFICANTLY DIFFER IN GROUPS OF EROSIve ESOPHAGITIS AND NON-EROsiVe FORM OF GASTROESOPHAGEAL REFLUX DISEASE (GERD) PATIENTS

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Introduction: Patients with gastroesophageal reflux disease (GERD) demonstrate a range of different symptoms (esophageal and extraesophageal) however the relationship between symptoms and types of reflux was not evaluated.

Aims & Methods: The aim of the study was to assess the relationship between GERD patients’ symptoms with characteristics of refluxes obtained by 24-h esophageal pH-impedance. One hundred fifty eight GERD patients (68 men, 89 women, age (M ± m) 42 ± 4.8 yrs and 49 controls (22 men, 27 women, age (M ± m) 46 ± 6.7 yrs) were examined using 24-hour esophageal pH-impedance recordings (Ohmega, MMS, the Netherlands; 2pH-6 impedance channels catheters, UnisensorAG, USA) and validated GERD-Q questionnaire. According to baseline endoscopy 91 patients were classified as non-erosive reflux disease (NERD) and 67 as erosive reflux disease (ERD) patients. Patients’ symptoms were classified according to Montreal classification.

Results: Extraesophageal symptoms as well as weak acid gastroesophageal refluxes were found significantly more often in patients with NERD compared to ERD group (table 1). However higher number of acid refluxes, higher GERD-Q score and DeMeester score were present in ERD. The total number of gastroesophageal refluxes didn’t differ between ERD and NERD groups of patients.

Table 1: Results of the study

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<tr>
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<th>Controls (n = 49)</th>
<th>NERD (n = 91)</th>
<th>ERD (n = 67)</th>
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<tr>
<td>Number of refluxes/ day, n</td>
<td>17 ± 1.3</td>
<td>55 ± 3.0*</td>
<td>55 ± 4.7*</td>
<td>≤0.729</td>
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<tr>
<td>Number of acid refluxes/day, n</td>
<td>6 ± 1.0</td>
<td>27 ± 2.2*</td>
<td>33 ± 3.7*</td>
<td>≤0.040</td>
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<tr>
<td>Number of weak acid refluxes/day, n</td>
<td>7 ± 0.93</td>
<td>22 ± 2.1*</td>
<td>15 ± 2.3*</td>
<td>≤0.038</td>
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<tr>
<td>Number of high gastro-esophageal refluxes/day, n</td>
<td>2 ± 0.47</td>
<td>15 ± 1.4*</td>
<td>12 ± 2.2*</td>
<td>≤0.347</td>
</tr>
<tr>
<td>DeMeester score</td>
<td>3.16 ± 1.75</td>
<td>13.3 ± 2.0*</td>
<td>26.92 ± 6.2*</td>
<td>≤0.0001</td>
</tr>
<tr>
<td>GERD-Q score</td>
<td>5 ± 0.31*t</td>
<td>10 ± 0.24*</td>
<td>13 ± 1.27*</td>
<td>≤0.0001</td>
</tr>
<tr>
<td>Extraesophageal sympoms (cough, laryngitis, etc.) (presence, % in group)</td>
<td>0</td>
<td>61.5*</td>
<td>31.3*</td>
<td>≤0.0001</td>
</tr>
</tbody>
</table>

Conclusion: ERD and NERD groups of patients are characterized by different symptom patterns and types of gastroesophageal refluxes registered with 24-hours esophageal pH-impedance monitoring. These findings could reflect differences in pathogenesis and clinical manifestations of mentioned forms of GERD. Disclosure of Interest: All authors have declared no conflicts of interest.

P0539 LARYNGEAL DISORDERS AND CHRONIC COUGH IN ADULTS WITH AND WITHOUT ESOPHAGEAL ESOPHAGITIS: A CASE-CONTROL STUDY IN ALBANIA

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Introduction: Several clinical-based studies from Western countries have investigated the prevalence of extra-esophageal symptoms in various degrees of reflux erosive esophagitis. However, the independent factors related to the development extra-esophageal manifestations remain unclear.

Aims & Methods: Our aim was to assess the prevalence of extra-esophageal symptoms (laryngeal disorders and chronic cough) in adults with (cases) and those without (controls) erosive esophagitis in Albania, a developing Southeast European country. A case-control study was conducted at the Regional Hospital of Durres, the second main district in Albania, a transitional country in South Eastern Europe, including 289 patients with erosive esophagitis (aged 16–55 years) and 273 controls (aged 46± 16.0 years; response rate: 70%) enrolled during the period January 2013 – June 2014. Both cases and controls underwent upper endoscopy. Information on socio-demographic characteristics and lifestyle factors were also collected. Binary logistic regression was used to assess the association of erosive esophagitis and extra-esophageal symptoms.

Results: Patients with erosive esophagitis had a higher prevalence of excessive alcohol consumption, smoking, sedentariness and obesity compared to their control counterparts (9% vs. 5%, 70% vs. 49%, 31% vs. 17% and 22% vs. 9%, respectively). The prevalence of hiatal hernia was higher in cases than in controls (21% vs. 8%, respectively), whereas the prevalence of gastric-duodenal ulcer was similar in both groups (13% vs. 14%, respectively). Upon adjustment for all sociodemographic characteristic and lifestyle/behavioral factors, there was evidence of a strong association of erosive esophagitis with chronic cough (OR = 3.1, 95%CI = 1.7–5.7), and even more so with laryngeal disorders (OR = 4.4, 95%CI = 2.6–7.4). In all models, the association of extra erosive esophagitis with extra-esophageal symptoms was strong and remained significant after adjustment of the symptoms separately (fully-adjusted model: OR = 4.6, 95% CI = 2.9–7.3).

Conclusion: Our findings indicate that the prevalence of extra-esophageal symptoms is higher among patients with erosive esophagitis in a transitional country characterized conventionally by the employment of a Mediterranean diet. Therefore, the upper esophageal should be part of the evaluation in patients with suspected reflux-related chronic cough and laryngeal disorders.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0540 ASSESSMENT OF EXHALED BREATH CONDENSATE FOR NON-INVASIVE DIAGNOSIS OF GASTROESOPHAGEAL REFLUX DISEASE IN CORRELATION WITH MII-PH AND PEPTEST

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Introduction: Gastroesophageal reflux disease (GERD) is a disease caused by backflow of gastric contents into the esophagus due to the failure of physiological anti-reflux mechanisms and is the main cause of extraesophageal symptoms. Extraesophageal reflux (GER) is a condition where refluxate penetrate above the upper esophageal sphincter (UES) in to the oral cavity, pharynx, upper and lower respiratory tract and leads to pathological changes like e.g. chronic cough, globus pharyngis, laryngitis, pharyngitis, rhinosinusitis, otitis media, bronchial asthma, COPD, sleep apnea and noncardiac chest pain. Currently there is no suitable, non-invasive diagnostic method applicable for GERD in clinical practice. Exhaled breath condensate (EBC) and saliva are two easily obtainable samples that could be used in monitoring of patients suffering from extraesophageal symptoms of GERD. The aim of this study was to compare the pH and total ionic profile of EBC with 24-hour multichannel intraluminal impedance and pH monitoring (MII-PH) and salivary Peptest in a group of patients with reflux (pH < 4), weak and strong acid reflux (pH 4–7) and healthy controls.

Aims & Methods: A portable EBC sampler was used for collection of EBC. 10 µL sample aliquots of EBC were analyzed. For pH measurement, the CO2 from EBC was trapped with Na2 gas for 24 hours. The pH was measured with a pH microelectrode and total ionic profile (amions, cations, organic acids - NH4+, K+, Ca2+, Na+, Mg2+, Cl-, CO3-, NO3-, SO42-, acetate, lactate, propionate, butyrate) was analyzed by capillary electrophoresis in each sample. Saliva was collected using the commercial Peptest sampling containers, applied to the Peptest lateral flow devices and analyzed using the device reader. The data from EBC were compared with MII-PH and Peptest. In total the study comprised of 39 participants. The patients were divided by dominant findings from MII-PH to groups with acid reflux (n = 17), weakly acid reflux (n = 8) and without reflux (n = 14).

Results: The values of pH (after CO2 removal with Na2) were significantly higher in the group with acid reflux (p < 0.01), (mean pH 7.13, interquartile ranges 6.83–7.47) and in the group with weak acid reflux (p < 0.01) (7.37, (7.18– 7.57)) vs. healthy controls (6.8, (6.65–6.99)). Butyric acid (BA) was the second most significant parameter that was significantly elevated (p < 0.01) in both patient groups (acid reflux- mean BA 2.29 µM, weak acid reflux- mean BA 3.31 µM) compared to healthy subjects (mean BA 0.69 µM).

Further statistically significant differences were found in chloride ([Cl]−), nitrate ([NO3]−) and sodium ([Na+] ions concentration. CI− was elevated (p < 0.01) in group with acid reflux vs. healthy controls and NO3− and Na+ were elevated (p < 0.01) in the group with with weak acid reflux vs. healthy controls. For saliva sampling and peptin analysis showed no statistically significant differences within the groups. In the groups of patients with acid reflux, the incidence of high peptin concentration (above 75 ng/ml) was found only in 50% of the patients.

We found statistically significant difference in pH in selected ions from EBC between different groups of patients and healthy controls. The analysis of selected parameters in EBC could provide a fast and non-invasive diagnostic method for GERD patients with EER symptoms in the future. This can
Introduction: Impedance-pH testing is actually considered the gold standard diagnostic tool for reflux assessment. In fact, it allows to characterize any type of gastro-esophageal reflux (GER), namely acid and non-acid, and therefore permits – in presence of typical reflux symptoms – to diagnose functional heartburn (FH) based on the lack of abnormal acidic or non-acidic refluxate (i.e. normal number of reflux episodes and negative reflux-symptom association). Gastrin-17 (G17) has been proposed as a non-invasive marker of GERD, due to the negative feedback between acidic output and this hormone. Indeed, preliminary data showed that intermediate values of G17, between very low to normal levels, may identify GERD subjects with abnormal non-acid reflux.

Aims & Methods: We aimed to correlate various patterns of refluxate (i.e. predominant acidic refluxate, predominant non-acidic refluxate and no reflux at all), as assessed by impedance-pH, with different levels of G17 in endoscopy-negative subjects with heartburn. Thirty-five consecutive patients (19F/16M, mean age 47 years, range 31–56 years), all reporting heartburn since 6 months with at least 3 episodes/week, entered the study. All patients underwent upper endoscopy off-therapy and blood determination of G17. In the Group A, the mean value of G17 was 2.6 pmol/l, and, in the Group C was 5.1 pmol/l any kind of GER (Group C). In the Group A, the mean value of G17 was 2.6 pmol/l, and, in the Group C was 5.1 pmol/l. Results: The results of impedance-pH: a) Group A: subjects with increased number of acid reflux episodes and normal AET. In the Group B, levels of G17 were always low, but higher than in case of acid reflux pattern (Group A) (p < 0.05). Finally, when impedance-pH did not show any kind of abnormal reflux, suggesting a diagnosis of FH, G17 levels were always normal.

Conclusion: In this preliminary study, G17 levels well correlated with the three different categories of patients suffering of heartburn and included in the NERD umbrella (i.e. NERD patients with increased acid reflux episodes or abnormal AET, endoscopy-negative patients with increased non-acidic reflux and subjects with FH), suggesting its use as surrogate marker of NERD or non-acid reflux disease, without the need of performing invasive tests.

Disclosure of Interest: E. Savarino: Consulting fee from Medtronic, Sofar, Takeda, Abbvie, MSD. All other authors have declared no conflicts of interest.

Introduction: As a treatment for gastro esophageal reflux disease (GERD), proton pump inhibitors (PPIs) are the mainstream of medical therapy. Laparoscopic fundoplication is generally advised when symptoms are poorly controlled with PPIs and is regarded as a gold standard of treatment, with excellent control in the short- and midterm. Long-term results, however, remain equivocal. Following on from the principles of surgical fundoplication, a variety of endoscopic procedures for GERD have been proposed to achieve non-surgical control. Linx procedure, Stretta have been proposed as less invasive options.

Aims & Methods: We recruited all patients who had GERD refractory to standard medical therapy to see whether anti reflux mucosectomy prevents acid reflux into the esophagus. We screened all GERD patients who were refractory to proton pump inhibitors, hydrogen 2 receptor blockers and alginates and had an endoscopy suggestive of a lax cardia with mucosal flap valving grading of 1 to 5. We performed a baseline screening endoscopy to rule out a hiatus hernia and to exclude helicobacter infection. A GERDQ questionnaire was filled by all the patients indicative of severity of reflux All patients had a high resolution manometry (Sandhill scientific) to exclude significant dysmotility and 24 hour pH measurements using Zephyr pH probe (Sandhill scientific) on therapy to demonstrate significant acid reflux. Only patients with mucosal flap valving grade 1, 2 or 3 were selected for anti reflux mucosectomy.

Results: Technique: Crescentic ARMS of the esophagogastric junctional (EGJ) mucosa was conducted with the standardized technique of endoscopic mucosal resection (EMR) of at least 3 cm length in the stomach, with the length of mucosal resection at the cardia measured in retroflexion from the gastric side. ARMS was conducted along the lesser curve of the stomach, thus preserving a sharp mucosal valve at gastric cardia. All the patients who underwent ARMS had a significant reduction in the DeMeester score, with predominant decrease in the recumbent acid reflux. 7/12 patients were able to discontinue all the medical therapy, PPI dose reduction was possible in the other patients with a mean reduction of 50%, all alginates were stopped in all patients and HRA were also discontinued.

Conclusion: Results suggest a potential anti-reflux effect of ARMS. The mechanism is presumed to be due to scar formation after healing of the mucosal defect. On the gastric side, this induces narrowing of the gastric cardia opening, while preserving and/or re-creating a robust his angle. After ARMS, the lesser curve of the gastric cardia takes on an almost “mechanically-stitched” appearance. The mucosal flap is robust and looks well-defined. Furthermore, the lesser curve side potentially reduce the diagnostic cost and avoid unnecessary invasive MII-pH testing in future. Unlike the EBC, pepsin analysis using Pepstep did not provide any diagnostic value.

Disclosure of Interest: This work was supported by Ministry of Health of the Czech Republic, grant nr. 17-31945A. All rights reserved.

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of the EGI is shortened with scar formation, and greater curve of EGI (his angle is not mentioned) is noted, and therefore retained resectability as a mucosal flap valve. The quantity of mucosa to be resected to induce appropriate (“not too tight and not too loose”) scar formation is a key issue in this procedure. Total circumferential resection causes strictureing as demonstrated in previous studies, while subtotal dissection, which we have termed crescentic, produces better results in this regard, while still resulting in symptom control. Mucosal flap valve grading is not only a good predictor of reflux in these patients but also is a prognostic marker of effectiveness of ARMs, i.e. higher the grade worse the outcome. The extent and type of mucosal resection (4R vs. 4S) according to the mucosal flap valve grading may be a better predictor of outcome than a box standard procedure. This technique has a potential role in people with oesophageal dysmotility wherein Nissen’s fundoplication is relatively contraindicated.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference


P0543 A RANDOMISED, DOBLE-BLIND, PLACEBO-CONTROLLED, MULTICENTRE 26 WEEK STUDY ON THE EFFECTS OF DEXLANSOPRAZOLE AND ESOMEPRAZOLE ON BONE HOMEOASTIS IN HEALTHY POSTMENOPAUSAL WOMEN

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Introduction: Observational and epidemiologic data have suggested an association between proton pump inhibitor (PPI) use and osteoporotic fractures. To evaluate potential mechanisms for this association, we measured bone turnover, except a small increase in CTX levels with DEX (0.12 ng/mL, 95% CI 0.03–0.23). The 26-wk median % increases in P1NP from baseline vs PBO (difference not significant (P = 0.05) increase in the pH in the esophagus for 120 minutes after ingestion [average pH values 6.04 ± 0.27 vs. 4.86 ± 0.23 during 0–60 min., and 5.93 ± 0.25 vs. 4.15 ± 0.26 during 60–120 min.]). In the gastric cardia (a typical place of formation of postprandial acid pocket) showed significant (P = 0.05) higher values for the first 60 minutes after intake of alginate [pH 4.3 ± 0.37 vs. 3.04 ± 0.25], during 60–90 min, pH values wasn’t significantly (P > 0.05) different [2.75 ± 0.45 vs. 2.43 ± 0.20]. In the stomach body no significant effect of the drug on pH was recorded [average pH values for stomach 2.56 ± 0.46 vs. 2.1 ± 0.18 during 1st postprandial hour and 2.29 ± 0.49 vs. 2.09 ± 0.18 during 2nd postprandial hour; P = 0.05].

Conclusion: Our findings demonstrate that raft-forming alginate is an effective antireflux treatment and is effective in the prevention of postprandial acid and gas reflux and to reduce the injurious effect of acid in the esophagus. At the same time alginate showed no effect on stomach content in the postprandial period, it means that the main mechanism of action is through the movement of postprandial acid contents from the lower esophageal sphincter, but not the neutralization of stomach acid, unlike nonraft-forming antacids and PPIs.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0545 EFFICACY OF S-PANTOPRAZOLE 10 MG IN THE SYMPTOM CONTROL OF NON-EROSIVE REFUX DISEASE: A PHASE III PLACEBO-CONTROLLED TRIAL

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Introduction: S-isomer (S) pantoprazole is more bioavailable and less dependent on cytochrome 2C19 than is racemic pantoprazole.

Aims & Methods: We aimed to evaluate the efficacy and safety of 10 mg S-pantoprazole for treatment of non-erosive reflux esophagitis (NERD). This study was designed as a multicenter, randomized, double-blind, placebo controlled trial. NERD was defined as reflux symptoms and normal endoscopy findings. Patients were allocated to take either 10 mg S-pantoprazole or placebo once daily for 4 weeks, after which reflux symptoms were reassessed. Recurrence of symptoms was assessed at 4 weeks after cessation of medication. The efficacy endpoints were complete relief of symptoms, improvement of reflux symptoms, and safety.

Results: Eighty-eight patients randomly assigned pantoprazole group (25 males, 43.7 years old) and 86 to the placebo group (32 males, 43 years old), and 163 patients were subjected to a per protocol analysis. A higher proportion of patients in the S-pantoprazole group had complete symptom relief (33.6% vs. 14%, P < 0.001). In the both groups, symptoms of heartburn, acid regurgitation and epigastric discomfort significantly improved after treatment compared with baseline; however, improvement of all symptoms was greater in the s-pantoprazole group compared to placebo group. Therapeutic gains in controls of heartburn, acid regurgitation and epigastric discomfort were 66 to 80%.

The factors associated with poor symptom responses to PPI were older age, female sex, greater body mass index and symptom severity in both groups.

Conclusion: S-pantoprazole (10 mg) was more efficacious than placebo in providing reflux symptom relief in patients with NERD, especially acid regurgitation.

Disclosure of Interest: All authors have declared no conflicts of interest.
**P0546**

**TAILED THERAPY GUIDED BY MULTICHLANAL CONTACT PH MONITORING FOR REFRACTORY NON EROSIVE REFUX DISEASE: PRELIMINARY EXPERIENCE**

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**Introduction:** Refractory non erosive reflux disease (NERD) is defined by absence of clinical response to a 12-week course of proton pump inhibitors (PPI) at full dose in absence of esophagitis. It accounts for about 20% of all NERD cases. 24-hour multichannel intraluminal impedance (pH/MII monitoring) should give useful patient-specific information about refractory NERD. Therefore, our aim was to assess whether this technique could be useful to guide a “tailed” therapy to refractory NERD patients.

**Aims & Methods:** We retrospectively recruited patients undergoing pH/MII monitoring for refractory NERD. All patients had undergone upper endoscopy, and cases of esophagitis were excluded. No patient received PPI during pH/MII monitoring. Subjects were subgrouped into 3 categories according to Zerbib’s classification: i) Acid reflux (exposure to pH ≤ 4 for at least 1.1% of record time), ii) Non acidic reflux (symptom association probability to pH > 4 reflux episodes > 95%), and iii) Functional heartburn (no pathologic reflux with symptom association probability < 50%). MII-pH guided therapy was performed as follows: patients with acid reflux received PPI at double dose, patients with non acid reflux PPI at full dose plus alginates and patients with functional heartburn levosulpride 75 mg/day for 4 weeks. A visual analogue scale (VAS) ranging 0–100 was administered before and after such tailored therapy to evaluate overall symptomatology. Responders were defined by VAS improvement of at least 70%. Comparisons between continuous variables were performed by ANOVA or paired/unpaired t-test where required, and Fisher’s exact test was applied to categorical variables. Variables with statistical significance p < 0.10 at univariate analysis were entered into a binary multivariate regression analysis, aimed to investigate factors predictive of response to tailored therapy.

**Results:** Thirty-four patients with refractory NERD were selected (female:male ratio 20:14, mean age 47.4 ± 12.8). Twelve had acid reflux, 7 non acid reflux and 15 functional heartburn. Overall effectiveness of tailored therapy was 82.3% (26 out of 34), and it did not differ between subgroups (91.7% acid reflux, 71.4% non acid reflux, 80.0% functional heartburn, p = 0.31). At univariate analysis, therapy failure directly correlated with dysphagia (OR = 0.15, p = 0.10) and inversely with sensation of slow digestion (OR = 7.70, p = 0.05). However, at multivariate analysis, these parameters were not statistically significant. We found a mean VAS reduction of 30.2 ± 24.9, which was similar between acid reflux (36.7 ± 22.7), non acid reflux (30.0 ± 27.7) and functional heartburn (38.2 ± 25.7) p = 0.76.

**Conclusion:** A tailored approach to refractory NERD, guided by pH/MII monitoring, demonstrated to be effective, independently from disease subtype. Therefore it should be advised to patients who complain of symptom persistence despite PPI therapy.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**References:**


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**P0548**

**THE EFFECT OF SPECIFIC REFUXATE COMPONENTS ON BILE RECEPTOR SIGNALING AND DEVELOPMENT OF METASTATIC BARRETT-LIKE GLANDS IN MICE**

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**Introduction:** Chronic reflux, a risk factor for the development of Barrett’s esophagus (BE), causes damage to the normal squamous epithelium of the esophagus, which eventually is replaced by a columnar type of epithelium. It has been shown that bile acids (BAs) play a role in the development of BE. The effect of different BAs in the refluxate has been poorly studied with respect to the pathogenesis of BE. Insights in the effects of the bile components in reflux can help provide more efficacious targets for preventing the development of metaplasia and the progression from BE to EAC. Before being released into the duodenum, BAs produced by the liver are conjugated with either taurine or glycine. BAs not only have detergent properties, but can also act as signaling molecules by activating the farnesoid X receptor (FXR) and G-protein coupled bile acid receptor (TGR5). Both receptors are upregulated in BE and EAC compared to normal squamous mucosa, suggesting a possible role in the progression of BE. (De Gottardi 2006; Hong 2010).

**Aims & Methods:** The aim of the study was to analyze refluxates of BE patients and evaluate the effect of these different bile components on metastatic gland development and bile receptor activation.

**Results:** Determination of the bile composition in refluxate of BE patients by HPLC showed the presence of both glyco-conjugated (67.6 ± 8.8%) and taurine-conjugated BAs (31.5 ± 9.1%). Only a low percentage of unconjugated BAs was found in the patient refluxates (0.5 ± 0.4%). Although unconjugated BAs were absent in our refluxates, they have shown their presence in GERD patients (Nehra 1999). Deoxycholic acid (DCA), a secondary bile, is formed through deconjugation by microbial enzymes present in the colon, but the increase in pH due to PPI use can cause gastric bacterial overgrowth, resulting in the presence of DCA in reflux (Theisen 2000). Each of the six conjugated bile components 

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**P0547**

**STW5 MODULATES TIGHT-JUNCTION GENE AND PROTEIN EXPRESSIONS IN REFUX-ESOPHAGITIS - POSSIBLE RELEVANCE FOR TUMORGENESIS**

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**Introduction:** STW5, a herbal combination preparation of nine different plant extracts (Iberis amara (L.), Menthae piperitae (L.) Chamomilla recutita (L.), Glycyrrhiza glabra (L.), Angelica archangelica (L.), Carum Carvi (L.), Silybum marianum (L.) Gaertn. Melissa officinalis (L.) und Chelidonium majus (L.)), Glycyrrhiza glabra (L.), Angelica archangelica (L.), Carum Carvi (L.), Silybum marianum (L.) Gaertn. has been extensively studied for the treatment of gastrointestinal disorders resulting in an recommendation for the German therapy guidelines for both upper and lower functional gastrointestinal disorders (1). We investigated the mode of action of this herbal medicine on reflux esophagitis as the most common condition treated by gastroenterologists with possible long-term implications such as Barrett’s esophagus and esophageal adenocarcinoma.

**Aims & Methods:** We were especially interested in the tight junction proteins (TJ), which are multi-protein complexes in epithelial and endothelial cells known to contribute to the barrier-function, but recently discovered to play an important role in tumorigenesis (3). TJ proteins like ZO-1 and 2 participate in cell-cycle regulation, occludin (OCLN) regulates the mitotic entry via centrosome separation, claudin-4 increased cell proliferation (CDP), claudin-1 is responsible for increased proliferation of the crypt cells (3). CLDN 1, 3, 4, 5, 7, 10 and 16 have been found altered in various types of cancer and OCLC is regarded an anti -transformation protein (3).

**Results:** In the model, RE was induced by surgical methods and rats (n = 6 per group) were treated with STW5 (0.5 or 2 ml/kg) or the proton pump inhibitor (PPI) omeprazole (O) (30 mg/kg) as described earlier (2). RNA was isolated from defined tissue areas of the esophag. In the inflamed tissue we found a simulta-neous transcript down regulation of claudin 4 (p < 0.0001), compared to DCA treated or untreated animals. DCA was able to activate FXR, while the addition of all conjugated BAs did not result in a signal change. Both receptors are able to activate bile receptors we transfected primary mouse esophageal epithelial cells (ME10) with TGR5 and FXR, too. Transcripts of MarvelD1 and JAM 2 were increased. The down regulation of ZO1 was seen by Western Blot, too. HLPC showed the presence of both glyco-conjugated (67.6 ± 8.8%) and taurine-conjugated BAs produced by the liver are conjugated with either taurine or glycine. BAs not only have detergent properties, but can also act as signaling molecules by activating the farnesoid X receptor (FXR) and G-protein coupled bile acid receptor (TGR5). Both receptors are upregulated in BE and EAC compared to normal squamous mucosa, suggesting a possible role in the progression of BE. References:


Aims & Methods: Organoid cultures are widely used because they mimic in vivo differentiation of self-organizing stem cells and represent the perfect model to study stem cell interaction in basic and translational research. We developed an in vivo organoid model of human BE to investigate the potential to modulate the metaplastic process using an innovative anti-BMP2/4 llama-derived Dwarfbody™ (DB). Endoscopic BE biopsies were implanted into immunocompromised nude mice intramuscularly and grown for a period of three months with DB or control. These structures were assessed histologically and immunohistochemically (IHC) using panels of squamous, intestinal and stem cell markers.

Results: A clustering phenomenon is seen at the epithelial layer containing goblet cells and recapitulated the crypt and villous regions seen within BE glands. IHC validation confirmed that the xenograft structures were of human origin and expressed markers of intestinal differentiation (CKS, CDX2 and villin). In contrast, treatment with the BMP inhibitor lead to the formation of multi-layered squamous epithelium expressing both the stem cell marker p63 and the squamous marker CK5.

Conclusion: Preliminary results demonstrate that inhibition of BMP2/4 in this model can prevent development of squamous epithelium. These pre-clinical results may be translated to the clinical setting in order improve treatment of BE and as such prevent the development of esophageal adenocarcinoma.

Disclosure of Interest: All authors have declared no conflicts of interest.

References


P0550 GASTRIC CARDIA GLANDS MANIFEST APPARENT BROAD DIFFERENTIATION POTENTIAL, AS EVIDENCED BY HOXA13 EXPRESSION, IMPLICATIONS FOR THE ORIGIN OF BARRETT’S ESOPHAGUS

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Introduction: Metaplastic phenomena in the upper gastrointestinal tract are still poorly understood. A prominent theory is that Barrett’s esophagus originates from gastric cardia glandular epithelium. However, in absence of evidence that the gastric stem cell has broad differentiation potential, this theory remains controversial. The gastroesophageal junction is a high prevalence area for metaplasia and subsequent cancer. Characteristic of this area are the gastric cardia glands which are only the most proximal part of the anatomic gastric cardia. Recent evidence from human and mouse studies has shown Barrett’s esophagus can originate from these gastric cardia glands. If it can be shown that gastric cardia glands contain elements associated with positional mis specification, this theory could be substantially bolstered. HOX genes are a family of transcription factors that convey positional information. The 3rd to 5th sequence of HOX genes corresponds to the sequence in which they act along the anterior to posterior axes of the gut. This property is termed collinearity and links clustering to function. In gastrointestinal physiology, HOX4.13, a 5’ member of the HOX 4 cluster, has an expression pattern restricted to the colonic epithelium. However, pathological metaplastic lesions of the esophagus and stomach are also characterized by HOXA13 expression. This in parallel with the similarities of these lesions with physiological embryonic morphology. Hence, investigating HOXA13 expression in gastric cardia glands appears a rational strategy in assessing the potential of this gastric cardia epithelium to serve as the origin of Barrett’s esophagus.

Aims & Methods: We aimed to determine HOXA13 expression in physiological gastric cardia glands. Firstly, strips of tissue from surgical specimens containing squamous esophageal epithelium, gastric cardia glands, and oxyntic stomach, were collected. These were continuous strips, from proximal to distal, to preserve morphological information. Material from three patients was selected, they suffered from either a neuroendocrine tumor, or decompensated achalasia, or an adenocarcinoma. Antibodies against HOXA13 were found not to be specific. Therefore, RNA in situ hybridization by RNA-scope was performed to visualize HOXA13 RNA. Secondly, a HOXA13GFP x C57BL/6J heterozygous mutant mouse model was used. In these animals, the cardiac glands were visualized directly for GFP expression using a fluorescence confocal microscope.

Results: All three patients showed HOXA13 expression of a portion of gastric cardia epithelial cells. The squamous epithelium, the oxyntic epithelium, and the cardia did not show any signal. The signal is located relatively close to the base of the crypts of the cardiac glands. The HOXA13GFP x C57BL/6J heterozygous mice showed GFP expression localized to the nucleus of some of the epithelial cells of the cardia gland. No nuclear signal was detected in the squamous or oxyntic epithelium. The colonic epithelium of the mouse showed nuclear GFP signal. Rectal squamous epithelium was negative as well as ileal epithelium, in accordance with HOXA13 colinearity in mouse and human. A littermate negative for HOXA13 was analyzed and showed no nuclear signal in either gastric cardia gland cells or in any intestinal cells.

Conclusion: Gastric cardia gland epithelial cells in both human and mouse exhibit HOXA13 expression. All other physiological upper gastrointestinal tract tissues are HOXA13 negative in line with HOX gene colinearity in the gut. This dichotomy proves positional information in these glands is discordant with their actual location. These findings suggest that gastric cardia glands have a broad differential potential. This is consistent with an origin of Barrett’s metaplasia in the gastric cardia and might be indicative of Barrett’s not being a true transdifferentiation.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

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Introduction: Barrett’s Oesophagus (BE) is an acquired condition resulting from of continuous reflux that causes chronic irritation of the Barrett’s metaplasia-dysplasia-adenocarcinoma sequence. Am J Gastroenterol 2013;108: 1082-93.

During progression from BE to EAC the infiltration of CD4+ cells was observed. The number of IL-22+ cells and IL-17A+ cells as well as the number of FOXP3+ cells/mg tissue increased in oesophageal cancer and in its peritumoral tissue as compared to healthy controls. The relative amounts of IL-22+ and IL-17A+ cells decreased while an increase of FOXP3+ cells was observed. Also more IL-10+ cells/mg tissue were observed in the tumours. In accordance to the latter finding high IL-10 mRNA expression levels were associated with poor survival in EAC patients. Interestingly, high mRNA expression levels of IL-10 in the non-malignant peritumoral tissue also correlated with poor survival.

Conclusion: During progression from BE to EAC the infiltration of CD4+ immune cells increases. While the relative amount of pro-inflammatory cells (CD4+ / CD8+ ) increases it is accompanied by a decrease of FOXP3+ regulatory T cells. Our results strongly suggest that especially regulatory T cells influence overall patient survival in EAC. Notably, high levels of IL-10 in the non-malignant peritumoral tissue also demonstrated to be unfavourable for patient survival. Thus, a pro-tumorigenic immune response is accompanied by increased IL-10 expression and high mRNA expression of IL-10 in BE patients.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0553 ANTI-INFLAMMATORY ENVIRONMENT CHARACTERISES BARRETT’S OESOPHAGUS ASSOCIATED ADENOCARCINOMAS AND INFLUENCES PATIENT SURVIVAL

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Introduction: Barrett’s Oesophagus (BE) is a premalignant condition associated with an increased risk of adenocarcinoma. The potential for BE to progress to dysplasia and ultimately lead to oesophageal adenocarcinoma presents a significant clinical challenge. The identification of environmental factors that can progress to dysplastic lesions, which ultimately lead to oesophageal adenocarcinoma (EAC). The incidence of EACs is rising in the Western world and 5-year survival rates are below 20%. Hence, new diagnostic and prognostic markers are needed. Since elevated levels of interleukin (IL)-6 in BE producing cells are associated with a poor prognosis in colorectal cancer we wanted to investigate their influence in EACs.

Aims & Methods: None of the patients enrolled in this study received chemoradiation therapy prior to surgery and all patients had pathologically confirmed BE. mRNA expression levels of interleukins in tumour tissue and non-malignant peritumoral specimens of 39 patients were measured. Immunohistochemical analysis was conducted to investigate interleukins during the progression from BE to EAC. Interleukins were investigated in formalin-fixed paraffin-embedded oesophageal cancer specimens and in their non-malignant peritumoral tissue (n = 11). During routine endoscopy samples from healthy volunteers were obtained and analysed by flow cytometry as controls (n = 5).

Results: During progression from BE to EAC an increase of CD4+ cells was observed. The number of IL-22+ cells and IL-17A+ cells as well as the number of FOXP3+ cells/mg tissue increased in oesophageal cancer and in its peritumoral tissue as compared to healthy controls. The relative amounts of IL-22+ and IL-17A+ cells decreased while an increase of FOXP3+ cells was observed. Also more IL-10+ cells/mg tissue were observed in the tumours. In accordance to the latter finding high IL-10 mRNA expression levels were associated with poor survival in EAC patients. Interestingly, high mRNA expression levels of IL-10 in the non-malignant peritumoral tissue also correlated with poor survival. 

Conclusion: During progression from BE to EAC the infiltration of CD4+ immune cells increases. While the relative amount of pro-inflammatory cells increases in BE it is accompanied by a decrease of FOXP3+ regulatory T cells. Our results strongly suggest that especially regulatory T cells influence overall patient survival in EAC. Notably, high levels of IL-10 in the non-malignant peritumoral tissue also demonstrated to be unfavourable for patient survival. Thus, a pro-tumorigenic immune response is accompanied by increased IL-10 expression and high mRNA expression of IL-10 in BE patients.

Disclosure of Interest: All authors have declared no conflicts of interest.

References


as genotypic evolution. Patients with dysplasia also show a significant increase in gland phenotype diversity (Shannon) per biopsy in adjacent to dysplasia glands compared with patients who do not have dysplasia.

**Conclusion:** BE is phenotypically diverse with a range of glandular phenotypes that are clonally related. An increase in phenotypic diversity may be a potential biomarker for assessment of patients progressing from BE to cancer with implications for diagnostic and surveillance policy.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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**P0555** A DEDICATED BARRETT'S OESOPHAGUS ENDOSCOPY LIST IMPROVES THE ACCURACY OF ENDOSCOPIC REPORTING AND QUALITY OF BIOPSY

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**Introduction:** The importance of skilled endoscopic assessment of Barrett's oesophagus (BO) has been clearly established and forms part of the British Society of Gastroenterology guidelines. Use of Prague classification when reporting on areas of BO improves standardisation, and adherence to the Seattle biopsy protocol (quadrant biopsies every 2 cm) when sampling Barrett's mucosa is thought to improve dysplasia detection. In East Kent Hospitals NHS Foundation Trust we have created a dedicated nurse-led BO surveillance endoscopy list with the aim of improving compliance with guidelines and the quality of biopsies taken. Here we present a retrospective observational study of patients who underwent upper GI endoscopy on a general endoscopy (GE) list compared with the dedicated BO endoscopy (DBO) list.

**Aims & Methods:** We searched our endoscopy software for patients who had had an endoscopy documented by a consultant gastroenterologist who had an endoscopy on a GE list from 2012–2013. The same search was performed for patients who were scoped on the DBO list from 2014–2016. Endoscopy reports were reviewed to assess the use of Prague classification and determine numbers of biopsies taken. Biopsy results were reviewed on our electronic pathology database.

**Results:** One hundred procedures for BO surveillance on GE lists were audited, comprising 65% male patients with median age 68 years; 60% were performed by a consultant gastroenterologist and the remainder were performed by other operators including surgical consultants and gastroenterology registrars. Of the 105 procedures on the DBO lists, 63% of patients were male, median age 70 years. Prague classification was used in 94% of endoscopy reports on the DBO lists compared with 5% on the GE lists. The Seattle biopsy protocol was observed in 70% of cases on the DBO lists as opposed to 30/100 (30%) on the GE lists. Dysplasia detection rate (low grade, high grade or indefinite) was similar in both groups: 8/105 (7.6%) on the DBO list and 6/100 (6%) in the GE group. All (100%) of the dysplasia detected on the GE lists occurred in procedures performed by consultant gastroenterologists.

**Conclusion:** Our comparison shows that observance of Prague classification is significantly higher on the DBO lists when compared with GE lists (94% vs 5%), and compliance with the Seattle biopsy protocol is similarly higher (74% vs 30%). These are indicative of higher quality endoscopic surveillance on DBO lists. However, this did not translate to a different dysplasia detection rate which appeared to be more influenced by the endoscopy operator since all of the dysplasia detected on GE lists was identified by consultant gastroenterologists. We believe that adding this additional familiarity of guidelines and possible greater experience of endoscopists regularly taking BO biopsies. We therefore recommend that all Barrett's oesophagus patients have their surveillance endoscopies performed on dedicated BO endoscopy lists.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**References**


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**P0556** ADHERENCE TO QUALITY INDICATORS AND SURVEILLANCE GUIDELINES IN THE MANAGEMENT OF BARRETT'S OESOPHAGUS: A RETROSPECTIVE ANALYSIS

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**Introduction:** Adherence to quality indicators and surveillance guidelines in the management of Barrett's esophagus (BE) promotes high-quality cost-effective care.

**Aims & Methods:** The aims of this study were to evaluate (1) adherence to standardized classification (Prague Criteria) and a systematic four-quadrant biopsy protocol, (2) identify predictors of practice patterns, and (3) to assess adherence to surveillance guidelines for non-dysplastic BE (NBDE).

This was a Single-center retrospective study of endoscopies (EGDs) performed for BE between June 2008 to December 2015. Data on patient demographics, procedure characteristics and histology results were obtained from a prospectively collected endoscopy database and chart review. Adherence to the use of Prague Criteria and systematic biopsy protocol were assessed based on operative report documentation. Guideline adherent surveillance EGD was defined as those performed within 6 months of the recommended 3–5 year interval. Uni- and multivariable analysis were performed to identify predictors of practice patterns.

**Results:** A total of 397 patients (66.5% male; mean age 60.1 ± 12.5 years) had an index EGD during the study period. Adherence to the use of Prague Criteria and systematic biopsies were 27.4% and 24.1%, respectively. Endoscopists who perform systematic interventions for BE were more likely to use the Prague Criteria (OR: 3.16; 95% CI: 1.47–6.82) than those who do not. Longer time in practice (in years) was positively associated with adherence to Prague Criteria (OR 1.07; 95% CI: 1.02–1.12; p < 0.01) but with a lower likelihood of performing systematic biopsies (OR 0.91; 95% CI: 0.85–0.97; p < 0.01). Nearly 41% of patients with NBDE (11/27) underwent surveillance EGD sooner (range 1–24 months) than the recommended interval.

**Conclusion:** Adherence to quality indicators and surveillance guidelines in BE is low. One major characteristic, including experience with endoscopic therapy for BE and time in practice predicted adherence to the use of Prague Criteria and systematic biopsies. Future efforts are needed to reduce variability in practice and promote high-value care.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**References**


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**P0557** EXPRESSION OF TGF-B AND CD-44 IN AGE SPECIFIC SUBGROUP OF PATIENTS WITH ADENOCARCINOMA OF GASTRIC CARDIA

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**Introduction:** Adenocarcinoma near the esophagogastric junction is one of the most lethal GI malignancies known. Surgical treatment of these cancers stay determinative factors of patient survival. Older persons often differ from the younger adult population in terms of biological and functional perspectives; as such, they may have particular needs which require an interdisciplinary approach and intervention, especially when faced with a cancer diagnosis.

**Aims & Methods:** The aim of this study was to detected expression of TGF-B and CD-44 in age specific subgroup. The expressions of TGF-B and CD-44 were evaluated immunohistochimically in 23 patients with adenocarcinoma of gastric cardia who underwent curative surgery (RO) without any neo/adjuvant therapy. Additionally we analyzed control group of patients with non-cancer lesion or normal tissue of upper digestive tract (13 patients). We divided the patients into two groups. Group A consisted of 13 cancer patients and 7 control patients 65 years of age or older, while Group B consisted of 10 cancer and 6 control patients younger than 65 years of age. The two groups were comparable - there were no differences between the two groups regarding tumor stage.

**Results:** Elderly patients have statistically significant better survival (median 20.2 month) compared with younger patients (median 15.4 month) (p = 0.045). The median survival rate of patients without TGF-B and/or CD-44 expression was significantly lower (7 m) than that of patients with positive expression (>15 m) (p = 0.003). Regardless of patients age, CD-44 was significantly higher in the cancer tissue of elderly patients than in younger (p < 0, 035). But no significant difference was observed in the TGF-B expression between group A and group B cancers tissue (p = 0.005).

**Conclusion:** The biology of tumors may be different in elderly patients, leading to a lower rate of tumor-related mortality.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**References**

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**Introduction:** Barrett’s esophagus (BO) is considered a premalignant condition for oesophageal adenocarcinoma (OAC). Once diagnosed, interval endoscopic surveillance is recommended to promote early detection of dysplasia and cancer. Occurrence and incidence of dysplasia and cancer among BO vary across populations. Recent studies show BO patients mortality is mainly related to non-oesophageal cancer and cardiovascular morbidity.
### Aims & Methods:
In this cross-sectional study, our aims were to describe the local BO clinical, endoscopic and histologic profile in our tertiary referral centre, and discover whether the Prague classification reporting requirements are filled. We identified and included all consecutive patients with oesophageal intestinal metaplasia (identified by the presence of goblet cells) from March 2009 to May 2015. All endoscopies and biopsy reports were reviewed: BO segment length, use of the Prague classification, endoscopic abnormalities, treatment modality and, histologic findings of dysplasia. Participants were sent a clinical questionnaire, via which pertinent clinical data including personal and familial cancer history, were collected.

### Results:
Clinical profile: Our cohort consists of 406 patients, with a mean age of 60.9 ± 13.3 years, 69% were male. Endoscopic profile: Mean maximal BO length (Prague classification M) was 2.8 ± 1.9 cm (reported in 49.6% of endoscopies). Mean circumferential BO (Prague classification C) was 4.9 ± 3.1 cm (reported in 18.1% of endoscopies). Histologic profile: Low-grade dysplasia (LGD) was seen in 4.4% of patients, high-grade dysplasia (HGD) in 3%, intramucosal carcinoma (IMC) in 0.7%, and OAC in 2%. A subgroup of 250 patients underwent more than one endoscopy, allowing for prospective incidence analysis. They had 914 years of follow-up, with a mean number of endoscopies of 4.7 ± 3. The incidence rates of LGD, HGD, IMC, OAC per 1000 patient-years were 20.8, 15.3, 2.2, and 5.7 years. A personal history of non-oesophageal malignancy was reported in 15.4%. A family history of BO, OAC and non-oesophageal cancer were reported in 5.2%, 4.5%, and 35.4%, respectively.

### Conclusion:
Compared to the information gathered by Katz et al. (1), we demonstrated a lower rate of LGD, but comparable rates of HGD and OAC. The personal and familial history of non-oesophageal malignancy was higher than the oesophageal malignancy rates. Our findings may support the importance of age appropriate non-oesophageal malignancy screening in BO patients. Physician compliance in reporting BO according to the Prague classification is lacking. Factors associated with our local BO profile as well as the implication of family history requires further prospective studies.

### Disclosure of Interest:
All authors have declared no conflicts of interest.

### Reference

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### P0556

**THE EFFICACY OF ENDOSCOPIC MUCOSAL RESECTION IN MANAGING EARLY NEOPLASIA IN BARRETT’S ESOPHAGUS, EXPERIENCES OF A TERTIARY REFERRAL CENTER IN THE UK**

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**Introduction:** Endoscopic mucosal resection (EMR) is an established diagnostic and treatment tool in the management of Barrett’s oesophagus (BO) with early neoplasia. Our objectives were to demonstrate EMR’s efficacy in removing early neoplasia within BO and its usefulness in obtaining comprehensive histological specimens to accurately stage the early neoplasia and effectively deliver therapy.

**Aims & Methods:** We have conducted a retrospective analysis using our electronic database for endoscopic procedures for patients with BO, who underwent EMR from October 2010 to December 2016. We analysed the resection margins for both en bloc and piecemeal EMRs. We compared the original histology from the referral endoscopy to the histology obtained from the EMR, to analyse any deviation and to demonstrate the importance of histological staging of the early neoplasia in BO. We also investigated the three-year survival in patients, who have had their EMR longer than 3 years ago, along with causes of death. A total of 99 patients underwent 134 EMR procedures and 259 EMRs. 84% were male, the mean age at first EMR was 71 years (SD = 8.2). 24 patients underwent 2 EMR procedures, 2 patients underwent 3 EMR procedures and 2 patients underwent 4 EMR procedures. The median length of the circumferential and maximum extent of the BO segments were 3 cm and 4 cm, respectively (interquartile range (IQR) 2–4). 44 patients underwent 60 en bloc resections. After histologic assessment of these EMR specimens, 34 (56.7%) had clear deep and radial resection margins, 14 (23.5%) showed least low-grade dysplasia at the radial margin and 8 (13.4%) at both margins. 2 (3.3%) were clear at the deep margin, but due to thermal damage the radial margins were indeterminate. Following the 60 EMRs there was no visible residual early neoplasia on the follow up endoscopy in 37 cases (61.7%), 55 patients underwent 74 piecemeal EMRs, of which 52 (70.3%) had clear deep margins on histologic assessment and 38 (51.4%) had no visible residual neoplasia on the follow up endoscopy. Pre EMR histology was available in 82 patients and it showed high-grade dysplasia (HGD) in 49 (59.8%), mucosal adenocarcinoma in 24 (29.2%) and low-grade dysplasia in 9 patients (11%). However the EMR histology resulted in altered grading in 59 (72%) patients, with 47 (57%) upgraded and 12 (14%) downgraded from the pre EMR histology and unchanged only in 22 patients (28%). The EMR histologies in the 82 patients showed HGD in 16 (19.5%) patients, intramucosal adenocarcinoma in 33 (40.2%), adenocarcinoma with submucosal invasion in 20 (24.4%) and LGD in 13 (15.9%). The remaining 52 EMRs were performed for visible lesions within BO without pre EMR histology result, predominately for patients in the radiofrequency ablation program. The 3 year survival rate for 42 patients was 81%, 8 patients died, 5 due to cardiac failure, 1 due to a PE and 2 due to advanced oesophageal adenocarcinoma.

**Conclusion:** In this moderately sized retrospective study EMR has been proven to be an effective tool in managing early neoplasia within BO. It not only allows the potential complete resection of the visible early neoplasia (61.7% for en bloc and 51.4% for piecemeal EMR), but also gives a histologic specimen with a more accurate grading of the neoplasia (upgraded in 57%, downgraded in 14% and unchanged in only in 23% of all EMRs), both aspects culminating in more effective and precise patient treatment. In all patients managed and assessed by EMR we have seen 19% mortality of which only 4.8% was cancer related.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P0560

**ADHERENCE TO BARRETT’S ESOPHAGUS SURVEILLANCE GUIDELINES: A SYSTEMATIC REVIEW AND META-ANALYSIS**


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**Objective:** To determine the adherence to surveillance guidelines for Barrett’s oesophagus (BO) in different countries using a systematic review and meta-analysis of prospective cohort studies.

**Methods:** A systematic review of prospective studies was conducted using a predefined protocol. Studies were identified through a comprehensive search of Embase, PubMed and CINAHL databases until 2015. The primary outcome was the percentage of patients that adhered to surveillance guidelines, i.e. the percentage of patients that underwent at least two endoscopies within the recommended surveillance interval. Results were presented as a meta-analysis of proportions using a random-effects model.

**Results:** A total of 11 studies were included. The total number of patients in the studies was 10,824. The adherence to surveillance guidelines was 51% (95% CI: 43%–58%). A meta-analysis of the studies revealed a significant difference in adherence among the countries. The adherence was significantly lower in the Netherlands (41%, 95% CI: 33%–48%) compared to the United States (57%, 95% CI: 52%–62%) and Australia (64%, 95% CI: 57%–70%).

**Conclusion:** The adherence to surveillance guidelines for BO varies significantly among different countries. The Netherlands has the lowest adherence, while the United States and Australia have higher adherence rates. Further studies are needed to investigate the reasons for the differences in adherence among the countries.

**Disclosure of Interest:** All authors have declared no conflicts of interest.
BE surveillance in non-dysplastic BE patients a prevalence ratio for adherence of
Results:
1 proportional hazard ratio of mortality for ESD compared with surgery was not
lymphovascular invation, submucosal invation, and ASA-PS, multivariate Cox
ESD compared with surgery has not been clarified.
54 lesions in the ESD group and 51 lesions in the surgery group met the
and surgery for cN0M0 relative indication lesions of ESCC. Between 2006 and
2016, patients with relative indication lesions of ESCC treated endoscopically or
surgically in Okayama University Hospital were retrospectively analyzed. We
and analysis of heterogeneity (I² statistic).
Results: From a total of 373 studies, 49 were eligible for this meta-analysis. For
BE surveillance in non-dysplastic BE patients a prevalence ratio for adherence of
percentage of mortality for ESD compared with surgery was not
lymphovascular invasion, submucosal invasion, and ASA-PS, multivariate Cox
Results: Eight FA subjects with a median age of 22.2 years at first endoscopy
(range 16–41) were identified. The median upper endoscopies number per patient
was 1.5 (range 2–14) with a median time of follow-up of 4.5 years (range 1–9
years). All subjects (100%) had an endoscopic evidence of reflux esophagitis: 3
(37.5%) had mild and 5 (62.5%) had moderate-severe reflux esophagitis. Three
subjects (37.5%) had complicated esophageal reflux disease (two subjects develop-
multiple squamous cell carcinomas). A retrospective cohort study had an endoscopic stente.
Two subjects (25%) developed esophageal squamous cell carcinoma during follow-
up, with interval time of 8 and 18 months from previous upper endoscopy. Both
had tumor expression of p16 protein suggesting human papilloma virus (HPV)
infection. The calculated standardized incidence ratio (SIR) for the development of
esophageal squamous cell carcinoma was 5.107.
Conclusion: FA patients are at an increased risk for developing esophageal cancer
and reflux esophageal disease with associated complications. Larger, prospective
studies are needed to determine the optimal interval for endoscopic screening in
these patients.
Disclosure of Interest: All authors have declared no conflicts of interest.
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P0563 RISK FACTORS FOR THE DEVELOPMENT OF DISPLASTIC SQUAMOUS EPITHELIUM IN THE DEVELOPMENT OF ESOPHAGEAL SQUAMOUS CELL CARCINOMA IN FANCONI ANEMIA
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Introduction: Multiple development of squamous cell carcinoma (SCC) in the
upper aerodigestive tract is known as the “field carcinization phenomenon,”
and alcohol is a definite carcinogen. Multiple dysplastic lesions in the esophagus
are a useful predictor of the risk for the field carcinization. However, what causes
the development of dysplastic squamous epithelium in the esophagus is still
unclear.
Aims & Methods: The aim of this prospective cohort study was to identify associa-
tions between patients’ lifestyle, including alcohol consumption, the genetic
trait of aldehyde dehydrogenase-2 (ALDH2), and the development of dysplastic
squamous epithelium in the esophagus. This is a post hoc analysis of the Japan
Esophageal Cohort (JEC) study (UMIN1676). Patients with superficial SCC
were carefully documented. To examine two single nucleotide polymorphisms included in the study. The drinking and smoking histories before and after ER for SCC of the oesophagus, based on a prospective study of 330 patients from 16 hospitals.

Aims & Methods: Between Sep 2005 and May 2010, 330 patients (M/F = 278/52) were registered. The proportions of the different grades of LVL were A = 50%, B = 52.7%, and C = 47.3%. After adjusting for sex and age, controls and the LVL grade was associated with progressively higher proportions of heavy drinkers (8.4%, 24.8%, 26.2%, and 52.5%, respectively, p < 0.0001), frequently strong alcoholic beverages (2.3%, 7.2%, 11.8%, and 11.6%, respectively, p < 0.0001), heavy smokers (34.6%, 38.7%, 65.7%, and 70.8%, respectively, p < 0.0001), liking high-temperature food (4.6%, 19.6%, 20.8%, and 20.7%, respectively, p < 0.0001), not eating green-yellow vegetables almost every day (55.0%, 48.9%, 54.9%, and 71.1%, respectively, p < 0.0001), and not eating fruit almost every day (51.6%, 74.3%, 68.0%, and 75.3%, respectively, p < 0.0001). The risk of LVL grade B and C was strongly associated with the amount of alcohol consumption especially in inactive ALDH2. Odds ratio (OR) of LVL grade B associated with heavy drinking was significantly stronger in moderate and heavy drinkers before ER (OR = 3.7; p < 0.0001) than non-temperate drinkers (OR = 2.3; p < 0.0001) and moderate and heavy drinkers after ER. Six of the seven patients had an inactive heterozygous ALDH2. We analyzed the 63 patients with inactive heterozygous ALDH2 and moderate and heavy drinkers before ER based on their temperance history and found 38 patients in the temperance group (light drinkers after ER) and 25 patients in the non-temperance group. The 3-year cumulative incidence of SCC was 3.4% in the temperance group and 16.2% in none. The 5-year cumulative incidence of SCC was 6.2% in 49.8%, respectively (p < 0.05). The 5-year cumulative incidence rate of a third SCC revealed an incidence of 0% vs 23.8%, respectively (p < 0.01). The 7-year cumulative incidence rate of a fourth SCC revealed an incidence of 0% vs 16.9%, respectively (p < 0.01).

Conclusion: The development of dysplastic squamous epithelium in the esophagus was associated with the amount of alcohol consumption and genetic trait of inactive ALDH2.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

P0564 EVALUATION OF THE RISK OF METACHRONOUS SQUAMOUS CELL CARCINOMA OF THE OESOPHAGUS AND THE HEAD AND NECK AFTER ENDOSCOPIC RESECTION FOR SQUAMOUS CELL CARCINOMA OF THE ESOPHAGUS BASED ON THE GENETIC POLYMORPHISMS OF ADH1B AND ALDH2
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Introduction: Metachronous multiple squamous cell carcinoma (SCC) of the oesophagus and the head and neck often occurs in patients who previously underwent endoscopic resection (ER) for SCC of the oesophagus. This has become a problem regarding the curability of ER. Katada et al reported that alcohol abstinence significantly decreased the risk of developing a secondary SCC of the oesophagus, based on a prospective study of 330 patients from 16 hospitals. However, there are few studies that have investigated the risk of developing a secondary SCC of the oesophagus and the head and neck based on the genetic polymorphisms of alcohol dehydrogenase-1B (ADH1B) and aldehyde dehydrogenase-2 (ALDH2) which are closely associated with developing oesophageal SCC. No studies have evaluated the risk of developing a third (or more) SCC after ER for SCC of the oesophagus.

Aims & Methods: The study group included patients who underwent ER for SCC of the oesophagus at Hokkaido University Hospital. All patients were followed up by endoscopic examination for ≥2 years. Overall, 126 patients were included in the study. The drinking and smoking histories before and after ER were carefully documented. To examine two single nucleotide polymorphisms (SNPs) on ADH1B and ALDH2 genotyping, we obtained approximately 1 ml of saliva with a pipette or cotton swab before the endoscopic review board at each hospital, and we obtained written informed consent from all patients. Using Lugol chromoendoscopy, we evaluated the dysplastic squamous epithelium in the esophagus. Lugol voiding lesion (LVL) was graded into 3 categories (A = no lesion; B = 1 to 9 lesions; C = ≥10 lesions per endoscopic view). Endoscopic images obtained from eligible patients at study entry were registered. The proportions of the different grades of LVL were A = 50% (15.2%), B = 52.7%, and C = 47.3% (32.1%). After adjusting for sex and age, the LVL grade was associated with progressively higher proportions of heavy drinkers (8.4%, 24.8%, 26.2%, and 52.5%, respectively, p < 0.0001), frequently strong alcoholic beverages (2.3%, 7.2%, 11.8%, and 11.6%, respectively, p < 0.0001), heavy smokers (34.6%, 38.7%, 65.7%, and 70.8%, respectively, p < 0.0001), liking high-temperature food (4.6%, 19.6%, 20.8%, and 20.7%, respectively, p < 0.0001), not eating green-yellow vegetables almost every day (55.0%, 48.9%, 54.9%, and 71.1%, respectively, p < 0.0001), and not eating fruit almost every day (51.6%, 74.3%, 68.0%, and 75.3%, respectively, p < 0.0001). The risk of LVL grade B and C was strongly associated with the amount of alcohol consumption especially in inactive ALDH2. Odds ratio (OR) of LVL grade B associated with heavy drinking was significantly stronger in moderate and heavy drinkers before ER (OR = 3.7; p < 0.0001) than non-temperate drinkers (OR = 2.3; p < 0.0001) and moderate and heavy drinkers after ER. Six of the seven patients had an inactive heterozygous ALDH2. We analyzed the 63 patients with inactive heterozygous ALDH2 and moderate and heavy drinkers before ER based on their temperance history and found 38 patients in the temperance group (light drinkers after ER) and 25 patients in the non-temperance group. The 3-year cumulative incidence of SCC was 3.4% in the temperance group and 16.2% in none. The 5-year cumulative incidence of SCC was 6.2% in 49.8%, respectively (p < 0.05). The 5-year cumulative incidence rate of a third SCC revealed an incidence of 0% vs 23.8%, respectively (p < 0.01). The 7-year cumulative incidence rate of a fourth SCC revealed an incidence of 0% vs 16.9%, respectively (p < 0.01).

Conclusion: Among the patients who underwent ER for oesophageal SCC, an inactive heterozygous ALDH2 with a continue drinking habit were the significant risk factors of developing metachronous multiple SCC. These are the greater risk factors for developing a third or more SCC. Patients with an inactive heterozygous ALDH2 and a drinking habit should receive strict instruction for temperance.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference
they were not recommended additional therapy. The remaining eight patients had undergone endoscopic submucosal dissection (ESD), and the clinicopathological characteristics of the patients and lesions between the 2 groups were analyzed. There were no significant differences in tumor size (A: 34.9±13.6 mm) and operation times (A: 95.4±131.9 min) in the 3 groups. Group A demonstrated the best results. There were no significant differences in tumor size (A: 34.9±13.6 mm) and operation times (A: 95.4±131.9 min) in the 3 groups. Group A demonstrated the best results.

References
The development of endoscopic submucosal dissection (ESD) of early gastric cancer: a prospective randomized trial

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Aims & Methods: All patients with endoscopic diagnosis of early gastric cancer (EGC) and biopsy confirmed to be high grade dysplasia or adenocarcinoma were recruited. They underwent staging investigations including image enhanced endoscopy, EUS and CT and those predicted to be T1a (intramucosal) neoplasia were randomly assigned to receive ESD or LAG. ESD were performed according to the EGJ (D2) lymph node dissection in the group with INFa, INFb, or lymphovascular invasion were 100% and 87%, respectively. The recurrence-free survival rate was significantly higher in the group with INFa and no lymphovascular invasion than in the group with INFb, INFb or lymphovascular invasion.

Conclusion: Our outcome data support the clinical validity of the curative precautions after ER for MM/S1 ESCC of the JES guidelines. However, MM/S1 ESCC with INFa and no lymphovascular invasion may have more possible curative precautions after ER without additional treatment.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
or those in which the biopsies were still taken from the different anatomical areas were excluded.

**Results:** Only 148 patients were admitted to the study. The mean age was 49.7±2.8 years, and 60% were female (CI: 52–67, 95%). 264 vials were sent with biopsies of normal gastritis or mucosa and 32 (21.6%) had endoscopic diagnosis of PCLS. From 148 patients with endoscopic diagnosis of gastritis or normal mucosa, LCPM was identified in 46 patients (39.6%) (p < 0.001) and 1 of them were low-grade dysplasia. From 32 of patients with suspected endoscopic PCLS, the diagnosis was confirmed with histology in 26 patients (81.2%). A total of 72 patients had PCLS vs. 32 who were initially suspected (p < 0.01), with a total patients of CI: 40.7–56.6, 95%).

**Conclusion:** Pre-malignant conditions and lesions of the stomach (PCLS) can show as normal mucosa or gastritis during endoscopic procedure. 39.9% of patients who underwent endoscopic procedure with presumptive gastritis had PCLS. PCLS may be under-diagnosed if random biopsies are not taken. Therefore, taking biopsies from areas without suspected PCLS causes a change in the clinical management of patients, both for the initial diagnosis and for the staging according to OLGA and OLGUSM systems.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**References**


**P0571 CORRELATION BETWEEN THE COMBINATION OF HELICOBACTER PYLORI ANTIBODY AND PEPSSINOGEN AND OLGA/OLGIM STAGING FOR RISK ASSESSMENT OF GaSTRIC PRECANCEROUS LESIONS**

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**Introduction:** Prognosis of GC has a noticeable relation with its clinical stage. Atrophic gastritis (AG), intestinal metaplasia (IM) and dysplasia are well-recognized risk factors for intestinal type GC (GC). A large cohort study confirmed that the annual incidence of GC were approximately 0.1% for patients with AG, controlled and their occurrence could be reduced with clipping prophylactic hemos.

**Aims & Methods:** We aimed to discuss the correlation between the combination of Helicobacter pylori antibody and pepsinogen and OLGA/OLGIM staging system in gastric precancerous lesions risk assessment. A total of 331 patients were enrolled after the examination of endoscopy at Endoscopy Center, the First Affiliated Hospital of Zhejiang Chinese Medical University from October 2014 to December 2015. According to the result of gastroscopy, gastric secretion and serum Helicobacter pylori antibody test, the patients were divided into four groups: Group A: Hp (+)P (−), Group B: Hp (+)P (+), Group C: Hp (−)P (+) and Group D: Hp (-)P (−). PG positive was defined as PG1<70µg/L and PGR<15%. According to the range and degree of atrophy/intestinal metaplasia, patients were assigned into five groups on the basis of OLGA/OLGIM staging system. The levels of Hp infection rate, PG I, PG II and PGR were compared between different groups, and the correlation between ABM method and OLGA/OLGIM staging system were evaluated. Statistical analysis was accomplished by chi-square test and logistic regression modeling analysis.

**Results:** A total of 331 patients were enrolled. 214 patients were classified into group A, 106 patients into group B, 8 patients into group C and 7 patients into group D, respectively. According to the pathological results, 177 cases were non-associated and 54 cases associated atrophic gastritis. The Hp infection rate was significantly higher in patients with AG than those in AG and PGR level correlated inversely with the rising OLGA stages (F = 5.127, P =0.0013). Logistic regression modeling showed significant correlations between Hp infection rate, OLGA stages and OLGIM staging system (P<0.001).

**Conclusion:** Serological ABC method and histological OLGA/OLGIM staging system are closely linked in gastric precancerous lesions risk assessment. Serum pepsinogen test could be applied for high risk population identifying and provide a recommendation for further endoscopy examination.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**References**


**P0572 ENDOSCOPIC MUCOSAL RESECTION FOR SPORADIC NON AMPULLARY DUODENAL ADENOMA (SADA) CAN WE REDUCE THE RISK OF RECURRENCE AND COMPLICATIONS IN TERTIARY CENTERS?**

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**Introduction:** Endoscopic treatment of sporadic duodenal adenoma is mainly performed in tertiary centers because it is technically challenging and associated in major complications (perforation 1–5% and delayed bleeding 10–15%). The aim of this study was to evaluate the safety and efficacy of the endoscopic treatment for non ampullary sporadic duodenal adenomas (SADA) in two tertiary centers in a large series and to try to determine the predictive factors of outcomes with a long follow-up.

**Aims & Methods:** This retrospective study was conducted in two tertiary centers between 12/2003 to 03/2016. All the patients who underwent at least one endoscopic treatment by EMR for SDA histologically proven were included. Patients with PAF and ampullary adenoma were excluded. All the following outcomes were systematically recorded in both centers: complete endoscopic resection, resection with negative lateral and vertical margins, recurrence, success of the en-bloc resection and adverse events (Perforation, intra-procedural bleeding, delayed bleeding, others). There were analysed with multivariate analysis.

**Results:** 134 procedures were performed. The mean patient age was 65 years (33–83), 50.7% were women. The mean SDA size was 20.7mm (5–50mm), mostly located in the second duodenum (47.8%), 64.9% of the adenomas had a villous component, 33.4% with high grade dysplasia and 7.5% with in situ intramusco. Discrepancy between biopsies and the final histology was demonstrated, 19.7% of the lesions being upgraded at the first biopsy and 7.5% being downgraded. An EMR was performed in 98.5% of the cases with a complete endoscopic resection rate of 96.2% which was associated in multivariate analysis with the lesion size and pronounced depression. The en-bloc resection’s rate was 44%. Vertical margins were negative in 91.8% of the cases. Negative lateral and vertical margins was associated in multivariate analysis with the lesion size and its en-bloc resection.

**Conclusion:** Endoscopic treatment of SDA appears to be effective and relatively safe in tertiary centers. The major complications were mostly associated with major complications (perforation 1–5% and delayed bleeding 10–15%). The aim of this study was to evaluate the safety and efficacy of the endoscopic treatment for non ampullary sporadic duodenal adenomas (SADA) in two tertiary centers in a large series and to try to determine the predictive factors of outcomes with a long follow-up.

**Disclosure of Interest:** All authors have declared no conflicts of interest.
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Introduction: Additional surgery should be recommended in patients with non-curative endoscopic resection for early gastric cancer (EGC). However, this decision has often been hesitated according to patient condition such as advanced age or comorbidities. After the recognition of recurrence, the salvage surgery has been considered difficult. However, little has been reported on it.

Aim of the study: The aim of this study was to clarify the results of salvage surgery for recurrence after non-curative ESD for EGC using data from multicenter retrospective study (EAST study). Of 15,785 patients who underwent ESD for EGC at 19 participating institutions from January 2000 to August 2010, we aimed to meet the current curative criteria for ESD were retrospectively reviewed. Among 1,585 patients who underwent ESD for EGC and were included in the study, 1,064 patients underwent additional surgery, and 905 patients were observed without any additional treatment. We evaluated first site of recurrence, clinical course after salvage surgery, and long-term survival on non-survival group. Recurrence was classified regional LNM, and distant metastasis.

Results: Over a median follow-up period of 64 months, recurrence was detected in 27 patients. Among them, 2 patients were excluded from this study due to missing data. Therefore, 25 patients with recurrence were only local site (intra-gastric relapse 3, regional LNM 7), and distant metastasis 15 (60%). The first treatments for recurrence were endoscopic treatment 1, salvage surgery 7 (28%), chemotherapy 6, and best supportive care 1. Only one patient was alive without any recurrence for 31 months after salvage surgery. And one patient died of acute myocardial infarction just one month after salvage surgery. In the remaining 5 patients, recurrence was detected at 0, 2, 3, 5, 30 months after salvage surgery, and all of them died of gastric cancer. Median survival time of all 25 patients with recurrence was 16 months after salvage surgery. All survival of patients who underwent salvage surgery was only 7 months from salvage surgery.

Conclusion: More than half of recurrence after non-curative ESD without additional surgery was distant metastasis, and the survival rate after salvage surgery was quite low.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

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Introduction: Since population-based screening for gastric cancer in Korea was implemented in 2002, endoscopic treatment of early gastric cancer (EGC) has been popularized. Most patients with early neoplasm have no alarming symptoms/signs. In addition, the strategy for detecting factors predicting curative endoscopic resection of EGC is being popularized, because the general population is aging and considering the quality of life after treatment.

Aims & Methods: This study investigates factors affecting curative endoscopic resection of EGC in the era of population-based screening for gastric cancer. The subjects consisted of patients newly diagnosed with stomach cancer at Seoul ST. Mary’s Hospital between May 2011 and May 2016. All patients completed questionnaires about symptoms, social history, family history, knowledge of national cancer screening program, the reason for screening, and the interval between endoscopy screening examinations for gastric cancer.

Results: Of a total of 469 patients, 147 (31.3%) had a curative endoscopic resection, 260 (55.4%) had a curative surgical resection and 62 (13.3%) were in non-curative surgical resection or an inoperable state. The patients with curative endoscopic resection had minimal abdominal symptoms and few alarm symptoms/signs (a family history of gastric cancer, anemia, and clinically important weight loss), whereas alarm symptoms were more common in patients with advanced cancer. In multivariate analysis, regular surveillance endoscopy was only the factor predicting the curative endoscopic resection [Odd ratio (95% CI) 6.099 (2.532 ~ 14.933), p = 0.000]. In addition, the proportion of curative endoscopic resection was significantly higher in the 1-year [Odd ratio (95% CI) 10.381 (4.081 ~ 26.405), p = 0.0000], 2-year endoscopy interval groups [Odd ratio (95% CI) 3.161 (1.106 ~ 9.035), p = 0.032] than patients who had no endoscopy within 2 years.

Conclusion: Most patients with the curative endoscopic resection have minimal abdominal symptoms and no alarming symptoms/signs. Regular surveillance endoscopy was the only factor predicting the curative endoscopic resection of gastric cancer. In addition, more frequent endoscopic surveillance could help to early detect gastric cancers with curative endoscopic resection.

Disclosure of Interest: All authors have declared no conflicts of interest.
P0576 USEFULNESS OF OPERATIVE LINK ON GASTRITIS ASSESSMENT (OLGA) AND OPERATIVE LINK ON GASTRIC INTESTINAL METAPLASIA (OLGIM) FOR DIAGNOSIS OF HELICOBACTER PYLORI-ASSOCIATED GASTRIC CANCER REGARDLESS OF TISSUE TYPE IN KOREA

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Introduction: Atrophic gastritis and intestinal metaplasia are the cancerization field in which gastric cancer (GC) develops in case of intestinal type. The OLGA and OLGIM staging systems have been suggested to provide risk estimation for GC.

Aims & Methods: The aim of this study is to evaluate the usefulness of OLGA and OLGIM staging according to Lauren’s histological classification of GC in considering with other risk factors of gastric cancer. From January 2006 to December 2015, 607 GC patients and 677 control subjects were enrolled who underwent esophagogastroduodenoscopy. Biopsies were taken from the greater and lesser curvatures of the antrum and mid-body, respectively. The OLGA and OLGIM stage (0-IV) was recorded by combining antral with body atrophy scores using the Updated Sydney System. Stage III and IV OLGA or OLGIM was classified as high-risk stage group and Stage 0-II as low-risk group. Helicobacter pylori infection was assessed by modified Giemsa stain, rapid urease test and culture and was defined by a positive result on any of these tests. Multivariate logistic analysis was performed for the age, sex, smoking, alcohol and family history of GC.

Results: GC patients had more high-risk OLGA stages (25.9%) than controls (6.8%, P < 0.001) and high-risk OLGIM stages (18.3%) than controls (4.9%, P < 0.001). In the multivariate logistic analysis, Old age [odds ratios (ORs), 1.932; P = 0.004 and 2.584, P < 0.001 for ages in the 40 ~ 59 and > 60, respectively], family history of GC (OR, 2.119; P < 0.001), and H. pylori infection (OR, 1.963; P < 0.001) were independent risk factors for GC in the diffuse type as well as intestinal type (Table). High-risk OLGA stages were significantly associated with increased risk of GC in comparison to low-risk (OR, 3.778; P < 0.001): intestinal-type (OR, 4.318; P < 0.001) and diffuse-type (OR, 2.920; P < 0.001) (Table). High-risk OLGIM stages were also significantly associated with increased risk of GC in comparison to low-risk (OR, 3.306; P < 0.001): intestinal-type (OR, 3.051; P < 0.001) and diffuse-type GC (OR, 3.981; P < 0.001).

Conclusion: High-risk OLGA and OLGIM stages were useful for intestinal type as well as diffuse type. This usefulness will be increased when combined with H. pylori status and family history of GC in regions with high prevalence of GC. Analysis regarding specific interaction among these three factors is undergoing.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0577 BODY MASS INDEX AND DIGESTIVE CANCER MORTALITY IN THE KOREAN GENERAL POPULATION: A NATIONWIDE COHORT STUDY

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Introduction: The association between body mass index (BMI) and digestive cancer mortality is not conclusive in East Asians.

Aims & Methods: We evaluated the relationship between BMI and digestive cancer mortality, using prospective cohort data by the National Health Insurance Service in Korea, which consisted of more than one million subjects. A total of 510, 148 Korean adults were followed-up until 2010. The adjusted hazard ratios (HRs) of cancer mortality were calculated using a Cox model.

Results: During follow-up, 7774 total deaths occurred from digestive cancer, HR for digestive cancer mortality across seven BMI categories. Below 25 kg/m², the HRs of death for each 5 kg/m² increase in BMI were 0.43 (95% confidence interval [CI] = 0.32-0.58) for esophageus cancer, 0.70 (0.62-0.79) for stomach cancer, and 0.70(0.65-0.90) for colorectal cancer. Over 25 kg/m², the HRs of death for each 5 kg/m² increase in BMI were 1.30 (95% CI = 1.04-1.64) for colorectal cancer, 1.28 (1.07-1.53) for liver cancer, and 1.28 (0.96-1.71) for gall-bladder cancer and biliary tract cancer. BMI were not associated mortality from small intestine cancer and pancreatic cancer.

Conclusion: Low BMI were predictors of mortality from esophageal cancer and stomach cancer. High BMI were predictors of mortality from liver cancer and gallbladder cancer and biliary tract cancer. Both low and high BMI were predictors of mortality from colorectal cancer. Further research is needed to evaluate whether interventions involving weight change (loss or gain) reduce the risk of cancer or improve the survival.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
BMI, body mass index; CI, confidence interval; GB, gallbladder; HR, hazard ratio. *Hazard ratios were calculated using Cox proportional hazards models after adjustment for age at baseline (continuous variable), smoking status (current smoker, former smoker, never-smoker, and missing smoking status), alcohol consumption (frequency, five or more times/week, one to four times/week, less than one time/week, past drinker [no alcohol for a year], never-drinker, or missing information), monthly household income (Korean won [KRW], 1 United States dollar = 1170 KRW as of August 1, 2004; < 500, 000, 500, 000–990, 000, 1, 000, 000–1, 490, 000, ≥ 1, 500, 000, missing information), and physical activity (yes, no). HRs were not presented for causes with less than 10 deaths.

Aims & Methods: A novel robotic suture manipulator is composed of control panel and a working arm, which grasp and move objects at the end of scope. A total of 10 porcine stomachs were used for the test. Pigs were sacrificed randomly to 2 groups and ESD was performed on mucosa of stomach using conventional technique and new endoscopic technique with robotic manipulator. Endoscopic experts and novice endoscopists performed ESD in 2 parts (antrum & body) of stomach. During procedure, robotic manipulator lifts up dissected tissue of stomach to make better visibility. Procedure time, complete resection rate, and complications such as perforation were recorded.

Results: The average procedure time for the robotic manipulator and conventional ESD was 42 minutes and 45.9 minutes. In novice endoscopists, the average procedure time using robotic manipulator is faster than conventional ESD group (42 minutes vs 53.5 min, p < 0.005). Both robotic expert and novice endoscopists completed the ESD procedure for en bloc resection of target lesions using KUMC robotic manipulator. There was no difference in complete resection rates between two groups. No complication such as perforation occurred in both groups during the procedures. There was no difference depending on resected location in stomach.

Conclusion: The robotic manipulator, which can perform ESD more easily showed feasible result comparing with conventional ESD. ESD using robotic manipulator could be helpful, especially in novice endoscopists. This research proposes a novel approach for safe and feasible method during ESD.

Disclosure of Interest: All authors have declared no conflicts of interest.

Aims & Methods: Newly developed endoscopic IRE ablative catheter works with single channel of endoscope. A pair of dipolar electrodes consist of pre-shaped f 0.63 mm nitinol wire and the distance between each electrode is 10 mm. The electrodes are loaded within braided tube for sient delivery system then deployed when IRE catheter put in stomach through the endoscope. We performed animal study. Results: We developed new endoscopic IRE device, and studied about its effectiveness and feasibility in animal model.

Conclusion: Irreversible electroporation (IRE) is a promising novel technique for the ablation of tumors. An advantage of IRE is its mechanism to remove undesired cells by affecting the cell membrane without thermally destructing blood vessels, nerves and the surrounding tissues. Several clinical trials for applying IRE to human organs such as liver, pancreas and kidney are being conducted. Furthermore, there are several clinical trials for applying IRE ablation for gastrointestinal tumors also have been conducted recently. Here, we developed endoscopic IRE device, and studied about its effectiveness and feasibility in animal model.

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Results: Ten male Yorkshire pigs and in vitro stomachs were used in this study. The tissue with H&E stain showed diffuse cell death 24 hr after IRE ablation.

Aim: To investigate the risk factors for lymph node metastasis in ulcerative type EGC. Methods: Our study consisted of 1450 EGC cases; 749 cases were patients with GB cancer and 701 cases were patients with no GB cancer. A Cox proportional hazards model was used to evaluate the risk factors for lymph node metastasis in ulcerative type EGC. Results: Hazard ratios were calculated using Cox proportional hazards models after adjustment for age at baseline (continuous variable), smoking status (current smoker, former smoker, never-smoker, and missing smoking status), alcohol consumption (frequency, five or more times/week, one to four times/week, less than one time/week, past drinker [no alcohol for a year], never-drinker, or missing information), monthly household income (Korean won [KRW], 1 United States dollar = 1170 KRW as of August 1, 2004; < 500, 000, 500, 000–990, 000, 1, 000, 000–1, 490, 000, ≥ 1, 500, 000, missing information), and physical activity (yes, no). HRs were not presented for causes with less than 10 deaths.

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Conclusion: The robotic manipulator, which can perform ESD more easily showed feasible result comparing with conventional ESD. ESD using robotic manipulator could be helpful, especially in novice endoscopists. This research proposes a novel approach for safe and feasible method during ESD.

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Results: We developed new endoscopic IRE device, and studied about its effectiveness and feasibility in animal model.

Conclusion: Irreversible electroporation (IRE) is a promising novel technique for the ablation of tumors. An advantage of IRE is its mechanism to remove undesired cells by affecting the cell membrane without thermally destructing blood vessels, nerves and the surrounding tissues. Several clinical trials for applying IRE to human organs such as liver, pancreas and kidney are being conducted. Furthermore, there are several clinical trials for applying IRE ablation for gastrointestinal tumors also have been conducted recently. Here, we developed new endoscopic IRE device, and studied about its effectiveness and feasibility in animal model.

Disclosure of Interest: All authors have declared no conflicts of interest.
Conclusion: The new endoscopic IRE device, which can perform IRE ablation on gastrointestinal tract using endoscopy showed safe and feasible result.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0581 DIAGNOSIS OF MICROVASCULAR PATTERN IS MORE IMPORTANT THAN MICROSCOPIC SURFACE PATTERN TO DELINATE GASTRIC CANCERS DETECTED AFTER H. PYLORI ERADICATION BY MAGNIFYING ENDOSCOPY

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Introduction: It is difficult to delineate gastric cancer that is detected after successful eradication of Helicobacter pylori. One reason is reportedly the difficulty in identifying the demarcation line between the cancerous lesion and non-cancerous gastric mucosa due to a mixture of non-neoplastic epithelial-lined structure inside the neoplasm. However, almost all previous studies have only used magnifying endoscopy (ME) at low magnification which could evaluate microendoscopy pattern (MSP) but could not evaluate microvascular pattern (MVP).

The highest power magnification was necessary to evaluate MVP accurately. ME findings of the demarcation line, irregular MSP and irregular MVP were not shown in any of the gastric cancers that were not accurately assessed in these studies.

Aims & Methods: The aim of this study was investigating diagnostic efficacy of ME with narrow band imaging (NBI) in delineating the gastric cancers after eradication HP, using ME at highest power magnification, and classifying ME features of the marginal area according to the vessel plus surface classification system (VSCS) to realize which was more important ME findings MSP or MVP to detect demarcation line. Endoscopic examination was performed using a magnifying endoscopy (GIF-H260Z, Olympus Medical Systems Co, Tokyo, Japan) and NBI system (EVIS LUCERA Spectrum system; Olympus Medical Systems Co, Tokyo, Japan). Endoscopic imaging procedures were performed at low-power magnification followed by highest power magnification. On the day of ESD, the resection line was marked 3–5 mm outside of the margin of the lesion. A lesion meeting all of the following criteria was defined as a lesion with successful delineation: (1) the demarcation line of the lesion is endoscopically identified with a high level of confidence; (2) According to histopathological findings, the lesion is identified as a demarcation line. The diagnostic accuracy of ME-NBI in delineating the lesions was evaluated. On the other hand the ME findings of the marginal area in each lesion were classified in terms of microsurface pattern (MSP) and microvascular pattern (MVP) according to the VSCS to identify the findings that were useful in delineating the lesions in patients with differentiated-type early gastric cancers. The classification according to the VSCS was made in the marginal area with the least irregular findings.

Results: Of 178 consecutive lesions of differentiated-type early gastric cancer treated by endoscopic submucosal dissection (EM-SD) between August 2013 and March 2017, the study included 59 lesions that were detected after successful H. pylori eradication. The result of ME-NBI findings are summarized in the table. Gastric cancer was successfully delineated in 98.3% (57/59) of the lesions with regular MVP or irregular MVP with a demarcation line. Among the ME findings of the demarcation line, irregular MSP and irregular MVP were present in 67.7% (40/59) and 93.2% (55/59), respectively, according to the VSCS, with a higher percentage of lesions with irregular MVP than those with irregular MSP. In addition, there was no finding which was irregular MVP and regular MSP, but 27.1% (16/59) was regular MSP and irregular MVP, which indicated that the ME findings of MVP was more important than MSP. One lesion showed regular MSP or regular MVP without a demarcation line in a portion of the marginal area, resulting in unsuccessful delineation.

Conclusion: The accuracy of ME with NBI in delineating gastric cancer detected after H. pylori eradication was 98.3%, which was higher than the values reported previously. In addition, the MVP as visualized by ME appeared to be a more reliable biomarker which we know that some play an important role in the cancer. However, the role of stress in cancer initiation is contradicted and debatable. Other natural factors such as nitrates, which are widely presented in daily food, are actively discussed as carcinogenic to humans. There is no clinical and epimediological evidences that the nitrosamines itself can induce the stomach cancer.

Aims & Methods: For the better understanding of carcinogenic effects of daily stress and nitrates in development of stomach cancer, here we studied the role of these factors in adenocarcinoma in stomach of rats. The experiments were carried out with male adult rats (n = 200). To examine the role of stress and nitrosamines in gastric mucosal injuries we used: 1) the model of chronic social stress (over-population during 9 months); 2) the daily using of toluidine (2 g/kg) in food and water with nitrates (2 g/l); 3) the combined effects of stress + nitrosamines. The

References

Disclosure of Interest: All authors have declared no conflicts of interest.

P0582 ENDOSCOPIC SMALL CAPACITY FORCEPS INCREASE THE PATHOLOGICAL DIAGNOSIS OF GASTRIC INDEFINITE NEOPLASIA

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Introduction: Endoscopic forceps biopsy (EFB) is the gold standard for gastric epithelial tumor diagnosis. However, definitive diagnosis is often difficult, and some cases are diagnosed as gastric indefinite neoplasia (GIN), which corresponds to category 2 in the revised Vienna classification. GIN lesions require short periods of follow-up. The most appropriate forceps size for gastric biopsy has yet to be determined. In the Japanese Classification of Gastric Cancer, diagnoses of GIN are attributed, at least partly, to the full size of biopsy specimens. Since specimens yielded by small biopsy forceps are small, the use of small biopsy forceps is expected to increase the rate of GIN diagnoses.

Aims & Methods: The relationship between forceps size and the frequency of GIN was investigated. The patients in this cohort were divided into two historical groups. The first group comprised patients evaluated during the period when standard biopsy forceps (SF) were used (April 2010–March 2011), and the second comprised patients evaluated during the period when small biopsy forceps (SmF) were used (April 2011–March 2013). Standard caliber endoscopy was used for all esophagogastroduodenoscopy(EGD). We count the number of GIN and gastric carcinoma lesions. Patient characteristics, lesion characteristics (e.g., size, macroscopic appearance, and color tone), endoscopist experience level, biopsy sample groups diagnoses as GIN, the clinical courses of GIN cases were followed for 3 years, and the timing of EGD after the GIN diagnosis and the final pathological result were investigated.

Results: Among the 5420 patients who underwent EGD in the first period, 2, 584 (30.7%) underwent gastric biopsy with SF. Among the 15,986 patients who underwent EGD in the second period, 4204 (26.3%) underwent gastric biopsy with SmF. Gastric carcinoma was diagnosed in 7.93% (205/2584) and 7.54% (317/4204) of the SF and SmF groups, respectively (P = 0.556). GIN was diagnosed in 10.01% (258/2584) and 12.5% (529/4204) of the SF and SmF groups, respectively (P = 0.048). The two groups diagnosed as GIN did not differ significantly in terms of the patient characteristics, the lesion characteristics, endoscopist experience level and biopsy related hemorrhage. The mean minor-axis lengths of the biopsy samples were 1.50 ±0.50 mm and 1.38 ± 0.40 mm in the SF and SmF groups, respectively. The SmF group samples tended to be shorter (P = 0.088). In both groups, 40% of the final diagnoses were epithelial neoplasia; no significant differences were observed.

Conclusion: SmF use may increase the rate of GIN. Thus, SmF use should be avoided with a standard caliber endoscopy.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P0583 THE ROLE OF STRESS AND NITROSAMINES IN THE DEVELOPMENT OF GASTRIC CANCER: A NEW MODEL OF ADENOCARCINOMA FORMATION WITH METASTASES IN RATS

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Introduction: Stomach cancer is a leading cause of cancer-related deaths in the eastern Europe. It well knows that stress play an important role in the cancer. However, for the role of stress in cancer initiation is contradicted and debatable. Other natural factors such as nitrates, which are widely presented in daily food, are actively discussed as carcinogenic to humans. There is no clinical and epimediological evidences that the nitrosamines itself can induce the stomach cancer.

Aims & Methods: For the better understanding of carcinogenic effects of daily stress and nitrates in development of stomach cancer, here we studied the role of these factors in adenocarcinoma in stomach of rats. The experiments were carried out with male adult rats (n = 200). To examine the role of stress and nitrosamines in gastric mucosal injuries we used: 1) the model of chronic social stress (over-population during 9 months); 2) the daily using of toluidine (2 g/kg) in food and water with nitrates (2 g/l); 3) the combined effects of stress + nitrosamines. The
upper endoscopy was performed using our in-house custom-made multichannel endoscopy system. Histological assay performed to analyze the changes in the gastric tissues.

Results: Using upper gastroscopy, we studies the stomach tissues during 9 months of lining of rats in chronic stress. There were no changes in the gastric mucosa during the first 2 months. In the third month 35% (7 of 20) animals demonstrated multiple small peptic ulcer (n = 11). These changes progressed during other time of observation. 9 months of experiment. So, this time all rats showed peptic ulcers both types with significant increase in the number of ulcers (n = 21) at the end of the experiment. Thus, this series of experiments clearly showed that chronic stress plays provoking role in the peptic ulcer formation in the stomach of rats. The deleterious effects of nitrosamines on the gastric mucosa observed 4 months after the beginning of daily using of toluidine and nitrides in 75% of the rats showed symptoms of atrophic gastritis. Other 25% (5 of 20) animals did not demonstrate any changes in gastric mucosa.

Thus, this series of experiments markedly showed that effect of long-term eating low-dose nitrosamines induced of atrophic gastritis in the stomach of majority of rats. Using similar protocol of the first and second parts of experiments, we observed the changes in the stomach tissues during 9 months. The same scenarios of typical gastric injuries induced by stress and nitrosamines were observed in rats, i.e. they showed development of peptic ulcers and atrophic gastritis. But, 7 months after the start of experiment, these pathological changes of gastric tissues were associated with intestinal metaplasia of goblet cells, which is the pre-cancer symptom. In 9 months of study, symptoms of gastric adenocarcinoma were observed in 82% of rats (131 of 160) with tumor lesions was accompanied by the migration of metastatic tumor cells through the bloodstream in the liver. The number of metastatic nodes varied from 1 to 5.

Conclusion: Thus, in our research we clearly show that only combination of two parameters: stress and nitrosamine, cause development of gastric cancer with metastasis in the liver while the presence of these factors alone contribute mucosal injuries without oncolgical changes in the stomach.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

PG085 RELEVANCE OF PTGS1 AND PTGS2 GENE POLYMORPHISMS TO GASTRIC CANCER RISK AND PHENOTYPE IN CAUCASIANS

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PG086 GASTRIC JUICE FREE AMINO ACID PROFILING AS A METHOD FOR DISCOVERING POTENTIAL BIOMARKERS OF GASTRIC CANCER

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Introduction: Gastric cancer (GC) contributes a heavy burden to the global health, especially in Asian countries. Early diagnosis is crucial to improve patients’ outcome, but reliable biomarkers are desperately needed. In our previous studies, we established several endogenous fluorescence spectra of gastric juice for GC diagnosis and screening [1, 2], isolated and identified three fluorescence signatures (aromatic amino acids, AA), which can be used to distinguish GC from non-neoplastic gastric diseases (NGD) regardless of the stage [3, 4]. However, the characteristic biosignature for the whole metabolic spectra of gastric juice free amino acids (GJFAs) in GC patients remain unclear. Although many investigators had reported on the changes of amino acids’ concentrations in the peripheral blood, urine and tissues of GC patients [5, 6].

Aims & Methods: In order to determine the metabolic patterns of GJFAs in GC and NGD patients, gastric juice samples were collected from GC patients (n = 47) and age-matched NGD patients (n = 83) from December 2015 to May 2016, and then measured by an automatic amino acid analyzer. Orthogonal partial least squares discriminant analysis (OPLS-DA) and Mann-Whitney U test are used for data analysis. The diagnostic value of GJFAs was evaluated by ROC curve. Furthermore, significantly altered metabolic pathways were identified by pathway analysis using public databases such as KEGG and MetaAnalysis 3.0.

Results: GJFAs profiles significantly differed between the GC and NGD patients. A total of 14 kinds of GJFAs, whose first principal component of variable importance in the projection (VIP) value exceeding 1 and P-value than 0.05, were screened as differential GJFAs. Compared with the NGD patients, GC patients had higher levels of threonine, serine, alanine, valine, methionine, isoleucine, leucine, tyrosine, phenylalanine, lysine and arginine,
together with lower levels of phosphoserine, ethanolamine phosphate and urea (Table 4). The 14 GFAAs revealed diagnostic values with AUC from 0.666 to 0.868, and the combined AUC of them reached to 0.902 (95% CI, 0.846–0.959) for the diagnosis of GC. Importantly, their AUCs were from 0.649 to 0.857, and the combined AUC reached to 0.880 (95% CI, 0.792–0.969) for the diagnosis of early GC, particularly, leucine, threonine and serine are the most altered three GFAAs between the two groups, whose fold change more than 2 and AUC value greater than 0.8. Moreover, the combined AUC of the 3 non-AAAs was 0.869 (95% CI, 0.805–0.934) for the diagnosis of GC. It was slightly higher than that in comparison with 3 AAPs 0.841 (95% CI, 0.773–0.908). Additionally, the pathway of aminoacyl-tRNA biosynthesis metabolism was excessively activated, which significantly responsible for the above alteration in amino acids metabolism.

Table 1: Differential GFAAs between GC and NGD patients and their discriminating performance

<table>
<thead>
<tr>
<th>Number</th>
<th>Abbreviation</th>
<th>GC Median</th>
<th>NGD Median</th>
<th>P-value</th>
<th>VIP</th>
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<td>0.797</td>
</tr>
<tr>
<td>AA07</td>
<td>Leu</td>
<td>0.026</td>
<td>0.007</td>
<td>0.001</td>
<td>1.343</td>
<td>0.812</td>
</tr>
<tr>
<td>AA08</td>
<td>His</td>
<td>0.075</td>
<td>0.020</td>
<td>0.001</td>
<td>1.626</td>
<td>0.888</td>
</tr>
<tr>
<td>AA09</td>
<td>Ile</td>
<td>0.066</td>
<td>0.026</td>
<td>0.002</td>
<td>1.288</td>
<td>0.882</td>
</tr>
<tr>
<td>AA10</td>
<td>Phe</td>
<td>0.060</td>
<td>0.032</td>
<td>0.002</td>
<td>1.745</td>
<td>0.802</td>
</tr>
<tr>
<td>AA11</td>
<td>Ala</td>
<td>0.033</td>
<td>0.016</td>
<td>0.001</td>
<td>1.138</td>
<td>0.793</td>
</tr>
<tr>
<td>AA12</td>
<td>Arg</td>
<td>0.036</td>
<td>0.008</td>
<td>0.001</td>
<td>1.332</td>
<td>0.772</td>
</tr>
</tbody>
</table>

P-value, Statistically significant difference using Mann-Whitney U test; VIP, variable importance; AUC, area under the ROC curve; 95% CI, 95% confidence interval.

Conclusion: GJFAA profiles may be helpful for improving GC diagnosing even in the early stage and for providing more information about its metabolism. Leucine, threonine and serine, three non-AAAs, warrant further validation as alternative metabolic biomarkers for GC.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

PO0587 THE ASSOCIATION BETWEEN MMP-2/9 AND TYPE IV COLLAGEN LEVELS OF AMINO ACIDS IN GASTRIC JUICE OF GASTRIC CANCER PATIENTS

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Introduction: It is reported that aromatic amino acids (AAAs) in gastric juice could be used as potential diagnostic biomarkers to screen gastric cancer (GC) [1–3]. However, the underlying mechanism remain elusive [4]. Our group had previously reported that 29 GC patients with MMP-2/9 mRNA levels in gastric juice were measured by liquid chromatography-tandem mass spectrometry (LC-MS/MS). Furthermore, the association between them was evaluated by Spearman correlation analysis.

Results: On the one hand, the expression intensity of MMP-2/9 in GC group were significantly higher than those in NGD group, while MMP-9 was markedly lower than that in NGD group (P < 0.001 for all). Moreover, there was a positive correlation between the expression level of MMP-2 and MMP-9 (rho = 0.439, P < 0.01), but they were both negatively correlated with Col IV (rho = −0.454, P < 0.01; rho = −0.392, P < 0.01). On the other hand, significantly higher level of AAAs in gastric juice were observed in GC patients than those in NGD individuals (P < 0.001 for all). Ultimately, the expression levels of MMP-2/9 in gastric mucosal tissues were both positively correlated with the concentrations of AAAs in gastric juice (MMP-2: rho = 0.282, 0.329, and 0.293, respectively, P < 0.01 for all; MMP-9: rho = 0.457, 0.455, and 0.417, respectively, P < 0.001 for all), but Col IV was negatively correlated with them (rho = −0.283, −0.280, and −0.273, respectively, P < 0.01 for all) (Table 1).

Table 1: Relationship between the expression levels of MMP-2/9 and Col IV in gastric tissues and the levels of AAAs in gastric juice

<table>
<thead>
<tr>
<th>Variable</th>
<th>MMP-2</th>
<th>Col IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tyrosine</td>
<td>0.262**</td>
<td>0.457***</td>
</tr>
<tr>
<td>Phenylalanine</td>
<td>0.295**</td>
<td>0.455***</td>
</tr>
<tr>
<td>Triptophan</td>
<td>0.283**</td>
<td>0.417***</td>
</tr>
</tbody>
</table>

**represents significant correlation using Spearman correlation analysis when the confidence level was 0.01; ***represents significant correlation using Spearman correlation analysis when the confidence level was 0.001.

Conclusion: The overexpression of MMP-2/9 resulting in the degradation of Col IV in basement membrane and extracellular matrix may lead to the variation of AAAs’ levels in gastric juice of GC patients.

Disclosure of Interest: All authors have declared no conflicts of interest.

PO0588 MISSING RATE OF GaSTRIC CANCER DURING UPPER GaSTRONTESTINAL ENDOCOpY AND INFLUENCE ON THE NATURAL HISTORY OF THE DISEASE

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Introduction: Gastric cancer (GC) is the fourth most common type of cancer and the second leading cause of cancer related death. The gold standard for diagnosis is the esophagogastroduodenoscopy (EGD) with targeted biopsies. The aim of this observational and descriptive study in patients diagnosed of gastric cancer from January 2013 to December 2016 in the area of Ciudad Real (Spain). Missing rate of gastric cancer was defined as the percentage patients who had a negative EGD three years before the diagnosis of CG. A survival analysis was performed with Kaplan Meier curves, mainly focussing on the influence of missing rate for gastric cancer. We studied the features related to EGD that could lead this issue.

Results: 162 patients were included, 65% male with a mean age at diagnosis of 72 years. Intestinal type was the most common histology (76%). A rate of 6.8% missing of gastric cancer was detected with an average of 20 months in delay of diagnosis. However, the survival rate was similar between patients with and without a previous EGD (7.08 vs. 5.05 months p = 0.60). Among the patients who passed away, a longer delay period was observed comparing to patients who were still alive (6 months vs. 25 months; p = 0.006). In the aforementioned subgroup, biopsias were taken in 72% with gastric atrophy in all these cases. Helicobacter pylori infection was detected in 30% of them. 55.6% of the EGDs were conducted without sedation. At no point chromoendoscopy was performed, pictures were taken and withdrawal times were not reflected.

Conclusion: Despite the fact that EGD is by far the most effective method to diagnose gastric cancer, 1 out of 10 cancers or premalignant lesions are not found during EGD. Therefore, it is of utmost importance to put in place quality protocols in EGD that may help to increase the diagnosis of early gastric cancer, and by this way, improve the survival rate of these patients.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P0959 INTERFERENCE OF PG2 TATA BOX REGION IN GASTRIC CANCER

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Introduction: Several studies have demonstrated serum PGII level as a marker of the functional gastric mucosa, and a marker of some tumor including the gastric cancer. However, the modulation of the protein and its role in cancer is not fully understood. The aim of this study was to analyse the polymorphisms in the TATA BOX region, which provides a binding site for the transcription factor and then the expression of the corresponding gene, are under investigation. This study will be important to deeper understand the physiopathological PG2 role in GC.

Aims & Methods: Genetic function of 180 patients (67 GC, 71 first-degree relatives of GC patients (FDR-GC) and 42 autoimmune chronic AG (ACAG)) was assessed by gastropanel test. We investigated the PG2 TATA BOX polymorphism frequencies in relation to serum PG2 (sPG2) expression level, HP positivity and risk for GC. TATA BOX DNA fragments were amplified by PCR and analyzed by the capillary-electrophoresis (GeneMapper software). Association among clinical data and PG2 polymorphisms were estimated by Receiver operating characteristic (ROC) curve and linear regression analyses.

Results: After ROC curve analysis, the sensitivity to discriminate GC at 15 ng/mL PG2 cut-off was 70.15% and 79, 65% sensitivity and specificity, respectively (AUC: 75, p < 0.0001). We obtained 26 different PG2 TATA box fragments (280 bp to 479 bp). These fragments were grouped into 4 sized categories (1 = 308–400 bp; 2 = 401–436 bp; 3 = 437–483 bp; 4 = 439–479 bp). A positive correlation among the increase of PG2 sized fragments and the sPG2 level was found in the GC group (linear regression y = 16, 4381 + 2, 6846 x, p = 0.02).

Conclusion: In the literature, we confirm sPG2 level as a marker discriminating between GC and individuals at risk for GC (i.e ACAG and FDR) in our series. In addition we reported a correlation between the shortest PG2 TATA BOX fragments and the lower PG2 level. Since highest PG2 level was related to the GC condition, our data suggest that carriers having longer TATA BOX region may produce higher sPG2 level than patients with shorter region. The clinical significance of the differences in PG2 level associated with the TATA BOX fragments, by interfering with the transcriptional factor and then with the expression of the corresponding gene, are under investigation. This study will be important to deeper understand the physiopathological PG2 role in GC.

Disclosure of Interest: All authors have declared no conflicts of interest.

MONDAY, OCTOBER 30, 2017

P0950 HELICOBACTER PYLORI INFECTION ASSOCIATED WITH NONALCOHOLIC FATTY LIVER DISEASE: A LARGE-SCALE COHORT STUDY

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Introduction: Previous studies suggested a link between Helicobacter pylori (H. pylori) infection and nonalcoholic fatty liver disease (NAFLD), yet large-scale longitudinal studies are lacking to elucidate this association.

Aims & Methods: A cohort study of 17,028 adults without NAFLD at baseline, who participated in a repeated health screening examination including an H. pylori-specific immunoglobulin G antibody test, was conducted to evaluate the association between H. pylori and NAFLD development. Fatty liver was diagnosed by ultrasonography.

Results: During the 83,130 person-years follow-up, participants with H. pylori infection had a higher rate of incident NAFLD than those who were uninfected. In a multivariable model adjusted for age, sex, body mass index, smoking status, alcohol intake, regular exercise, year of screening exam, and education level, the hazard ratio (HR) for NAFLD development in participants with H. pylori-infection compared to those without infection was 1.21 (95% confidence interval [CI], 1.10–1.34). The association persisted after further adjustment for metabolic variables, inflammatory marker, and liver enzymes. The association between H. pylori and NAFLD was still evident in an analysis using fatty liver index as a surrogate marker of NAFLD. In addition, the association between H. pylori infection and incident NAFLD did not differ across clinically relevant subgroups evaluated.

Conclusion: H. pylori infection was significantly associated with the development of NAFLD, independent of metabolic and inflammatory risk factors. H. pylori infection may play a pathophysiological role in NAFLD development, indicating that H. pylori eradication might play a role in reducing risk of NAFLD.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
H. pylori infection reduces the risk of Barrett's adenocarcinoma and is independent from the geographical location, a meta-analysis

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Introduction: The European and Northern American populations a decreasing prevalence of H. pylori infection has been observed, along with an increasing prevalence of Barrett’s oesophagus and an increasing incidence and prevalence of the adenocarcinoma of the oesophagus and gastro-oesophageal junctional cancers. HP has been proven a constructive factor against Barrett’s oesophagus, but some individual studies suggested the opposite.

Aims & Methods: Our aim was to scrutinize all data available on the relationship between H. pylori infection and Barrett’s oesophagus prevalence, to see, if H. pylori has a protective role for Barrett’s oesophagus and if it is dependent from the geographical location. A meta-analysis was performed using the preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P). We conducted a systematic search in PUBMED, EMBASE and COCHRANE databases from inception to December 2016, for the keywords of Barrett’s, Barrett’s metaplasia, Barrett’s oesophagus, Barrett’s oesophagus, Barrett oesophagus, Helicobacter pylori, H pylori and Helicobacter. We also used information from the references of relevant publications to find further eligible studies. We have conducted a meta-analysis of the data from all studies included. We used the random effects DerSimonian and Laird.

Results: We have found 568 articles in PUBMED, 741 in EMBASE and 15 in COCHRANE databases. After exclusion of the articles without sufficient data on the prevalence of H pylori and Barrett’s oesophagus, we have identified 83 articles suitable for statistical analysis. This meta-analysis involved 98 665 patients with Barrett’s oesophagus and 720 800 patients without Barrett’s oesophagus. The statistical analysis from all 83 studies from five continents and 27 countries showed a protective effect of H pylori for Barrett’s oesophagus, not in Africa, overall Odds Ratio = 0.63 (95% CI:0.55, 0.71). The OR and 95% CI values were 0.34 (0.17, 0.67) for Asia, 0.71 (0.55, 0.91) for Europe, 3.05 (0.59, 15.73) for Africa, 0.60 (0.51, 0.71) for North America, 0.95 (0.56, 1.64) for South America and 0.56 (0.39, 0.83) for Australia. The OR and 95% CI values were 0.84 (0.43, 1.64) for Eastern Europe; 0.68 (0.52, 0.90) for Western Europe and 0.71 (0.55, 0.91) for all of Europe, suggesting that the protective role of H pylori infection is not different across Europe.

Conclusion: This large meta-analysis has given further evidence, that Helicobacter pylori infection has a protective role for Barrett’s oesophagus and this protective role is independent from the geographical location, apart from Africa. In view of the decreasing prevalence of H pylori in developed countries and the epidemiological rise of Barrett’s oesophagus and adenocarcinoma, it would be important to conduct further large, prospective, multinational studies on the effect of H. pylori infection on Barrett’s oesophagus.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

The reference list for all studies involved in this meta-analysis will be presented at the conference, if this abstract was to be accepted, as the reference list is too long for the constraints on the number of characters in the abstract.

The IMPACT OF HELICOBACTER PYLORI ON MORTALITY AND OTHER OUTCOMES IN PATIENTS WITH HEPATIC ENCEPHALOPATHY: A NATIONWIDE ANALYSIS

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Introduction: Helicobacter Pylori (H. Pylori) has been implicated in worsening outcomes in patients with hepatic encephalopathy. This is believed to be the result of its urease enzyme that increases the production of ammonia. Small studies so far have yielded contradictory results on whether the presence of H. pylori worsens treatment outcomes in hepatic encephalopathy. Therefore, the aim of this study was to assess the impact of H. pylori on mortality, morbidity and resource utilization among patients with hepatic encephalopathy using a national database.

Aims & Methods: This was a case-control study using the National Inpatient Sample 2013, the largest publicly available inpatient database in the United States. All patients with an ICD-9 CM code for a principal diagnosis of hepatic encephalopathy were included. There were no exclusion criteria. Patients positive for H. pylori were identified using the appropriate ICD-9CM codes. The primary outcome was all cause mortality. The secondary outcome was resource utilization as measure by use of abdominal imaging (CT scan and ultrasound of the abdo-

Multivariate regression analyses were used to adjust for the following confounders: Age; sex; race; income in patients’ zip code; Charlson Comorbidity Index, hospital region, location, size and teaching status.

Results: A total of 55,360 patients with hepatic encephalopathy were included in the study, of which 20 had H. pylori infection. The mean patient age was 60 years and 42% were female. After adjusting for confounders using multivariate analysis, patients with and without H. pylori had similar adjusted odds of mortality (adjusted Odds Ratio (aOR): 1.71, 95% CI: 0.62-4.74, p = 0.30). As far as resource utilization, patients with and without H. pylori had similar adjusted odds of hospitalization (aOR: 0.92, 95% CI: 0.88–1.00, p = 0.08), LOS (adjusted mean difference: 1.7 days, 95% CI: –0.02-3.42, p = 0.52), and total hospitalization charges (adjusted mean difference: $16888, 95% CI: $4499 - $37675, p=0.12). However, patients with H. pylori had higher adjusted total hospitalization charges ($6128, 95% CI: $1141 - $11115, p=0.01)

Conclusion: Presence of Helicobacter Pylori has no impact on inpatient mortality among patients with liver cirrhosis and hepatic encephalopathy. In addition, the presence of Helicobacter Pylori is not associated with any increase in resource utilization among this patient population, with the exception of total hospitalization costs. It is surprising to note that, although total hospitalization costs differed between the two groups, they received the same total hospitalization charges from admitting hospitals.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

Table 1: H. pylori eradication rates in patients with and without previous intake of macrolides.

<table>
<thead>
<tr>
<th></th>
<th>Previous use of Macrolides</th>
<th>No previous use of Macrolides</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>A: Triple therapy (n = 113)</td>
<td>24/45 (53, 3%)</td>
<td>65/68 (95, 5%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>B: Concomitant (n = 106)</td>
<td>37/44 (84, 1%)</td>
<td>61/62 (98, 4%)</td>
<td>0.0085</td>
</tr>
<tr>
<td>Total (n = 219)</td>
<td>61/89 (68, 5%)</td>
<td>126/130 (96, 9%)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Conclusion: Previous use of macrolide antibiotics predicts a low response to triple and to concomitant clarithromycin-containing regimens. In addition, our study shows that in patients without previous use of macrolides triple therapy achieves per-protocol eradication rates over 90%.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P0597 EFFICACY OF THREE-IN-ONE CAPSULE BISMUTH QUADRUPLE THERAPY FOR HELICOBACTER PYLORI ERADICATION IN CLINICAL PRACTICE IN A MULTINATIONAL PATIENT POPULATION
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Introduction: Due to increasing prevalences of clarithromycin resistance in H. pylori infection, current guidelines recommend quadruple therapies as first-line therapy1-3. Bismuth quadruple therapy (BQT) has been proven superior to standard triple therapy in clinical trials, however little is known about the efficacy of BQT in clinical routine practice.

Aims & Methods: In a prospective single center cohort study we analyzed consecutive patients in whom three-in-one capsule BQT (Pylér® + omeprazole) has been prescribed between 1/2013 and 12/2016. All patients were instructed in a standardized fashion and a prospective follow-up was planned. In a subgroup of patients, genotypic susceptibility testing for clarithromycin and levofloxacin by PCR was carried out on gastric biopsies before treatment. Treatment outcome was assessed by 13C urea breath test or by histology not earlier than 4 weeks after end of treatment.

Results: Three-in-one capsule BQT has been prescribed in 322 patients (mean age 41 years (18-80), 65% female, 26% active smoker). 71% of patients had a migrational background including Southern/Eastern Europe, Eurasia/Central Asia, Southeast-Asia, Africa, and Central/South America. PCR results were available in 163 patients (50.6%) and identified resistance to clarithromycin and levofloxacin in 29 (17, 8%) and 20 (12, 3%) of cases, respectively. BQT was administered as firstline, secondline and rescue treatment in 74%, 17% and 9% of cases, respectively. 5 patients discontinued treatment prematurely due to side effects (1, 8%) and 43 patients were lost to follow-up (13, 4%). By modified intention-to-treat and per-protocol analysis the H. pylori eradication rates were 94, 9% (95% CI: 92.1-97.5%) and 96.7% (95% CI: 94.4-98.8%), respectively. The low number of treatment failures (n=9) did not allow to identify risk factors for failure.

Conclusion: Three-in-one capsule bismuth quadruple therapy is highly effective and safe for treatment of H. pylori infection in clinical routine practice, irrespective of the patient’s migrational background or the number of previous treatment failures.

Disclosure of Interest: S. Mielcke: Speakers honoraria: Allergan, Kibion, Olympus
All other authors have declared no conflicts of interest.

References
Introduction: Background: Eradication of Helicobacter pylori (H. pylori) infection represents a clinical challenge. The current requirements demand eradication rates above the 90%, which has made that the use of triple treatment including clarithromycin or metronidazole alone has been given up on those countries, such as Spain, with high resistance rates. Quadruple therapy with a proton pump inhibitor (PPI) plus a single three-in-one capsule containing bismuth subcitrate potassium 140 mg, metronidazole 125 mg, and tetracycline 200 mg has shown high eradication rates in clinical trials.

Aims & Methods: We aimed to evaluate the efficacy and safety of a PPI-bismuth based quadruple therapy in patients diagnosed of H pylori infection in a clinical setting of a Private Hospital, located at the North of Madrid (Spain). A prospective and real-life study was conducted, between March 2016 to February 2017, on consecutive patients with confirmed H pylori infection eradication indication. Patients were treated for ten days with a daily regimen containing bismuth subcitrate potassium 140 mg, metronidazole 125 mg, and tetracycline 125 mg, three capsules four times daily, and esomeprazole 40 mg twice daily and proton pump inhibitors (PPIs) for a first-line Helicobacter Pylori eradication.

Results: A total of 100 patients, 60 (60.0%) women and 40 (40.0%) men, who fulfilled the respective demands of the inclusion and exclusion criteria, were enrolled consecutively. Five of these were lost to follow-up. Mean (standard deviation) [95% confidence interval] age was 47.1 (15.4) [44.0 to 50.2] years. Twenty-five (25.0%) patients had a prior history of using medications to treat H. pylori. The urea breath test performed, at least 28 days, after the end of treatment. Intent-to-treat (ITT) efficacy analyses included all patients who received study medication and took at least one dose of study medication; patients without an observed outcome were considered as treatment failures. Patients included in the ITT population, which excluded patients who did not complete the study or who had major protocol violations, were also conducted to confirm the ITT results.

Conclusion: In patients with confirmed H pylori infection, 10 days of treatment with vonoprazan, bismuth, metronidazole and tetracycline plus esomeprazole provides high eradication rates not only as first-line but also as rescue therapy, with an acceptable safety profile.

Disclosure of Interest: All authors have declared no conflicts of interest.

Introduction: This study was evaluated the effectiveness and safety of Vonoprazan, a potassium-competitive acid blocker (P-CAB) compared with proton pump inhibitors (PPIs) for a first-line Helicobacter Pylori eradication.

Aims & Methods: We retrospectively analyzed data from first-line H. pylori eradication treatment (vonoprazan or PPIs with 400 mg clarithromycin and 400 mg pantoprazole) in Japan during a single hospital setting, which included patients who did not complete the study or who had major protocol violations, were also conducted to confirm the ITT results.

Results: ITT and PP analysis of the first-line H. pylori eradication for vonoprazan, lansoprazole, rabeprazole, and esomeprazole were 75.5%/86.8%, 63.9%/76.2%, 59.1%/76.0%, 68.0%/79.5%, and 63.2%/70.8%, respectively. The vonoprazan eradication rates were significantly higher than those of these PPIs (P < 0.05), respectively. There was no significant difference in the adverse events between the two therapies.

Conclusion: Aims & Methods: The aim of the current study was to evaluate the efficacy and safety of VPZ (400 mg/day), and amoxicillin (ABPC: 1500 mg/day) triple therapy in post-marketing use in Japan. A randomized, open-label, single-center study was conducted to verify the superiority of VPZ to esomeprazole (EPZ) as part of first-line triple therapy in patients with HP infection. Three hundred and forty-nine Japanese patients with HP infection diagnosed using a rapid urease test were enrolled between June 2015 and October 2016. The patients were randomly allocated to VPZ group (VPZ 40 mg/day, ABPC 1500 mg/day, and CAM 400 mg/day) or EPZ group (EPZ 40 mg/day, ABPC 1500 mg/day, and esomeprazole 400 mg/day) with stratification according to acid-related gastrointestinal sequelae. A phase III study revealed that VPZ is superior to esomeprazole as part of first-line therapy for Helicobacter pylori (HP) infection when combined with 400 or 800 mg/day clarithromycin (CAM).

Aims & Methods: The aim of the current study was to evaluate the efficacy and safety of VPZ, CAM (400 mg/day), and amoxicillin (ABPC: 1500 mg/day) triple therapy for vonoprazan-resistant H. pylori infection. Patients were randomly allocated to VPZ group (VPZ 40 mg/day, ABPC 1500 mg/day, and CAM 400 mg/day) or EPZ group (EPZ 40 mg/day, ABPC 1500 mg/day, and esomeprazole 400 mg/day) with stratification according to acid-related gastrointestinal sequelae. A phase III study revealed that VPZ is superior to esomeprazole as part of first-line therapy for Helicobacter pylori (HP) infection when combined with 400 or 800 mg/day clarithromycin (CAM).

Results: In patients with confirmed H pylori infection eradication rate in patients with CAM-sensitive HP (87.2% [82/94] versus 84.6% [81/96]) was significantly lower than that in the patients with CAM-resistant HP (91.5% [108/119] versus 84.6% [81/96]) using a random urease test were enrolled between June 2015 and October 2016. The patients were randomly allocated to VPZ group (VPZ 40 mg/day, ABPC 1500 mg/day, and CAM 400 mg/day) or EPZ group (EPZ 40 mg/day, ABPC 1500 mg/day, and esomeprazole 400 mg/day) with stratification according to acid-related gastrointestinal sequelae. A phase III study revealed that VPZ is superior to esomeprazole as part of first-line therapy for Helicobacter pylori (HP) infection when combined with 400 or 800 mg/day clarithromycin (CAM).

Disclosure of Interest: All authors have declared no conflicts of interest.
the patients with low eGFR, 65.3% [34/53] in the patients with high eGFR [P = 0.0342], which was significantly higher in the VPZ group than that in the EPZ group (79.3% [23/29] versus 50% [11/13], respectively, [P = 0.025]). The first-line eradication rate in continuous smokers was significantly lower than that in non-smokers (81.0% [187/231] in non-smokers vs. 64.3% [27/42] in continuous smokers [P = 0.016]). However, there were no significant differences between the VPZ and EPZ groups in non-smokers (84.2% [96/114] versus 77.8% [91/117], respectively, [P = 0.21]) and in continuous smokers (84.2% [12/16] versus 57.7% [15/26], respectively, [P = 0.33]). Furthermore, the first-line eradication rates in both groups were not influenced by age, sex, body mass index, drinking habit, and the endoscopic findings of gastric duodenal ulcers/scars. There were no significant differences with regard to adverse effects between the two groups.

Conclusion: In contrast to the previous reports, the first-line eradication rate of VPZ-based triple therapy with 400 mg/day CAM and 1500 mg/day ABPC was similar to that of EPZ-based triple therapy in all groups except in patients with CAM-resistant HP and high eGFR. It is necessary to determine the most appropriate conditions that will maximize the therapeutic effect of VPZ-based triple therapy.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

P0602 THE IMPACT OF AMOXICILLIN RESISTANCE ON THE EFFICACY OF AMOXICILLIN-CONTAINING REGIMENS FOR HELICOBACTER PYLORI ERADICATION - A POST-HOC ANALYSIS OF RCTs AND HTTRIALS

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Introduction: The impact of amoxicillin resistance on the efficacy of regimens containing amoxicillin for Helicobacter pylori (H. pylori) eradication remains inconclusive. Therefore, we aimed to investigate whether the efficacy of amoxicillin containing regimens is affected by amoxicillin resistance and to identify the optimal breakpoint of amoxicillin resistance.

Aims & Methods: This was a post-hoc analysis of five randomized trials conducted in Taiwan from 2007 to 2016. Patients who received amoxicillin-containing regimens were recruited. The minimum inhibitory concentrations (MICs) were determined by agar dilution test. Meta-analysis was performed to assess the frequencies of all polymorphisms between AG patients and controls were 33/80/50%. There was no difference between the 3 groups in these parameters. However, a significant difference in the rate of submucosal invasion is presented that the pigmentation in GAFG may relate with PPI (p=0.025). The first-line eradication rate in continuous smokers was significantly lower than that in non-smokers (81.0% [187/231] in non-smokers vs. 64.3% [27/42] in continuous smokers [P = 0.016]). However, there were no significant differences between the VPZ and EPZ groups in non-smokers (84.2% [96/114] versus 77.8% [91/117], respectively, [P = 0.21]) and in continuous smokers (84.2% [12/16] versus 57.7% [15/26], respectively, [P = 0.33]). Furthermore, the first-line eradication rates in both groups were not influenced by age, sex, body mass index, drinking habit, and the endoscopic findings of gastric duodenal ulcers/scars. There were no significant differences with regard to adverse effects between the two groups.

Conclusion: In contrast to the previous reports, the first-line eradication rate of VPZ-based triple therapy with 400 mg/day CAM and 1500 mg/day ABPC was similar to that of EPZ-based triple therapy in all groups except in patients with CAM-resistant HP and high eGFR. It is necessary to determine the most appropriate conditions that will maximize the therapeutic effect of VPZ-based triple therapy.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

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Conclusion: In contrast to the previous reports, the first-line eradication rate of VPZ-based triple therapy with 400 mg/day CAM and 1500 mg/day ABPC was similar to that of EPZ-based triple therapy in all groups except in patients with CAM-resistant HP and high eGFR. It is necessary to determine the most appropriate conditions that will maximize the therapeutic effect of VPZ-based triple therapy.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

P0604 ASSOCIATION BETWEEN GASTRIC ADENOCARCINOMA OF THE FUNDIC GLAND TYPE AND H. PYLORI INFECTION

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Introduction: Gastric adenocarcinoma with low-grade atypia occurring in the mucosa of the fundic gland without atrophy, and is recognized that it is not related to H. pylori (Hp) infection. However, HpAGFAG is also found in Hp-infected and past Hp-infected patients. It may not deny the relationship between the progress of GAFG and Hp infection.

Aims & Methods: Ten lesions of GAFG resected endoscopically or surgically in our hospital from December 2010 to October 2016 were classified as Hp-uninfected, Hp-infected and past Hp-infected (n=3) past Hp-infected (n=2), and each endoscopic and clinicopathological features were examined.

Results: Median age of Hp-infected/past Hp-infected/Hp-uninfected were 65/71/54.5 years old, respectively, male ratio were 100/80/0, occupied site U area were 33/80/50%. There was no difference between the 3 groups in these parameters. However, a significant difference in the rate of submucosal invasion is recognized between the Hp-uninfected and past Hp-infected group and the Hp-uninfected group (submucosal invasion was found at 80/100/0%, p=0.035). According to endoscopic features, background mucosa of gastric fundus gland mucosa without atrophic change was found in 100/100/100%, whitish color in 67/60/50%, submucosal tumor shape in 67/60/0%, dilated vessels with branching architecture in 100/100/50%. The association with Hp infection was not clear. In immunohistochemical staining, MUC6 positive and MUC5AC positive, MUC2 negative, CD 10 negative in all cases, whereas the rate of MUC5AC positive was significantly higher in the Hp-infected group as 0.2/100/0% (P=0.045). We reported that black pigmentation is recognized in GAFG (stomach and intestine 50:1521-1531, 2015), but no association between Hp infection and black pigmentation was observed. On the other hand, the rate of PPI administration divided pigmentation (n=6) no pigmentation (n=4) are 50/0%, and it is suggested that the pigmentation in GAFG may relate with PPI (p=0.091).
The prevalence of hepatic disorders in celiac patients is estimated at...

Results: 28). A cryptogenetic hypertransaminase is found in 12.3% of cases (1.062–109.634), p = 0.0001, df (Q) = 2) of the cases and ascitic decompensation in slightly more than half of cases 55.6% (n = 5).

Conclusion: Hp infection is suggested to be related to the invasion depth of CD. The infection may also be an important profile in GAFG cases. Pigmentation in GAFG is found frequently, but it may be related to taking PPI.

Disclosure of Interest: All authors have declared no conflicts of interest.

References


Monday, October 30, 2017
Small intestinal 1: hall 7

P0605 MUCIN EXPRESSION IN THE SMALL BOWEL OF CELIAC DISEASE – A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: Mucins, heavily glycosylated glycoproteins, synthesized by mucosal surfaces and have an important role in healthy and malignant states. Changes in mucin synthesis, expression and secretion may be a primary event or may be secondary to inflammation and carcinogenesis.

Aims & Methods: Since untreated celiac disease (CD) is associated with intestinal mucosa abnormalities, we aimed to assess the current knowledge about mucin expression in the small bowel of CD patients, and to look for a possible association between mucin profile and gluten-free diet. English Medical literature searches were conducted for “mucin” and “celiac”. Observational studies were included. Meta-analysis was performed by using Comprehensive meta-analysis software. Pooled odds ratios and 95% confidence intervals were calculated.

Results: Out of 18 titles initially generated by the literature searches, 3 observational studies that fulfilled the inclusion criteria remained eligible for meta-analysis. They included 58 patients and 68 controls from 3 countries (Finland, Japan, USA). Mucin expression was significantly increased in small bowel mucosa of CD patients than in normal small bowel mucosa [OR 10.789, 95%CI (1.062–109.634), p = 0.044] (random-effect model). Heterogeneity was significant: Q = 4.470, df (Q) = 3, P = 0.024, I² = 62.832%, ORs for MUC2 and MUC5AC expression in the small bowel mucosa of untreated CD patients were 1.143, 95%CI 0.060–21.870, P = 0.929 and 21.429, 95%CI 3.883–118.255, P < 0.0001, respectively.

Conclusion: We found that expression of certain mucin genes in the small bowel mucosa of CD patients may serve as a diagnostic tool, and assist in surveillance programs.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0606 HEPATIC ABNORMALITIES ASSOCIATED WITH CELIAC DISEASE

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Introduction: Celiac disease (CD) is a gluten-sensitive enteropathy that resolves with a gluten free diet (GFD). It’s now considered as a multisystem disorder. A number of studies have shown the occurrence of liver diseases at a higher frequency in patients with CD compared with that in the general population. Cytokine- and growth factor-mediated events in the small intestinal mucosa of untreated CD patients are involved in the pathogenesis of liver disease.

Aims & Methods: The aim of this work is to determine the prevalence and clinical characteristics of the chronic liver disease observed during CD. Prospective multicenter work involving 154 adult celiac patients (42H, 112F), with an average age of 36.1 years ±13.6, recruited between 01-01-2013 and 30-06-2014 with a minimum follow-up of 12 months. The diagnosis of CD was made in all cases by clinical, serological and histological arguments. Thrombotic complications were noted as well as their modalities of occurrence.

Results: Vascular thrombosis was involved in 13 patients (8.4%), and occurred almost exclusively in women (84.6%) (11 F - 2 H). There are 6 cases of portal cavernoma, one associated with lower limb thrombosis, 4 cases of stroke and 3 cases of thrombosis of the lower limbs. The diagnosis of thrombosis revealed the diagnosis of MC in 8 patients (61.5%) with an average delay of 11.6 months and extreme delays of 1 to 43 months. These include 4 cases of a portal cavernoma, one associated with deep limb thrombosis, 3 cases of stroke, and one case of deep thrombosis of the lower limbs. The diagnosis of CD was made on average 72 months after that of thrombosis in 4 patients (30.8%). In one case, thrombosis was complicated 39 years after diagnosis of CD diagnosed in childhood at the age of 5 years without gluten-free diet. The thrombophilia assessment was carried out in all patients and. The thrombophilia assessment was was negative in 11 cases (84.6%). A S protein deficiency associated with the CD in one case and an antithrombin III deficiency in another case were detected. The use of oral contraceptives and in all cases a micro-dosed oestro-progestin was found in 7 women (63.6%). 7 cases women involved intrahepatic thrombosis.

Conclusion: The diagnosis of CD must be evoked when there is a thrombosis disease without obvious cause, factors of thrombophilia may be present during the CD. Early CD diagnosis with respect to the gluten-free diet may prevent the development of this complication.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0607 CELIAC DISEASE ASSOCIATED WITH VASCULAR THROMBOSIS

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Introduction: Celiac disease (CD) is a life-long autoimmune disease affecting multiple organs of genetically susceptible individuals. One of the extra intestinal manifestations of the disease is thromboembolic events like strokes and veins’ thrombosis.

Aims & Methods: The aim of this work is to determine the prevalence and clinical characteristics of the thrombosis observed during CD. Prospective multicenter work involving 154 adult celiac patients (42H, 112F), with an average age of 36.1 years ±13.6, recruited between 01-01-2013 and 30-06-2014 with a minimum follow-up of 12 months. The diagnosis of CD was made in all cases by clinical, serological and histological arguments. Thrombotic complications were noted as well as their modalities of occurrence.

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Conclusion: The diagnosis of CD must be evoked when there is a thrombosis disease without obvious cause, factors of thrombophilia may be present during the CD. Early CD diagnosis with respect to the gluten-free diet may prevent the development of this complication.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0608 DIFFERENT PROFILES OF TLR 2, 4, 7 AND 9 MRNA IN PBMC AND BIOPSY SPECIMENS OF PATIENTS WITH CELIAC DISEASE

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Introduction: Celiac disease (CD) is an organ-specific autoimmune disease, and both adaptive and innate immunity are involved in its development. Recent studies suggest the dysregulation Toll-like receptors (TLRs) in innate immunity can confer risk to autoimmune diseases such as CD.
Introduction: The mucus layer, covering the gastrointestinal mucosa, is considered the first line of defence against mechanical, chemical, or microbiological aggressions arising from the luminal contents1. Among all different cell types of the intestinal epithelium, the goblet cell functions are specialised in the secretion of mucus constituent2. As an example of failing barrier function, patients with coeliac disease (CD) have been reported to have altered intestinal barrier3. Human colonic mucus-secreting cells HT-29-16E are valuable tools to explore the effect of a specific treatment on permeability and mucus production by the human intestinal epithelium.

Aims & Methods: We investigated the new and innovative gluten detoxified bread (GFB; patent PCT/IB2013/000797) effects on mucus production by means of Alcian blue staining in comparison to the control bread (CB). In addition, MUC2 and MUC3 were quantified by ELISA and the permeability of the intestinal epithelium monolayer was evaluated by transepithelial resistance (TEER) measurement. The statistical analysis was conducted by one-way ANOVA followed by a Bonferroni post-hoc t-test.

Results: Mucin production by Alcian blue staining was expressed as % background subtracted from Image J measurement. GFB increased MUC2 expression by 24.2% after 24 hours by Alcian blue staining (10.28 ± 1.82; P = 0.01), whereas CB did not (9.94 ± 0.67; P = 0.05). Higher MUC2 concentrations expressed as ng/ml were found on cells treated with GFB (10.82 ± 1.35; P = 0.01) compared to controls (9.24 ± 0.18; P = 0.03). Alcian blue TEER values, expressed as a percentage of initial TEER, were observed after 24 hours of incubation with GFB in comparison to the control (163.2 ± 33.8, P = 0.01) which was not observed or CB (139.4 ± 28.8, P = 0.05).

Conclusion: It could be concluded that GFB has a potential of inducing MUC2 secretion by intestinal epithelial cells and improving intestinal epithelium permeability in vitro. Such observed potential may effectively contribute to consequent benefits such as higher gut barrier defence, decreased susceptibility to infections and better absorption regulation, thus ameliorating such alterations in colonic patients.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P0609 IMMUNOHISTOCHEMICAL LYMPHOCYTE PATTERN OF NON CELIAC GLUTEN SENSITIVITY MAY SUPPORT THE INVOLVEMENT OF INNATE IMMUNE

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Introduction: Non-celiac gluten sensitivity (NCGS) is a gluten-related enteropathy with distinct features compared to celiac disease. Patients with NCGS experience symptoms, such as diarrhea or abdominal pain, shortly after gluten exposure. Differently from celiac disease, serology is negative, and histological picture is characterized by no lesion or a mild enteropathy (Marsh 1 stage). Few studies have investigated possible histopathological characteristics of NCGS. An immune response against gluten elicited exclusively by innate immunity has been hypothesized. On these bases, we attempted to depict an immunohistochromatograph pattern of NCGS by exploring markers of lymphocyte and innate immunity activation.

Aims & Methods: Duodenal biopsy samples of patients diagnosed of NCGS according to Salerno criteria were retrieved. Duodenal biopsy samples of positive controls ( overt seropositive celiac disease at Marsh 1 stage) and negative controls (functional dyspepsia and normal microscopic picture) were selected. Immunohistochemistry for CD3 (intraphelial lymphocytes), CD4 (T-helper lymphocytes), CD7 (T-cytotoxic lymphocytes) and CD1a (Langerhans cells) was performed. Cell count was carried out both in the epithelial layer (expressed as positive cells/100 enterocytes) and in the lamina propria (positive cells/mm2).

Comparison of means was performed by ANOVA test with Bonferroni’s post-hoc analysis.

Results: Twenty NCGS, 12 celiac patients (positive controls) and 16 negative controls were selected. CD3+ intraphelial lymphocytes in NCGS were expressed at intermediate levels (18.5 ± 6.4) between negative controls (11.9 ± 2.8) and celiac disease (40.8 ± 8.1, p < 0.0001). CD4+ T-helper lymphocytes were present only in lamina propria and NCGS had a lower level (3.1 ± 0.6) than controls (7.2 ± 2.9) and celiac disease (10.3 ± 15.7, p < 0.0001). Intraphelial CD7+ cells were similar between NCGS and negative controls (14.0 ± 7.4 versus 17.8 ± 4.2), but lower than celiac disease (34.0 ± 7.1, p < 0.0001). CD1a+ Langerhans cells were over-expressed in the lamina propria of NCGS (1.9 ± 1.1) in comparison to celiac disease and negative controls (respectively 0.3 ± 0.8 and 0.4 ± 0.5, p < 0.0001).

Conclusion: NCGS is characterized by a mild immunologic reaction, as shown by the slight increase in CD3 intraphelial lymphocytes. The over-expression in the
lamina propria of Langerhans cells, which are antigen presenting cells mainly involved in innate immunity, seems to support previous hypotheses of the predisposition of NGCS. Additionally, this finding could represent an useful pathological feature of NGCS.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0612 FUNCTIONAL DYSPESIA SYMPTOMS ARE STRONGLY ASSOCIATED WITH COELIAC DISEASE: RESULTS FROM A POPULATION-BASED STUDY

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Introduction: Coeliac disease (CD) is estimated to affect up to 1 in 100 Australians (1). Although CD has a wide range of clinical manifestations, patients frequently present with gastrointestinal (GI) symptoms which overlap with functional GI disorders, particularly irritable bowel syndrome (IBS) and functional dyspepsia (FD); the prevalence of biopsy proven CD is higher in IBS (2) and in dyspepsia (3). Patients with CD have been shown to experience persistent GI symptoms despite long term treatment with a gluten-free diet (4).

Aims & Methods: The aim of this study was to define GI symptoms reported in an Australian cohort with a doctor diagnosis of CD and compare with those not reporting CD. A total of 3825 people (mean age 58.4 years, age range 18–100 years and 47.5% males) randomly selected from the Australian population returned a mail survey (Digestive Health & Wellbeing Survey, response rate =45%) which contained questions on whether the participant had ever been told by a physician that they had CD, and questions regarding GI symptoms to establish whether they had co-existent functional GI disorders. Adherence to a gluten-free diet was not assessed. Prevalence of CD, FD and IBS are reported with 95% exact confidence intervals. The difference between symptoms in those with CD compared with the unaffected population was tested for significance by the Pearson chi-square test.

Results: The prevalence of doctor-diagnosed CD was 1.2% (95% CI 0.84–1.59) in this cohort. Subjects with CD reported significantly higher levels of GI symptoms than unaffected individuals, including abdominal pain associated with abnormal bowel habit, diarrhoea, bloating, distension, epigastric burning and early satiety (see Table). There was no significant difference observed in symptoms of post-prandial fullness, nausea, constipation, abnormal stool consistency, or straining with defecation. The prevalence of FD as defined by Rome III criteria in the CD cohort was 37.5% (95% CI 22.7–54.2) compared to 13.9% (95% CI 12.8–15.1) in the non-affected population (OR 2.7, 95% CI 1.9–7.1, p<0.001). There was no significant difference in the prevalence of IBS in the affected compared with the non-affected cohort (30.8% versus 22.2%, p=0.2).

Table: Gastrointestinal symptoms reported by patients with and without self-reported coeliac disease (CD). Items reported as greater than one day per week (*) or greater than or equal to “often” (**) Symptoms

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Self report CD (%)</th>
<th>Self report CD - Yes (%)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal pain associated with loose bowel motions **</td>
<td>16/37 43.2%</td>
<td>600/3234 18.6%</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>More bowel motions associated with pain **</td>
<td>13/38 34.2%</td>
<td>504/3248 15.5%</td>
<td>&lt; 0.002</td>
</tr>
<tr>
<td>Bloating *</td>
<td>13/40 32.5%</td>
<td>436/3381 12.9%</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Distension *</td>
<td>12/40 30%</td>
<td>395/3771 11.7%</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Abdominal pain *</td>
<td>9/39 23.1%</td>
<td>362/3738 10.7%</td>
<td>0.014</td>
</tr>
<tr>
<td>&gt;3 bowel motions per day **</td>
<td>7/40 17.5%</td>
<td>7/40 17.5%</td>
<td>0.046</td>
</tr>
<tr>
<td>Epigastric burning *</td>
<td>8/40 20%</td>
<td>165/3380 4.9%</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Early satiety *</td>
<td>8/40 20%</td>
<td>230/3378 6.8%</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

Conclusion: The prevalence of gastrointestinal symptoms and in particular functional dyspepsia symptoms are significantly higher in patients with a doctor diagnosis of CD than in unaffected individuals. Studies on whether biopsy proven coeliac disease in IBS is higher in IBS cohorts than healthy controls (2) and the value of screening with duodenal biopsy testing for CD in FD is concluded to be useful (3), this study supports these views.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P0613 MALE GENDER AND UNDERWEIGHT ARE ASSOCIATED WITH OSTEOPOROSIS IN PATIENTS WITH NEW DIAGNOSIS OF COELIAC DISEASE

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Introduction: Osteoporosis is a systemic skeletal disorder characterized by low bone density and micro-architectural deterioration with increase of bone fragility and consequent fracture risk. About 50–75% of patients (pts) with untreated coeliac disease (CD) suffer from bone mass loss (osteopenia or osteoporosis). Despite this strong correlation, guidelines do not express with certainty on the need to undergo a dual-energy X-ray absorptiometry (DEXA) scan in every patient with new diagnosis of CD. Recently, the DEXA screening was suggested for CD peri-post menopausal females, males over 55 years, pts with overt malabsorption or with a history of fragility fractures. Studies on bone mineral density (BMD) in CD pts led to discrepant results, probably due to heterogeneous designs.

Aims & Methods: The aim of this study was to evaluate, in a cohort of consecutively newly diagnosed CD adults, the prevalence of BMD alterations at diagnosis time and to evaluate associated clinical features. From January 2004 to December 2016, 258 consecutive pts (F = 72.4%) were diagnosed with CD. All pts were adults (median age 38, range 18–72 years), had atrophic disease and were invited to undergo a DEXA within 3 months from diagnosis to screen for osteoporosis (T-score < −2.5) or osteopenia (T-score < −1 and ≥ −2.5). A total of 214 (82.9%) pts underwent the DEXA scan and were included in the study (F = 71.5%, median age 38, range 18–72 years). On the basis of DEXA results (classified according to WHO classification) pts were divided into 3 groups: pts with normal BMD, with osteopenia, and with osteoporosis. For each patient, reported risk factors for low BMD (underweight, alcohol intake, drugs, menopause, smoke) and serological PTH values were assessed. The signs/symptoms leading to CD and their duration before diagnosis, autoimmune/nutritional comorbidities, familiarity for CD, previous fractures and serological assays (specific antibodies for CD, ferritin, cholesterol, triglycerides, and albumin) were also assessed. All the variables described were analyzed and compared between the 3 groups. Logistic regression was performed including into the model those independent variables which showed a significant difference at univariate analysis.

Results: At the DEXA scan, 85 (39.7%) and 129 (60.3%) pts had normal or low BMD, respectively. Among pts with low BMD, 91 (42.5%) had osteopenia and 38 (17.8%) osteoporosis. At logistic regression, clinical features significantly associated with osteoporosis were male gender (OR 4.7; 95%CI 1.3 to 17.4), underweight (OR 8.1; 95%CI 1.8 to 35.3) and increased PTH values (OR 5.1; 95%CI 1.4 to 18.8), while age, gender and gastrointestinal symptoms at diagnosis time, menopause, alcohol intake and previous fractures were not associated. Clinical features significantly associated with osteopenia were underweight (OR 4.0, 95% CI 1.4 to 10.2) and increased PTH values (OR 2.6, 95%CI 1.1 to 6.4).

Conclusion: In newly diagnosed coeliac pts, the overall prevalence of BMD alterations was more than 60%, with osteoporosis in nearly 1/5. Osteoporosis was more frequently associated with male gender, underweight and increased PTH. This study suggests that at CD diagnosis, DEXA scan might be of benefit, in particular in male underweight pts.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P0614 SELF-REPORTED WHEAT SENSITIVITY IN AN AUSTRALIAN POPULATION STUDY

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Introduction: Coeliac disease (CD) affects 0.6–1% of the population worldwide (1). Wheat avoidance in the absence of CD is common, and studies report a population prevalence of self-reported wheat or gluten sensitivity (SRWS) of
up to 13% (2, 3). SRWS is defined as gastrointestinal (GI) or extra intestinal symptoms on ingestion of wheat or gluten-containing food (2, 3).

Aims & Methods: The aim of this study was to determine the prevalence of SRWS in an Australian population, define associated GI symptoms, and relate the diagnosis to demographic, lifestyle and medical factors. A total of 3825 people (mean age 58.4 years, age range 18–80 years and 47.5% males) randomly selected from the Australian population returned a mail survey (Digestive Health & Wellbeing Survey, response rate = 45%) which contained questions on wheat avoidance, GI symptoms, demographic, medical and lifestyle factors. We defined SRWS as people who reported gastrointestinal symptoms on ingestion of wheat based foods, but did not suffer from doctor diagnosed coeliac disease, inflammatory bowel disease or bowel cancer. Prevalence of SRWS is reported with 95% exact confidence intervals. The association between SRWS prevalence and potential risk factors was reported using unconditional logistic regression. The degree of differentiation of SRWS from health was evaluated through the area under the receiver-operator-characteristic curve.

Results: The prevalence of SRWS in this cohort was 13.5% (455/3331, 95% CI 12.5–14.9%). Only 11% (50/455) of these 113 doctor diagnosed had received a diagnosis of celiac disease. The most commonly reported GI symptoms (reported as more than weekly or often) associated with SRWS included abdominal pain relieved by bowel movements (54.5%), bloating (37.6%) and abdominal distention (30.8%). In a multivariate analysis, a diagnosis or SRWS was significantly associated with irritable bowel syndrome (IBS) and functional dyspepsia (FD) (Rome III criteria), female gender, and food allergy (see Table). Older age was negatively associated with SRWS. In this multivariate model, factors with no observed association included body mass index, depression, anxiety, sleep problems, proton pump inhibitor use, gastrointestinal infection, rheumatoid arthritis, scleroderma, migraine, Parkinson’s disease, asthma, pollen allergy, animal allergy, and recent antibiotic use. The model provided useful although imperfect differentiation of SRWS from health (AUC = 0.76).

Conclusion: SRWS has a prevalence of 13.5% in this Australian cohort. Those with SRWS are likely to report abdominal symptoms, including abdominal pain associated with bowel habits, bloating or abdominal distention. SRWS is significantly associated with IBS and FD, younger age, female gender, and food allergy.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P0616 WHEAT PROTEIN ALLERGY OR SENSITIZATION TO WHEAT PROTEIN IN A CELIAC POPULATION
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Introduction: Epidemiological studies estimate a worldwide prevalence of CD of approximately 1:100 individuals, with a considerable proportion of patients remaining undiagnosed and untreated. According to a study performed by the National Health and Nutrition Examination Survey in the United States, the prevalence of self-prescribed GFD in an unselected population of subjects aged 6 years or older was 0.5%. Epidemiological studies report a prevalence of WA in American population of around 0.4% until 0.6%.

The diagnosis of WA is classically based on skin prick tests (SPT), in vitro specific Immunoglobulin E (sIgE) assays and functional assays. SPTs and sIgE in vitro assays are the first-level diagnostics for WA. However, they are affected by a low predictive value. In particular, their low sensitivity can be explained by the fact that the commercial test reagents are mixtures of water/salt-soluble wheat proteins that lack allergens from the insoluble gluten fraction. The association between food allergy and celiac disease (CD) is still to be clarified. Gluten-related disorders are an epidemiologically relevant phenomenon with a global prevalence that is estimated around 5%, drawing the attention of the scientific community.

Aims & Methods: We visited in our unit of celiac disease and gluten-related conditions during 2016 423 (F/M:312/111) new patients with clinical suspicion of CD. Of these 113 they were not celiac but were investigated for suspected non-celiac gluten sensitivity. After in vitro tests for the exclusion of celiac disease, to verify the real prevalence of food allergy particularly to wheat protein, in non celiac patient referred our unit for symptoms after gluten ingestion, all these patients underwent allergologic workup consists on: skin prick tests for food including wheat (Alk-abello), LTP (lipid transfer protein) (peach Alk abello), alpha amylase, wheat flour, barley, corn, rice, grass pollen and histamine. Also all they performed patch tests for suspected allergy to nickel, if they reported contact dermatitis. After in vitro tests for the exclusion of gluten. Molecular-based allergy (MA) diagnostics could overcome some limitations of sIgE in vitro assay using wheat flour extracts. We have used omega-5 gliadin (TR1 a 19) and mLTP (TR1a 14), gh, ghin, wheat, gluten that are available in the immunoCap assay, whereas the Alfa Aesar: α-amylase/trypsin inhibitor (Alfa A/Ti) is available only in the Pharmacia ISAC assay. The sIgE to omega-5 gliadin assay is highly reliable and now widely used to identify the patient with WDEIA.

Results: In our overall population, 113 (26.7%) non celiac patients had a history of immediate or not immediate reaction after ingesting gluten: the Allergologic tests found wheat protein sensitization in 14 patients of these 12 (4.9%). In addition we also found 5 (4.3%, 4F) patients with real allergy to wheat or wheat protein.

Conclusion: In our population 19/113 (16.8%) non celiac patient had real reaction after ingesting gluten: 14 (12.3%) had wheat protein sensitization and 5 (4.5%) had WA. These Percentages are different and very high than that reported in the literature.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

P0617 A QUESTIONNAIRE-BASED SYMPTOM EVALUATION STUDY IN 381 PATIENTS DIAGNOSED WITH BILE ACID MALABSORPTION BY SEHCAT FROM 2003 TO 2016
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Introduction: Excessive amounts of bile acids entering the colon cause chronic diarrhoea (bile acid diarrhoea (BAD)). Diagnosis of BAD is possible by measuring the retention level of orally ingested 3H-Selenium homoaooarcic acid (SeHCAT). Standard treatment of BAD is bile acid sequestrants (BAS), such...
as colestyramine. Short-term outcome of having BAD is well-described, but long-term effects remain unclear. The aim of the present study was to describe long-term symptoms, adherence to treatment and quality of life in a well-defined group of patients with BAD.

Aims & Methods: Between 2003 and 2016, 559 patients referred to our hospital for differently low self-CAT retention levels (<15% at day 7). Questionnaires about medical history, bowel function, use of medication, and quality of life were sent to all patients.

Results: Among 559 patients, 381 (68.2%) responded (242 women (63.5%), median age: 53 years (range 22 to 89), median age at diagnosis 47 years (range 16 to 85). In 123 respondents (32.3%) BAD was due to ileal dysfunction (type 1), 199 (52.2%) had idiopathic BAD (type 2), and 59 (15.5%) had BAD due to cholecystectomy (type 3). At follow-up, 272 patients (73.9%) still reported both enterocoele diarrhea and 248 (65.5%) regularly used anti-diarrheal medication. Treatment included BAS in 45.1% while 32.3% of patients used other treatment. 184 patients (49.9%) reported that treatment had improved their symptoms, while 116 (31.4%) reported that they were the same, and 69 (18.7%) felt worse. In 242 patients (65.5%) symptoms were either alleviated or free from cycle 1 to cycle 2 in 242 patients (65.5%).

Conclusion: BAD must be considered as a chronic disease and despite correct diagnosis and treatment, most patients continue to have significant diarrhoea and reduced quality of life. This supports the need for further research in pathophysiology and new therapy principles.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0618 EFFICACY OF PERCUTANEOUS ENDOSCOPIC GASTRO-JEJUNOSTOMY (PEG-J) DECOMPRESSION THERAPY FOR PATIENTS WITH CHRONIC INTESTINAL PSEUDO-OBSTRUCTION (CITO)

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Introduction: Chronic intestinal pseudo-obstruction (CITO) is an intractable rare digestive disease manifesting persistent small bowel distension without any mechanical cause. Intestinal decompression is a key treatment, but conventional methods including a transnasal small intestinal tube is invasive and painful. Therefore, a less invasive and tolerable new decompression method is urgently desired. We conducted a pilot study and assessed the efficacy and safety of percutaneous endoscopic gastro-jejunostomy (PEG-J) decompression therapy in CITO patients.

Aims & Methods: Eight definitive CITO patients (2 males and 6 females) were enrolled. All patients received PEG-J decompression therapy. The number of days with any abdominal symptoms in a month (NODASIM), body mass index (BMI), serum albumin level (Alb), and small intestinal volume before and after PEG-J were compared in all patients.

Results: PEG-J was well tolerated and oral intake improved in all patients. NODASIM has significantly decreased (24.3 vs 9.3 days/months) and BMI/Alb have significantly increased (4.9 vs 17.2 kg/m² and 2.6 vs 3.8 g/dl, respectively), whereas total volume of the small intestine has not significantly reduced (4.05 vs 2.59 L, p = 0.18). Reflex esophagitis and chemical dermatitis were observed in one case but was successfully treated conservatively.

Conclusion: PEG-J decompression therapy was found to be a safe and invasive novel decompression therapy for CITO patients available at home. However, accumulation of more CITO patients and long-term observation is needed.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0619 DIFFERENT ORAL GLUTEN LOADS INDUCE AN INFLAMMATORY AND ANTIOXIDANT RESPONSE IN HEALTHY VOLUNTEERS

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Introduction: Gluten-susceptible subjects, gluten exposure determines celiac disease, but it has also been shown that gluten ingestion could alter intestinal absorption even in patients with non-intestinal diseases (Doherty, Lancet 1981) and in healthy subjects (Levine, NEJM 1966). However, whether gluten causes intestinal or extra-intestinal inflammation is still a matter of debate: in Doherty we recently demonstrated that gallbladder motility and gastric emptying were not affected by the ingestion of gluten, while a slight increase of intestinal fermentation was evident (Di Stefano, LDL 2015). A cytotoxic effect of gluten on intestinal cell lines was also previously shown (Rivabene, BBJ 1999). We recently demonstrated that in dyspeptic patients the ingestion of a standard meal induces both an inflammatory and an antioxidant response, correlated with symptom occurrence (De Stefano, UEGW 2016). It is therefore possible that food-related alterations of the intestine could be responsible for post-prandial activation of inflammation and anti-oxidant systems.

Aims & Methods: We therefore studied whether gluten intake induces alterations of post-prandial activation of inflammation and anti-oxidant systems. Twenty consecutive, non-smoking, normal-weight HV (8 females, mean age 27.9 ± 6 years) were enrolled. The presence of another monostotic disorders was excluded in all of them. After an overnight fast and at the same time in the morning, all the subjects underwent evaluation of post-prandial modifications of serum levels of pro-inflammatory cytokines (IL-1β, IL-6, TNFα), endogenous antioxidant system (uric acid), glucose, insulin and serum lipopolysaccharide (LPS), measured as putative factors responsible for inflammatory response. Serum samples were collected at fasting and every 30 minutes for 4-hour period after an oral gluten load of 2 gr (in 10 HV) or 20gr (in the other 10 HV). The presence and severity of a post-prandial symptom, epigastric burning, fullness, early satiety, abdominal pain, abdominal distension, bloating, flatulence, nausea, vomiting, belching, heartburn, regurgitation, diarrhea, and headache, were evaluated by visuo-analog score at fasting and every 30 minutes in the post-prandial period.

Results: In comparison with mean fasting values, none of the measured parameters showed a significant increase in the post-prandial period after the ingestion of 2 gr of gluten. On the contrary, after the ingestion of 20 gr of gluten mean post-prandial values of TNFα and IL-8 showed a significant increase (2.45 ± 1.75 pg/mL and 0.65 ± 0.31 pg/mL) as compared to mean fasting values (1.17 ± 1.49 pg/mL and 0.29 ± 0.15 pg/mL, p < 0.05). Mean post-prandial values of glucose were also significantly higher (74.98 ± 5.02 mmol/L) as compared to fasting values (45.34 ± 10.08 mmol/L, p < 0.05). No significant differences were detected in IL-6, glucose, insulin and LPS a after the ingestion of the 20 gr gluten oral load. Symptoms were absent after both oral loads.

Conclusion: The ingestion of gluten does not alter oral load of gluten induces a significant post-prandial inflammatory response causing the manifestation of the main endogenous anti-oxidant system. In HV, these activities are not accompanied by a symptomatic response. Further studies are needed to investigate the inflammatory and anti-oxidant post-prandial response in patients with gluten-related disorders.

Disclosure of Interest: All authors have declared no conflicts of interest.

MONDAY, OCTOBER 30, 2017 09:00-17:00
NUTRITION I – HALL 7

P0620 THERAPEUTIC ACTION OF KETOCENIC ENTERAL NUTRITION IN OBSESE AND OVERWEIGHT PATIENTS: A RETROSPECTIVE PROSPECTIVE, CONTROLLED, STUDY

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Introduction: Ketogenic Enteral Nutrition (KETON3) is a modification of Blackburn’s protein-sparing modified fast, using a hypocloric, ketogenic liquid diet. The study is about Ketogenic enteral nutrition (KETON) in overweight and obese patients during treatment of the obese of weight loss with a 24 h hour infusion. It is a retrospective analysis that examines safety, weight loss and body composition changes after three sequential 10-days cycles of KETON therapy.

Aims & Methods: Anthropometric and bio-impedance data from 629 patients were collected before and after 1, 2 and 3 complete cycles. The study focuses on the change in outcomes from the first cycle to the second cycle and from the first cycle to the third cycle. The following outcomes were explored: weight, waist circumference, BMI, fat mass, lean mass, phase angle, waist marker, water mass as a percentage of total body weight. The cycle 1, 2 and 3 outcomes were analyzed using descriptive statistics (mean, standard deviation, n) summarizing the outcome at each cycle. Statistical tests were used to test for significance between paired cycle 1 and cycle 2 outcomes and also between paired cycle 1 and cycle 3 outcomes. For normally distributed outcomes, the paired t-test was used. Whereas for skewed outcomes, the Wilcoxon signed-ranks test was used. Scatter plots were used to plot percent change in weight loss against phase angle. The Pearson’s correlation coefficient was calculated. Regression analysis for the outcome percent change in weight from cycle 1 to cycle 2 for phase angle and basal metabolic rate (BMR)/Weight ratio as predictors was carried out.

Results: The results suggested significant changes for all analyzed parameters. There were significant decreases in weight, waist circumference, BMI, fat mass, lean mass, dry lean mass and phase angle. Quantitative changes in lean mass and dry lean mass were negligible with respect to changes in fat mass. There was also a statistically significant increase in the weight of total body weight and water mass marker from cycle 1 to cycle 3. The Pearson’s correlation coefficients r = 0.18, p = 0.004 and r = 22, p = 0.04 indicated changes in cycle 1 and cycle 3 in percentage of weight excess to be significantly, positively correlated to phase angle. The Pearson’s correlation coefficient was calculated. Regression analysis for the outcome percent change in weight from cycle 1 to cycle 2 for phase angle and basal metabolic rate (BMR)/Weight ratio as predictors was carried out.

Conclusion: KEN treatment is safe, well tolerated and results in rapid fat loss without detriment to dry lean mass.

Disclosure of Interest: All authors have declared no conflicts of interest.
P0621 ANALYSIS OF LONG-TERM WEIGHT REGAIN IN OBSESE PATIENTS WITH INTRAGASTRIC BALLOON

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Introduction: Obesity is a global disease and its management includes pharmaco-
ologic and surgical approaches. The intragastric balloon (IGB) is an option.

Objective: To analyze the obesity regained after balloon removal. The previ-
ous studies of the IGB had shown only follow-up of weight loss and not weight regain.

Method: All obese patients (BMI > 35) treated with IGB in a specialized obesity
center, and that underwent balloon removal from June 2009 to June 2013 were
invited to participate in the study. Exclusion criteria: pregnancy or bariatric
surgery after balloon removal, impossibility to contact, and refusal to participate.

Results: Out of the study of patients, 81.3% (182) were women. The average weight
at the moment of IGB implantation was 110.4 ± 28.2 kg. The average weight loss was
4.6 ± 4.9 kg; 3 years (n = 83): 8.66 ± 6.96 kg; 4 years (n = 54): 9.99 ± 8.44 kg and 5 years (n = 3): 19.96 ± 12.24 (p = 0.51). The lower the BMI at the beginning of the treatment, the greater the weight regain after the IGB withdrawal. This correlation was inverse (r = -0.20) and significant (p < 0.01).

Conclusion: The correlation between patient BMI and weight regain after the IGB withdrawal is a significant factor for weight regain after the removal of the device.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0622 LONG TERM EFFECT OF DUODENAL-JEJUNAL BYPASS LINEAR IMPLANTATION ON WEIGHT REDUCTION AND GLYCEMIC CONTROL

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Introduction: The Duodenal Jejunostomy Bypass Linear (DJBL) is an endoscopic device which prevents ingested nutrients absorption in the duodenum and first part of jejunum. The resultant effects are weight reduction and improvement in glycemic control in patients with type 2 diabetes mellitus (T2DM).

Aims & Methods: The study aim was to assess weight regain in insulin and glycemic
control changes resulted from the device implantation and a year after the device removal. Between February 2013 and September 2016, 51 diabetic patients were treated with DJBL in our center. This prospective observational study included a total of 306 follow-up periods for 9 months of active treatment. However, adverse events and early removals were analyzed for the whole cohort. Blood tests, body weight and medications data were collected during scheduled visits and phone interviews. The primary end points were body weight and glycemic control changes a year after the end points were the same
parameters after device removal. The protocol was approved by the local ethic committee.

Results: Thirty six patients (52.8% male) were treated for at least 9 months with the device. 10 of which completed a whole year follow-up after device removal. At the end of 12 months post implantation, the average body weight and BMI dropped from 109.5 ± 19.1 kg and 37.4 ± 5.0 kg/m² to 93.7 ± 20.4 kg and 29.6 ± 4.1 kg/m² (P = 0.001). Although the HbA1c dropped from 7.3 ± 1.1% to 6.9 ± 0.9% (P = 0.001) followed by those in which
<10% 20% (2) 15.6% (13) 18.5% (10) 33.3% (1)
10 to 19% 70% (5) 62.7% (52) 59.3% (32) 66.7% (2)
20 to 29% 10% (1) 14.5% (12) 14.8% (8) 0
30 to 49% 20% (2) 2.4% (2) 1.9% (1) 0
50 to 69% 20% (2) 1.2% (1) 5.6% (3) 0
70 to 89% 20% (2) 2.4% (2) 0
90 to 100% 0
<10% 20% (2) 15.6% (13) 18.5% (10) 33.3% (1)
10 to 19% 70% (5) 62.7% (52) 59.3% (32) 66.7% (2)
20 to 29% 10% (1) 14.5% (12) 14.8% (8) 0
30 to 49% 20% (2) 2.4% (2) 1.9% (1) 0
50 to 69% 20% (2) 1.2% (1) 5.6% (3) 0
70 to 89% 20% (2) 2.4% (2) 0
90 to 100% 0

Conclusion: DJBL is an effective tool for weight reduction glycemic control
among insulin and non-insulin dependent diabetic patients. Moreover, substan-
tial clinical achievements were observed at least a year after device removal.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0623 SYNTHETIC (INULIN, LACTOBACILLUS, BIFIDOBACTERIUM AND SACCHAROMYCES BOULARDI) IMPROVES FATTY LIVER DISEASE BY VIRTUE OF ITS ACTION ON ADIPOSE PROFILES, LEPTIN, ADIPONECtin, AND INFLAMMATORY BIOMARKERS

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Introduction: NASH is the most important cause of chronic liver disease and is
considered the hepatic manifestation of the metabolic syndrome associated with
type 2 diabetes. The prevalence of NASH in the general population reaches 15–
20% and it goes up to 70 to 90% in the obese population. The search of new non-
toxic drugs for prevention of the development of obesity is the most important
challenge of modern science. The question about impact of probiotics and
biotics on fat metabolism and obesity is being actively debated in the scientific
literature. So the aim of the study was to investigate the effect of synthetic (S) on
development of experimental obesity in rats with NAFID.

Aims & Methods: The study was carried out on 60 white rats, that were divided
into 6 groups (I-III – males, IV-VI – females). I and IV groups were intact control
(4-month old). Newborn rats of groups II and III s.c. in volume 8
mL saline or monosodium glutamate (MSG) (4 mg/g) at 2–10 days of age
were administered a saline or monosodium glutamate (MSG) (4 mg/g) at 2–10 days
of life. Since the age of 1 month, rats of III and V group had been injected with
water, rats III and VI groups - S (Inulin, Lactobacillus, Bifidobacterium and
Saccharomyces boulardii) (“Opferla” World Medicine) in a dose of 1, 94 ± 109
mg/kg/day and insulin. Interventions were performed by 13 months (3 months
courses alternated with two-week breaks) for 3 months. In 4-month rats anthropometric parameters and visceral adipose (VAT) tissue mass were esti-
minated, and adiponectin in serum and leptin in VAT were measured by ELISA.

Results: In our study we observed increased levels of the anthropometric para-
eters and significant increase of VAT mass that confirmed development of
visceral obesity. In male rats, there were more pronounced changes. It was estab-
lished that under condition of obesity caused by the introduction of MSG, the
level of adiponectin in serum decreased but leptin in VAT was increased. S
significantly improvement lipid profiles and histological state of liver: decrease
of dystrophy, inflammation and necrosis and reduction of the NASH incidence.
Also consumption of S led to reduction of pro-inflammatory cytokines and leptin and increased anti-inflammatory cytokines and adiponectin.

Conclusion: The introduction of S reduced the obesity, that shows the effectiveness of therapy for the prevention of obesity.

Disclosure of Interest: All authors have declared no conflicts of interest.

Introduction: Endoscopic bariatric approaches are gaining traction as possible treatment modalities for obesity. Especially, intragastric balloon was demonstrated to be associated with a significant weight loss in obese patients. Despite many advances in the design and material of intragastric balloon devices, there still remains a need for improved devices which is safer, faster, and less expensive than before. In the present study, we evaluated feasibility of newly developed intragastric balloon.

Aims & Methods: We used a newly developed intragastric balloon with improved employment for this study. The intragastric balloon was supplied as delicately rolled up inside a thin silicon sheath and mounted by surrounding the endoscope. Endoscopic intragastric balloon placement and positioning was simply performed by two endoscopists. 10 pigs were subjected to the novel intragastric balloon placement. We evaluated feasibility of the intragastric balloon and compared procedure time between the novel intragastric balloon and End-ball (Endalis, Brignais, France) intragastric balloon.

Results: In all cases, the novel intragastric balloons were successfully placed under usual sedation of diagnostic endoscopy. The procedures were simple and fast; the mean insertion time was 41.34±13.43 sec and 158±134.8 sec in novel intragastric balloon group and end ball group, respectively. The mean inflation time was 421.64±152.83 sec in novel intragastric balloon group and end ball group, respectively.

Conclusion: This preliminary data suggest that the procedure with the new intragastric balloon attain technical improvements in the placement without severe adverse events. The new intragastric balloon could offer constantly effective procedure regardless of the ability of the endoscopy practitioner.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

Disclosure of Interest: All authors have declared no conflicts of interest.

Table 1: Body weight, BMI and HbA1c changes at different timepoints

<table>
<thead>
<tr>
<th>Timepoint (months)</th>
<th>Mean weight in kg (±SD, range)</th>
<th>Mean BMI (±SD, range)</th>
<th>Mean HbA1c in % (±SD, range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>115.8 (45.4; 88–196)</td>
<td>40.9 (10.3; 35.3–59.2)</td>
<td>9.1 (1.3; 8.7–10.7)</td>
</tr>
<tr>
<td>6</td>
<td>97.4 (39.8; 72–164)</td>
<td>29.9 (2.1; 26.4–51.2)</td>
<td>7.6 (0.8; 6.6–8.3)</td>
</tr>
<tr>
<td>12</td>
<td>95.0 (38.8; 72–164)</td>
<td>33.5 (9.0; 29.549)</td>
<td>6.7 (0.9; 5.9–7.8)</td>
</tr>
<tr>
<td>16 (0)</td>
<td>91.7 (37.8; 75–164)</td>
<td>34.3 (8.6; 29.3–49.5)</td>
<td>7.7 (1.6; 6.2–9.9)</td>
</tr>
<tr>
<td>22 (6)</td>
<td>93.2 (40.6; 63–164)</td>
<td>32.8 (9.7; 24.6–49.5)</td>
<td>7.1 (0.7; 5.7–7.7)</td>
</tr>
<tr>
<td>28 (12)</td>
<td>92.5 (43.6; 61–160)</td>
<td>31.5 (9.1; 23.8–48.6)</td>
<td>7.0 (0.7; 6.3–7.7)</td>
</tr>
</tbody>
</table>

Conclusion: The results of this observational study show that re-implantation of the DJBL is viable and safe even after 4 months after explantation. After re-implantation, weight and HbA1c levels decreased one more time.

Disclosure of Interest: J. Stein has received speakers’ honoraria from GI Dynamics. All other authors have declared no conflicts of interest.

Conclusion: Obesity in the young population is becoming increasingly prevalent. It is associated with short- and long-term consequences. Early and effective interventions are paramount. Current treatment options include: lifestyle modifications, pharmacological therapies, endoscopic treatments and bariatric surgery. However, the relative effectiveness of these treatments in this cohort remains unclear.

Aims & Methods: To systematically identify and meta-analyse studies evaluating treatments that reduce body mass index (BMI) in overweight and obese young people. A systematic literature review of EMBASE and MEDLINE databases was conducted. Studies were included/excluded based on pre-specified eligibility criteria. Included patients were 21 years or younger. Lifestyle modification and pharmacological therapy searches were restricted to randomised control trials.

Results: 16,372 studies were identified with 80 studies complete with sufficient data for meta-analysis. Bariatric surgery caused the most weight loss in the short- and medium-term [pooled estimate of mean BMI loss: 13.77 kg/m²]. Lifestyle modifications and pharmacological therapy had a more modest impact on weight [pooled estimate of mean BMI loss: 0.99 kg/m² and 0.94 kg/m² respectively]. Individual studies demonstrated that endoscopic treatment results in short-term BMI reduction, however insufficient data prevented meta-analysis.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
Results: All analyzed microRNAs were present in all studied foods with highest expression found in poultry and meat. Especially, hash, beef and salmon showed the highest miRNA expression, while lowest expression was found in cheese and milk. Food processing led to only marginal changes (max. 1.5-fold) in miRNA expression and thus demonstrating its stability against degradation. Short-term changes in diet (from usual to vegetarian and to meat-rich diet) in healthy subjects was not associated with variation in miR-21, miR-155 and miR-16 expression. Interestingly, in comparison to several previous reports, we repeatedly failed to detect any plant miR-168 in sera. However, we did observe a slight increase in miR-155 expression in sera (up to 8-fold), while meat-rich diet was associated with slight decrease if compared to the starting time point (mean ± SD 0.031 ± 0.002 for no diet vs 0.025 ± 0.042 for vegetarian vs. 0.0016 ± 0.00096 for meat-rich; p = 0.03 Kruskal-Wallis test, with p = 0.05 for Dunts multiple comparison test for vegetarian vs. meat-rich).

Conclusion: The results of this study show that various foods provide a great source of miRNAs, which remains stable despite processing. We further demonstrate that short term changes in diet have only minor impact on the miRNA expression pattern in sera and blood supporting its value as biomarkers. Functional role of diet-induced increase in plant-derived miRNA expression needs further evaluation.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0628 NEUROMEDIN U BLOCKS GASTRIC EMPTYING THROUGH VAGAL-DEPENDENT MECHANISMS AND IMPROVES ORAL GLUCOSE TOLERANCE

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Introduction: The gut and brain peptide neuromedin U (NMU) is reported to contribute to its anorexigenic effect. During OGTT, blood was sampled to measure insulin secretion. [14]C-glucose tests were performed after an intraperitoneal injection of NMU or PBS in C57Bl6 mice. The gut and brain peptide neuromedin U (NMU) is reported to contribute to its anorexigenic effect. During OGTT, blood was sampled to measure insulin secretion. [14]C-glucose tests were performed after an intraperitoneal injection of NMU or PBS in C57Bl6 mice. Oral (OGTT) and intraperitoneal (IPGTT) glucose tolerance tests were performed after an intraperitoneal injection of NMU or PBS in C57Bl6 mice. The gut and brain peptide neuromedin U (NMU) is thus considered as a promising candidate for the treatment of obesity and diabetes. However, in contradiction with previous observations, NMU was recently presented as a “decretin” hormone able to decrease insulin secretion. The pathways through which NMU controls glucose are thus uncertain and we sought to clarify some of NMU mechanisms of action on glucose homeostasis.

Aims & Methods: Oral (OGTT) and intraperitoneal (IPGTT) glucose tolerance tests were performed after an intraperitoneal injection of NMU or PBS in C57Bl6 mice. Oral (OGTT) and intraperitoneal (IPGTT) glucose tolerance tests were performed after an intraperitoneal injection of NMU or PBS in C57Bl6 mice. The gut and brain peptide neuromedin U (NMU) is thus considered as a promising candidate for the treatment of obesity and diabetes. However, in contradiction with previous observations, NMU was recently presented as a “decretin” hormone able to decrease insulin secretion. The pathways through which NMU controls glucose are thus uncertain and we sought to clarify some of NMU mechanisms of action on glucose homeostasis.

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Disclosure of Interest: All authors have declared no conflicts of interest.

P0629 LOW FODMAP DIET & PREBIOTIC GALACTOOLIGOSACCHARIDES IMPROVE IRREVERSIBLE BOWEL SYNDROME SYMPTOMS AND RESPONSE TO LOW FODMAP DIET THROUGH VAGAL-DEPENDENT MECHANISMS AND IMPROVES ORAL GLUCOSE TOLERANCE

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Disclosure of Interest: B. Wilson: BW is funded by a PhD studentship provided by Clasado Biosciences

All other authors have declared no conflicts of interest.

P0630 THE ANALYSIS OF PROTEIN CONSUMPTION PATTERNs IN PATIENTs WITH SIBO

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Disclosure of Interest: None declared.

Table 1

<table>
<thead>
<tr>
<th>Type of SIBO</th>
<th>Response Rate (% of Responders)</th>
<th>Adequate Relief (≥50% improvement)</th>
</tr>
</thead>
<tbody>
<tr>
<td>High LDA</td>
<td>51.4 mg/100g</td>
<td>24.3%</td>
</tr>
<tr>
<td>Low LDA</td>
<td>31.9 mg/100g</td>
<td>23.8%</td>
</tr>
<tr>
<td>Antibiotics</td>
<td>42.9 mg/100g</td>
<td>23.8%</td>
</tr>
<tr>
<td>Prebiotics</td>
<td>44.4 mg/100g</td>
<td>23.8%</td>
</tr>
</tbody>
</table>

VOC profiles, stool SCFA and VOC profiling are relatively low-cost and non-invasive techniques that may predict response to the LFD as well as helping to further understand the underlying mechanisms. Prospective clinical trials to test these algorithms are warranted and may lead to personalisation therapy for patients with IBS.

Disclosure of Interest: B. Wilson: BW is funded by a PhD studentship provided by Clasado Biosciences

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Table 1

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Disclosure of Interest: B. Wilson: BW is funded by a PhD studentship provided by Clasado Biosciences

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FODMAP intake was successfully reduced, and main additional changes were used to evaluate HRQOL. A 3-day food record was used to estimate base-line intake of FODMAPs, to reveal dietary changes and to assess adherence to LFD throughout a 4-week intervention period. IBS Severity Scoring System (IBS-SSS) and IBS Symptom Questionnaire (IBS-SQ) were used to assess symptoms. An Ad hoc questionnaire measured grade of tissue damage and typical RISBD complaints (fecal incontinence, rectal mucus and rectal bleeding). Short Form Nepean Dyspepsia Index (SF-NDI) and 12-item Short Form Health Survey (SF-12) were used to evaluate HRQOL. A 3-day food record was used to estimate baseline intake of FODMAPs, to reveal dietary changes and to assess adherence to the diet. All schemes were completed at baseline and at 4 weeks. The study included no control group.

Results: FODMAP intake was successfully reduced, and main additional changes in the diet were reduced intake of energy, carbohydrates and fiber. The adherence to the diet was high (mean 94.8%). IBS symptoms improved significantly based on mean total score of IBS-SSS and IBS-SQ, which changed from 310.2 ± 9.4 to 18.3 ± 8.2 (p = 0.001) and based on mental (p = 0.047) and physical (p = 0.134) component summary score of SF-12.

Conclusion: The low FODMAP diet seems effective in alleviating IBS symptoms, and improving HRQOL in patients with RISBD. High compliance to LFD is possible with adequate diet counseling and continuous guidance. Further controlled studies with larger sample size should be conducted to verify our results and hopefully enable the implementation of LFD as a future management strategy for chronic RISBD.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
is similar to the oral glucose-stimulated secretion of glucagon-like peptide 1 (GLP-1) and nitric oxide from enterointerine L cells (EEC) from the distal gut. GLP-1 and glucagon, both originate from the same proglucagon precursor, differentially processed by prohormone convertase 2 (PC2) into glucagon in pancreatic α cells and by prohormone convertase 1/3 (PC1/3) into GLP-1.

Aims & Methods: We hypothesized that, after pancreatectomy, proglucagon can also be processed into glucagon in EEC. We developed a 75% subtotal pancreatectomy model in C57Bl/6 mice. Control (Ct) mice underwent a laparatomy. Post-surgery, blood samples were measured for blood glucose and oral glucose tolerance tests (OGTT) were performed after 1 week. Insulinemia and glucagonemia were also measured in fed and fasted mice and during OGTT. After 2 weeks, animals were sacrificed and the remnant pancreas was sampled for glucagon and insulin immunohistochemistry in whole-organ alpha- versus beta-cell mass quantification. Proximal and distal intestinal segments were sampled for morphometric analyses as well as measurement of proconvertase and proglucagon mRNA levels. Colonic segments were incubated in a glucose-enriched medium for one hour and glucose-induced secretion of glucagon and insulin were measured in the supernatant and in the supernatant.

Results: As soon as one day post-surgery, pancreatomezzized (Px) mice developed a hyperglycemia that maintained for over a week (351 mg/dl in Px mice vs 140 mg/dl in Ct mice, P < 0.05, 5 days post-surgery). This hyperglycemic state was accompanied by an oral glucose intolerance (area under the curve +278% in Px mice, P < 0.01 vs Ct mice, 1 week post-surgery). During OGTT, intestinal glucose absorption increased (slope between 0 and 15 min +69.9% in Px mice vs 0% in Ct mice, 1 week post-surgery). Glucagonemia increased in fasted pancreatomezzized mice (+146.6% in Px mice P < 0.01 vs Ct mice 1 week post-surgery). After sacrifice, alpha cell mass was decreased in the remaining pancreas (~79.25% in Px mice P < 0.05 vs Ct mice, 2 weeks post-surgery). However, the proximal colon to secret glucagon and vaso was observed (+290.6% in Px mice P < 0.05 vs Ct mice, 2 weeks post-surgery). In pancreatomezzzed mice, an hypertrophy of the duodenum was associated with an increase in crypt depth (+77.7%, in Px mice P < 0.05 vs control mice, 2 weeks post-surgery) and villus height (+53.8% in Px mice P < 0.05 vs control mice, 2 weeks post-surgery).

Conclusion: These data establish an ability of the whole gut to adapt in response to pancreatectomy. The upper intestine (duodenum) become hyperplasic and more glucose-induced intestinal response to absorb glucose. The distal intestine (colon) is able to produce glucagon and may participate to the development of the reported hyperglycagonemia.

Disclosure of Interest: All authors have declared no conflicts of interest.

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PO036 COMPLICATIONS AND EARLY MORTALITY IN PERCUTANEOUS ENDOSCOPIC GASTROSTOMY PLACEMENT IN LOMBARDY: A MULTICENTER PROSPECTIVE STUDY


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Introduction: Percutaneous endoscopic gastrostomy (PEG) is currently one of the most common endoscopic procedures performed worldwide. To date, the mortality of patients after PEG insertion or PEG replacement. This is a relative (without legal guardianship) in 49.6%, patient in 28.2%, legal guardian in 10.5%, legal guardian in 16.25%, medical director in 7% of patients. Thirty-days mortality was 2.4%

Conclusion: Our data confirm that PEG placement is a safe procedure with a mortality rate of 30 days of 8%. To our knowledge this is the largest prospective study on the use of PEG. Surprisingly in more than 50% of patients the consent form was not properly signed, leading to possible medico-legal consequences. Moreover, in 9% of the cases PEG was placed for an early discharge (more than for clinical indication).

Disclosure of Interest: All authors have declared no conflicts of interest.

References


PO037 MEDICAL REGISTRAR REPORTING OF CHEST X-RAYS FOR NASOGASTRIC TUBE POSITION: HOW CAN IT BE MADE SAFER?


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Introduction: Nasogastric tube (NG) feeding is an essential part of in-patient care. Tubes can be placed at the bedside with no need for specific equipment or sedation. However placement of NG tubes is not without risk and avoiding the introduction of substances into the respiratory tract through a misplaced NG tube was highlighted as a UK National Patient Safety Agency alert in 2005. In 2011 the NPSA made this a ‘never event’. The only acceptable methods of checking the position of an NG tube are: pH < 5.3 on aspiration or confirmation of flow of NG (CRM) by competent medical staff. Reporting a CXR for NG tube position is a frequent request particularly for junior doctors out of hours. Practise varies across the UK - some trusts require NG checking to be done only by senior clinicians (medical registrars or consultants) and some only allow reporting by a consultant radiologist. We assessed documentation of NG position on CXR by medical registrars from the region to find out if documentation was adequate, as would be expected of senior clinicians. NPSA guidance suggests four points should be documented in the medical notes to confirm NG position: 1. Does the tube follow the contours of the oesophagus and avoid those of the bronchi? 2. Does the tube clearly bisect the carina or the bronchi? 3. Does it cross the diaphragm in the midline? 4. Is the tip clearly visible below the left hemi-diaphragm? All four criteria were met in only 17.6% of responses and answers were considered incorrect in 20.5%. An aide-memoir sticker with an abbreviated version of the above four points, time, date, doctor signature and whether tube is safe to use or not with Yes/No answers, is used on some wards in Southampton and we assessed whether its use would improve quality of reporting both a correctly placed and misplaced NG tube.

Aims & Methods: Medical registrars from first to final year of specialist training and from various specialties were presented with a CXR showing a correctly sited NG tube and were asked to complete a sticker answering yes or no, to check position and whether it was safe to use. Following this they were presented with a CXR showing an incorrectly sited NG tube and asked to use the sticker to assess position. The CXR was projected and anonymous responses collected after sufficient time for the group to complete both stickers. Results: 31 complete responses were obtained for the correctly sited tube with 58% stating that it should be used and 42% that they would not use the tube without further review. 10 incomplete responses were obtained and therefore 86% of responses met NPSA guidance for reporting CXR for NG position. 28 complete responses were obtained for the incorrectly sited tube and 100% stated that the tube should not be used.

Conclusion: Use of the sticker increased compliance with NPSA guidance for CXR reporting for NG tube position from 17.6% to 86%. The misplaced tube was correctly reported and not used in 100% of responses. The correctly sited tube was reported as safe to use in 58%. The CXR used was of an anonymous real patient and was slightly rotated to reflect a real-life scenario which meant the tube was slightly off the midline. In this real-life scenario some trainees would be happy to make a judgement considering these factors and others may be cautious and follow the sticker statements exactly prompting further review by radiology or removal of the tube. Overall this increases patient safety and avoids use of a misplaced tube in accordance with UK guidelines. We recommend the use of a CXR sticker on all wards which use NG tubes to rapidly improve documentation and patient safety. The other option we may consider is developing a pathway for radiology consultants to report all these CXRs before the NG tube is used; however this is likely to take considerable time and is unlikely to be available out of hours.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P0638 MICRONUTRIENT MONITORING IN HOME PARENTERAL NUTRITION PATIENTS: AN AUDIT OF PRACTICE IN A REGIONAL REFERRAL CENTRE

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Introduction: Intestinal failure patients by definition have reduced ability to absorb fluid and macronutrients through the gastrointestinal tract. Type two intestinal failure patients require months of intravenous nutrition (parenteral nutrition) for weeks or months either in hospital or at home. Type three intestinal failure patients generally require long-term parenteral nutrition (PN), which is given at home (HPN) and may be life-long. In addition to a reduction in the ability to absorb macronutrients, patients on long-term PN have a reduction in absorption of micronutrients (copper, zinc, selenium and manganese) and vita-
mins (A, B12, D and E) which are required for metabolism and enzymatic reac-
tions at a cellular level. PN is routinely supplemented with micronutrients and show that therapy can occur at high levels and deficiency can cause a variety of symptoms. ESPEN guidelines recommend that serum vitamin and trace element levels be checked at baseline and at least once per year. NICE guidelines specify more frequent monitoring for in-patients and that selenium; manganese and vitamin D should be checked three to six monthly in HPN patients. Some trace elements (copper and zinc in particular) are affected by acute illness. Current local practise is to avoid checking levels until there is evidence that inflammation or infection has resolved.

Aims & Methods: Our aim was to audit the frequency of micronutrient screening in our cohort of HPN patients. All type two and three intestinal failure out-
patients were included. Current in-patients were excluded due to the effect of acute illness on micronutrient levels. Patients on parenteral fluid rather than nutrition were excluded as current guidelines give recommendations for HPN patients and do not specify recommendations if fluid alone is required. A search of the blood results system was performed for all micronutrient results from one full year to the date of the search. Results were recorded in spreadsheet format and analysed. Many patients live out of the region; however, many local trusts do not have the laboratory facilities to check micronutrient levels so they tend to be done in Southampton. If no results were available on the Southampton system then the local hospital was contacted for local results if available.

Results: 57 home parental nutrition patients were identified. 51 (89.5%) of these patients had micronutrients checked at some point during their care. 44 of 49 (88.7%) had micronutrients checked within one year (two of the 51 had other recently so did not have results within a year). 32 (61.5%) of those who had micronutrients checked had them done within the last six months. 6 patients had never had micronutrients checked. One had them requested just prior to the time of audit but results were not yet available. Two were out of area and had not been in hospital that year. One of these commenced PN in 2015 and found it difficult to attend clinic. The other had not been seen in clinic due to an administrative error and has now been seen with micronutrients requested. Two further patients had never had micronutrients checked due to a persistently raised CRP.

Conclusion: Despite a lack of clarity between guidelines about the frequency of monitoring of micronutrients, it is recommended that HPN patients receiving long-term intravenous nutrition should have regular monitoring to reduce risk of deficiency or toxicity. The majority of our cohort of HPN patients had micro-
nutrients checked annually and over half were checked six monthly. This is compliant with ESPEN guidelines; however, we need to aim for 100%. We have introduced a template to use in clinic to trigger review of results and request micronutrient levels when required. Alongside this we have introduced a virtual ward round to remotely review all out-patients regularly and plan ahead to request blood tests when required. Following the introduction of these measures we will repeat the audit to find out if the situation has improved.

Disclosure of Interest: All authors have declared no conflicts of interest.

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Nutrition support for adults: oral nutrition support, enteral tube feeding and parenteral nutrition NICE Clinical guideline [CG332] Published date: February 2006

P0639 CLINICAL NUTRITION - ARE WE IGNORANT OR NEGLIGENT?

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Introduction: Early recognition and delivery of nutritional care by physicians has been shown to improve outcomes in malnourished hospitalized patients. However, physicians encounter multiple barriers in providing appropriate nutrition intervention. These are interspecial and nutritional train-
ing in medical education have been introduced to overcome these barriers, there appears to be a discrepancy in practice amongst physicians despite the availabil-
ity of these resources.

Aims & Methods: We aim to assess the knowledge and attitudes of physicians towards clinical nutrition in a large tertiary teaching hospital in Singapore. An anonymous questionnaire comprising 15 multiple-choice questions from stand-
ard nutrition textbooks was administered. The questionnaire was designed to assess (a) recognition of nutritional needs of hospitalized patients, (b) knowledge on the role of clinical nutrition, and (c) application of nutritional intervention in common clinical practice. We included consultants, fellows and residents working in units where nutritional problems were common. Finally, we conducted a separate 5-question opinion survey to assess each participant’s nutri-
tional training and exposure, based on a 5-point Likert scale ranging from “strongly agree” to “strongly disagree”.

Results: A total of 305 physicians volunteered to participate in this study. Forty (15%) did not reveal their specialty or staff grade and were excluded from ana-
lysis. Of the remaining 265 responders comprised 77 (29%) consultants, 88 (22%) fellows, and 130 (49%) residents. Amongst them, 232 (87%) were from medical disciplines and 33 (13%) from surgical disciplines. The median aggregate score (out of a maximum score of 15) obtained by consultants, fellows and residents was 6.0 ± 2.2 (range 2–12), 7.0 ± 1.8 (range 3–11), 7.0 ± 1.8 (range 1–10) respectively. All 3 grades of physicians achieved less than 50% of the maximum possible score. No significant difference in median aggregate score was observed between physicians from medical disciplines (6.5 ± 1.9) and those from surgical disciplines (6.5 ± 1.9). However, gastroenterologists performed significantly better than non-gastroenterologists (median aggregate score 9.0 ± 2.2 vs 6.0 ± 1.8, p < 0.001). In the opinion survey, a majority of physicians (63%) believed that nutrition-related teaching was inadequate during residency training and 44% felt that clinical nutrition was accorded insufficient attention during ward rounds. Only 33% of responders reported that they performed nutritional screening on admission, and a mere 10% were confident in providing nutrition counselling to malnourished patients. Interestingly, their overall performance was not different from that of other participants (see Table 1).

Table 1: Median aggregate scores by grade, specialty and response in opinion survey

<table>
<thead>
<tr>
<th>Specialty</th>
<th>Physician Grade</th>
<th>Median aggregate score ±SD</th>
<th>Range</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical disciplines (n = 232)</td>
<td>Consultants (n = 77)</td>
<td>6.0 ± 2.2</td>
<td>2.0–12.0</td>
<td>0.617</td>
</tr>
<tr>
<td>Surgical disciplines (n = 33)</td>
<td>Fellows (n = 58)</td>
<td>7.0 ± 1.8</td>
<td>3.0–11.0</td>
<td></td>
</tr>
<tr>
<td>Non-gastroenterologists (n = 240)</td>
<td>Residents (n = 130)</td>
<td>7.0 ± 1.8</td>
<td>1.0–11.0</td>
<td></td>
</tr>
<tr>
<td>Gastroenterologists (n = 25)</td>
<td>Specialty</td>
<td>6.5 ± 1.9</td>
<td>1.0–12.0</td>
<td>0.193</td>
</tr>
<tr>
<td>Non-gastroenterologists (n = 240)</td>
<td>7.0 ± 1.8</td>
<td>2.0–10.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-gastroenterologists (n = 240)</td>
<td>Gastroenterologists (n = 25)</td>
<td>9.0 ± 2.2</td>
<td>3.0–12.0</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Non-gastroenterologists (n = 240)</td>
<td>Performing nutrition screening on admission</td>
<td>6.0 ± 1.8</td>
<td>1.0–11.0</td>
<td></td>
</tr>
<tr>
<td>Confident in providing nutrition counselling</td>
<td>Disagreed (n = 81)</td>
<td>7.0 ± 1.0</td>
<td>2.0–12.0</td>
<td>0.321</td>
</tr>
<tr>
<td>Confident in providing nutrition counselling</td>
<td>Disagreed (n = 99)</td>
<td>7.0 ± 2.2</td>
<td>2.0–11.0</td>
<td></td>
</tr>
<tr>
<td>Confident in providing nutrition counselling</td>
<td>Disagreed (n = 23)</td>
<td>7.0 ± 2.0</td>
<td>3.0–11.0</td>
<td>0.467</td>
</tr>
<tr>
<td>Confident in providing nutrition counselling</td>
<td>Disagreed (n = 137)</td>
<td>7.0 ± 2.0</td>
<td>3.0–11.0</td>
<td></td>
</tr>
</tbody>
</table>

Conclusion: Our study highlights that knowledge on nutrition and its clinical application to hospitalized patients remains inadequate across all physician grades, especially amongst non-gastroenterologists. The current state of clinical nutrition-related teaching during residency training falls short of achieving its goals, and may need re-examination.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
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Introduction: Per-oréal endoscopic myotomy (POEM) is a novel treatment mod-
ality for achalasia cardia (AC). The studies are limited in paediatric population. Aims & Methods: In this study our aim was to analyse the feasibility, safety and efficacy of per-oréal endoscopic myotomy in children We retrospectively evalu-
ate the data of all children (<18 years) who underwent POEM at our institution from September 2013 to February 2017. All POEM procedures were performed under general anaesthesia in an endoscopy suit. Technical feasibility, safety and efficacy were analysed. Clinical success was defined as Eckardt score ≤ 3. Objective postoperative indwelling-timed barium swallow and high resolution mano-
metry were assessed and compared before and after POEM.

Results: Thirty children (15-boys, 15-girls) with mean age of 14.1 ± 3.2 (4–18) years, underwent POEM during the specified period. The sub-types of AC were-
type I (6), type II (19) and type III (1). Eight children had prior treatment with pneumatic balloon dilatation. POEM was successfully performed in all children. Anterior myotomy was performed in majority of children 23 (76.7%). Mean total length of myotomy was 10.9 ± 2.2 cm, with 7.9 ± 2.0 cm on esophageal and...
Aims & Methods: We aimed to study the composition of the microbiota in the biopsy material of the antral part of the stomach, according to the 16S-rRNA sequencing, of children with chronic gastritis, in the presence or absence of HP, and also to compare it with the histological data. Biopsy materials of mucous coat from antral part of the stomach were taken from 16 children aged 10–17 with chronic gastritis and after the preliminary extraction the biopsy materials were examined using the method of sequencing with a pair of oligonucleotide primers, which are specific for the conservative regions of the 16S-rRNA gene, on the Life Technologies Ion Torrent sequencer using the 318v2 chip. Bioinformatic processing was conducted using the QIIME package. The results were compared with the data from the histological examination of the biopsy materials from the same part of the stomach as well as with the results of diagnosis using rapid urease test AMA RUT Expert with digital Reader.

Results: 8 out of 16 patients were identified as HP(+) positive, 2 of them had HP in small amounts, 6 of them – in significant amounts. The dominant types of bacteria in the stomach of all children were Proteobacteria, Bacteroidetes, Firmicutes; in a lesser extent - Actinobacteria, Cyanobacteria, Fusobacteria. 64.1% of HP(+) patients’ microbiome was constituted of HP, among Proteobacteria it reached 75–99%, the amount of other bacteria herewith shor- tened, and the microbiota diversity decreased. Non-helicobacter microbiota of children with small amount of HP was almost identical in composition as HP(-) patients’, the amount of other microbes was more numerous and diverse, also within Proteobacteria. The signs of inflammation in mucous coat of the stomach in case of HP presence were more pronounced than in HP absence, they corre- lated with the amount of HP.

Conclusion: Microbiome of the children’s stomach is diverse, it is similar to adults’. The infection from HP inhibits another microbiota and it is accompanied with the signs of mucous coat inflammation, which correlates with the amount of HP.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

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Introduction: Because of high prevalence of gastric malignancies in the adult population, high Helicobacter pylori (Hp) prevalence in Armenia is suspected. Rising antibiotic resistance of Hp both in children and adults lead to decrease of effectiveness of standard eradication therapy [1, 2]. The aim of this study is to determine frequency of Hp antibiotic resistance in Armenian children.

Aims & Methods: 47 children with suspected gastroduodenal disease (GDD), hospitalized in Arabkir MC, were selected from April to December 2016 (23 boys and 24 girls, average age 8.98±4.40). Hp-associated GDD were diagnosed according to clinical, endoscopic and histological criteria. Antral biopsy was cultured on 3% sheep blood Columbia agar and selective Hp media. Antibiotic susceptibility test by disk diffusion method was conducted.

Results: Hp-associated GDD was diagnosed in 40 patients out of 47: 37 (92.5%) had gastritis and/or duodenitis, 3 (7.5%) had peptic ulcer disease (PUD). Seven out of 47 children were excluded from the study due to both histology and culture negative for Hp. Thirty-four (85%) were treatment-naive patients and 6 (15%) had received eradication therapy previously. Main clinical symptoms were recurrent epigastric pain 34 (85%), nausea 28 (70%) and vomiting 13 (32.5%). By Hp eradication therapy, Hp(+) and/or duodenitis was seen in 18 (45%), non-erosive gastritis in 16 (40%), PUD in 3 (7.5%), normal mucosa in 3 (7.5%). Rapid urease test was positive in all antral biopsies (100%). Histology showed chronic gastritis and/or duodenitis in 28 (70%), atrophic gastritis in 5 (12.5%), gastric glandular dysplasia in 2 (5%), gastric metaplasia of duodenal mucosa in 3 (7.5%), normal mucosa in 2 (5%). Hp was positive in 38 (95%) and negative in 2 (5%). Cultures were positive for Hp in 14 of 40 patients (35%). Susceptibility test was possible in 12 Hp strains from available 14: all but 2 were resistant to metronidazole (83.3%), 4 to clarithromycin (33.3%), 3 double resistant to both metronidazole and clarithromycin (25%), and 66.6% to doxycycline. All strains were susceptible to amoxicillin and levofloxacin (100%), 6 strains were tested and found susceptible to rifuratol.

Conclusion: The data indicate a high rate of resistance to conventional triple therapy antibiotics: metronidazole (83.3%) and clarithromycin (33%). High resistance to doxycycline also was seen, despite limited use of this antibiotic in Armenian paediatric practice. High susceptibility to rifuratol might be useful for further development of specific eradication schemes for Armenia. High frequency of both erosive and non-erosive gastritis as well as high rate of gastric atrophy and dysplasia in these patients were noticed.

Disclosure of Interest: All authors have declared no conflicts of interest.
**P0645 CURRENT STATUS OF THE FIRST AND SECOND LINE THERAPY FOR HELICOBACTER PYLORI INFECTION IN SYMPTOMATIC CHILDREN: A SINGLE CENTER STUDY**

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Introduction: Current evidence suggests the decline of the eradication rates of *H. pylori* infection in children treated with standard first line therapy, partly determined by its antibiotic resistance.

Aims & Methods: To evaluate the effectiveness of current first and second-line therapies for *H. pylori* eradication in children. We conducted a prospective open-label study of 158 symptomatic children (age 6 months−18 years; 106 girls) who required a first upper digestive endoscopy over the past year. Active *H. pylori* infection was documented in 122 of the 158 investigated children (77.2%). Infected children were randomly assigned to receive either a 7−14 days standard empiric triple therapy consisting of esomeprazole (Eso) plus amoxicillin (AMO) and clarithromycin (CLA) or metronidazole (MET), either a sequential therapy for 10−14 days. Bismuth salts are not easily available in our country.

Results: Thirty CD patients completed the study. After 12-weeks intervention, the biochemical blood parameters remained normative in all CD patients, and the gut microbiota counts within each experimental group did not differ from their counts at baseline. However, in comparison with placebo group, bifidobacterium counts was significantly (*p* < 0.01) higher in CD children consuming OEF−supplemented GFD. Moreover, the counts of Clostridium leptum group in children of prebiotic group did not show the decreasing tendency among the time of GFD intervention was observed in placebo group. These changes were reflected into bacteria after the intervention that was constant in prebiotic group but tended to fall in placebo group. Microbiota corresponded well with microbial metabolic activity. In comparison with placebo group, concentration of short chain fatty acids (SCFA) was higher in prebiotic group (50.27 ± 69.55 μmol/g, *p* < 0.05) mainly due to a significantly higher acetate formation (28.82 ± 44.06 μmol/g, *p* < 0.05).

Conclusion: Imbalanced gut microbiota is suggested to be involved in the pathogenesis of celiac disease (CD). In many CD patients, despite a long-term treatment with a gluten-free diet (GFD), the intestinal dysbiosis is not completely restored. Prebiotics, substances of the unique ability to shape intestinal microbial composition, low-risk GFD supplement to remedy the intestinal dysbiosis in CD patients.

Aims & Methods: The aim of the present study was to assess the effect of prebiotic oligofructose-enriched inulin (OEI) administration on the quantitative gut microbiota characteristics of CD children following a strict GFD for ≥1 year. A randomized, placebo-controlled 12-weeks dietary intervention was conducted on 34 CD children (62 % female, mean age 10 years) on GFD who were randomly assigned to prebiotic (OEI: 10 g/day) or placebo group (multidextrin; 7 g/day). Before (baseline) and after the intervention, the anthropometric (weight, height) and biochemical blood parameters (C-reactive protein, creatinine, aspartate aminotransferase, alanine aminotransferase), quantitative gut microbiota characteristics (by real-time PCR) and concentration of short-chain fatty acids (by gas chromatography with a flame ionization detector) were assessed.

Results: Treatments were analysed by x2 test and the Odds Ratio (p < 0.05) was considered statistically significant. There were no association between *H. pylori* infection and Ig E mediated food allergy. Undernutrition and overnutrition were not associated with the *H. pylori* infection and food allergy in our patients.

Disclosure of Interest: All authors have declared no conflicts of interest.

**P0646 GUT MICROBIOTA MODULATION UNDER OLIGOFRUCTOSE-ENRICHED INULIN ADMINISTRATION IN PAEDIATRIC CELIAC DISEASE PATIENTS ON A GLUTEN-FREE DIET: RANDOMIZED CONTROLLED TRIAL**

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Introduction: Imbalanced gut microbiota is suggested to be involved in the pathogenesis of celiac disease (CD). In many CD patients, despite a long-term treatment with a gluten-free diet (GFD), the intestinal dysbiosis is not completely restored. Prebiotics, substances of the unique ability to shape intestinal microbial composition, low-risk GFD supplement to remedy the intestinal dysbiosis in CD patients.

Aims & Methods: The aim of the present study was to assess the effect of prebiotic oligofructose-enriched inulin (OEI) administration on the quantitative gut microbiota characteristics of CD children following a strict GFD for ≥1 year. A randomized, placebo-controlled 12-weeks dietary intervention was conducted on 34 CD children (62 % female, mean age 10 years) on GFD who were randomly assigned to prebiotic (OEI: 10 g/day) or placebo group (multidextrin; 7 g/day). Before (baseline) and after the intervention, the anthropometric (weight, height) and biochemical blood parameters (C-reactive protein, creatinine, aspartate aminotransferase, alanine aminotransferase), quantitative gut microbiota characteristics (by real-time PCR) and concentration of short-chain fatty acids (by gas chromatography with a flame ionization detector) were assessed.

Results: Treatments were analysed by x2 test and the Odds Ratio (p < 0.05) was considered statistically significant. There were no association between *H. pylori* infection and Ig E mediated food allergy. Undernutrition and overnutrition were not associated with the *H. pylori* infection and food allergy in our patients.

Disclosure of Interest: All authors have declared no conflicts of interest.

**P0644 HELICOBACTER PYLORI INFECTION AND SPECIFIC IMMUNOGLOBULIN E ANTIBODIES TO FOOD ALLERGENS IN SYMPTOMATIC CHILDREN ADMITTED IN A DIGESTIVE ENDOSCOPY UNIT**

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Introduction: *H. pylori* is one of the most widespread bacterial infections worldwide, therefore nowadays its prevalence is decreasing, mostly in developed countries. There are some studies which support that *H. pylori* could favor the development of food allergy.

Aims & Methods: To assess the relationship between *H. pylori* infection and specific immunoglobulin E (Ig E) antibodies to food allergens in symptomatic children. We conducted a prospective study of 394 symptomatic children (249 girls, age range 6 months−18 years), mostly with uninvestigated dyspepsia requiring an endoscopic evaluation in our unit, from January 2015 to December 2016. All patients were evaluated for *H. pylori* infection by at least two standard invasive tests and for specific immunoglobulin E antibodies to major food allergens (R-Biopharm, Germany). The nutritional status of patients was assessed in all cases by the new World Health Organization (WHO, 2007) growth charts. EPI−INFO version 7 was used for statistical analysis. A two sided p-value less then 0.05 was considered statistically significant.

Results: Active *H. pylori* infection was documented in 246 (62.3%) cases. The allergic sensisation to at least one of the food allergens was identified in 134 of 394 patients (34%). The majority of Ig E positive children (109 of 134 cases; 80.55%) were positive for cow’s milk followed by egg (17.9%), wheat (7.46%), potato (5.95%), soybean (3.73%). The allergic sensitization to food allergens was associated with abnormal levels of specific Ig E antibodies to common inhalatory allergens in 55 of 134 cases (41.04%). Regarding the association of *H. pylori* infection with an elevated serum Ig E level to at least one of the food allergens tested, there was a weak but present correlation (p = 0.14, 77 of 134 (51.30%) patients positive for food specific Ig E antibodies were *H. pylori* infected and 57 of them (38.55%) were *H. pylori* negative (Fisher exact test = 0.08). The assessment of the patients nutritional profile in relationship with *H. pylori* infection and food allergy not revealed any statistical significance between the two the poor nutritional status (undernutrition and overnutrition).

Conclusion: The recent decline of *H. pylori* infection is not evident in our study. There was no association between *H. pylori* infection and Ig E mediated food allergy. Undernutrition and overnutrition were not associated with the *H. pylori* infection and food allergy in our patients.

Disclosure of Interest: All authors have declared no conflicts of interest.

**P0648 EVALUATING GLUTEN IMMUNOGENIC PEPTIDES AS NON-INVASIVE MARKER OF GLUTEN-FREE DIET ADHERENCE IN PAEDIATRIC CELIAC DISEASE**

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Introduction: Treatment for celiac disease (CD) is a lifelong strict gluten-free diet (GFD). Patients should be followed-up with dietary interviews and serology as CD markers to ensure adherence to the diet. However, none of these methods is sufficiently sensitive. The current study aims to use a non-invasive method to evaluate adherence to dietary restriction in children and adolescents with CD.

Methods: A total of 62 children and adolescents (32 males, 30 females; mean age 7.3 ± 3.1 years) with CD followed up for at least 1 year were included in this study. The patients were questioned using a validated questionnaire to identify adherence to dietary restrictions. A protein antigen mixture enriched in gluten immunogenic peptides was used to evaluate the adherence to dietary restriction. A second-line therapy was recommended in 26 of cases with an overall eradication rate of 80.76% (21/26 cases) for ITT analysis and respectively 87.5% (21/24 cases) for PP analysis.

Conclusion: This endoscopic series reveals a high rate of *H. pylori* infection (77.2%). The sequential therapy achieved a significantly higher eradication rate than the standard empiric triple regimens regardless of using ITT (78.57% versus 61.35%) or PP (85.93% versus 65.30%) analysis. The eradication rates for the second-line therapy was significantly higher (87.5% for PP analysis) compared with standard first line triple therapy (76.99% for PP analysis).

Disclosure of Interest: All authors have declared no conflicts of interest.

**A390 United European Gastroenterology Journal 5 (S5)**
offer an accurate measure of dietary compliance. Presence of gluten related sub-
stances in faeces may falsely suggest that transit through gastrointestinal tract happened and 
confirms gluten ingestion.

**Aims & Methods:** Detection of gluten immunogenic peptides (GIP) in stools as a marker of GFD adherence in CD paediatric patients was evaluated and compared against traditional methods of GFD monitoring. A prospective, non-randomized, multi-centre follow-up study, 2 years long, including 64 CD patients started on GFD when diagnosed (age range 9–18 years). Fecal GIP was quantified by enzyme-linked immunosorbent assay (ELISA). Anti-tissue transglutaminase (anti-TTG) IgA and anti-deamidated gliadin peptide (anti-DGP) IgA antibodies were measured simultaneously, during basal and follow-up visits at 6, 12, 6 and 24 months. Correlations between fecal GIP and serum antibodies were established by Cochran’s and Friedman tests.

**Results:** 62 patients (97%) had detectable GIP levels in stools, during basal visit, before initiation of the GFD, whereas 20.3% of the patients were found to have positive GIP after treated with a GFD. Dietary transgressions were more frequent in the first 6 months of starting GFD. 11% of them showed more than one detected transgression. Anti-TTG IgA remained in high concentrations in 48, 34 and 20% of the patients at 6, 12 and 24 months of follow-up. Anti-DGP was positive in 13, 4.5 and 0% of cases when tested at 6, 12 and 24 months follow-up. Both serological methods did not correlate with GIP in stools (P < 0.05).

**Conclusion:** The GIP ELISA enabled direct and quantitative assessment of gluten exposure early after ingestion. Detection of GIP in stools revealed lack of trau-

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P0652 CLINICAL SIGNIFICANCE OF TRANSFORMING GROWTH FACTOR - β1 AND TUMOR NECROSIS FACTOR - C IN CHILDREN WITH FOOD PROTEIN INDUCED ENTEROCOLITIS SYNDROME

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Introduction: Nowadays food allergy continues to increase, especially in western countries and is now recognized as a worldwide problem. Transforming growth factor-β1 (TGF-β1) is a profibrotic cytokine, which plays an important role in promoting the structural changes in food allergy. Also for patients with food protein - induced enterocolitis syndrome TNF-α appears to have an important role.

Aims & Methods: The aim was to determine the significance of the Transforming Growth Factor - β1[TGF – β1] and Tumor Necrosis Factor – α (TNF – α) in children with food protein induced enterocolitis syndrome. It was examined 38 patients with FPIES at the age from 4 months to 3 years, the average age was 19 ± 4 months. The control group consisted of 11 healthy children of the same age. The determination of TGF-β1 and TNF-α in serum was performed by an enzyme immunoassay kits from Bender MedSystem (Austria).

Results: The level of TGF-β1 in patients with FPIES exceeded the norm and was respectively 33.5 ± 1.6 ng/ml, at norm 20.2 ± 2.1 ng/ml, p < 0.001. The indices of TNF-α were also increased and amounted to 8.8 ± 1.3 ng/ml in comparison with the control group, p < 0.001. For comparison, it was characterized by an increase in specific antibodies IgE to cow’s milk in 18 (47.3%) children. In these cases disease was more severely with vivid clinical manifestations (indomitable increase in specific antibodies IgE to cow’s milk in 18 (47.3%) children. It is likely that an increase in TNF-α level was significantly higher than in the control group, amounting to 42, 01 ± 7.5 ng/ml. TNF-α indicators were also increased: 11 ± 2.1 ng/ml.

Conclusion: It is believed that TGF – β1 promotes allergic inflammation, but in our observations its increase in its values was established, especially the case of children with high specific IgE levels to cow’s milk. It is likely that an increase in TGF – β1 stimulates the release of TNF – α, which supports chronic inflammation in allergic diseases.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P0653 THE ROLE OF GST1 & GSTM1 GENE POLYMORPHISMS IN NEWBORNS’ OBESITY RISK

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Introduction: Newborns’ birth weight is influenced by maternal factors (mother’s weight at the onset of pregnancy, gestational weight gain - GWG), genetic, obstetrical and environmental factors, but also socio-economic ones. Excessive GWG, mother’s increased BMI and the adipose tissue mass determine a bigger birth weight and increase the risk of newborns’ obesity. Glutathione S-transferases (GSTs) is an oxidative stress-related gene which is associated with androst interactions.

Aims & Methods: The aim of the study was to investigate the role of mother-child GST1 and GSTM1 polymorphisms as independent risk factors for newborns’ weight, but also to establish correlations between these polymorphisms and anthropometrical parameters, and bioimpedance (BIA) ones, respectively. We assessed the anthropometrical parameters in both mothers and their newborns (BMI- body mass index, MUAC – medium upper arm circumference, TST – tricipital skin thickness, weight - W), BIA parameters in mothers, but we also determined the clinical, paraclinical and genetic parameters in both mothers and newborns.

Methods: We performed a cross-sectional study on 202 mothers and their newborns in a Clinic of Neonatology & Gynecology and Obstetrics from Romania. Results: We noticed that in newborns with W > 3000 gr there was a significant statistically correlation between weight and mother’s GST1 polymorphism (p = 0.046), birth at term (p < 0.001), with mother’s percentage of fat mass assessed by BIA (p < 0.001), and multi parity, respectively (p < 0.001). We obtained a tendency towards correlations between W > 3000 gr and basal metabolism rate (p = 0.086), and GWG seemed to be a protective factor for this W (p = 0.072). We also found that GSTM1 in newborns was a risk factor with tendency towards statistical significance in newborns with increased birth weight. We did not find any interaction effect between newborns’ and mothers’ GST1 polymorphisms and anthropometrical parameters (p = 0.545 for newborns’ clinical parameters).

Conclusion: Mother’s GSTM1 is an independent risk factor for newborns’ W > 3000 gr, while mother’s GWG seems to be a protective factor for W > 3000 gr. Further studies are needed in order to determine the clear role of the polymorphisms in newborns’ obesity risk. This research was supported by the Research Grants of the University of Medicine and Pharmacy Tirgu Mures, Romania - “The role of genetic determinism of the mother in child’s obesity correlated with measurements of bioimpedance and anthropometry” no.275/4/11.01.2017.

Disclosure of Interest: All authors have declared no conflicts of interest.

References


**P0655 GENETIC PREDISPOSITION TO PRIMARY LACTOSE INTOLERANCE AND ITS INFLUENCE ON CHILDREN'S QUALITY OF LIFE AND DAIRY INTAKE**

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**Introduction:** Primary lactose intolerance (PLI) is a frequent condition caused by a genetically programmed and progressive loss of lactase expression. It is considered that PLI is the ancestral variant, while lactase persistence is caused by 2 polymorphisms: the dominant C/T13910 and G/A22018. Homozygotes (CC or GG) have undetectable lactase levels. In clinical practice only half of people with PLI have symptoms. However, some studies showed that PLI subjects have lower dairy intake.

**Aims & Methods:** To investigate whether genetical predisposition to PLI influences the quality of life and dairy intake in a group of Romanian children. We conducted a prospective study, recruiting consecutive children evaluated in our unit in May-August 2016. Our study population included 87 children aged 6–17 years (mean age 10.64 ± 3.51 years), 45 (51.72%) girls. We used strip genotyping to identify key genetic determinant to PLI. Subjects were asked to complete a validated quality of life questionnaire and a dairy intake questionnaire. We used Spearman's test to evaluate the correlation between IPL and quality of life and dairy intake.

**Results:** (51.7%) subjects had a CC genotype. 30 (34.5%) subjects had a GG genotype. Our results were consistent with Hardy-Weinberg equilibrium. We found no correlation between homozygosity for PLI and dairy intake (CC: r = 0.11, p = 0.34). There was evident tendency to be lower in patients with more extent steatosis (grade 2 and 3) compared to those without or with mild steatosis (grade 0 and 1) (p = 0.049). However, ROC analysis showed poor discriminant power for FGF21 serum level in differentiation between more and less extensive steatosis with AUC = 0.666. There was evident tendency to higher levels of hepatic FGF21 mRNA in patients with lobular inflammation and fibrosis, and to lower levels in the case of ballooning degeneration and steatosis. There was positive mutual correlation between hepatic FGF21 and omentin-1 mRNA levels (r = 0.73, p < 0.001). Fibrosis stage was associated with serum glucose and HOMA-IR (p = 0.03 and p = 0.02, respectively). Serum omentin was not associated with histopathological features. Hepatic omentin-1 mRNA levels exerted the tendency to be lower in patients with advanced steatosis and hepatocyte ballooning.

**Conclusion:** In conclusion our study, which focused on hepatic FGF21 and omentin-1 mRNA expression, confirmed a marked expression of both molecules in the liver of morbidly obese patients with NAFLD. mRNA levels were affected by clinical and pathological abnormalities. More extent steatosis was associated with evident change in serum FGF21 concentration in morbidly obese women with NAFLD. The vast amount of fat, both visceral and subcutaneous in severely obese patients may affect FGF21 and omentin-1 serum levels. **Disclosure of Interest:** All authors have declared no conflicts of interest.

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**P0658 LOUREIRIN B INHIBITS THE PROLIFERATION OF HEPATOCYTE STELLATE CELLS VIA DOWN-REGULATING FRIZZLED-7**

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**Introduction:** Liver fibrosis is the result of repeated healing repair and interstitial reconstruction after chronic liver injury. Activation of hepatic stellate cells represents a critical event in fibrosis because these cells become the primary source of extracellular matrix in liver upon injury. Inhibiting HSCs' activation, proliferation, extracellular matrix production and promoting HSCs' apoptosis are the important therapeutic approaches of liver fibrosis.

**Aims & Methods:** We aimed to investigate the anti-liver fibrosis ability of lourierin B and the molecular mechanisms involved it. After hepatic stellate cells controlling liver fibrogenesis. Its role in a liver fibrosis scenario needs to be further investigated.

**Disclosure of Interest:** All authors have declared no conflicts of interest.
(HSCs), which were separated from Sprague-Dawley rat, were treated with dif- fering concentrations of Loureirin B, MTX such of steatohapatitis.

HSCs proliferation, western blot were used to test the expressions of Frizzled-4 receptor protein and α-SMA. In addition, enzyme-linked immunosorbent assay (ELISA) was performed to measure the content of α-SMA, TGF-β1 and VEGF in the treated HSCs’ supernatant, and reverse-transcription PCR (RT-PCR) were utilized to detect the expressions of Frizzled-4 and α-SMA genes.

Results: MTX test showed that the proliferation of HSCs was inhibited significantly with a time and dose dependent relationship by the treatment of Loureirin B at 1.0 μM, and the inhibitory concentrations of 11.80±0.53 % (IC50 = 0.180±0.08 μg/mL). Western blot analysis showed that the expressions of Wnt receptor Frizzled-4 protein and α-SMA were obviously lower in the group of Loureirin B treatment than that in the control group. Moreover, the Loureirin B allele (GC/TG) 0.01, TGFβ1 (p = 0.05) secretion in the cultured HSCs’ supernatant in different degree by the ELISA assay, and RT-PCR results revealed that Loureirin B down-regulated the expressions of Frizzled-4 and α-SMA genes in the level of mRNA.

Conclusion: CONCLUSIONS: The Loureirin B mediated anti-hepatic fibrosis by inhibiting the proliferation of HSCs through restraining the Wnt signaling pathway.

Disclosure of Interest: All authors have declared no conflicts of interest.

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P0659 MACROPHAGE CONTRIBUTES TO STEATOHAPATITIS THROUGH MEDIATING INFLAMMATORY CYTOKINES, AUTOPHAGY AND THE CROSSTALK WITH HEPATOCYTES J.K.C. Lau1, X. Zhang2, E.S. Chu2, J. Yu2
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Introduction: Macrophages play a pivotal role in the pathogenesis of non-alco-
holic steatohepatitis (NASH) and are a major component of inflammatory cells
infiltrated in NASH. However, the precise mechanism by which macrophages contribute to the pathogenesis of NASH remains unexplored.

Aims & Methods: We aimed to characterize the role and molecular regulators of macrophages in NASH and the therapeutic effects of macrophage depletion on NASH. C57BL/6 wildtype (WT) mice and transgenic LysM-Cre:DTI mice were fed a high-fat diet and a high lipid diet for 5 weeks. The liver tissue was collected for RNASeq analysis. Hepatocytes were isolated from the liver by collagenase digestion and cultured with selected derivatives efficiently prevented FFA-induced cell death and lipid accumulation. Pre-incubation of HepG2 cells with BA derivatives co-incubated with oleic and palmitic acids (2:1) for assessment of cellular cytotoxicity and intracellular lipid accumulation.

Results: From the compound library, five BA derivatives showed stronger activation of FXR, similar with their natural precursors. Incubation of HepG2 cells with FAs led to a ~25% reduction in cell viability and ~55% increase in cell death, with a dose-dependent accumulation of lipid droplets. Pre-incubation of cells with selected derivatives efficiently prevented FFA-induced cell death and lipid accumulation. Finally, incubation of both HepG2 cells and primary mouse hepatocytes with BA derivatives strongly increased FXR, RXR, SHP, BSEP, FGFl9 and VLDLR mRNA levels, and repressed PARP1, LXR, SREBP1-c and CYP7a1 mRNA expression. Molecular docking studies and FXR reporter assays confirmed ligand affinity to FXR. Furthermore, chenodeoxycholic acid (CDCA) co-incubation and CYP-based derivatives were identified as activators of FXR at lower concentra-
tions comparing with the parent molecule.

Conclusion: In conclusion, we identified novel BA derivatives that directly mod-
ulate liver nuclear receptors, such as Fxr and Lxr, thus protecting liver cells from steatosis. Our results showed that CDCA co-incubation and CYP-based derivatives were identified as activators of Fxr at lower concentra-
tions comparing with the parent molecule.

Disclosure of Interest: All authors have declared no conflicts of interest.

(Supported by PTDC/BIM-MEC/0995/2014, SFRH/BD/110672/2015, and SFRH/BD/89975/2011, FCT, Portugal).

P0660 NEWLY SYNTHESIZED BILE ACID DERIVATIVES PREVENT LIVER STEATOSIS IN VITRO THROUGH TARGETING OF NRI SUBFAMILY NUCLEAR RECEPTORS H.M.D.S. Brito1, M. Batista2, M. Silva2, J. Salvador2, R. E. Castro1, C.M.P. Rodrigues1
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Introduction: Non-alcoholic fatty liver disease (NAFLD) is considered the hepa-
tic manifestation of metabolic syndrome, with simple liver steatosis being capable of gradually progressing to inflammation, fibrosis, cirrhosis and even hepatocellu-
lar carcinoma. Still, disease pathogenesis is complex and no targeted therapies have yet been approved for NAFLD. Bile acids (BAs) constitute a wide class of steroid molecules with pleiotropic functions, contributing to the homeostasis of lipids and glucose. In the liver, they specifically modulate nuclear receptors from the NRI subfamily, such as Farnesoid X Receptor (FXR) and Liver X Receptor (LXR), thus tightly regulating bile acid synthesis and oxidation and storage of triglycerides.

Aims & Methods: Our aim was to screen BA derivatives for their potential to selectively activate Fxr, thus protecting liver cells against free fatty acid (FFA)-
induced lipid accumulation and lipotoxicity. Nineteen novel BA derivatives were analyzed in silico molecular docking studies for Fxr and Lxr, and further evaluated in human cells using a FXR reporter assay. Assessment of Fxr-depend-
tent gene and protein expression was analyzed upon incubation of primary mouse hepatocytes and HepG2 cells with selected BA derivatives. In parallel, BA derivatives were co-incubated with oleic and palmitic acids (2:1) for assess-
ment of cellular cytotoxicity and intracellular lipid accumulation.

Results: From the compound library, five BA derivatives showed stronger activa-
tion of Fxr, with similar efficacy as their natural precursors. Incubation of HepG2 cells with FAs led to a ~25% reduction in cell viability and ~55% increase in cell death, with a dose-dependent accumulation of lipid droplets. Pre-incubation of cells with selected derivatives efficiently prevented FFA-induced cell death and lipid accumulation. Finally, incubation of both HepG2 cells and primary mouse hepatocytes with BA derivatives strongly increased FXR, RXR, SHP, BSEP, FGFl9 and VLDLR mRNA levels, and repressed PARP1, LXR, SREBP1-c and CYP7a1 mRNA expression. Molecular docking studies and FXR reporter assays confirmed ligand affinity to Fxr. Furthermore, chenodeoxycholic acid (CDCA) co-incubation and CYP-based derivatives were identified as activators of Fxr at lower concentra-
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tions comparing with the parent molecule.

Disclosure of Interest: All authors have declared no conflicts of interest.

(Supported by PTDC/BIM-MEC/0995/2014, SFRH/BD/110672/2015, and SFRH/BD/89975/2011, FCT, Portugal).
alone and in combination with 100 mM Bafilomycin and 2 mM Caffeine. RT-qPCR was performed and also real time fluorescence monitoring of HepG2 cells stably expressing ectopic MAP1LC3B-GFP-RFP-tag was performed with Incucyte.

**Results:** FLS-ob/ob mice, representing a NASH mouse model, showed an over-expression of the autophagy markers Becn1, Map1lc3b, Uvrag and Tfeb, Prkaa1_1 and Prkaa2_1 in comparison with FLS mice that represent the NAFL model. Furthermore, the protein level of Becn1 and Map1lc3b was down-regulated in FLS-ob/ob mice, whereas SQSTM and UVRAG were up-regulated. Interestingly, the phosphorylation of AMPK and AKT was found up-regulated in FLS-ob/ob mice, while FLS mice did not show a significant phosphorylation of P-AMPK. AMPK was found stably expressed in both FLS-ob/ob and FLS mice. HepG2 cells treated with oleic acid showed a down-regulation of Becn1, Map1lc3b, UVRAG and SQSTM2 proteins. AMPK and its phosphorylated form remained unvaried. Interestingly, Caffeine treatment caused a stronger reduction of autophagy markers, including the reduction of P-AMPK. The combination of Caffeine and oleic acid caused a stronger suppression of autophagy markers protein level. Bafilomycin caused a reduction of MAP1LC3B and UVRAG only. Its combination with OA caused a stronger reduction of protein level. HepG2 MAP1LC3B-GFP-RFP showed an increase of red fluorescence after 48 h of treatment with 2 mM OA.

**Conclusion:** Autophagy mechanism is significantly activated in FLS-ob/ob mice, leading to an increase of red fluorescence after 48 h of treatment with 2 mM OA.

**P0662 MODULATION OF MITOCHONDRIAL DYNAMICS BY MIRNAS IN NAFLD**

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**Introduction:** Non-alcoholic fatty liver disease (NAFLD) pathogenesis associates with intracellular lipid accumulation in the liver. In addition, recent evidence supports a functional role for both mitochondrial dysfunction and microRNAs (miRNA/miRs) in NAFLD pathogenesis. In particular, deregulation of mitochondrial dynamics proteins, like mitofusin-2 (Mfn2) is frequently observed in obese and diabetic patients.

**Aims & Methods:** Our aims were to profile global liver mRNA expression changes during NAFLD progression and correlate them with the development of liver steatohepatitis. Expression of mitochondrial and human NAFLD, C57BL6 mice were fed either a standard or a fast food (FF) diet for 25 weeks; or a methionine- and choline-deficient (MCD) diet for 2 and 8 weeks. miRNA profiling was performed using liver RNA from 8 weeks MCD-fed mice, in TqMan MicroRNA arrays. qPCR array data was analyzed using the HTqPCR package in Bioconductor. Liver biopsies were obtained from patients with simple steatosis or NAFLD. mRNA and protein expressions were analyzed by qRT-PCR and immunoblotting, respectively. miRNA targeting was evaluated by dual-luciferase reporter assays.

**Results:** Both FF- and MCD-fed mice developed NAFLD-like features, including liver steatosis, inflammation and insulin resistance; as well as progressive steatohepatitis, severe liver damage and fibrosis. Strikingly, liver Mfn2 protein levels significantly decreased in both models (p < 0.05). Inversely, expression of Drp1, a mitochondrial fission protein, was found increased (p < 0.05). Other mitochondrial proteins, such as the voltage-dependent anion channel (VDAC), presented no expression changes. In human patients, Mfn2 protein levels decreased from steatosis to NASH (p < 0.05). Microarray profiling indicated that liver miRNAs are significantly modulated during NAFLD progression. Specifically, 25 miRNAs were found significantly increased in the liver of MCD-fed mice, while, inversely, 27 miRNAs were decreased. Curiously, in silico analysis revealed that several of the up-regulated miRNAs could target Mfn2 in at least, one Mfn2 3’UTR binding site. Binding of miRNAs to Mfn-2, including mir-34a, was validated in HepG2 cells using a dual-luciferase reporter vector containing the Mfn2 3’UTR. Finally, overexpression of mir-34a in C212 muscle cells lead to Mfn2 inhibition and insulin resistance (p < 0.05).

**Conclusion:** In conclusion, mitochondrial dysfunction, particularly downregulation of Mfn2, plays a key role in human and experimental NAFLD and is targeted by miRNA/miRs such as mir-34a. A better understanding of the potential role of miRNAs targeting mitochondrial proteins during NAFLD may help in the development of novel targeted therapies for metabolic diseases associated with mitochondrial dysfunctions. (Supported by PTDC/BIM-MEC/0989/2014, STREP-651404/2010, FCT, PT and Gilead Sciences International Research Scholars Program 2015).

**Disclosure of Interest:** All authors have declared no conflicts of interest.
mononuclear layer containing stem cells is a novel approach for regeneration of liver cells. However, this therapeutic option is not currently approved and requires repeated PBMC transplantation.

Aims & Methods: To determine the outcome after intrasplenic or intrahepatic injection of autologous bone marrow stem cells (ABMSC) transplantation in patients with liver cell failure secondary to chronic hepatitis C infection. Sixty chronic hepatitis C patients with liver cell failure were prospectively enrolled. They were classified into 3 groups; group I: 20 patients underwent (ABMSC) injected intrasplenic. Group II: consisted of 20 patients underwent (ABMSC) injected intra hepatic (right portal branch). Group III: Control Group, consisted of 20 patients treated with their conventional medical therapy. The aim of this study was to determine how much impact the risk factors of metabolic syndrome has on ultrasoundographic fatty liver, especially NAFLD.

Results: Our study included 60 patients (78.33% males) with mean age ±SD (49.9 ± 6 years). Patients who had ABMSC injection showed improvement in clinical parameters as bleeding tendency, ascites, lower limb edema and hepatic encephalopathy. There was statistically significant improvement in serum albumin, ascites, lower limb edema and hepatic encephalopathy. There was improvement in serum albumin, ascites, lower limb edema, bleeding tendency and physical activity. Also there was improvement in MELD score and performance status. Additionally, there was recovery of platelets count. The improvement in biochemical parameters as bleeding tendency, ascites, lower limb edema and hepatic encephalopathy were expressed as percentage ratios. Statistical analysis was done by Wilcoxon signed-rank test using Statistica v.12 software. p value ≤ 0.05 was considered significant. Females gender (OR-1.78, p < 0.001) and unhealthy eating (p < 0.001) were associated with prevalent CO. Inadequate physical activity was not associated with either. 2137(72%) attended follow-up in 2014. Of those who were initially non-obese who attended follow-up, 189(64.9%) had developed GO (annual-incidence 2.27%, p < 0.001) and 206/947(21.9%) [56.3% women] had developed CO (annual incidence 3.12%) after 7 years. TBF and VFP significantly correlated with incident GO and CO (p < 0.001). Females gender (OR-1.8, p < 0.001; 2.81, p < 0.001) and NAFLD (OR-2.93, p < 0.001) independently predicted incident GO and CO respectively.

Conclusion: The prevalence and incidence of GO and CO were high in this cohort. Both incident GO and CO were associated with female gender and

Blood biochemical data in patients with alcoholic liver cirrhosis. However, effect of this therapeutic option is not currently approved and requires repeated PBMC transplantation.

Disclosure of Interest: All authors have declared no conflicts of interest.

In vitro, the proliferation of BPA-exposed HepG2 cells at two different concentrations (0.025 and 0.05 μM) was evaluated, both at high (H-HepG2), in order to simulate human hyperglycemia, and at low (L-HepG2) glucose concentrations, for better-replicating periporatorium conditions experienced by T2DM patients.

Results: BPA levels were significantly higher in 60 NAFLD subjects, both in urine and in plasma (p < 0.0001) if compared to controls and, among this group, it appeared to be higher in 30 non-alcoholic steatohepatitis (NASH) patients compared to 30 simple steatosis (NAFL) ones (p < 0.05), independently from the presence of T2DM. After following a BPA-free diet for one month, NAFLD patients showed a significant reduction of BPA circulating levels (p < 0.05) without a significant reduction of urine levels, which represents the only way to eliminate BPA amount released into circulation by the adipose BPA reservoir. In fact subjects with a higher fat percentage in body composition showed higher BPA levels in plasma and urine. In our population study, NASH patients showed a higher fat percentage in body composition in comparison to NAFL ones. Only H-HepG2 cells treated with the BPA amount released in urine showed higher proliferation compared to controls at 48 h (p < 0.0001). Moreover, BPA increased TBARS levels at 48 h in H-HepG2 cells versus controls.

Conclusion: Our study reveals a possible role of BPA as an environmental factor influencing the progression of NAFLD, particularly in obese and/or T2DM patients.

Disclosure of Interest: All authors have declared no conflicts of interest.
P0671 SERUM THYROID STIMULATING HORMONE IS INDEPENDENTLY ASSOCIATED WITH HEPATIC STEATOSIS AND STEATOHEPATITIS IN EUTHYROID SUBJECTS

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Introduction: Non-alcoholic fatty liver disease (NAFLD) is a rapidly growing disease worldwide. The pathogenesis of NAFLD is not well recognized. Thyroid is totally involved in regulation of lipid and carbohydrate metabolism, body weight, and energy homeostasis. Therefore, the role of thyroid hormones in pathogenesis of hepatic steatosis is anticipated.

Aims & Methods: This study aimed to investigate thyroid hormone abnormalities in euthyroid subjects with hepatic steatosis. A cross-sectional study was conducted between September 2012 and September 2015 at Namazi hospital, Shiraz, Iran. Study subjects were healthy individuals who had undergone liver biopsy. In liver histology, liver histology was categorized into steatosis 2500C > T and a nontumor pretransplant checkup before living related liver transplantation. Liver function tests, age, gender, weight, height, fasting plasma glucose, thyroid hormones, and lipid profile were recorded. Liver biopsy specimens were reviewed by an expert pathologist for steatohepatitis and steatosis. Individuals with a history of chronic liver disease, hepatitis B or C infection, hepatitis-biliary cancers, those with >20 grams/day alcohol consumption, and individuals receiving medications causing hepatic steatosis were excluded from the study.

Results: A total of 210 individuals (130 women and 80 men) were included. Seventy six individuals (36.19 %) had hepatic steatosis and 19 individuals had hepatic steatosis were excluded from the study.

<table>
<thead>
<tr>
<th>Odds Ratio (OR)</th>
<th>95% Confidence Interval (CI)</th>
<th>P-Value</th>
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<tr>
<td><strong>Weight</strong></td>
<td></td>
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<tr>
<td>1.05</td>
<td>0.96–1.16</td>
<td>0.245</td>
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<tr>
<td><strong>Triglyceride</strong></td>
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<tr>
<td>1</td>
<td>0.98–1.01</td>
<td>0.989</td>
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<tr>
<td><strong>ALT</strong></td>
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<td>1.007</td>
<td>0.93–1.08</td>
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<td><strong>TSH</strong></td>
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<td>2.11</td>
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Conclusion: Higher serum TSH is associated with hepatic steatosis and steatohepatitis in euthyroid subjects. Thyroid hormones may have crucial role in hepatic steatosis and may be targeted for treatment of NAFLD patients.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

P0673 DIFFERENCES BETWEEN BY-PASS AND SLEEVE GASTRECTOMY ON CLINICAL AND LABORATORY STATUS 6 AND 12 MONTHS AFTER INTERVENTION IN BARIATRIC SUBJECTS

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Introduction: In patients with morbid obesity, dietary treatment and physical activity are the first line of treatment, but if not responding, bariatric surgery is a properly validated alternative. The main surgical procedures are sleeve gastrectomy (SG) and gastric bypass (GBP), and they are chosen in function of BMI, age and comorbidity. Both techniques have proven effective in weight loss. It is known that liver fibrosis evaluation with Point Shear Wave Elastography (pSWE) is difficult in these patients.

Aims & Methods: To study the difference between SG and GB and their impact on main clinical and laboratory hepatic metabolic indicators and scores 6 and 12 months after the intervention and pSWE at 12 months. We studied 68 obese subject candidate to bariatric surgery (45 female, 23 male). 28 underwent GBP and 40 GB. Blood tests, physical examination were assessed before surgery, after 6 months (68 patients) and after 12 months (51 patients) and pSWE after 12 months.

Results: In the comparison between GBP vs SG there was a statistically significant difference in the reduction in Fatty Liver Index (61% vs 37%, p = 0.015), waist circumference (26% vs 18%, p = 0.045), BMI (34% vs 28%, p = 0.016), total cholesterol (23% vs 0.05%, p = 0.001), ALT (increased by 15% in GBP, decreased by 27% in SG, p = 0.023) while no differences were observed in the other indicators considered. Ferritin level increased (52%) in SG and decreased (25%) in GBP (p = 0.02). No difference was observed for pSWE.

Conclusion: This study showed some significant differences in clinical and laboratory terms between the two types of intervention, in fact GBP seems to have a more powerful effect on weight loss and all related markers: all steatosis scores (FLI, HSI, LAPI), BMI, waist circumference. This can be explained by better malabsorptive effect of this intervention and by a lower BMI starting point for reasons related to the intervention technique.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

with use of anti-diabetic agents and the absence of highly fatty pancreas, indicating its potential protective role. Simple new noninvasive scoring system was designed from multivariate logistic regression analysis to estimate the occurrence of severely FP in NAFLD with best ability in the prediction in score values above 6.5.

Disclosure of Interest: All authors have declared no conflicts of interest.

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Introduction: Glucosidase II is part of the functional pathway of co-translational protein translocation and maturation in the endoplasmic reticulum. It is implicated in autosomal dominant polycystic liver disease (ADPLD) and autosomal dominant polycystic kidney disease (ADPKD). The Φ-subunit of glucosidase II, encoded by PRKCSH, has been identified as one of the causative genes of ADPLD. Recent data suggest that the Φ-subunit of glucosidase II (ΦΓ), encoded by GANAB, is associated with ADPKD and ADPLD. We aimed to identify GANAB mutations in an independent cohort of patients with the primary phenotype of polycystic liver disease (PLD) and to predict the influence of these mutations on glucosidase II function.

Aims & Methods: We identified genetic mutations in GANAB using molecular inversion probe (MIP) analysis in a cohort of PLD patients. Both patients with ADPKD and ADPLD were included for analysis. Mutations identified with MIP analysis were validated using Sanger sequencing. Bioinformatics prediction tools (PolyPhen-2, Align GVGD, SIFT, MutationTaster) were used to predict the functional significance of the mutations. YASARA&WHAT IF were used for analysis of the structural effects of the mutations. Primary cholangiocytes obtained from a patient with GANAB mutation (c.2515C > T) were used to study loss of heterozygosity.

Results: We identified and validated 6 new bona fide GANAB mutations in 7 unrelated families. These are 2 frameshift (c.687delT and c.11_16delTAGGG), 1 splicing (c.2691-28C > G), 2 nonsense (c.2509C > T and c.11_16delTAGGG, and 1 missense (c.1835G > C) mutation. In silico analysis showed c.687delT and c.11_16delTAGGG are located in N-terminal domain of the protein. These mutations probably lead to a total defective protein, c.1835G > C is located in the active site of the protein. It is predicted to disrupt the composition of the active site and reduce enzymatic activity. The remaining mutations (c.2691-28C > G, c.2509C > T) are located in catalytic C-terminal domain, which interacts with PRKCSH. The mutations could result in early termination of this domain. It is speculated this disrupts the ability of the two subunits to interact. Western Blot showed no differences in Glhase expression in an ADPKD patient with GANAB mutation c.2515C > T compared to primary cholangiocytes obtained from a patient without PLD. This indicates in this patient no loss of heterozygosity occurs in cholangiocytes lining the hepatic cysts.

Conclusion: We describe six novel GANAB mutations that can cause PLD in a mixed population of ADPKD and ADPLD patients. These mutations are found in functionally important domains of Φ-subunit of glucosidase II, which may lead to impaired enzymatic activity of the complex. In contrast to other PLD related genes no loss of heterozygosity was found for GANAB in cyst epithelium.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
J Clin Endocrinol Metab 2016;101(8):3204–11

Aims & Methods: We included 95 patients with NAFLD, from which 53 were with MS and 42 without MS.

Results: Out of a total 1674 patients in the PLD registry, 1222 patients (1110 ADPKD, 112 ADPLD) could be selected. In the ADPKD group, height adjusted total liver volume was measured prior to liver reducing therapy. Liver reducing therapy was typically reported using semi-quantitative scores. Inter- and intra-observer variability in the current scoring systems may impact upon histological staging, and consequently upon the interpretation of responses to interventions in clinical trials.

Conclusion: We developed an automated method for steatosis and fibrosis quantification using biopsies of NAFLD patients. We further validated Liver Stiffness Measurements (LSM) and controlled attenuation parameter (CAP) in this group, using quantitative assessment as reference. 246 consecutive patients with biopsy-confirmed NAFLD and transient elastography within 3 months of the biopsy were evaluated. Biopsies were independently scored by two histopathologists and digitalised at 2x magnification. Areas of steatosis and fibrosis were annotated manually using the NDP.view2 to facilitate machine learning. Each image was then analysed by the automated software: fat percentage (fat%) and collagen Proportionate Area (CPA) computed by the software were compared with the manual annotation. They were also correlated with LSM and CAP.

Disclose of Interest: All authors have declared no conflicts of interest.

Disclosure of Interest: All authors have declared no conflicts of interest.

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Introduction: Today, non-alcoholic fatty liver disease (NAFLD) is the most prevalent form of liver disease and it is an increasingly frequent cause of cirrhosis. Although several factors have been associated with the disease, the biological basis of the histological diversity of severity of NAFLD remains unknown. Several relatively noninvasive parameters have been identified as predictive for advanced fibrosis stage in patients with NAFLD, but none of them has sufficient sensitivity or specificity to replace liver biopsy.

Disclosure of Interest: All authors have declared no conflicts of interest.

Contact E-mail Address: d.neagoa2014@gmail.com

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Aims & Methods: Aim of our study was to compare two non-invasive methods: fibrosis score on serum markers and transient elastography (TE). We included 152 patients with NAFLD, 40 males (26.31%) and 112 females with age from 23 to 79 years.35 patients (23.02%) were overweight, 9 patients had normal weight and 24 (15.79%) had severe obesity. In all patients we calculated BMI and fibrosis scores: BARD, FIB-4 and NAFLD FIBrosis score (NAFLD-FS). Blood samples were collected to determinate aminotransferases, glucose, albumin level, platelet count. The abdominal ultrasonography was performed by the same physician and steatosis was graded using a semi-quantitative scale from 0 to 3. TE was also performed by a single physician using conventional M probe or XL probe, with 10 valid acquisitions. We considered significant fibrosis (F2) when estimated cutoff of F2 was 7.1 kPa, severe fibrosis (F3) when cutoff value was 9.5 kPa, and cirrhosis (F4) with cutoff value conventional M probe or XL probe, with 10 valid acquisitions. We considered significant fibrosis (F2) when cutoff value was 9.5 kPa, and cirrhosis (F4) with cutoff value 10.09 kPa.

Results: 86.84% patients had metabolic syndrome and 51.31% had diabetes mellitus.40 patients had mild steatosis, 59 had moderate and 53 had severe steatosis. After we performed TE 69.07% of patients had no significant fibrosis, 14.47% had F2, 9.86% had F3 and 7.23% had F4. The area under the receiver-operating characteristic curve (AUROC) of TE was 0.823 (95%, 0.252–0.394) (p < 0.0001). Sensibility and specificity for cutoff 7.1 kPa was 0.74 respectively 0.79 to exclude significant fibrosis. NAFLD-FS correlated statistically significant with TE (p < 0.0001); BARD score did not correlate with TE and NAFLD-FS for significant fibrosis FIB-4 correlated with TE for high degree fibrosis (p = 0.004).

Conclusion: NAFLD-FS, FIB-4 and TE can be used together to evaluate the progression of fibrosis in NAFLD and to select the patients for liver biopsy. In our study BARD score was not useful in detection of high degree fibrosis.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0678 EFFECTS OF UDCA AND STATIN COMBINATIONS ON LIPID PROFILE IN NAFLD PATIENTS
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Introduction: Dyslipidemia has an important role in NAFLD and inflammation progress and insulin resistance development. The studies suggested the role of UDCA in lipid profile correction. UDCA replaced bile acid balance and improved triglyceride and cholesterol levels in NAFLD patients, has immunomodulatory action.

Aims & Methods: The aim of study was estimation of the efficacy of different dosage of ursoodeoxycholic acid (UDCA) with statin combination treatment in patients with NASH and NAFLD. There are 180 patients with NAFLD. It was divided into two subgroups: fatty liver (90 subjects) – patients with normal level of ALT, and nonalcoholic steatohepatitis (NASH, 90 subjects) – patients with elevated level of ALT (the median is 78.5 U/l). All patients were divided in 3 groups. The blood test, liver enzymes, lipid profile, HOMA-IR, Fibroscan and stool test was checked every 2 weeks of treatment. First group was taken UDCA 10 mg/kg/day + Statin. Second group was taken UDCA 15 mg/kg/day + Statin. Third group was fed the low-liquid and low-glucose diet index only (900 kcal/day). After 1 months of treatment patients of third group (diet only) add UDCA 15 mg/kg/day to treatment for 3 months.

Results: The subgroups did not show any difference in terms of initial total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), and triglycerides (TG). Analysis of the lipid spectrum showed a more intense dynamics in the group of patients taken UDCA combined with statin. After 3 months of follow-up there was a significant reduction in TC to 4.2 mmol/l, LDL-C to 1.8 mmol/l and TG to 1.2 mmol/l in the fatty liver subgroup, and TC to 4.1 mmol/l, LDL-C to 1.8 mmol/l and TG to 1.2 mmol/l in the NASH subgroup. Changes were similar in the subgroups. The level of total cholesterol, triglyceride and liver enzymes were decreased faster in group taken UDCA and statin independent from UDCA dosage. There are no side effects or liver enzyme elevation in group treated with UDCA and statins. In the NASH subgroup there was a significant decrease in ALT to 35 U/l. At the end of the first month of statin therapy combined with UDCA in the NASH subgroup a significant positive dynamics of ALT was found in patients with NASH (initially 78.5 U/l; after treatment decrease to 38.5 U/l). Stage of liver fibrosis was significant in patients taken UDCA and statin, as evidenced by the decrease in the index of fibrosis.

Conclusion: 3-month statin therapy in combination with UDCA showed significant lipid-lowering effects in patients with NAFLD, as well as normalization of ALT. In the first 2 weeks, the NASH subgroup had shown a decrease in both ALT and TS. The NASH subgroup had a significant decrease in ALT and in the index of fibrosis.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P0679 EFFECT OF GRANULOCYTE COLONY-STIMULATING FACTOR (G-CSF) ON MORTALITY AND COMPLICATIONS VIZ. SEPSIS, ENCEPHALOPATHY, HEPATORENAL SYNDROME AND GASTROINTESTINAL BLEED IN SEVERE ALCOHOLIC HEPATITIS: A RANDOMIZED CONTROLLED STUDY
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Introduction: Severe alcoholic hepatitis has very high short-term mortality. Compared to standard medical therapy (SMT), GCSF improves clinical and biochemical profiles, morbidity and mortality in these patients. We evaluated efficacy of G-CSF in modulating the disease course of severe alcoholic hepatitis over period of 3 months in terms of mortality, morbidity by Discriminant function (mDF), Child–Turcotte–Pugh (CTP) and Model for End-Stage Liver Disease (MELD) scores and various complications viz. sepsis, GI bleed, encephalopathy, hepatorenal syndrome (HRS) in comparison to SMT. We also studied the mobilising effect of GCSF on bone marrow stem cells measured by CD34+ cells from peripheral blood.

Aims & Methods: The present study was performed to evaluate the safety and efficacy of GCSF on mortality and complications viz. sepsis, encephalopathy, hepatorenal syndrome (HRS) and gastrointestinal bleed (GI Bleed) and also to investigate whether G-CSF therapy could improve the indices of severity of liver disease, such as Discriminant function (mDF), Child–Turcotte–Pugh (CTP), Model for End-Stage Liver Disease (MELD) score in patients with severe alcoholic hepatitis. 50 patients with severe alcoholic hepatitis were randomly assigned to groups A and B (25 in each). Both groups were given SMT, while in addition, patients in group A were given 5µg/kg GCSF subcutaneous (10 doses for 5 days).

Results: The baseline parameters in both groups were comparable. On day 6 group A had higher mean leucocyte and CD34 counts than group B (p < 0.0001). In 90 days follow up 17 patients in group A (68%) and 9 in group B (36%) survived (p = 0.04). Mean changes for different scores were greater in group A then group B i.e. CTP (−41.97% vs −8.84%), MELD (−50.89% vs 10.09%) and mDF (−74% vs 18%) (p < 0.001). The percentages of patients who developed HRS, HLN, or sepsis were lower in group A (28% vs 64%, 32% vs 64%, and 28% vs 68%, respectively) (p < 0.001). There was no significant difference in GI bleed in both groups.

Conclusion: In severe alcoholic hepatitis, GCSF therapy significantly improves the survival. It also significantly reduces CTP, MELD and mDF scores and prevents the development of complications.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0680 ALCOHOLIC LIVER DISEASE/NON ALCOHOLIC FATTY LIVER DISEASE INDEX (ANI): HOW TO DISTINGUISH ALCOHOLIC FROM NON ALCOHOLIC LIVER DISEASE WITHOUT HISTOLOGY
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Introduction: Steatosis/steatohepatitis is one of the most common liver diseases with increasing prevalence and results from excessive alcohol consumption (alcoholic liver disease) or nonalcoholic fatty liver disease (NAFLD). The differential diagnosis is of paramount importance as they have different management and therapeutic approaches, being liver biopsy the gold standard for establishing the diagnosis. The distinction between these two entities without biopsy is...
difficult due to the unreliable history of alcohol consumption and lack of sensi-
tivity of a single marker. In order to overcome these difficulties, a ANI (alcoholic liver disease/nonalcoholic fatty liver disease index) was created for a non-invasive determination of fatty liver diagnosis.

Aims & Methods: The aim of this study was to evaluate the reliability of ANI as a non-invasive diagnostic tool. A retrospective study between 2010 and 2015 in patients with definite diagnosis of NAFLD and ALD based on clinical, biochemical and histological criteria was performed. ANI scoring system in the differentiation of ALD and NAFLD was evaluated through the area under receiver operating curve (AUROC). ANI score was calculated through Mayo Clinic formula.

Results: This study was carried out in 22 patients with ALD and 120 with NAFLD, 87 men (61.3%) with a median age of 51 ± 13 years. NAFLD patients presented a body mass index (BMI) of 29.0 ± 5.9 vs 23.9 ± 6 in ALD. ANI showed a sensitivity of 81% and specificity of 79% for the diagnosis of ALD with a cut-off value of −1.96 [AUROC 0.806 (0.715–0.898), p < 0.001]. ANI greater than −1.96 indicates a diagnosis of ALD whereas ANI less than −1.96 indicates a diagnosis of NAFLD.

Conclusion: ANI scoring system is a non-invasive diagnostic and reliable tool that may be used to distinguish NAFLD from ALD, decreasing the need for liver biopsy. ANI greater than −1.96 suggests the diagnosis of ALD and ANI lesser than −1.96 suggest NAFLD.

Disclosure of Interest: All authors have declared no conflicts of interest.

References:


the CTCAE scale was used. Overweight was detected in 40 patients: BMI = 25–29.9 – in 29 (34.5%), BMI ≥ 30 – in 11 (13.1%) patients. Depending on overweight presence the patients were divided into 2 groups: I (n = 44) – patients with AL with normal body weight, II (n = 40) – patients with AL and overweight.

**Results:** In AL patients of group I before the start of chemotherapy functional liver dysfunction was not significantly different from healthy people. In group II there was an increase of ALT activity in 1.5 times, AST – in 1.2 times, ALP and GGT in 1.4 times compared to the norm (p < 0.05) and reached grade I level, and no change in bilirubin and total protein levels. On the 28th day of treatment in 3 (6.8%) patients of group I the violation of the functional liver state was revealed, which was characterized by the increased activity of ALT in 1.5 times, AST – in 1.2 times, ALP – in 1.3 times, GGT – in 1.5 times compared to normal levels, that consistent with grade I level, the bilirubin and total protein levels remained in the normal range. In group II the hepatocytotoxicity was detected in 19 (47.5%), which was characterized by the increased activity of ALT and AST in 2.3 and in 2.2 times respectively, GGT and ALP in 1.9 and 2.4 times respectively, the level of total bilirubin increased in 2.1 times (p < 0.05), of which in 17 (42.5%) patients hepatopathy of grade I and in 2 (5%) – of grade II level, with no statistically significant changes in protein synthesis liver function. On the 56th day of treatment in 7 (15.9%) patients of group I the violation of the functional liver state was revealed, which was characterized by the increased activity of ALT in 1.8 times, AST – in 1.3 times, ALP – in 1.6 times, GGT – in 1.9 times compared to normal levels, the bilirubin and total protein levels remained in the normal range, that consistent with grade I level. In group II hepatotoxicity was detected in 26 (65%), which was characterized by the increased activity of ALT and AST in 2.6 and in 2.3 times respectively, GGT and ALP in 2.6 and 3.7 times respectively, the level of total bilirubin increased in 3.6 times (p < 0.05), of which in 10 (25%) patients hepatotoxic reactions were of grade I and in 16 (40%) – of grade II level.

**Conclusion:** The presence of the overweight results in a significant increase in the frequency and degree of hepatotoxic reactions in patients with AL during chemotherapy.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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**References**


Abstract No: P0685

P0687 LOW LYSOPOPHOSPHATIDYLCHOLINE LEVELS MAY PREDICT SEVERE ALCOHOLIC HEPATITIS

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Introduction: Severe alcoholic hepatitis (SAH) remains a condition which bears high mortality and morbidity rates, as well as high healthcare costs. This is why adequate selection of patients who would benefit the most from corticotherapy is of utmost importance. Although serum biomarkers are available (Maddrey Discriminant Function - MDF), the diagnostic of SAH relies on liver biopsy. Previous metabolic studies have shown a core metabolic phenotype represented by decreased serum lysophosphatidylcholines (LPC) and increased serum bile acids that occurs relatively early in liver diseases regardless of etiology, and remains stable in their evolution, including liver cirrhosis and hepatocellular carcinoma (1). Our previous work also showed that decreased LPC levels are associated with alcoholic liver disease (ALD).

Aims & Methods: The aim of the study was to assess the metabolic profile of patients with ALD and to identify potential new biomarkers associated with severity. Between December 2015 and September 2016, 64 patients with biopsy proven AH were included (38 with SAH - MDF ≥ 32 and 24 with non-severe AH - MDF < 32). Fasting serum was stored at −80 degrees after centrifugation at 5000 rpm for 10 minutes. Specific purification protocol metabolic analysis was performed using Thermo Scientific UHPLC UltiMate 3000 system, equipped with a Dionex quaternary pump delivery system and a Bruker Daltonics MaXis Impact MS detection equipment (version 2012). Biostatistical analysis The chromatograms obtained were processed using CompassDataAnalysis_4.2 software (Bruker, Germany) and about 3000–4000 molecular masses were identified. Those data were further processed using ProfileAnalysis (Bruker, Daltonics): time alignment, normalization by sum of bucket values in analysis, 80% bucket filter, internal recalibration, etc. The matrix obtained was further processed by MetaboAnalysis, to analyze samples through univariate and multivariate statistical analysis. Results: Univariate and multivariate statistical analysis by MetaboAnalysis identified 10 potential biomarkers. Among them, LPC (18:0) showed good discrimination for SAH (AUROC = 0.804) with significantly lower values as compared with non-severe AH (0.38 fold change, p = 6 × 10−11).

Conclusion: SAH appears to have a different metabolic profile, mainly due to changes in lysophosphatidylcholine metabolism. Targeted metabolic studies are required in order to confirm the results and to evaluate the possible applications in current clinical practice.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference
P0688 APPLICATION OF THE ICA-AKI CRITERIA IN THE DIAGNOSIS OF ACUTE KIDNEY INJURY IN PATIENTS WITH ACUTE DECOMPENSATION OF CIRRHOSIS

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Introduction: Acute kidney injury (AKI) is a common complication in patients with decompensated liver cirrhosis. Recently, the International Club of Ascites (ICA) defined new diagnostic criteria: the ICA-AKI criteria.

Aims & Methods: This study aims to identify patients hospitalized for acute decompensation of cirrhosis with AKI, according to the ICA-AKI criteria, and to determine if its application leads to a greater prognostic accuracy and a better identification of outcomes.

Methods: Retrospective analysis of hospitalized patients in a gastroenterology department for acute decompensation of cirrhosis, without acute-on-chronic liver failure, between January 2014 and December 2015. Identification of AKI patients was based on ICA-AKI criteria. Data collected: severity of liver disease and in-hospital and short-term mortality among patients with and without AKI. Compared the accuracy of the conventional criteria vs. ICA-AKI criteria in the prediction of mortality.

Results: 161 patients included, 85.7% male, mean age of 65 ± 10.8 years. Average length of stay of 11.6 ± 9.5 days. 39.8% of patients had AKI on admission or during hospitalization according to the ICA-AKI criteria (60.9% in stage 1, 20.3% in stage 2 and 18.8% in stage 3). Patients with AKI according to ICA-AKI had longer hospitalizations (14.55 ± 9.7 days, p < 0.05), higher severity of hepatic disease quantified by the MELD and MELD-Na scores (17.62 ± 12.83 vs. 10.05 ± 0.05) and higher in-hospital, 28 and 90-day mortality compared to patients without AKI (33.4 vs. 6.2% vs. 9.3%, p < 0.05, 42.9 vs. 23.7%, p < 0.05). There was a statistically significant association between the presence of infection and the development of AKI (p < 0.05). The ICA-AKI area under the curve (AUC) to predict in-hospital, 28 and 90-day mortality was significantly higher than the AUC of conventional criteria (0.682 vs 0.533; 0.678 vs. 0.588; 0.618 vs. 0.509, p < 0.05).

Conclusion: The ICA-AKI criteria allow the identification of decompensated cirrhotic patients in whom a worse prognosis is predicted. Thus, they constitute a useful tool in daily clinical practice.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P0689 NESTED CASE-CONTROL STUDY FOR RISK FACTORS OF HEPATIC ENCEPHALOPATHY IN PATIENTS WITH LIVER CIRRHOSIS

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Introduction: The pathophysiology of hepatic encephalopathy is not fully understood. A nationwide nested case-control study was conducted to investigate risk factors in the development of hepatic encephalopathy (HE) among patients with liver cirrhosis (LC) in Taiwan.

Aims & Methods: A total of 913 patients with incident HE and 3499 patients without HE (control) were identified from a cohort of liver cirrhosis (n = 14,428) using the population-based, Longitudinal Health Insurance Database 2000 in 1997–2012. Controls were matched to case patients on age at LC diagnosis (< ± 2 years), sex, Charlson Comorbidity index score, year of LC and follow-up time at 1:1 ratio. A multivariate logistic regression model for HE was developed to explore the relative contribution of various risk factors, including patient demographics, infections, cirrhosis-related complications (hepato cellular carcinoma, spontaneous bacterial peritonitis, H. pylori therapy, bleeding ulcer and bleeding).

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Results: 714 cases of HE and matched to 714 controls were enrolled in the analysis. Infections (adj. OR, 3.41; 95% CI, 2.7–4.31; p < 0.001) and frequency of infection yearly (≥3 days/adj. OR 11.26, 95% CI, 5.7–22.2); 1–3: adj. OR 2.82, 95% CI, 2.26–3.53) were significantly associated with increased risk of HE. H. pylori infection (13.31% vs. 8.68%, p = 0.0052) and sites of infections such as pneumonia (14.99% vs. 10.50%, p = 0.0011), peritonitis (14.29% vs 2.52%, p < 0.0001), sepsis (25.63% vs. 9.52%, p < 0.0001), biliary tract infection (7.14% vs. 3.22%, p = 0.0008) and cellulitis (11.62% vs. 3.98%, p = 0.0207) increased risk for HE. HE (adj. HR, 0.90, 95% CI, 0.76–1.06, p = 0.02) and infections (adj. HR, 1.13, 95% CI 0.93–1.38, p = 0.23) increased hazards of death but did not reach statistical significance.

Conclusion: This is the first reported case-control study of HE in Taiwan. The study provides further evidence that infections are strongly associated with HE development in cirrhotic patients, and that the hospital site and severity of infection can provide useful data to identify relative frequencies and sites of infections. These data provide important information relevant to the prevention and management of cirrhotic patients at risk for HE.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
predictors of in-hospital mortality. Patients with Sepsis-3 had higher incidence of acute kidney injury (36 vs. 11%) and hypothermia (17% vs. 2%), septic shock (15 vs. 0%), p < 0.001) and transfer to the ICU (16 vs 2%; p = 0.001) than those without Sepsis-3. Similar findings were found for qSOFA.

Conclusion: Sepsis-3 criteria are more accurate than SIRS criteria in predicting the severity of infections in patients with cirrhosis. qSOFA is a useful bedside tool to assess risk for worse outcomes in these patients. Patients with Sepsis-3 and positive qSOFA deserve more intensive management and strict surveillance.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

P0691 A SUBCLINICAL HIGH TRICUSPID REGURGITATION PRESSURE GRADIENT IS A RISK FACTOR FOR SURVIVAL AFTER LIVING DONOR LIVER TRANSPLANTATION
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Introduction: Portopulmonary hypertension (PHOP) is characterized by pulmonary vasconstriction, while hepatopulmonary syndrome (HPS) is characterized by vasodilation. Given that HPS could be resolved after orthotopic liver transplantation (OLT) even when hypoxemia were severe (PaO2 < 80 mmHg), implications for OLT is accepted not only for deceased donor LT (DDLT), but also to living donor related LT (LDLT). However, the post-OLT course of POFH complicated patients are often unsatisfactory and severe (mPAP > 45 to 50 mmHg) patients are considered as an absolute contraindication for OLT. The International Liver Transplantation Society Practice Guidelines indicate that, unlike HPS, there are no data to support the concept that POFH (treated or untreated) should be an indication for OLT. Furthermore, the Practice Guidelines recommend that patients with mPAP < 35 mmHg be indicated for OLT, and PA-targeted therapy should be initiated in patients with mPAP>35 mmHg. However, almost all of the patients in these articles had received DDLT, and no such analyses have been for LDLT patients. Given that left or right lobe LDLT grafts are smaller than DDLT grafts, PH-induced hepatic venous pressure may result in a strong congestive impact on the LDLT grafted liver. Although patients with confirmed PHOP and HPS are rare, relatively pulmonary hypertensive patients and mild HPS patients may be more common.

Aims & Methods: The present objective is to investigate the clinical impact of subclinical PH on the inevitably small survival in grafted living donor OLT (LDLT). We recruited 84 OLT candidates for liver cirrhosis in a retrospective cohort study. Patients exhibiting a tricuspid regurgitation pressure gradient (TRPG) >25 mmHg (median) on echocardiography were categorized as poten- tially having PH (subclinical PH; n = 34), and the mean pulmonary artery pressure (mPAP) measured after general anesthesi with FIO2 0.6 (mPAP-FIO20.6) was also also included as advisory data. Patients exhibiting O2 < 80 mmHg and an alveolar-arterial oxygen gradient (AaDO2) >25 mmHg were categorized as potentially having subclinical HPS. The clinical course after LDLT was investigated according to subclinical PH or HPS.

Results: Subclinical PH was correlated with a worse 1-year survival (p = 0.003). Severe PH (New York Heart Association: IV) and older donor age (p = 0.008) were correlated with a poor 40-month survival. Although a higher mPAP-FIO20.6 was expected to correlate with a worse survival, a high mPAP-FIO20.6 was not a significant risk factor for the post-LDLT survival. When the post-LDLT survival was inves- tigated according to the TRPG and mPAP-FIO20.6 status, it was worst in patients who had a high TRPG and low mPAP-FIO20.6. The patients with a high mPAP-FIO20.6 and low TRPG showed a good survival, probably because co-existing HPS released the regurgitation pressure.

Conclusion: In cirrhosis patients, mPAP-FIO20.6 may not accurately reflect the congestive pressure to the liver, as the pressure might escape via a pulmonary shunt. Subclinical high TRPG is an important marker for predicting congestive pressure to a grafted small liver, resulting in a worse survival after LDLT.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0692 CARVEDILOL VERSUS PROPRANOLOL EFFECT IN THE PRIMARY PROPHYLAXIS OF VARICEAL BLEEDING IN CIRRHOTIC PATIENTS WITH PORTAL VEIN THROMBOSIS
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Introduction: Portal vein thrombosis (PVT) is recognized as an independent factor of variceal bleeding. Beta blockers are the mainstay treatment to prevent variceal bleeding in cirrhotic patients. Carvedilol has been shown to be equal to propranolol in preventing first bleeding in cirrhotic patients, however, the efficacy of this policy in patients with PVT is unknown.

Aims & Methods: The aim of this study was to evaluate the efficacy of carvedilol versus propranolol as primary prophylaxis of variceal bleeding in cirrhotic patients with occlusive portal vein thrombosis. Between January 2014 and December 2015, cirrhotic patients with occlusive non-malignant PVT were enrolled in a tertiary center. PVT was suspected by Doppler ultrasound and confirmed by computed tomography. Cirrhotic patients with esophageal varices and no previous variceal bleeding were randomized to carvedilol 6.125 mg daily or Propranolol 40 mg daily. End points were esophageal variceal bleeding or death.

Results: During the study period forty eight patients were evaluated. Twenty one and twenty seven patients were randomized in carvedilol and propranolol arms respectively. Mean age was 49 ± 12.2 years; 33 (68.7%) were males; 60.4% had viral cirrhosis; mean Child-Pugh score was 7.2 ± 2.6 and mean follow up was 12.3 ± 9.1 months (range 1-25 months). All the patients had exclusive non-malignant PVT, most of them involving only the trunk, and grade 2 or 3 esophageal varices. Both carvedilol and propranolol groups had comparable variceal bleeding rates (14.2% vs. 14.8%, P = 0.062), bled related mortality (9.5% vs. 11.1%, P = 0.027) and overall mortality (23.8% vs. 22.5%, P = 0.044) respectively. Adverse events in carvedilol group were hypotension (n = 2), requiring cessation of therapy, while and dyspnea (n = 3) resolved spontaneously. In the propranolol group there was 1 adverse event that required discontinuation of treatment (grade 2 intraventricular block).

Conclusion: Our study suggests that carvedilol is probably not superior to pro- pranolol in preventing first variceal bleeding in cirrhotic patients with occlusive PVT, and they both can be used as primary prophylaxis.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0694 ASSESSMENT OF PROGNOSTIC PERFORMANCE OF ALBI, PHTllen, CHILD-PUGH AND MELD SCORES IN PATIENTS WITH LIVER CIRRHOSIS COMPLICATED WITH ACUTE UPPER GASTROINTESTINAL BLEEDING
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Introduction: The ALBI score was recently developed to assess the severity of liver dysfunction, taking into account albumin and bilirubin levels. We aimed to assess its prognostic performance in patients with liver cirrhosis complicated with upper gastrointestinal bleeding (UGIB) while comparing it with Child-Pugh (CP) and MELD scores.

Aims & Methods: Retrospective uncenter study, including consecutive adult patients with cirrhosis admitted for UGIB between January 2011 and November 2015. Clinical, analytical and endoscopic variables were assessed and ALBI, CP and MELD scores at admission were calculated. Statistical analysis was performed using SPSS v21.0 and MedCalc v16.4.3, and a two-tailed p value < 0.05 was defined as indicating statistical significance.

Results: Included 111 patients with a mean age of 57 ± 12 years, 76.6% were males. Liver cirrhosis was most frequently alcoholic (89.2%) and the most common cause was hepatitis C virus infection in 75.5% of patients. During the first 30 days of follow-up 12 patients (10.8%) died, and during the 1st year of follow-up another 10 patients died (1st year mortality of 19.8%). When comparing the three scores, regarding in-stay and 30 days mortality, only ALBI score showed statistical significant results, with an area under the curve (AUC) of 0.82 (p < 0.001) for both outcomes. Regarding 1st year mortality, AUC for ALBI, CP and MELD scores, were 0.71 (p < 0.01), 0.72 (p < 0.05) and 0.66 (p = 0.02), respectively. While for global mortality AUC were 0.75 (p < 0.01), 0.72 (p < 0.01) and 0.72 (p < 0.01), respectively. When comparing the AUC of the three scores, no significant differences were found regarding 1st year mortality and global mortality.

Conclusion: In our series, ALBI score accurately predicted both in-stay and 30 days mortality (AUC 0.82 (p < 0.01)), while CP and MELD scores weren’t able to predict these outcomes. All scores showed a fair prognostic prediction performance regarding 1st year and global mortality. These results suggest that ALBI score is particularly helpful in the assessment of short term outcomes, with a better performance than the most commonly used scores, and may assist the clinician in the stratification of care at admission and maybe even in the referral to liver transplant.

Disclosure of Interest: All authors have declared no conflicts of interest.
PROTON PUMP INHIBITORS IN CIRRHOTIC PATIENTS: IT'S URGENT TO RETHINK THEIR USE

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Introduction: Despite the progress in the treatment of cirrhosis, infections remain a common problem, being responsible for the great majority of morbidity and mortality in these patients.

Aims & Methods: The aim of this study was to identify predictive factors for infection in the first hospitalization for decompensated cirrhosis (DC).

Retrospective analysis of patients with the first hospitalization for DC between January of 2009 and March of 2016. Demographic, clinical and biochemical data was compared between patients with and without infection in the first hospitalization for DC.

Results: From the 175 patients with a first hospitalization for DC, 6% had ascites on admission, 45.8% had upper gastrointestinal bleeding, 38.5% had jaundice, and 28.5% had hepatic encephalopathy. Regarding medication, 29.6% of the patients were taking proton pump inhibitors (PPI), 22.3% had beta-blockers prescribed, and 1.7% were on prophylactic antibiotic. In those 53 patients with proven infection, spontaneous bacterial peritonitis was the most common infection (34%), followed by urinary tract infection (30.2%) and pneumonia (13.2%).

Among those with urinary tract infection, the indication for the use of these drugs should be strictly reviewed and their interruption considered in cirrhotic patients.

Disclosure of Interest: All authors have declared no conflicts of interest.

CRITICAL FLICKER FREQUENCY TEST PREDICTS THE FIRST EPISODE OF OVERT HEPATIC ENCEPHALOPATHY IN PATIENTS WITH COMPENSATED LIVER CIRRHOSIS

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Introduction: Critical flicker frequency (CFF) values ≤3 Hz identify cirrhotic patients with minimal hepatic encephalopathy (mHE) and predict their risk of developing overt hepatic encephalopathy (oHE). However, these results have been obtained in cirrhotics with advanced liver disease suffering a previous episode of liver decompensation (74% of patients) or oHE (14% of patients).

Aims & Methods: Herein, we evaluated the effectiveness of CFF in predicting the first episode of oHE in compensated outpatients undergoing a long-term follow-up. A total of 134 selected patients and 150 healthy subjects were evaluated using CFF.

Results: At baseline, we evaluated demographic characteristics, laboratory tests, model for end-stage liver disease (MELD) score, and Child-Pugh class in all patients. Then, they were followed up for 31.5 ± 18.9 months and received clinical examinations and laboratory tests every six months.

Results: At baseline, all controls had a CFF > 39 Hz with a mean value significantly higher than that observed in 93 patients with CFF > 39 Hz (p < 0.001), while the remaining 41 patients showed a CFF ≤39 Hz. Our analysis demonstrated a significant correlation between CFF and MELD score (r = -0.0003, p = 0.0003), while the prevalence of CFF values ≤39 Hz significantly increased with the progression of the Child-Pugh class (p = 0.003). Interestingly, the CFF value at baseline was predictive of the first episode of oHE both by log-rank test (p = 0.001) and Cox regression analysis (HR = 5.623; 95% CI = 2.433–12.991; p < 0.001).

Conclusion: We demonstrated, for the first time, that CFF predicts the first episode of oHE in a population of compensated cirrhotics that never experienced an HE attack. Cirrhotic patients should be routinely screened by CFF to identify patients at risk of oHE.

Disclosure of Interest: All authors have declared no conflicts of interest.

REFERENCES

OMNIPRESENCE OF LIVER FIBROSIS, BUT PORTAL HYPERTENSION ONLY IN SELECTED ADULT PATIENTS

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Introduction: The Fontan circulation causes some degree of hepatic congestion by its nature of anatomical reconstruction. This may lead to liver fibrosis or even cirrhosis, but to what extent is unknown. A profound hepatic evaluation, incorporating several non-invasive and invasive modalities, in an asymptomatic Fontan patient cohort may further elucidate this.

Aims & Methods: Consecutive patients with a Fontan circulation are prospectively included for screening of liver fibrosis. This screening consists of a blood panel including biomarkers, liver ultrasound, transient elastography (Fibroscan), contrast-enhanced liver MRI or CT-scan and liver biopsy. Liver biopsies were systematically scored with the Fontan specific fibrosis score. Mild fibrosis was defined as a maximum score of 2 of sinusoidal and portal fibrosis component, severe fibrosis as score 3 or 4 on at least one component. Non-invasive markers for portal hypertension (PHT) such as presence of collaterals and splenomegaly on imaging, platelet count (N/L mm³) spleen diameter (mm) ratio (PSR) and von Willebrand factor (VWF) were measured.

Results: From November 2015 until March 2017, 52 Fontan patients were included (mean age 27.5 ± 7.5 years, 60% male). The majority of patients had one or more elevated liver enzymes (elevated GGT in 68%, median 67 μmol/l IQR 51–107). Median platelets were 174 × 10^9/l (IQR 147–213) and mean VWF 104 ± 23%. Mean liver stiffness was 1.8 ± 0.45 kPa. The majority (77%) of ultra-sonographies showed no sign of cirrhosis or splenomegaly (mean spleen size 11.9 ± 1.8 cm). However, 54% of advanced imaging (MRI or CT-scan) showed cirrhosis, 23% congestion and in 21% signs of PHT were observed. Of 33 patients with histology, none were without fibrosis or sinusoidal dilatation and cirrhosis was present in 21%. Of these only 57% also showed signs of cirrhosis on imaging. Of all patients with signs of PHT on imaging only one (13%) patient had histologically confirmed cirrhosis whereas five (63%) had mild fibrosis. Liver stiffness was equal in patients with mild (22.3 ± 9.3 KPa). The majority (77%) of ultra-sonographies showed no sign of cirrhosis or splenomegaly on imaging. Of all patients with signs of PHT on imaging only one (13%) patient had histologically confirmed cirrhosis whereas five (63%) had mild fibrosis.

Conclusion: All Fontan patients are at risk of developing severe liver fibrosis, irrespective of age, duration of Fontan circulation and even when asymptomatic. Portal hypertension may occur in the absence of severe fibrosis. Assessment by solely non-invasive modalities may both under- and overestimate the incidence of fibrosis. For generalizability of the current findings, Fontan patients should be prospectively assessed with multimodality assessment in larger cohorts.

Disclosure of Interest: All authors have declared no conflicts of interest.

A RANDOMIZED DOUBLE BLIND CONTROLLED TRIAL OF THE EFFECT OF LACTOBACILLUS RLG001 PROBIOTICS IN PATIENTS WITH MINIMAL HEPATIC ENCEPHALOPATHY

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Introduction: Probiotics has been recently used to treat cirrhotic patients with any grade of acute or chronic hepatic encephalopathy (HE). Herein, we evaluated the efficacy of Lactobacillus Rhamnosus GG (LRG001) on the treatment of minimal HE (mHE) in compensated cirrhotics.

Aims & Methods: 134 patients were screened by critical flicker frequency (CFF) to diagnose mHE. Among them, 41 patients were CFF+ (≤39 Hz) and were
randomized to placebo or LRGG treatment, for 2 months. In all intention to treat analysis, 124 patients were evaluable for outcome analysis, 61 patients in the placebo group and 63 patients in the LRGG group. The primary end point was measured by the change in the mean CFF value from baseline to week 6. Results: The frequency of the C allele of TLR 7 rs3853839 polymorphism was significantly higher in both HCV spontaneous clearance (SVC) and control groups when compared to chronic HCV group [OR 0.42 (95% CI 0.21 to 0.82, Pc < 0.0372) and OR 0.40 (95% CI 0.23 to 0.71, Pc < 0.0054)] respectively. The same results was also reported in the male subpopulation as the same allele was found to be significantly higher in both HCV spontaneous clearance (SVC) and control groups when compared to chronic HCV group [OR 0.289 (95% CI 0.14 to 0.59, Pc < 0.0021) and OR 0.17 (95% CI 0.1009 to 0.28, Pc < 0.0001)] respectively.

Table(1): Association of the allele T of TLR3 rs3775291 polymorphism among the studied groups.

<table>
<thead>
<tr>
<th>Allele</th>
<th>SVC vs Control</th>
<th>SVC vs CHC</th>
</tr>
</thead>
<tbody>
<tr>
<td>C</td>
<td>0.0234</td>
<td>0.0003</td>
</tr>
<tr>
<td>T</td>
<td>0.0078</td>
<td>0.0001</td>
</tr>
<tr>
<td>P</td>
<td>0.9306</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

Conclusion: The risk of development of chronic HCV infection was associated with T allele carriage of TLR3rs3775291 SNP. While the carriage of C allele of TLR3 rs3853839C allele was associated with spontaneous HCV clearance in both male and female subpopulations in Egyptian families.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P0701 ACTIVATED HEPATIC STELLATE CELLS CAN DIRECTLY INDUCE PATHOGENIC TH17 CELLS IN CHRONIC HEPATITIS B VIRUS INFECTION

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Introduction: TH17 cells are involved in liver fibrosis by activating hepatic stellate cells (HSCs). We aimed to investigate whether HSCs could regulate the function of TH17 cells and the relevant mechanism.

Aims & Methods: Sixty-five patients diagnosed with chronic hepatitis B (CHB) were enrolled in this study. To unravel the effect of HSCs on T cells, naïve CD4+ T cells and TH17 cells were sorted from CHB patients and cultured with or without activated-HSCs, and cytokines expression and genes transcription were analyzed. In addition, the regulatory mechanism of HSCs was also investigated.

Results: ELISA and qRT-PCR showed that TH17 cells from CHB patients were more pathogenic via the expression of IL-17A, IL-23R, RORC, CCL20 and CCR6, and meanwhile, they could activate the primary HSCs. The co-culture experiment indicated that activated HSCs dramatically promoted the proliferation of CD4+ T cells in a time- and dose-dependent manner. In addition, they could also induce the naïve CD4+ T cells into TH17 cells which had a more pathogenic phenotype. Moreover, activated-HSCs-mediated induction of TH17 cells might depend on IL-1β and IL-6 release as well as COX-2/PGE2 pathway. Conclusion: TH17 cells cooperated with HSCs in a proinflammatory feedback loop provide us a more understanding of the pathogenic role of TH17 cells in the chronicity of HBV infection.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
P0703 OPTIMIZATION OF DAA TREATMENT SCHEDULE: FOCUS ON HCV GENOTYPE 3
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Introduction: Direct antiviral agents (DAAs) have led to high sustained virological responses (SVR) in HCV patients. However, genotype 3 patients respond to treatment in a suboptimal way.

Aims & Methods: This study aims to identify which of the several treatment schedules for genotype 3 would constitute the best option.

Results: Twenty-four Italian centers were involved in this real-life study where HCV genotype 3 patients treated with DAAs. To evaluate the number of cases, we conducted a systematic review of literature on the outcome of genotype 3 patients treated with DAAs.

Results: A total of 233 patients with HCV genotype 3 were enrolled. Cirrhotic patients accounted for 83.7%. Overall, the SVR12 rate was achieved by 205 subjects (88.0%); the SVR rates were 78.8% after sofosbuvir/ribavirin, 92.5% after sofosbuvir/daclatasvir and 100% after sofosbuvir/ledipasvir.

Conclusion: Our results reinforce the concept that HCV genotype 3 should not have more considerable difficulty to treat individuals. The optimal therapeutic regimens for these patients appears to be the combination sofosbuvir/daclatasvir, administered for 12 weeks without the use of RBV in non-cirrhotic patients.

Disclosure of Interest: All authors have declared no conflicts of interest.

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Introduction: The therapeutic regimens for chronic hepatitis C are now tending to

Aims & Methods: We aimed at comparing the 8 weeks versus the 12 weeks regi-

Results: No significant demographic and clinical differences were found between

Previous treatment with INF + Ribavirin

Yes

No

HIV co-infection

RNA – week 4, n (%)

<15 U/mL

≥15 U/mL

Virologic response

SVR, n (%)

No response (no compliance) *

Awaiting response (in follow up)

Lost for follow up

Mild adverse effects, n (%)

* Patient retreated with ledipasvir + sofosbuvir + ribavirine during 12 weeks with

Conclusion: In patients with chronic HCV genotype 1 infection and RNA <6000000 UI/mL, the 8 weeks regimen of ledipasvir plus sofosbuvir without ribavirin has similar high cure rates with less adverse effects.

Disclosure of Interest: All authors have declared no conflicts of interest.

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Disclosure of Interest: None declared.

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Introduction: Direct-acting antivirals (DAAs) are novel antiviral drugs for hepa-
titis C virus (HCV) and have enabled the achievement of a high rate of sustained

Conclusion: Low level of serum albumin as well as the progression of hepatic fibrosis could be associated with the development of HCC after achieving SVR with DAA to HCC.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0707 EARLY OCCURRENCE OF HEPATOCELLULAR CARCINOMA IN PATIENTS WITH HEPATITIS C VIRUS TREATED WITH DIRECT-ACTING ANTIVIRALS


Disclosure of Interest: None declared.

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Introduction: Direct-acting antivirals (DAAs) are novel antiviral drugs for hepa-
titis C virus (HCV) and have enabled the achievement of a high rate of sustained

Disclosure of Interest: All authors have declared no conflicts of interest.

P0705 8 VERSUS 12 WEEKS OF LEDIPASVIR/SOFOSBUVIR REGIMEN IN PATIENTS WITH CHRONIC HEPATITIS C GENOTYPE 1 INFECTION


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Disclosure of Interest: None declared.
virological response (SVR) [1]. However, the impact of DAAs on the occurrence of hepatocellular carcinoma (HCC) and HCC recurrence after curative hepatic resection of HCC has been recently discussed [2, 3], but remain unclear.

**Aims & Methods:** The clinical data of 97 patients who underwent curative hepatic resection for primary HCC with HCV at our department between January 2012 and March 2017 were reviewed to clarify the impact of DAAs on HCC occurrence and recurrence. SVR was defined as no detection of HCV RNA in the serum at 24 weeks after the cessation of antiviral therapy.

**Results:** SVR was achieved in 21 patients treated with interferon (IFN)-based regimens and in 21 with DAAs at hepatectomy. Between the two groups, there were no significant differences in the clinical characteristics, including the age, prevalence of diabetes mellitus, drinking history, preoperative liver function, operative procedures, tumor size and presence of liver cirrhosis, but the median duration from the date of SVR to the date of HCC incidence was significantly shorter in patients treated with DAAs (14 days, range: 123 to 235 days) than in those treated with IFN-based regimens (324 days, range: 33 to 4190 days). In particular, HCC was detected within 24 weeks after the cessation of antiviral therapy in 3 patients treated with DAAs. After hepatectomy, SVR was achieved in 21 (DAAs: 16 patients, IFN-based regimens: 5 patients) of the 67 patients without SVR when hepatectomy was performed, and the 1- and 3-year disease-free survival (DFS) rates were 93.3% and 83.0% in patients after SVR treated with DAAs and 90.9% and 71.8% in patients with IFN-based regimens (n = 26) and 57.8% and 19.7% in patients without SVR (n = 40), respectively, regardless of the timing of hepatectomy, respectively. The DFS rate was significantly higher in patients with SVR than in those without SVR (p < 0.001), but was not markedly different according to the antiviral treatments (p = 0.594).

**Conclusion:** While DAAs were able to reduce the DFS rate, the early occurrence of HCC in patients after SVR treated with DAAs is more frequent than that among patients treated with IFN-based regimens. Therefore, careful follow-up with imaging series is needed even for patients with SVR treated with DAAs.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**References**


**P0709 CHRONIC HEPATITIS C MAJOR HEALTH – RELATED QUALITY OF LIFE BURDEN IN COMPASSIONATED CIRRHOTIC PATIENTS**

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**Introduction:** Chronic hepatitis C infection is a systemic disease, one of the leading causes towards cirrhosis and hepatocellular cancer and it is to be considered nowadays a major health-related quality of life (HRQoL) burden.

**Aims & Methods:** The aim of this study was to assess HRQoL, impairment of hepatitis C virus (HCV) infection among a broad sample of compensated HCV cirrhotic patients. We conducted a prospective study between January 1st 2016 to January 31, 2017, in a tertiary center, in which we included 110 patients with compensated HCV cirrhosis, aged between 50 and 75, with no history of neuropsychiatric illness but associated comorbidities (diabetes type 2, hypertension, dyslipidemia). The patients were completely evaluated according to the national protocol. Health status and fatigue of our patients were evaluated using the FACIT- F (version 4) and SF-36 survey. Respondents with HCV compensated cirrhosis were compared with a control group matched for age and sex with no prior history of HCV infection on the Mental (MCS) and Physical (PCS) Component Summary scores.

**Results:** Unadjusted comparisons between subjects infected with HCV (n = 110) and controls (n = 60) revealed that HCV patients had lower FACIT- F utility scores (43.2 ± 35.5 ± 0.05 vs 49.5 ± 5.5 vs 0.05). Severe fatigue was present in 30% (33 patients) of the HCV group compared to 11.5% (7 patients) in controls. Subgroup analyses of respondents age 60 years and older revealed lower MCS score in HCV patients compared to controls (41.95 vs 49.72, p < 0.05). Control group registered higher PCS score (53.30 vs 45.2, P < 0.05) compared to the study group.

**Conclusion:** Although the results were obtained on a small group we observed that in untreated patients with chronic HCV infection, HRQoL is significantly impaired due to fatigue severity and age. Our result underline the need for effective antiviral treatment to decrease the burden of fatigue in this segment of population.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**P0708 EFFICACY AND SAFETY OF SOFOSBUVIR AND RIBAVIRIN IN HCV POSITIVE PATIENTS WITH RENAL IMPAIRMENT**

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**Introduction:** Hepatitis C virus infection is a leading cause of chronic liver disease affecting more than 170 million people worldwide. HCV infection in the setting of renal impairment is not uncommon. Despite the major developments in the treatment of HCV, treatment of this subgroup of patient with impaired renal function is still a challenge.

**Aims & Methods:** The aim of this study is determine the efficacy and safety of sofosbuvir and ribavirin in HCV positive patients with renal impairment. All consecutive patients of HCV related liver disease with creatinine clearance less than 50 ml/min were included in the study. Data was collected for tolerability, efficacy and on treatment adverse events. All the patients received Sofosbuvir and dose adjusted Ribavirin according of CrCl. Virological response was checked at 1 month (RVR), 3 months (EVR) and at the end of treatment.

**Results:** A total of 31 patients were included in the study were 31 out of which 17 (54.8%) were male. Mean age was 52.3 ± 17.6 years while the mean BMI was 25.0 ± 4.30 kg/m². 10 (32.3%) patient were on regular hemodialysis. 26 (83.9%) patients had CTP-A while 5 (16.1%) had CTP-B disease. Majority of the patients 22 (71%) were genotype 3 while 7 (22.6%) were genotype 1. 24 (77.4%) patients were treatment naïve, while those who were treatment experienced. 3 patients received each Interferon and Peg interferon therapy. Treatment was stopped in 2 (6.5%) patients because of disease decomposition while 3 (9.7%) were lost to follow up. ETR was achieved in 25 (86.1%) out of 26 patients who completed treatment. Similarly 12 (80 %) out of 15 patients have achieved SVR-12 so far. During the therapy 10 (32.3%) patients had adverse events, 6 (19.4%) suffered from depression while 4 (12.9 %) developed grade H anemia.

**Conclusion:** In resource constraint population where newer DAAs are not available combination of sofosbuvir and low-dose ribavirin in patients with renal impairment seems to be better tolerated and efficacious in terms of achieving the virological response.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**P0709 SOFOSBUVIR IN COMBINATION WITH RIBAVIRIN IN GENOTYPE 3 HEPATITIS C PATIENTS WITH CIRRHOSIS. AN EXPERIENCE FROM TERTIARY CARE HOSPITAL**

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**Introduction:** Hepatitis C virus (HCV) is the most common cause of cirrhosis in this part of the world. Advent of Directly acting antivirals (DAAs) like Sofosbuvir (SOF) has dramatized the treatment and is the corner stone in treatment of (HCV). Most trials have been conducted in HCV genotype 1 and data for Interferon free regimen in genotype 3 (GT-3) is limited especially in cirrhotics.

**Aims & Methods:** We aimed to evaluate the safety and efficacy of SOF plus Ribavirin (RIB) in patients with compensated and decompensated cirrhosis. This is a prospective real-world cohort study of HCV with compensated or decompensated cirrhosis. Efficacy was assessed by Sustained Viral Response after 6 months of completion of treatment. Adverse events were recorded on designed proforma on serial follow-up visits.

**Results:** The cohort consisted of 9 1consecutive patients out of which 41 were compensated cirrhotics and 50 had decompensated cirrhosis. The mean age was 53.4 ± 11years. Males were 9 (51.6%) and females were 44 (48.4%). Mean CTP and MELD score were 7.71 and 9.21 respectively. In compensated cirrhosis, SVR was achieved in 25 (84.%) treatment naïve patients compared to treatment experienced patients where 5 (80%) achieved SVR. In decompensated cirrhosis SVR was achieved in 22 (77.3%) treatment naïve patients, whereas 13 (76.9%) patients achieved SVR in treatment experienced group. In 72% patients with cirrhosis, there were no side effects whereas most common adverse event was fatigue and drop of Hemoglobin by 1.0 gm/dl. Furthermore, CTP and MELD scores decreased to 6.9 and 8.7 respectively after treatment.

**Conclusion:** Sofosbuvir in combination with Ribavirin in GT-3 HCV patients achieved good SVR in compensated cirrhosis than decompensated cirrhosis whereas fatigue and drop of Hb were the most common adverse effects.

**Disclosure of Interest:** All authors have declared no conflicts of interest.
A411

United European Gastroenterology Journal 5(5S)
P0711 RECURRENCE OF HEPATOCELLULAR CARCINOMA (HCC)
IN PATIENTS WITH COMPENSATED LIVER CIRRHOSIS AND HCC
TREATED WITH PARITAPREVIR/OMBITASVIR/RITONAVIR,
DASABUVIR WITH RIBAVIRIN: A NATIONAL COHORT STUDY
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Introduction: New direct-acting antivirals (DAA) have changed the management
of HCV infection by being effective in more than 90% of cases [1, 2].
Unfortunately, it has been reported an unexpected high rate of HCC early recurrence following DAA treatment, but more data are needed [3–5].
Aims & Methods: From a national prospective cohort, enrolling 3717 Romanian
patients with hepatitis C virus compensated liver cirrhosis who received reimbursed DAA with Paritaprevir/Ombitasvir/ritonavir, Dasabuvir and Ribavirin
(OBV/PTV/r þ DSV þ RBV) for 12 weeks, from December 2015 to August 2016,
we analyzed 21 patients with previous HCC. Most of them were treated through
surgical resection (9/21), followed by radiofrequency ablation (RFA) 6/21, transarterial chemoembolisation (TACE) 5/21 and only one percutaneous ethanol
injection (PEIT). The patients received DAA treatment only if they had no
cancer relapse 6 months after their last therapy session for HCC. All these
patients were evaluated through CT scan or MRI 3 to 6 months after having
finished their DAA therapy. The median follow-up is 6 months (3 12). Data
were obtained from the Romanian National Health Agency.
Results: Two female patients decompensated and died because of acute liver
failure (9.5%), the first one after having finished the 12 weeks therapy, and the
other one in week 7 of DAA therapy. This cohort was 52% females, median age
64 years (51 - 77), 76% IFN pre-treated, 50% associated NASH, 67% with severe
necroinflammatory activity (severity score 3 - Fibromax), 30% with co-morbidities, 24% with Child Pugh A6. The median MELD score was 9 (6 11). SVR
was reported in 19/21 as per protocol analysis (90.5%). Recurrence rate of HCC
was 29%, higher in males (40%) than females (18%), higher in patients treated
with TACE (40%) than in those with hepatic resection (33%), and the lowest risk
of recurrence was encountered in RFA (17%). These differences were not statistically significant because of the small sample size. The pattern of recurrence was:
intrahepatic growth (1 patient), new intrahepatic lesion (1 nodule in 2 patients,
up to 3 nodules less or equal to 3 cm in 1 case) and infiltrative ill-defined
hepatocellular carcinoma in 2 patients. We found no correlation between the
HCC-free interval of time and recurrence rate (p ¼ 0.62).
Conclusion: Early recurrence rate of HCC in treated patients with compensated
liver cirrhosis that received DAA with OBV/PTV/r þ DSV þ RBV was 29%,
significantly increased compared to the natural recurrence rate. This rate is
higher in males (40%) and in patients treated with TACE (40%).
Disclosure of Interest: All authors have declared no conflicts of interest.
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40.
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5. Villani R, Facciorusso A, Bellanti F, . DAAs Rapidly Reduce Inflammation

P0712 SHEAR WAVE ELASTOGRAPHY FOR THE DIAGNOSIS OF
ESOPHAGOGASTRIC VARICES
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Introduction: Shear wave elastography (SWE) has been used in clinical practice as
a noninvasive method to diagnose liver fibrosis by measuring tissue stiffness.
Aims & Methods: The usefulness of SWE in the diagnosis of esophagogastric
varices (EGVs) associated with portal hypertension was evaluated. 550 patients
who underwent measurements of liver stiffness (LS), spleen stiffness (SS) and
EGV evaluation between January 2011 and July 2016 were included (no varices,
n ¼ 340; esophagus only, n ¼ 107; stomach only, n ¼ 14; esophagus and stomach,

n ¼ 89). Virtual Touch Quantification (VTQ) was used for measurements of LS
and SS, and the spleen index (SI) was calculated. EGVs were evaluated according
to forms and red colour sign (RC sign) based on the General Rules for Study of
Hypertension in Japan.
Results: LS, SS and SI showed significant increase in accordance with the severity
of forms (p 5 0.01). The area under the receiver operating characteristic curve
(AUROC) of LS, SS and SI for detecting EGVs were 0.8526, 0.9048, 0.8199, with
the cut off values 1.67 m/s, 2.81 m/s, 18.5cm2, respectively, and SS showed usefulness in detecting EGVs. When LS, SS and SI were compared for their ability to
detect EGVs which were 5F2 or with RC sign positive, LS, SS and SI were
significantly higher for EGVs which require treatment (p 5 0.001). The AUROC
of LS, SS and SI for detecting EGVs which require treatment were 0.8131,
0.8693, 0.8270, respectively. All modality showed good detecting ability, and
SS particularly showed better performance. When each modality was compared
in detection of gastric varices, LS and SS were significantly higher with the
presence of gastric varices, but SI did not show a significant difference. The
AUROC of LS, SS and SI for detecting gastric varices were 0.7359, 0.8611,
0.6470, respectively, and SS showed a superior detecting ability while LS and
SI showed decreased abilities.
Conclusion: LS, SS and SI were all useful in detecting EGVs and predicting the
presence of EGVs which require treatments. SS particularly showed the highest
diagnostic ability.
Disclosure of Interest: All authors have declared no conflicts of interest.

P0713 STAGING HEPATIC STEATOSIS IN NONALCOHOLIC
FATTY LIVER DISEASE BY QUANTITATIVE CONVENTIONAL
ULTRASOUND IMAGING, VALIDATED WITH HISTOPATHOLOGY
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Introduction: Nonalcoholic fatty liver disease (NAFLD) is the most common liver
disorder in developed countries with a global prevalence of approximately 25%.
NAFLD represents a spectrum of disorders and starts with benign steatosis
(NAFL, 5% hepatic steatosis but may lead to nonalcoholic steatohepatitis
(NASH), inflammation with hepatocyte injury with or without fibrosis, which
may lead to cirrhosis. Liver biopsy still is the gold standard for staging steatosis.
The BRUNT score stages steatosis in 4 categories (5%, 5–33%, 34–66%,
66%), which provides a limited sensitivity to detect changes in steatosis content.
For evaluation of treatment and disease activity a quantitative and preferably
non-invasive tool is needed urgently. Therefore we developed and tested a computer aided ultrasound (CAUS) protocol for the non-invasive assessment of
hepatic steatosis using ultrasound (US) B-mode images, which showed high predictive values (area under the curve (AUC) up to 0.95) in cows and similar
correlations in a human pilot study. The current study was conducted in order
to assess the predictive values of CAUS in staging hepatic steatosis in-vivo.
Aims & Methods: Consecutive patients indicated for a liver biopsy received a
simultaneous transabdominal US examination (Siemens Acuson X150; Siemens
Healthcare GmbH, Erlangen, Germany, with CH5-2 transducer). Currently 205
patients with liver biopsies and QUS images are included. Biopsies were qualitatively scored using the Brunt-score for steatosis grading. Metavir, Ishak and/or
Roenigk scores were used for disease specific fibrosis staging. All US images were
further post-processed using the CAUS method. In CAUS corrections are
applied for the: look up table (linearization); beam-profile; attenuation caused
by the superficial tissue layers. Furthermore segmentation of large blood vessels
and bile ducts is performed automatically. Finally echo-level and texture parameters are estimated on average and as a function of depth by estimation of slope
and intercept of a linear fit.
Results: Best correlating CAUS parameter with BRUNT steatosis stage was
found to be the residual attenuation coefficient (RAC, R ¼ 0.79, p 5 0.01).
Parameters used in the multiple linear regression analysis using the leave one
out method were: Residual attenuation coefficient (RAC ¼ slope of the mean
echo level (MU)); MU; slope of the Signal to noise ratio; and the lateral speckle
size. AUC for HS was found to be 0.95 (n ¼ 71) with a sensitivity and specificity
of 86% and 85% respectively, which are in line with previously performed studies. 87% of the included patients were found to have NASH with fibrosis.
However, no significant correlations of the CAUS parameters to a pure fibrosis-group (N ¼ 106) was found.
Conclusion: CAUS is able to classify steatosis accurately and does not suffer from
the presence of fibrosis, making CAUS a feasible tool for screening and evaluation of hepatic steatosis.
Disclosure of Interest: All authors have declared no conflicts of interest.

P0714 UTILITY OF A NEW FUNCTION IN 3D SIM-NAVIGATOR:
ELECTRIC FIELD, WHICH INDICATES THE PREDICTED
ABLATIVE AREA
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Introduction imaging technique has been reported as useful for radiofrequency ablation (RFA) and various models of ultrasound equipment have been developed to include fusion imaging systems. The 3D Sim- Navigator (HITACHI) is a navigation system that can be used in real-time with volumetric tomography and navigating the 3D positions of electrodes. As an addition, the 3D Sim-Navigator is now equipped with a new system that shows the predicted ablative area. This function indicates the electric field that occurs around the electrodes as the predicted ablative area on MP images. The E-field Simulator (E-field) can manage various electrodes, such as monopolar and bipolar RF systems. E-field can be used to predict the ablative areas from not only a single electrode but also multiple electrodes, which was difficult to do in the past. We therefore examined the accuracy of E-field on 3D Sim-Navigator.

Aims & Methods: We evaluated 10 nodules treated using a bipolar RF system (CelonPOWER: Olympus Medical Systems) with multiple electrodes and 72 nodules treated using a monopolar RF system (VIVARF system: STARmed) between April 2016 and March 2017 prospectively. We compared the major and minor axes of maximum axial ablative area for 72 nodules ablated by the monopolar RF system on both E-field and on post-RFA contrast-enhanced CT. Finally, we compared treatment efficacy using a grading system (J Gastroenterol 2013 Aug;48(8):951-65.) on E-field and on post-RFA contrast-enhanced CT.

Results: On the evaluation of maximum axial ablative area by monopolar electrodes, major and minor axes were smaller on E-field than on CT, but these differences were not significant. On the evaluation of ablative volume by bipolar electrodes, the activity coefficient for an ablative area of CEUS for the predicted area was greater than 0.96. On comparing treatment efficacy based on the grading system, the degree of agreement between E-field and CT was 0.691 and the weighted kappa coefficient was 0.929.

Conclusion: Ablative volume on E-field correlated well with that on post-RFA contrast-enhanced CT. Furthermore, good agreement was observed between the treatment efficacy based on E-field and post-RFA contrast-enhanced CT. E-field can be used to predict the ablative area from not only a single electrode, but also multiple electrodes, which was difficult to do in the past. The present results suggest that contrast-enhanced CT may become unnecessary for confirming therapeutic effects in the future.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

Usefulness of a New Three-Dimensional Simulator System for Radiofrequency Ablation in Various Clinical Conditions


P0715 ATTENUATION COEFFICIENT MEASUREMENT (ACM) AS NOVEL REAL TIME ULTRASOUND ALTERNATIVE TO CAP (FIBROSCAN)

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Introduction: The presence of fat droplets in the hepatocytes (micro- or macrovesicular hepatic steatosis) under condition of chronic diffuse liver disease (CDDL) increases the attenuation of ultrasound (US). A group of Ukrainian scientists proposed an original algorithm for real-time US attenuation measurement (attenuation coefficient measurement – ACM – patent UA №2014 111234). Aims & Methods: From total of 327 patients we underwent to comprehensive analysis of ACM in our clinic: 979 were diagnosed with HDD on ultrasonography according to Hamaguchi criteria. All these patient we provide ACM (dB/cm) measurement on SonoP 7 device (Ultrason, Ukraine), with a 1-6 MHz convex transducer in the right and left lobes. For diagnostic accuracy assessment (used ACM values standard and comparison with CAP measured by Fibroscan (Echosens, France) we included 142 patients for subanalysis. Evaluation of diagnostic accuracy of ACM performed by ROC-analysis.

Results: Depending on the stage of steatosis according to B-mode median, 25 and 75 IQ are as follows: control group: 1.57 (1,32; 1,53); 1.16 (1,78-2,11); S2-2, 26 (2,0-2,49) and respectively for 52-2,7 (40-2,82) dB/cm. ACM value increase parallel the hepatic steatosis progression (p < 0.001), which was also accompanied with presence of very strong correlation between these parameters (r = 0.814, p < 0.001). In patient with NAFLD the association between maximum value of ACM and duration of T2DM and triglycerides (model 1, multiple correlation coefficient = 0.55; R² = 0.26; p = 0.004) and ALT (model 2, multiple correlation coefficient = 0.55; R² = 0.25; p = 0.005) were observed. After adjustment by the duration of T2DM the level of triglycerides (r = 0.44, p = 0.012) and activity of ALT (r = 0.44, p = 0.012) significantly correlated with ACM. The AUROC of ACM for steatosis diagnosis was 0.925 (95% CI 0.877-0.973). The optimal cutoff point was > 2.272 dB/cm, with sensitivity, specificity, PPV and NPV respectively 91.5, 77.3, 84.6 and 83.8%. ACM value significantly correlated with CAP (r = 0.630, p = 0.001).

Conclusion: The ACM as novel real-time ultrasound approach can be used for noninvasive hepatic steatosis diagnosis, allows clinicians to monitor disease progression and response to treatment.

Disclosure of Interest: All authors have declared no conflicts of interest.

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Disclosure of Interest: All authors have declared no conflicts of interest.

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Disclosure of Interest: All authors have declared no conflicts of interest.

References


Disclosure of Interest: All authors have declared no conflicts of interest.

References
overexpressed. Knock-down of CUX1 determined a significant down-regulation of HIF-1α, FH1-1 and VEGF. Interestingly, the expression of CDKNA1 was only attenuated after CUX1 knock down and hypoxic stress. HIF1α and transcriptional activity is dependent by CUX1 expression.

Conclusion: CUX1 exerts an oncogenic role in liver cancer by sustaining the survival mechanism and hypoxia. CUX1 silencing results in suppression of the hypoxia inducible factor and its target VEGFA causing a block of cell cycle in liver cancer cells modulated by the stable expression of CDKNA1.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

Conclusion: Our results support the hypothesis that overexpression of BRG1 increases cell growth and cell invasion in HCC. Furthermore, the data highlight genes promoting proliferation and invasion that are regulated by BRG1 during hepatocarcinogenesis. In particular, CyclinB, D, E and MMP7 appear to play a major role in this context and might be an important link between BRG1 expression and HCC development.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0720 PROGNOSTIC ROLE OF NEUTROPHIL-TO-LYMPHOCYTE RATIO IN HEPATOCELULAR CARCINOMA (HCC)
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Introduction: Inflammation may play an important role in progression, and a high neutrophil-to-lymphocyte ratio (NLR) has been reported as a poor prognostic indicator in several malignancies.

Aims & Methods: This study was aimed to investigate the prognostic value of NLR in patients with HCC. We performed a retrospective study including patients with hepatocellular carcinoma admitted in the hepatogastroenterology department of Sousse between January 2010 and December 2015.

Results: A total of 76 patients were included in this study. Mean age was 59.8 (33–87 years). The sex ratio was 3.22 (M/F = 58:18). Hepatocellular carcinoma occurred on a liver of cirrhosis in the majority of cases (90.7%). The main causes of cirrhosis were hepatitis B virus infection (43 patients-62.3%), hepatitis C virus infection (11 patients-16%), non alcoholic steatohepatitis (6 patients-8.6%) and alcohol consumption (5 patients-7.2%). Our results showed that high NLR was associated with poor overall survival (OS) in HCC regardless of therapeutic choice (P < 0.05). Otherwise, high NLR was significantly correlated with the presence of vascular invasion (P = 0.002), lymph node metastasis (P = 0.04), tumor multifocality (P = 0.01) and higher incidence of AFP > 200 ng/mL (P = 0.04).

Conclusion: Elevated NLR indicates a poor prognosis for patients with HCC. The NLR is a readily available and inexpensive biomarker, and its addition to established prognostic scores for clinical decision making warrants further investigation.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0721 REIC/DKK-3 PROTEIN CONCENTRATION INDUCE THE POSITIVE EFFECT TO THE MORTALITY OF HEPATOCELULAR CARCINOMA
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Introduction: The Wnt/b-catenin plays essential roles in the growth of hepatocellular carcinoma (HCC). The Dickkopf (Dkk) protein family (Dkk1–4) is known as Wnt signal antagonists, and reduced expression in immortalized cells (REIC)/Dkk-3 over-methylcytidylation is associated with poor prognosis of HCC patients. But the roles of REIC/Dkk-3 in inhibiting Wnt signaling remains still unclear.

Aims & Methods: In our previous study, REIC/Dkk-3 protein induced significant proliferation of inter foam liverocytes incubated with pancreatic cancer cells, indicating that REIC/Dkk-3 protein might activate cancer immunity in the tumor-bearing patients.1 We hypothesized that REIC/Dkk-3 expression was correlated with cancer immunity in HCC patients. Thus, we investigated the correlation between serum REIC/Dkk-3 protein level and the prognosis in HCC patient. We retrospectively studied 58 HCC patients who underwent primary liver resection for HCC admitted to out unit from 2008 to 2017. Patient serum was gathered before resection. Serum REIC/Dkk-3 protein level was measured by an enzyme-linked immunosorbent assay.

Results: 58 HCC patients were divided into two groups, 41 REIC/Dkk-3 high concentration group (protein level > 800) and 17 Dkk-3 low concentration group (protein level < 800), according to the presence of REIC/Dkk-3 proteins in the blood, as detected by ELISA spectrometry. There was no significant difference in age, sex, Child-Pugh score and HCC stage in the patient groups. REIC/Dkk-3 Protein tended to be declining in liver cancer patients with poor prognosis. (p=0.186)

Conclusion: Our results demonstrated that the serum Dkk-3 protein levels might be a prognosis marker in HCC patients. Further study is necessary with more number of HCC patients.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

P0722 SURGICAL OUTCOME OF PATIENTS WITH FIBROLAMELLAR HEPATOCELULAR CARCINOMA: DOES IT DIFFERS FROM COMMON HEPATOCELULAR CARCINOMA?
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Introduction: Fibrolamelluar hepatocellular carcinoma (FL-HCC) has conventionally been considered to be a histologic variant of hepatocellular carcinoma (HCC), with distinct clinicopathologic features. It is a rare primary hepatic malignancy that was first described as a pathological variant of HCC by Edmondson in 1956 [1]. The etiology of FL-HCC remains unclear. It typically occurs in normal livers without underlying liver fibrosis or cirrhosis [2]. In contrast to HCC which usually found in the presence of cirrhosis or chronic hepatitis [3], FL-HCC has been reported to occur in association with focal nodular hyperplasia (FNH) a type of benign liver lesion. Many series have mentioned that FL-HCC is less aggressive than conventional HCC [4]. However, other studies have failed to confirm the observation of a better outcome in FL-HCC [6]. Other studies reported that the survival was similar between common HCC and FL-HCC, and that may be related to the higher resectability rate which improve the survival of patients with FL-HCC [1].

Aims & Methods: The aim of this study was to evaluate the clinicopathological features and the surgical outcomes of patients with FL-HCC who were referred to our tertiary referral center over a 15-year period. This is a retrospective study including 22 patients with a pathologic diagnosis of FL-HCC who underwent hepatectomy over a 15-year period. Tumor characteristics, survival and recurrence were evaluated.

Results: There were 11 male and 11 female with a median age of 29 years (range from 21 to 58 years). Two (9%) patients had hepatitis C viral infection and only 2 (9%) patients had alpha-fetoprotein level > 200 ng/mL. The median size of the tumors was 12 cm (range from 5–20 cm). Vascular invasion was detected in 5 (23%) patients. Four (18%) patients had lymph node metastases. The median follow up period was 42 mo and the 5-year survival was 65%. Five (23%) patients had a recurrent disease, 4 of them had a second surgery with 36 mo median time interval. Vascular invasion is the only significant negative prognostic factor.

<table>
<thead>
<tr>
<th>Factor</th>
<th>No. (%)</th>
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<td>Age (year)</td>
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<tr>
<td>&lt;40</td>
<td>15(75%)</td>
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<tr>
<td>Male</td>
<td>11(50%)</td>
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<td>Tumor size (cm)</td>
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<td>14(64%)</td>
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<tr>
<td>1</td>
<td>19(86%)</td>
<td>89</td>
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</tr>
<tr>
<td>&gt;1</td>
<td>3(14%)</td>
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<tr>
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<tr>
<td>Hepatectomy</td>
<td>16(73%)</td>
<td>86</td>
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</table>

(continued)
Conclusion: Percutaneous ablation of HCA using Microwave or Radiofrequency thermal Ablation is safe, feasible and able to eradicate the targeted hepatic focal lesion and prevent known complications of HCA. Of note Microwave ablation is much more efficient in treating larger lesions through single puncture in contrast to Radiofrequency which needs more than one puncture.

Disclose of Interest: All authors have declared no conflicts of interest.

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Introduction: Metabolic disorders, such as obesity and diabetes, are well known risk factors for hepatocellular carcinoma (HCC). Conversely, their impact on the natural history of HCC patients has not been established.

Aims & Methods: This study aimed at evaluating the impact of metabolic disorders on clinical features, treatment and survival of HCC patients regardless of its etiology. We analyzed the Italian Liver Cancer (ITA.LI.CA) database regarding 839 HCC patients prospectively collected from 2009 to 2014. The following metabolic features were analyzed: BMI, diabetes, arterial hypertension, hypercholesterolemia and hyperglycemia. According to these features, patients were divided into 3 groups: 0–1 metabolic features, 2 metabolic features, 3–5 metabolic features.

Results: As compared with patients with 0–1 metabolic features, patients with 3–5 features showed lower percentage of HCC diagnosis on surveillance (p = 0.021), larger tumors (p = 0.038), better liver function (higher percentage of patients with Child-Pugh A [p = 0.007] and MELD < 10 [p = 0.003]), higher percentage of metastases (p = 0.024), and lower percentage of portal vein thrombosis (p = 0.010). The BCLC stage and treatment options were similar among the 3 groups, with the exception of a less frequent access to locoregional therapies for BCLC stage B patients with 3–5 features (p = 0.012). Overall survival and survival according to BCLC stage and/or treatment did not significantly differ among the 3 groups. Diabetic patients showed a lower survival (p = 0.046). MELD score, HCC
Grade 1 or higher HFS was observed in 22 patients (53%), and it was significant predictive factors. The following were not significant predictive factors. The presence of HFS (hazard ratio, 0.41; 95% CI, 0.19 to 0.88; p = 0.045) was also associated with higher risk for HCC. (P < 0.001), whereas age, sex, alpha-fetoprotein and HCV RNA level were not significant predictors of HCC. Multivariate analysis show that LVI > 1 and presence of LC were independent predictors of HCC (HR: 63.53, CI. 1.24-1244.28, P < 0.001: HR: 3.10, CI. 1.28-7.51, P = 0.12, respectively).

Conclusion: Decreased liver volume is an independent predictor of HCC in chronic hepatitis C. Liver volume index is useful in predicting risk of HCC in CHC.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0727 HAND AND FOOT SYNDROME AS A PREDICTOR OF OUTCOME IN PATIENTS WITH HEPATOCELLULAR CARCINOMA TREATED WITH SORAFENIB

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Introduction: Sorafenib is a multi-thyrosine kinase inhibitor classified as a neo-vascularization inhibitor. A previous study indicated that the administration of a thyrosine kinase inhibitor, cetuximab, significantly prolonged the survival of patients with dermal disorder1. However, few studies have reported the efficacy of sorafenib administration in patients with hand and foot syndrome (HFS).

Aims & Methods: In this study, we investigated the prognosis of sorafenib-treated patients with HFS. HFS grading was conducted according to the Common Terminology Criteria for Adverse Events (CTCAE) v.4.0. Patients with grade 1 or higher dermal disorder were regarded as having HFS, and grade 0 patients as not having HFS. For HFS evaluation, a double-check system was adopted: primary evaluation based on a specific evaluation sheet at the Pharmacists' Outpatient Clinic and final evaluation by physicians at the outpatient clinic.

We examined the influence of HFS on the effects of treatment after the introduction of sorafenib in 42 patients with a history of multidisciplinary treatment, such as transcatheter arterial chemoembolization (TACE), between May 2009 and March 2017.

Results: Grade 1 or higher HFS was observed in 22 patients (53%), and it was absent in 20 (47%). Overall, the median sorafenib administration period was 2.1 months. In the HFS-free and HFS groups, it was 0.9 and 2.7 months, respectively (p < 0.001). Survival analysis was performed using the Kaplan-Meier method. Overall, the median survival was 5.2 months. In the HFS-free and HFS groups, it was 3.0 and 7.8 months, respectively (p = 0.001). Multivariate analysis showed that the presence of HFS (hazard ratio, 4.01; 95% CI, 0.19 to 0.88; p = 0.023) and administration period (hazard ratio, 0.45; 95% CI, 0.20 to 0.98; p = 0.045) were significant predictive factors. The following were not significant predictive factors: age, BCLC staging, dosage, and tumor markers.

Conclusion: The prognosis of hepatocellular carcinoma patients receiving sorafenib treatment was closely related to the presence of HFS and administration period. HFS was a predictor of outcome in patients with hepatocellular carcinoma treated with sorafenib. This study indicated that a multi-thyrosine kinase inhibitor, sorafenib, prolonged survival in patients with HFS, as demonstrated for cetuximab. HFS reduces the quality of life (QOL), and it is a sorafenib administration-inhibiting factor. In our hospital, a system for patients to initially consult the Pharmacists' Outpatient Clinic, followed by the feedback of grade-based HFS control strategies to physicians at the outpatient clinic, was established. Skin control for sorafenib-treated patients with HFS may have prolonged the administration period, improving the prognosis.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

P0729 UNUSUAL METASTASIS OF HEPATOCELLULAR CARCINOMA

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Introduction: Hepatocellular carcinoma is the most common primary tumor of the liver and is estimated to cause more than a quarter of a million deaths each year throughout the world. Extrahepatic metastasis of HCC occurs in about 30-50% of patients, and it depends on HCC stages. I The most frequent site is lung, followed by lymph node, bone, and adrenal gland.2 Extrahepatic metastases to unusually sites from HCC have been reported in a few case reports. We report cases of patients with unusual extrahepatic metastatic sites from HCC.

Aims & Methods: We carried out a retrospective study of 16 patients with unusual extrahepatic metastases of hepatocellular carcinoma out of 1047 cases of HCC treated at the hepatagastroenterology department "Medicine C" of the Ibn SINA University Hospital during the past 22 years. The diagnosis was suspected based on clinical signs and imaging data, and confirmed by histology when the biopsy of the metastasis was possible, were excluded from this study, patients with lung metastasis, lymph node and portal thrombosis.

Results: Our study included 16 patients, 10 men and 6 women with a mean age of 58.5 years ranging from 37 years to 75 years. 13 patients had cirrhosis due to hepatitis C virus, 1 patient had a cirrhosis due to viral B infection and 2 patients had HCC with anacirrhotic liver. All patients had one or more HCC, ranging in size from 2 to 10 cm. The AFP was normal in 11 cases and elevated in 4 cases (> 200ng/ml). We collected 4 cases of adrenal metastases, 5 costovertebral metastases, 2 brain metastases, 1 cranial metastasis, 1 caval metastasis, 1 ovarian metastasis, 1 nasopharyngeal metastasis, and a case of metastasis in the path of percutaneous biopsy of HCC. In 4 cases the diagnosis of HCC and metastasis was synchronous while in 12 cases median time from diagnosis of hepatocellular carcinoma and extrahepatic HCC was 15.5 months.

Therapeutic abstention was decided in 14 patients for the advanced stage of the disease. cutaneous metastasis was resected surgically and HCC occurring in healthy liver was treated by lumbectomy and upper pole gastrectomy in gastric metastasis. The average survival was estimated at 14 months with a decline of 17.3 months, 6 cases were lost to follow and 6 deaths occurred in our series.

Conclusion: The incidence of unusual and extrahepatic metastasis of HCC diagnosed during clinical course was not frequent. The prognostic diagnostic procedures for extrahepatic metastasis has not been standardized, however considering the significantly high survival of patients with dermal disorder1, we performed a retrospective study of 16 patients with unusual extrahepatic metastatic sites from HCC. The detection of extrahepatic HCC is crucial for patients to receive appropriate therapy, which ultimately determines patient survival.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0730 EPIDEMIOLOGICAL STUDY OF HISTOLOGICALLY PROVEN ADVANCED HEPATOCHELIOANGIOMA: AN AGED MULTICENTER RETROSPECTIVE STUDY IN FRANCE

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Introduction: Hepatocellulargliocarcinoma is a rare primary hepatic tumor comprising features of both, cholangiocarcinoma and hepatocellular carcinoma (CHC-ICC). Few data concerning the epidemiology of chHCC-ICC have been reported, mainly from surgical series in Asian and American populations.

Aims & Methods: The main objective of this retrospective multicenter study was to evaluate epidemiological features and overall survival of histologically proven advanced CHC patients in a French population. Data from patients treated for histologically proven chHCC-ICC in six French university hospitals between 2008 and February 2017, were retrospectively collected. The main clinical, biological, therapeutic features and OS were reported. Statistical analysis was performed using Graph Pad Prism 6.

Results: Thirty patients had HCC. 367 patients were included (76.6% of men, median age 64 years [extreme 37-88]. Cirrhosis was associated in 33.3% of cases (Child-Pugh score A: 70%). Positive serology for hepatitis B virus and C was found in respectively,
5 (16.6%) and 2 (6.6%) patients; and 1 co-infection was observed. Chronic alcoholism in 33.3%, diabetes and obesity (body mass index ≥30 kg/m²) were both present in 26.6% of cases. Alpha-fetoprotein, Carbohydrate Antigen 19-9 and carcinoembryonic antigen serum levels were above normal in respectively 35% (median = 5.3 μg/L [2.2–47.9]), 50% (median = 21.8 IU/mL [4.5–20 000]) and 14% (median = 2.4 μg/L [2–88]) of cases. Six patients (20%) were initially treated by surgical resection. At the diagnosis of advanced non resectable disease, 66.6% of patients presented a multifocal hepatic lesions, 50% presented distant metastases (bones metastases (21.3%), lungs metastases (20%) and peritoneal metastases (13.3%). Twenty-seven patients (90%) received first line of systemic treatment. Twenty-four patients were treated by chemotherapy: Gemcitabine (Gem) alone (n = 1), Gem + oxaliplatine (n = 12), Gem + oxaliplatine + bevacizumab (n = 9), Gem + cisplatine (n = 2). Two patients were treated by chemobezolization and 1 patient received sorafenib. Twenty-nine (70%) and 4 (13.3%) patients received a second and third line of treatment, respectively. Median overall survival was 14.5 months.

Conclusion: Advanced eHCC-ICC appear to be aggressive tumors with a poor prognosis. Cirrhosis was associated in one third of patients. Systemic treatments are not standardized and must be evaluated in a dedicated study.

Disclosure of Interest: All authors have declared no conflicts of interest.

Aims & Methods: The aim of this study was to evaluate the clinical manifesta-
tions, risk factors and prognosis in lymphomas with hepatic involvement. We conducted a retrospective study of patients diagnosed with hepatic lymphoma at our center between 2005 and 2016.

Results: During the 12 years, 36 hepatic lymphomas were identified, 27 primary hepatic lymphomas and 9 with secondary hepatic involvement. The mean age at diagnosis was 53.5 ± 14.6 years and 50% were males. Only one patient had hepatitis B and none had hepatitis C. The majority (94.4%) had symptoms at the time of diagnosis, with fatigue (83.3%), night sweats (61.1%) and loss of weight (61.1%) being the most common. The imaging presentation was of a single mass in 47.2% of cases, multiple masses in 30.6% and infiltrative mass in 22.2%. The most common lymphoma subtypes were diffuse large B-cell lymphoma (52.8%), MALT lymphoma (11.1%) and Hodgkin’s lymphoma (11.1%). Survival at the end of one year was 63.8% and 27.8% at 3 years. Age > 60 years (p = 0.004) was the only factor that was significantly associated with higher mortality.

Conclusion: Hepatic lymphomas are rare entities that may occur in different ways, with diffuse large B-cell lymphoma being the most common subtype. They presented a 3-year survival of only 27.8% and the age over 60 years was the only factor significantly associated with mortality.

Disclosure of Interest: All authors have declared no conflicts of interest.

References:
2. Giannini EG, Moscatelli A, Pellegatta G et al. Application of the Disclosure of Interest: between groups (P value = 0.722), while original BCLC showed the biggest AIC value (AIC = 7088.01) and largest IAUC (IAUC = 0.705). The modified BCLC stage C was further sub-classified into C1, C2, C3 and C4 according to the variables which selected by statistical and clinical importance. The C1-C4 sub-groups showed significant difference of OS distribution between groups (P < 0.001).

Conclusion: Modification of BCLC system based on PS derived accurate and relevant modified BCLC system for HCC patients.

Disclosure of Interest: All authors have declared no conflicts of interest.

References:

P0732 HEPATIC LYMPHOMAS: A RARE ENTITY
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Introduction: Primary tumors of the liver, beyond hepatocellular carcinoma, are difficult to characterize and are associated with poor prognosis. Hepatic involve-
m ent in the lymphomatous process is uncommon and primary hepatic lympho-
mas are rare. The etiology is not yet known but it is thought that hepatitis B and C may be risk factors. The therapeutic approach is not yet fully defined.

Aims & Methods: We aimed to evaluate the effects of various kinds of bile acids on microbiotas are very diverse. Each individual have a characteristic microbiotal distribution and composition within the intestinal tract, presumably related to the composition of their respective char-
geracteristic bile acids. The bile acids, released into the intestinal tract, are mostly reabsorbed (about 95%) through the enterohepatic circulation and recycled. If a certain bile acid is continuously orally supplied, the ratio of supplied bile acid to the total bile acid is gradually increased due to the continuous enterohepatic circulation. It has been reported that changes in the composition of intestinal bile acids cause dysbiosis, and it is presumed that an artificial change in the composition of bile acid can be an effective method of controlling the proliferation of target microbiota.

Aims & Methods: First, we wanted to identify the effects of certain bile acids on each microbiotas. We observed the effect of bile acids in human body (cholic acid, deoxycholic acid, lithocholic acid, and UDCA). We cultured several organims by the disk diffusion method, used for antibiotic susceptibility test. Second, we intended to observe actual intestinal microbial changes through the supply of specific bile acids in animal models. Specific bile acid (UDCA), which is not reabsorbed, was fed to rats for 1 month after bile duct ligation rat model. Next generation sequencing (NGS) method was used to analy-

References:


P0734 MI RNA-21 IS OVEREXPRESSED IN PRIMARY BILIARY CHOLANGITIS AND MEDIATES LIVER INJURY AND NECROTOPSIS IN EXPERIMENTAL CHOLESTASIS

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Introduction: Inhibition of microRNA-21 (miR-21) prevents necroptosis in the mouse pancreas. In turn, we recently showed that necroptosis contribute to hepatic necro-inflammation in the common bile duct ligation (BDL) murine model.

Aims & Methods: We aimed to evaluate the role of miR-21 in mediating deleterious processes associated with cholestasis. The functional crosstalk between miR-21 and necroptosis was investigated in vitro. miR-21 expression was evaluated in the liver of primary biliary cholangitis (PBC) patients. C57BL/6 wild-type (WT) or miR-21-deficient (miR-21−/−) mice were subjected to BDL or sham surgeries, with biochemical, molecular and histological analysis of hepatic damage, fibrosis, necroptosis and bile acid metabolism, after either acute (3 days) or chronic (14 days) injury.

Results: Studies in miR-21−/− primary mouse hepatocytes established a functional link between miR-21 and necroptosis through cyclin dependent kinase 2 associated protein 1 (CDKAP1). miR-21 expression increased in the liver of PBC patients (P=0.02). miR-21−/− mice displayed decreased serum levels of liver injury markers compared with WT mice, accompanied by reduced hepatocellular degeneration, oxidative stress and pro-fibrotic gene expression. Hallmarks of necroptosis were decreased in the liver of BDL miR-21−/− mice, via relieved repression of CDKAP1. Further, miR-21−/− mice displayed improved adaptive response in the expression of bile acid homeostasis-associated genes.

Conclusion: miR-21 ablation ameliorates liver damage and necroptosis in BDL murine model. miR-21 should be a promising approach to treat cholestatic liver diseases. Supported by FCT, Portugal through grants PTDC/ HMI-MEC/08953/2014 and UID/DTP/04138/2013, and fellowships SFHR/BD/ 9119/2012 (MBA), SFHR/BD/82212/2012 (FMR), and SFHR/BD/191460/201 (ALS).

Disclosure of Interest: All authors have declared no conflicts of interest.

P0735 THE RENDEZVOUS PROCEDURE FOR THE MANAGEMENT OF BILIARY TRAUMA AFTER CHOLECYSTECTOMY: SHORT AND LONG-TERM OUTCOMES AND PREDICTORS FOR SUCCESS

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Introduction: Bile Duct Injury (BDI) following laparoscopic cholecystectomy is a persisting problem. The rendezvous procedure (RV) provides a combined endoscopic and percutaneous approach in order to re-establish bile duct continuity in complex BDI.

Aims & Methods: The aim of this study is to assess short-term and long-term outcomes of the RV. All consecutive patients with BDI referred to our tertiary center were analyzed retrospectively. RV procedure was performed when endoscopic stenting or PTC failed and when deemed feasible by a dedicated multidisciplinary team including a hepato-pancreato-biliary surgeon, gastroenterologist and interventional radiologist. Classification of BDI, technical success of RV, procedure-related complications and outcomes were assessed.

Results: Among a total of 812 patients, RV was performed in 47 (5.8%) patients, of which 31 (66%) were diagnosed with complete transaction of the bile duct (type D3/Narseth type E injury). Primary success rate of RV was 94% (44/47 patients). Reasons for failure (N = 3) were inability to pass a stricture and inability to make contact between the two wires. In 26/47 patients (55%) RV was the final successful treatment. In 17/47 patients (36%) RV acted as a bridge to during the endoscopic procedure, and total number of endoscopic procedures did not significantly differ between the two groups. The median number of stent change was one (range 0–5) and two (range 1–5) (P = 0.013), while the median diameter of the largest stones was 9 mm (range 0–27) and 14 mm (range 5–32) (P = 0.001) in the complete and incomplete stone removal groups, respectively. During the follow-up period, OS was 33.5% and 41.9% and DSS was 5.66% and 3.23% in the complete and incomplete stone removal groups, respectively. Kaplan-Meier analysis found no significant difference in OS and DSS between the two groups (P = 0.187 and P = 0.581, respectively). Conclusion: Patients in the incomplete stone removal group tended to have more numerous and larger stones. This single-centre retrospective study revealed no significant difference in OS and DSS between the two groups. Complete stone removal might not be always necessary in extremely elderly patients aged 90 years and older.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0736 THE EVALUATION OF TRANSPAPILLARY ENDOSCOPIC GALLBLADDER DRAINAGE WITH THE USE OF INTRADUCTAL ULTRASONOGRAPHY


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Introduction: The number of indications for endoscopic transpapillary gallbladder drainage (ETGBD) to treat biliary colic in elderly patients aged 90 years was increased due to the aging of the population and prescribing antithrombotic agents. ETGBD is one of the challenging procedure because it is difficult to identify the cystic duct (CD) orifice. From November 2015, we performed with ETGBD using intraductal ultrasonography (IDUS) complementarily. The CD orifice can be identified using IDUS, resulting in cannulation to the CD. We investigated the success rate and clinical outcomes of ETGBD in combination with using IDUS.

Aims & Methods: ERCP was performed in 1000 patients (1400 times) at New Tokyo Hospital between January 2012 and December 2016. Among them, a total of 97 patients underwent ETGBD, 58 patients with IDUS and 39 without IDUS. In this study, we investigated the success rate of ETGBD retrospectively. The success of ETGBD was defined as cannulation into the gallbladder within two trials. Results: The mean age and male proportion of patients in the group with IDUS was similar to that in the group without IDUS (74.5±11.4 vs 73.3±11.3; P = 0.600 and 18/40 and 13/26; P = 0.828). The procedure success rate was 78.4% (76/97) in total; 86.2% (50/58) in the group with IDUS and 66.7% (26/39) in the group without IDUS (P = 0.026). Using IDUS under fluoroscopic image allowed all patients in the group with IDUS to identify the CD orifice. ETGBD procedures in eight patients were unsuccessful because of a highly flexion of the CD in seven patients and an obstruction of the CD orifice caused by tumor invasion in one patient. Although both groups developed mild pancreatitis (one patient in the group with IDUS, and two patients in the group without IDUS), no significant difference was observed in the two groups (P = 0.563). All patients were successfully managed with conservative treatment. There were no any other complications in the two groups.

Conclusion: The success rate of ETGBD in the group with IDUS was significantly higher than that in the group without IDUS. IDUS is may be useful as a complementary option of endoscopic gallbladder drainage.

Disclosure of Interest: All authors have declared no conflicts of interest.

Disclosure of Interest: All authors have declared no conflicts of interest.
surgery; although the RV was initially successful, late complications (stenosis, stent dysfunction) required elective hepaticojjunostomy (HJ). Procedure-related adverse events occurred in 10 patients (18%) with cholangitis being the most frequent complication (N = 4.7%). No life-threatening adverse events and no 30-day mortality occurred.

Conclusion: In experienced hands, RV is safe with a final non-surgical success rate of 55%. When endoscopic stenting fails in patients with complex BDI, RV can be considered as a viable treatment option before surgical repair.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
2. Booij KAC, de Reuver PR et al. Morbidity and mortality after minor bile duct injury or bleeding. Recurrent biliary symptoms were significantly more in delayed LC. Procedure-related adverse events occurred in 10 patients (18%) with cholangitis being the most frequent complication (N = 4.7%). No life-threatening adverse events and no 30-day mortality occurred.

Conclusion: In experienced hands, RV is safe with a final non-surgical success rate of 55%. When endoscopic stenting fails in patients with complex BDI, RV can be considered as a viable treatment option before surgical repair.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0739
TRANSCRECTAL GALLBLADDER PRESERVING ChoLecystolithotomy and PolyPectomy by pure NOTES
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Introduction: Transcolonic and transrectal NOTES in human cases was greatly restricted by the fact of fecal contamination. We developed a detachable intracolonic balloon to help keep the colon sterile by blocking the colonic lumen. Although cholecystectomy is widely used for treating gallbladder polyps and gallstones, there is still a controversy about whether or not the gallbladder should be preserved. However, postcholecystectomy syndromes, such as biliary duct injury and the correlation with colon cancer, remind us of the importance of gallbladder preservation.

Aims & Methods: Approved by the Independent Ethics Committee, we’ve completed 8 transrectal gallbladder preserving cholecystolithotomy (TRGCP) and 3 transrectal gallbladder preserving polypectomy (TRGPP) and 2 combined cases by pure NOTES. Moreover, 1 case of TRGCP was done by hybrid NOTES. As the figures show, the balloon was placed in the transverse colon to block the colonic lumen, and the distal colon cavity was disinfected with povidone-iodine solution. An incision was made on the anterior rectal wall 12–17 cm from the anus. The endoscope was advanced into the peritoneal cavity with liver and gallbladder identified. The bile was aspirated before an incision on the gallbladder wall was made. Stones and/or polyps were found inside of the gallbladder. Stone extractor and biopsy forceps were used to take out the stones. The polyps were coagulated and removed by electric biopsy forceps. The muscular layer and the adventitial layer were successively closed with endolips. Peritoneal cavity lavage was performed with sterile saline. The rectal incision was closed with endoclips and endoloops tightly. At the end of the procedure, the balloon was pulled out after being deflated.

Results: The mean operation time (from incision making till the last clipping) was 180.5 min. (89–467 min.). 6 hours after anesthesia, the patients could drink water, and liquid diet was resumed 24 hours later. Postoperatively, 4 of the 14 patients felt mild abdominal distention which disappeared within 12 hours when they were able to get off the bed. For 1 patient with acute cholecystitis, a hybrid NOTES with laparoscopy was performed. Moreover, gallbladder drainage and peritoneal lavage were used, and the abdominal pain relieved soon. All the patients were discharged without any adverse events and all felt good during the follow-ups.

Conclusion: The usage of the detachable balloon can prevent the operative field from fecal contamination effectively. TRGCP and TRGPP by pure NOTES are suitable for both males and females. Transrectal route provides a novel alternative approach for the treatment of gallbladder polyps and gallstones. To our knowledge, this is the first human case series of transrectal gallbladder preserving cholecystolithotomy and polypectomy by pure NOTES. However, multi-centered, prospective, controlled researches with more cases are needed in the future.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0740
KML001, AN ORAL ARSENIC COMPOUND, AS PALLIATIVE CHEMOTHERAPY IN ADVANCED BILIARY TRACT CANCERS AFTER FAILURE OF GEMCITABINE-BASED CHEMOTHERAPY
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Introduction: Sodium metarsenite (NaAs2O3: code name KML001) is an orally bioavailable arsenic compound with potential anti-cancer activity. However, the effect of KML001 has not been evaluated in patient with biliary tract cancers. We investigated the potential of KML001 as palliative chemotherapy in patients with advanced biliary tract cancers who non-respond to gemcitabine-based chemotherapy.

Aims & Methods: The study was designed to evaluate safety, tolerability and effectiveness of KML001 as palliative chemotherapy in advanced biliary tract cancer. Inclusion criteria were 1) inoperable or metastatic cholangiocarcinoma and gallbladder cancer, and 2) previous history of failure to gemcitabine-based chemotherapy. Exclusion criteria were 1) naïve patient to chemotherapy, 2) ECOG PS > 3, and 3) history of decompensated congestive heart failure, uncontrolled arrhythmia, and QT prolongation (QTc > 480 ms). KML001 (Kominos, Komipharm International Co., Ltd.) was administered as 7.5 mg daily to eligible subjects. Every two months, patient took response evaluation by biliary CT scan.

Results: A total of 44 patients (21 females and 23 males) were enrolled prospectively between November 2011 and October 2014. Mean age of the patients was
Conclusion: KML001 was safe and well tolerated in respects of adverse events. The percentage of drained segments. This percentage was calculated by dividing intubated patient. The quality of the drainage was evaluated by calculation of ques could be associated. A Ct-scan or MRI was performed before and after operators performing ERCP, EUS-drainage, and per-cutaneous drainage. The drainage of malignant stenosis of the hilum. Drainage were performed by 5 unilateral or bilateral palliative drainage has to be perform for this kind of drained in case of unresectable hilary liver stenosis, however it remains unclear if ESGE stated in 2012 that more than 50% of the liver had to be Morphin requirement, n (%) increased 8 (18.6%) ECOG, n (%) Increased 19 (43.2%) Progression, n (%) Decreased 11 (24.7%) Table 1: Treatment outcomes Study period, mean, mo (range) 1.5 (0.5–10.0) Progression free survival, mo (IQR) 1.7 (0.8–2.3) Survival from study-enroll, mo (IQR) 2.5 (1.4–4.9) Best response, n (%) SD 3 (6.8%) PD 23 (53.2%) Not evaluated 18 (40.9%) ECOG, n (%) Increased 19 (43.2%) Main 24 (54.5%) Morphin requirement, n (%) increased 8 (18.6%) maintain 31 (72.1%) decreased 4 (9.3%) Adverse event, n (%) Grade 1 16 (36.4%) Grade 2 29 (65.9%) Grade 3 12 (27.3%) Grade 4 0 (0%) Drop out cause, n (%) - drug reaction 1 (2.3%) - Adverse event 4 (9.1%) - Patient’s death 7 (15.9%) - Disease progression 22 (50.0%) - Withdrawal consent 5 (11.4%) - Loss of follow-up 2 (4.5%) - Poor general condition 3 (6.8%) Conclusion: KML001 was shown promising result in disease control and pain control. The other factors with impact on the survival was an invasion of the liver > 50% by tumor. There was no impact on the survival according to the different techniques used to drain the bile ducts. To confirm the efficiency of the quality of the drainage, a ROC curve was performed establishing a correlation between patients receiving chemotherapy and percentage of liver drained (area curve = 0.77 (0.65–0.88)). Disclosure of Interest: All authors have declared no conflicts of interest.

Aim & Methods: The study is a retrospective analysis of a prospective registry of patients with malignant stenosis of the biliary confluence. The aim of our study was to evaluate the efficiency of hilar drainage in function of the number of segments drained. The number of liver segment drained with the number of liver segment measured by removing the segments with the segments resected in case of surgery, and/or the segments with invasion of more than 50% by tumor. The aim of the study was to evaluate the effect of the quality of the drainage on the patients survival. Quality of the drainage was defined by the percentage of liver segments drained.

Results: 60 (38 men) patients were included from from 01/2015 to 07/2016. Mean age = 69.84 years old. The classification of the stenosis was type II for 17 (29%) patients, type III for 20 patients (34%), type IV for 22 (37%). Histology corre- sponded to hepatic cell carcinoma (53%), metastasis from colorectal cancer for 15 patients (25%) and others cancers for 19 (32%). Median follow-up was 8.5 months (5.5–16.5). The median of survival was 5 months (2.3–12.3). In univaried and multivaried analysis there was a significant correlation between the percentage of segments drained > 50% (p < 0.05) and the survival. The other factors with impact on the survival was an invasion of the liver > 50% by tumor.

Disclosure of Interest: The patient with a malignant stenosis of the biliary confluence is highly correlate with the rate of the liver segment drained.

Aims & Methods: The aim was to determine and compare the accuracy of TAUS and EUS for diagnosis of gallbladder polyps. The decision to perform cholecystectomy is based on presence of gallbladder polyp on transabdominal ultrasound (TAUS) or endoscopic ultrasound (EUS), or both. This decision also influences whether the polyp is to be removed or to be left alone (true or pseudo polyp. Pseudo polyps are non-neoplastic and do not need surgery. True polyps are neoplastic, either benign (adenoma) or (pre)malignant (dysplastic polyp/carcinoma). True polyps usually need surgery, as they are thought to have malignant potential through the adenoma-carcinoma sequence. (Pre)malignant lesions should be operated sooner than benign lesions. There has been no systematic review and meta-analysis on the accuracy of TAUS and EUS in the diagnosis of gallbladder polyps, true gallbladder polyps and (pre)malignant polyps.

Results: A total of 17 studies were included in this review. For diagnosis of gallbladder polyps six studies on TAUS were included. The sensitivities and specificities of the studies ranged from 0.45 to 1.00, and 0.91 to 0.98 respectively. There were no studies on EUS for this topic. For differentiating between true and pseudo polyps, seven studies were included. All seven studies reported on TAUS, four studies also reported on EUS. The sensitivities and specificities of the studies ranged from 0.47 to 1.00 and 0.51 to 0.98 for TAUS, and from 0.63 to 1.00 and 0.84 to 0.96 for EUS. For differentiating between (pre)malignant and benign polyps, five studies were included. Four studies reported on TAUS and three studies on EUS. The sensitivities and specificities of the studies ranged from 0.22 to 0.99 and 0.46 to 1.00 for TAUS and from 0.69 and 0.92, and 0.87 to 0.95 respectively.

No studies were of high methodological quality. The results of the pooled sensitivities, specificities and test–post–test probabilities are shown in Table 1. HSROC analysis showed no significant difference between the diagnostic accuracy of TAUS and EUS for differentiating between true and pseudo polyps and for
determining diagnostic accuracy of TAUS for diagnosis gallbladder polyps is moderate and decreases further when differentiating between polyp types. TAUS would regularly provide false positive results, leading to unnecessary surgery. There was no evidence that diagnostic test accuracy of EUS was better than TAUS. Further studies of high methodological quality are needed to determine diagnostic accuracy of EUS and TAUS for differentiating between polyp types.

This abstract is based on a pre-peer review draft of a Cochrane Review.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference


P0743 DIAGNOSTIC VALUE OF CONTRAST-ENHANCED ULTRASONOGRAPHY IN HIGH MECHANICAL INDEX CONTRAST MODE FOR POLYPOID LESIONS OF THE GALLBLADDER

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Introduction: In its early stages, gallbladder cancer is an asymptomatic disease, and is associated with a poor prognosis if found in an inoperable condition. Several investigators have reported the utility of contrast-enhanced ultrasonography (CEUS) in low mechanical index (MI) contrast mode using a microbubble contrast agent for gallbladder lesions. However, CEUS images with low MI setting are influenced by the echogenicity of background B-mode and cannot depict precise vessel images, in contrast with high MI contrast mode.

Aims & Methods: The aim of this study was to assess the diagnostic value of CEUS in high MI contrast mode for characterizing polypoid lesions of the gallbladder (PLG). Thirty-six patients with PLG, including 17 with gallbladder cancer and 19 with benign polyps, who underwent CEUS were enrolled. The institutional review board approved this study and informed consent was obtained. Two blinded readers retrospectively evaluated images obtained in B-mode and CEUS. Kappa values, which reflect inter-observer agreement, were calculated. Subsequently, patients were stratified according to lesion size at the largest diameter, and the diagnostic accuracy for gallbladder cancer in B-mode and CEUS were assessed.

Results: Two patients with malignant PLG could not be evaluated in B-mode due to sludge. Kappa values for CEUS were graded as good or excellent, and were better than in B-mode. Age and size of malignant PLGs were significantly larger than benign lesions. In B-mode, 80% (12/15) of malignant PLGs exhibited heterogeneity (p < 0.01). On CEUS, malignant PLGs exhibited sessile-shape (76% [13/17]), dilated vessels (71% [12/17]), irregular vessels (82% [14/17]), and heterogeneous enhancement (59% [10/17]) (p < 0.01). Except for heterogeneous enhancement, all features remained significantly different after stratification according to size of PLG between 11 mm and 20 mm on CEUS. The sensitivity, specificity, and accuracy for diagnosis of gallbladder cancer was 80% (12/15), 79% (13/19), and 73% (25/34) in B-mode, 94% (16/17), 89% (17/19), and 92% (33/36) on CEUS, and 88% (7/8), 91% (10/11), and 89% (17/19) on CEUS after stratification according to size, respectively.

Conclusion: CEUS in high mechanical index contrast mode was a useful modality for differentiating gallbladder cancer and benign PLGs.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0744 ASSOCIATION OF CIRCULATING ADIPONECTIN LEVELS AND TUMOR STAGE IN BILIARY TRACT CANCER

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Introduction: Multiple recent studies have indicated that some of adipose tissue-derived hormones may significantly influence the growth and proliferation of GI tumors including liver cancer (1, 2). However, the role of adipokines such as adiponectin and leptin in biliary tract cancer have not been well studied before. The aim of the study was to analyze plasma concentrations of adiponectin and leptin in cholangiocarcinoma (CC) patients and to compare these concentrations to clinopathological parameters.

Aims & Methods: Baseline levels of adiponectin and leptin were determined in 38 consecutive patients with newly diagnosed cholangiocarcinoma and 38 healthy control subjects. The association between adiponectin and leptin and tumor stage was evaluated using nonparametric Spearman’s correlation test. Control subjects were matched to case patients by age, sex and BMI. Survival analysis used the Kaplan-Meier curve and the Cox proportional hazards model.

Results: Overall median adiponectin concentrations were lower in CC patients versus control subjects (5.1 vs 9.3 mg/mL, P = 0.001). In CC patients with T stage 2–4 (n = 22) median adiponectin concentrations were significantly lower than in CC patients with T stage 1 (n = 16) (3.8 vs 6.6 mg/mL, P = 0.001). The mean leptin levels were not significantly decreased in CC patients (P = 0.45). Adiponectin concentrations were inversely correlated with tumor T stage (r = -0.811, P = 0.01) of CC patients. Higher adiponectin levels at baseline were associated with increased overall survival in T stage 2-4 patients (Cox F test = 2.139, P < 0.05).

Conclusion: This study identified an association between adiponectin levels and tumor stage suggesting a potential role for adiponectin in progression of cholangiocarcinoma. Furthermore these results suggest, for the first time, that serum adiponectin levels might represent a prognostic indicator in patients with CC. Our results support the hypothesis linking adipose-tissue derived hormones levels to growth of obesity-associated cancers (3). Adipokines appear to play an important role in risk prediction and management of cholangiocarcinoma patients.

Disclosure of Interest: All authors have declared no conflicts of interest.

References


Table 1: Results of meta-analysis and post-test probabilities

<table>
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<tr>
<th>Index Test</th>
<th>Target condition</th>
<th>Number of studies (patients)</th>
<th>Summary sensitivity (95% CI)</th>
<th>Summary specificity (95% CI)</th>
<th>Minimum, median and maximum prevalence of target condition = pre-test probability</th>
<th>Positive post-test probability (95% CI)</th>
<th>Negative post-test probability (95% CI)</th>
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<td>TAUS</td>
<td>Gallbladder polyp</td>
<td>6 studies (16260 patients)</td>
<td>0.80 (0.55–0.98)</td>
<td>0.97 (0.95–0.98)</td>
<td>Minimum: 0.4%</td>
<td>Median: 6.4%</td>
<td>0.04 (0.00–0.05)</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Maximum: 53.3%</td>
<td></td>
<td>0.28 (0.12–0.54)</td>
</tr>
<tr>
<td>TAUS</td>
<td>True gallbladder polyp</td>
<td>7 studies (1272 patients)</td>
<td>0.77 (0.48–0.92)</td>
<td>0.78 (0.59–0.90)</td>
<td>Minimum: 9.1%</td>
<td>Median: 20.2%</td>
<td>0.03 (0.01–0.07)</td>
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<td></td>
<td></td>
<td>Maximum: 60.0%</td>
<td></td>
<td>0.28 (0.12–0.51)</td>
</tr>
<tr>
<td>EUS</td>
<td>True gallbladder polyp</td>
<td>4 studies (267 patients)</td>
<td>0.84 (0.54–0.96)</td>
<td>0.84 (0.70–0.92)</td>
<td>Minimum: 9.1%</td>
<td>Median: 20.2%</td>
<td>0.02 (0.00–0.07)</td>
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<td></td>
<td>Maximum: 60.0%</td>
<td></td>
<td>0.27 (0.02–0.51)</td>
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<tr>
<td>TAUS</td>
<td>Dysplastic polyp</td>
<td>4 studies (1637 patients)</td>
<td>0.60 (0.22–0.89)</td>
<td>0.89 (0.76–0.96)</td>
<td>Minimum: 4.1%</td>
<td>Median: 20.1%</td>
<td>0.02 (0.00–0.05)</td>
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<td></td>
<td>carcinoma</td>
<td></td>
<td></td>
<td></td>
<td>Maximum: 59.6%</td>
<td></td>
<td>0.10 (0.00–0.26)</td>
</tr>
<tr>
<td>EUS</td>
<td>Dysplastic polyp</td>
<td>3 studies (350 patients)</td>
<td>0.85 (0.56–0.96)</td>
<td>0.91 (0.75–0.97)</td>
<td>Minimum: 4.1%</td>
<td>Median: 20.1%</td>
<td>0.04 (0.01–0.13)</td>
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<tr>
<td></td>
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<td></td>
<td></td>
<td></td>
<td>Maximum: 95.6%</td>
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<td>0.78 (0.51–0.92)</td>
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weigh, 23–24.9 kg/m²; obese, retrospectively reviewed. The relationship between BMI (kg/m²) and overall incidence. Vary in different cancers. Biliary tract cancer was less frequently analyzed and most of the studies were on the relationship between obesity and cancer incidence. Aims & Methods: We performed this study to investigate the association between BMI and survival in advanced biliary tract cancer patients with chemotherapy. Between January 2005 and December 2015, two hundred and eighty-four patients who underwent chemotherapy for biliary tract cancer were retrospectively reviewed. The relationship between BMI (kg/m²) and overall survival (OS) was assessed. Based on World Health Organization BMI category and 2014 Clinical Practice Guidelines for Overweight and Obesity in Korea, BMI was classified as follows: underweight, <18.5 kg/m²; normal, 18.5–22.9 kg/m²; overweight, 23–24.9 kg/m²; obese, ≥25 kg/m². Results: Median OS was 12.1 months for underweight patients, 10.5 months for normal-weight patients (BMI 23–24.9 kg/m²) had a reduced risk of mortality in significantly associated with better survival. Compared with normal patients, overweight patients (BMI 23–24.9 kg/m²) had a reduced risk of mortality in multivariate analysis (HR 0.491, CI 0.334–0.721; 95% p = 0.036). In the additional analysis for the effect of change in body weight and BMI to the overall survival, larger amount of change in body weight was associated with further decrease in overall survival. Conclusion: Slightly overweight status and the maintenance of body weight during the initial period of chemotherapy is independent predictor of better overall survival in advanced biliary tract cancer patients with good performance status. Disclosure of Interest: All authors have declared no conflicts of interest.

P0746 THROUGH THE CATHETER BIOPSY METHOD FOR BILIARY CARCINOMA

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Introduction: To perform curative operation of biliary carcinoma, the pre-operative identification of exact proximal and distal margins is important. A biopsy forceps is conventionally inserted to common bile duct via duodenal ampulla, guided with an antecedent guide wire. Cannulation of the bile duct with the biopsy forceps may sometimes be difficult in cases where no sphincterotomy is performed, placing the patient at risk of post-ERCP pancreatitis after multiple attempts to advance the forceps into the duct. Pancreatobiliary endoscopists have reported the biopsy methods. Aims & Methods: The aim of this study was to assess the feasibility and safety of the technique. This was a retrospective review of bile duct biopsies with this new method conducted in Sendai Kousei hospital from February 2015 to October 2016. All patients who had biliary stenosis were included. Patients’ demographic data, technical success, adverse events and the diagnostic accuracy were evaluated. Results: A total of 95 biopsy procedures were performed in 40 patients. The technical success rate was 95% (90/95). Post-ERCP pancreatitis occurred in 1 of 40 patients (2.5%, 1 grade 1 patient). There were no other adverse events like perforation or bleeding. The diagnostic yield of biopsy procedures was 100% (7 of 7 patients). Conclusion: The new biopsy methods to biliary stricture were feasible and safe. It opens up exciting possibilities for endoscopic preoperative diagnosis of the biliary carcinoma. Disclosure of Interest: All authors have declared no conflicts of interest.

Reference
Meier curves, and calibration curves revealed good predictive abilities. The risk scores identified patients with a 1-year survival probability ranging from 15 to 73%.

Conclusion: We developed a prognostic score to predict overall survival for PHC patients using eight independent poor prognostic factors available at presentation. This score may help to inform patients and guide individualized treatment decision making.

Disclosure of Interest: All authors have declared no conflicts of interest.


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Introduction: Malignant biliary obstruction has a poor prognosis unless secondarily to a resectable primary cancer. Recent data on PTC for the relief of malignant obstruction in a palliative setting demonstrated a high early mortality. We have therefore examined outcomes of ERCP in inoperable malignant obstruction.

Aims & Methods: The Hospital Episode Statistics (HES) database contains diagnostic and procedural data for all hospital attendances in England. HES is linked to the Office for National Statistics (ONS) to provide mortality data. All subjects from April 2001 to April 2015 in England with an ICD10 code for cancer 2 years prior to ERCP or in the following 6 months were examined. Subjects undergoing a curative surgical procedure were excluded. Associations between demographics, co-morbidities, unit ERCP volume and mortality were examined by logistic regression.

Results: 49055 subjects were included in the study of whom 48.7% were male, median age 74.5 years (range 19–104). Pancreatic cancer was the most common aetiology (63.5%), followed by liver and intrahepatic bile duct malignancy (19.4%). Mortality was 4.16%, 10.9% and 19.6% for 7 day, in hospital and 30 day mortality respectively. Multivariate analysis male gender (OR 1.14, (95% CI 1.08–1.20) p < 0.001); increasing by age quintile 64–71 (1.34, (1.23–1.47) p < 0.001), 72+ (1.12, (1.04–1.20) p < 0.001), 1.68–2.00) p < 0.001); increasing co-morbidity score 1 to 5 (1.09, (1.02–1.16) p < 0.001), 6–8 (1.32–1.35, p < 0.001); 11 to 15 (1.19, (1.33–1.66) p < 0.001); 16 to 20 (1.21, (1.14–1.30) p < 0.001); male gender, increasing co-morbidity score 1 to 5 (1.09, (1.02–1.16) p < 0.001), 6–8 (1.32–1.35, p < 0.001); 11 to 15 (1.19, (1.33–1.66) p < 0.001); 16 to 20 (1.21, (1.14–1.30) p < 0.001); and upper tertile of unit ERCP activity (p = 0.024) were associated with increasing 30 day mortality. Asian ethnicity (0.82, (0.67–0.99), p = 0.036), Cancer of extrahepatic and unspecified parts of biliary tree (0.60, (0.47–0.74), p < 0.001); advancing year of ERCP 2013/14 (0.78, (0.68–0.89), p < 0.001), 2014/15 (0.85, (0.74–0.98), p = 0.028); and previous renal failure (1.92, (1.77–2.09), p < 0.001) were associated with increasing 30 day mortality.

Conclusion: Short-term mortality in subjects with malignant biliary obstruction following ERCP was high. A better prognosis was observed in; high-volume ERCP units, Asian ethnicity and extrahepatic primary cancers. Male gender, advancing age, increasing co-morbidity score, greater deprivation and previous renal failure predicted death at 30 days.

Disclosure of Interest: All authors have declared no conflicts of interest.

TUESDAY, OCTOBER 31, 2017 09:00-17:00

P0750 EARLY DEVELOPMENT OF NONALCOHOLIC FATTY LIVER DISEASE IN GENETICALLY PREDISPOSED CHILDREN WITH OVERWEIGHT AND OBESITY DOES NOT COINCIDE WITH METABOLIC DERANGEMENTS

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Introduction: Non-alcoholic fatty liver disease (NAFLD) is a common chronic liver disease and in particular a health threat in obese children. Single nucleotide polymorphisms in genes encoding PNPLA3 (rs738409) and TM6SF2 (rs58542926) contribute to the development of NAFLD. It is however unknown whether liver parameters and cardiometabolic disturbances coincide in non-carriers and non-carriers of these risk alleles in an at-risk obese pediatric population. Therefore, we assessed cardiometabolic derangements, genetic predisposition for NAFLD and liver transaminase levels in children with overweight and obesity.

Aims & Methods: One hundred and seventy-four children (49% boys) from the Centre for Overweight Adolescent and Children’s Healthcare (COACH) at the Maastricht University Medical Centre were genotyped for PNPLA3 I148M and TM6SF2 E167K. Anthropometric, cardiometabolic risk and liver-related parameters were determined.

Results: Anthropometric parameters did not differ significantly between carriers and non-carriers of the risk alleles. ALT and AST were significantly higher in PNPLA3 G allele carriers as compared to the C allele carriers (ALT; CC 21 (0, 101), GG 26 (0, 101); p = 0.034, 0.000; GG 27, 50 (21, 00, 40, 00); p = 0.015) for the PNPLA3 G genotype, compared to the CC genotype. Carriers of the PNPLA3 risk allele did not show a deteriorated metabolic profile compared to non-carriers.

Conclusion: Despite significantly higher liver transaminase levels and a positive correlation between ALT levels and triglyceride and fasting insulin concentrations in PNPLA3 G allele carriers, these children did not have a more deteriorated cardiometabolic profile compared to non-carriers. The metabolic syndrome was more prevalent in risk allele carriers. These results suggest that hepatic aberrations and metabolic disturbances apparently do not develop concordantly in this specific population. Furthermore, these children with a high liver health risk may not be identified by measuring cardiometabolic parameters.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0751 TWO-DIMENSIONAL SHEAR WAVE ELASTOGRAPHY IN CHILDREN: WHAT IS THE MEANING OF MEASUREMENTS NEEDED FOR A HIGH QUALITY EVALUATION?

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Introduction: Pediatric chronic liver diseases are becoming a public health issue. Ultrasound based elastographic techniques have emerged as non-invasive methods of pediatric liver fibrosis assessment. The most recent are two dimensional (2D) SWE techniques. While elastography appears to be highly reproducible in children, there is still no consensus regarding the number of measurements to be performed for a high-quality evaluation.

Aims & Methods: We aimed to investigate the number of liver stiffness measurements (LSM) needed for a high-quality evaluation using a 2D SWE technique. We conducted a prospective study which included 73 children (age range: 3–17 years, mean age 11.73 ± 3.35 years, 37% girls, mean body mass index (BMI) 25.12 ± 7.38 kg/m²). We used the 2D-SWE.GE (Logiq E9, GE Healthcare, Chalfont St. Giles- UK), with a C1-Transducer. One examiner performed 10 LSM for each child. We randomly extracted 1 LSM, 2 LSM, 3 LSM and 5 LSM from all 10 and calculated their respective medians. We employed the Friedman test to compare the medians of 1, 2, 3, 5 and 10 LSMs. We used the interclass correlation coefficient (ICC) to assess the agreement between the medians of 1, 2, 3, 5 and 10 LSMs.

Results: Medians calculated from 1, 2, 3, 5 and 10 LSMs were similar (ICC = 0.893 (0.72–0.95) vs 4.22 ± 0.91 kPa, 4.25 ± 1.03 vs 4.2 ± 0.99 kPa vs 4.19 ± 0.99 kPa, p = 0.94). Furthermore, the agreement between medians calculated from 1, 2, 3, 5 and 10 LSMs was excellent (ICC = 0.960, 95% confidence interval: 0.944–0.974).

Conclusion: We suggest obtaining 5 LSM for a high-quality evaluation using this 2D SWE technique.

Disclosure of Interest: S.A. Popescu: I hereby confirm that I have received financial support (Congress travel grants, speaker fee) from: Philips, General Electric, Abbvie, AbxiZeAme, Zentiva

All other authors have declared no conflicts of interest.

I. Sporea: I hereby confirm that I have received financial support (Congress travel grant or speaker fee) from Philips, Siemens, General Electric, Abbvie, Zentiva, Bristol Meyers Squibb

TUESDAY, OCTOBER 31, 2017 09:00-17:00

P0752 PERCUTANEOUS EMBOLIZATION OF VISCERAL ARTERY PSEUDO-ANEURYSMS – A TERTIARY CENTER EXPERIENCE

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Introduction: Visceral artery pseudo-aneurysms are rare, but potentially fatal if rupture. Pseudoaneurysm usually occurs most frequently after pancreatitis. Angiembolization with conventional trans-catheter approach is the standard treatment. Direct percutaneous embolization has been commonly used for treatment of peripheral artery pseudoaneurysm when trans-catheter approach is not feasible. However, very limited data is available regarding its safety and efficacy in visceral artery pseudoaneurysm.
Aims & Methods: We aimed to assess the technical feasibility, safety and effic- iency of percutaneous embolization as an alternative treatment option for visceral pseudo aneurysms. We retrospectively evaluated the data of patients who underwent percutaneous embolization at our institution from Feb 2007 to March 2017. All procedures were performed under ultrasound (US) guidance and both embolization techniques (transarterial and transvenous) were used. Technical feasibility, safety and efficacy of percutaneous embolization were analysed. At 30 days follow up US with color Doppler/dual phase computed tomography was done to see for recurrence of pseudoaneurysm.

Results: 23 patients (18 male) with mean age of 34.47 ± 21.28 (7–72) years, under- went direct percutaneous embolization for visceral pseudo aneurysm. Most common aetiology for pseudo aneurysm was pancreatitis (16) followed by trauma (3), paracentesis (3) and surgery (1). The site of pseudo aneurysm was splenic artery (3), left gastric artery (3), hepatic artery (3), inferior epigastric artery (3) and gastroduodenal artery (1). Mean size of pseudo aneurysm was 1.8 ± 0.6 (1–3.5) cm. Reasons for choosing percutaneous approach over transcatheter embolization included: technical difficulties in 11 patients, excess collat- erals that would obstruct the feeding artery in 5 patients, and recurrence after pre- vious embolization in 6 patients. Agents used for embolization-glue with lipiodol (21), coil (1) and coil with glue (1). Mean procedural time was 11.3 ± 2.11 (8–16) minutes and fluoroscopy exposure time was 2.4 ± 1.14 (1–6) minutes. Percutaneous embolization was successfully performed in all patients (technical success 100%). Mild adverse events included: local site pain in 19 (80%) patients. Moderate adverse event included: splenic infarct in 5 patients, all of which responded to conservative management. There were no major adverse events and no occurrence of distant embolization. At median follow up of 910 days (30–3186) there was no recurrence of pseudoaneurysm (clinical success 100%).

Conclusion: Percutaneous embolization is safe and effective for treatment of visceral artery pseudoaneurysm. Percutaneous technique may be considered as an alternative to trans-catheter embolization in cases of challenging anatomy, multiple collaterals and recurrence after previous embolization precluding transcatheter approach.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0753 DEVELOPMENT OF AUTOIMMUNE PANCREATITIS IS INDEPENDENT OF NON-CANONICAL NFkB PATHWAY ACTIVATION IN PDECs

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Introduction: Chronic (CP) and autoimmune pancreatitis (AIP) are characterized by different pathophysiologic mechanisms. Whether CP is a preseucibility for autoimmunity is still unclear. AIP is considered mostly a T-cell mediated disease; however, in induction of chronic pancreatitis macrophages play a pivotal role. Cytokine dependent kinase (cdk) inhibitors are critical regulators in inflammatory disease and pancreatic fibrosis, activating autophagy, differentiation of macrophages, and apoptosis. In particular, p21 has been described as a mediator of inflammation and various autoimmune diseases by regulating T-cell activation and promoting macrophage development. We therefore examined the role of p21-mediated inflammation in AIP.

Aims & Methods: Human pancreas samples from CP and AIP patients were evaluated for p21 expression. To investigate the effects of p21 in pancreatitis, we intercrossed lymphotixin overexpressing mice (Tg(Elf-1/L-a,b)−/−) a model to study CP and AIP – with p21 deficient (p21−/−) mice. Infiltrating cells were visualized by immunohistochemistry, supported by gene expression analysis in an early and a progressive phase. Circulating autoantibodies and the presence of circulating autoantibodies and the presence of circulating autoantibodies and neutrophil infiltration to the pancreas. Interestingly, neutrophils do not recruit into the interstitium, suggesting that they are present as a result of local processes.

Results: p21 was upregulated in human CP patients but remained unchanged in AIP patients. p21 deficiency in LT mice (LtP21−/−) prevented early pancreatic injury. LtP21−/− mice had normal serum amylase, reduced inflammatory gene expression and histopathology. In acinar cells diminished proliferation and aberrant activation of non-canonical NF-kB pathway was observed. In contrast, 12 months old LT mice with and without p21 had similar inflammatory gene expression and T & B cell infiltration. Interestingly, Lt and LtP21−/− mice had comparable tertiary lymphoid organs (TLOs), autoreactive and elevated IgG levels. However, acinar cell proliferation, acinar-to-duodenal metaplasia and acinar non-canonical NF-kB pathway activation remained impaired in LtP21−/− pancreata.

Conclusion: Our findings indicate that p21 is crucial for pancreatitis in LT-driven pancreatic injury. p21 is involved in early acinar secretion of inflammatory mediators that attract innate immune cells. However, p21 is not essential for humoral immune response, accountable for autoimmunity and lack of p21 does not rescue AIP. Notably, p21 interventional NF-kB activation and renders acinar cells less susceptible to proliferation and transdifferentiation. We therefore suggest that chronic and autoimmune pancreatitis follow different inflammatory processes.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0754 GRANULOCYTES DRIVE PANCREATITIS IN A NOVEL MODEL OF INTERLEUKIN-17A-PERITIDYL ARGININE DEIMINASE-DEPENDENT EXTRACELLULAR TRAP FORMATION


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Introduction: Various forms of pancreatitis (e.g. severe acute pancreatitis, auto- immune pancreatitis type 2) are characterized by an infiltration of neutrophil granulocytes. Yet, despite sharing the feature of granulocytic infiltration, these diseases take opposing natural courses of disease. A novel function of granulo- cytes, the formation of aggregated neutrophil extracellular traps (aggNETs), has been described and called for a reevaluation of the specific role of neutrophils in pancreatitis. We were interested in the specific function of granulocytes in various models of pancreatic inflammation.

Aims & Methods: Experimental models of pancreatic inflammation were employed including caerulein-induced pancreatitis and a novel model of IL-17A-induced pancreatitis. The outcome of disease was characterized by immu- nohistochemistry, DNA expression and flow cytometric analyses.

Results: Transgenic systemic delivery of IL-17A alone can induce granulocytosis and neutrophil infiltration to the pancreas. Interestingly, neutrophils do not recruit into the interstitium, suggesting that they are present as a result of local processes.

Conclusion: Granulocytes aim to contain an inflammatory focus and enter pan- creatic ducts with potentially detrimental consequences to dependent areas of the organ.

Disclosure of Interest: M. Leppkes: M.L. has received a research scholarship from MSD Sharpe & Dohme GmbH, Germany. No financial or non-financial conflict of interest exists related to this study.

All other authors have declared no conflicts of interest.

P0755 MITOCHONDRIAL FUNCTION AND DISTRIBUTION IN PANCREATIC DUCTAL EPITHELIAL CELLS

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Introduction: Mitochondrial dysfunction is a hallmark of several disease patho- genesis including acute pancreatitis (AP). Our results suggest that mitochondrial damage is crucial in bile acid induced inhibition of pancreatic ductal HCO3− secretion, however the details of mitochondrial function and dysfunction in pan- creatic ductal epithelial cells (PDEC) is not known yet.

Aims & Methods: The aim of our study was to characterize the mitochondrial function and distribution in pancreatic ductal epithelial cells under physiological and pathophysiological conditions. Guinea pig and Cyclophilin D WT and knock out (KO) mouse pancreatic ducts were used. Mitochondrial distribution was studied by electron microscopy (EM). Mitochondrial membrane potential (ΔΨm) was measured by confocal microscopy and pancreatic ductal HCO3− secretion by microfluorometry.

Results: EM measurements revealed that the mitochondrial density is signifi- cantly higher on the apical side of the guinea pig PDEC compared to the middle or the basal segment in HEPES solution. The apical mitochondrial den- sity increased further in CO2/HCO3− buffered solution, or during the adminis- tration of 5 µM forskolin. It was also confirmed by the ΔΨm measurements as we detected increased TMRM fluorescence on the apical side of the PDEC during stimulation. The genetic KO of cyclophilin D WT markedly reduced the loss of ΔΨm and protected pancreatic ductal HCO3− secretion during the adminis- tration of 500 µM chenodeoxycholic acid.

Conclusion: Our results revealed that mitochondrial function has a central role in the function of PDEC presumably by providing ATP for fluid and ion secretion. On the other hand the opening of MPTP seems to be crucial in the bile acid induced toxicity offering a potential therapeutic target in AP.

Disclosure of Interest: All authors have declared no conflicts of interest.

United European Gastroenterology Journal 5(5S)

Introduction: Inflammatory complications are major causes of mortality in severe acute pancreatitis. Most infections in AP are intestinal origin (2). The Nucleotide oligomerization domain 2 (NOD2) is a NOD-like receptor family member that senses and responds to bacterial wall peptides (3). Guenther et al. reported that p.R702W mutation was found to be associated with multiple organ failure and mortality in patients with AP (4). We aimed to investigate whether there is a correlation between NOD2 variants and AP severity in this study.

Aims & Methods: Group 1 (n = 27) was healthy. Group 2 (n = 36) and Group 3 (n = 32) were composed of mild and severe pancreatitis patients according to the Atlanta 2012 classification (5). Four NOD2 variants and serum interleukin-6 (IL-6), Tumor Necrosis Factor-α (TNF-α) and lipopolysaccharide-binding protein (LBP) levels were studied.

Results: We detected p.R702W variant in 3 patients (3/32, 9.4%) in severe pancreatitis group, but this variant was not seen in the other two groups. 1007fs variant was found in 3, 3 and 1 patient in mild (3/36, 8.3%) and severe pancreatitis (3/32, 9.4%) groups, and in healthy group (1/27, 3.7%), respectively. There was no significant difference in the frequencies of NOD2 variants between groups. Serum IL-6, TNF-α and LBP levels were significantly higher in the severe pancreatitis group than in the healthy group and mild pancreatitis group (all p < 0.001). However, there was no significant difference between these cytokine levels and NOD2 variants.

Conclusion: Our results suggest that there may be a relationship between the presence of p.R702W variant and severe pancreatitis.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P0758 A LAMMEN ADO METAL STENT WITH ANTI-REFLUX VALVE FOR ENDOSCOPIC ULTRASOUND-GUIDED DRAINAGE OF PSEUDOCYST AND WALLED-OFF NECROSIS

Conclusion: Our results suggest that there may be a relationship between the presence of p.R702W variant and severe pancreatitis.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P0757 DETERMINANTS OF SEVERITY IN ACUTE PANCREATITIS - A NATION-WIDE PROSPECTIVE MULTICENTER STUDY

Introduction: Pancreatic pseudocyst (PC) and walled-off necrosis (WON) are frequent complications of acute pancreatitis. Drainage procedure is required for complications such as pain, biliary obstruction, infection, or reflux of bowel contents while improving the stent patency. The aim of this study is to investigate the efficacy and the rate of complications of EUS-guided drainage using novel LAMS with anti-reflux valve for PC and WON.

Aims & Methods: We compared the technical success, outcomes of the LAMS group compared to the plastic stent group. Ten patients underwent EUS-guided drainage using the novel LAMS (LAMS group) and eighteen patients using conventional plastic stents (plastic stent group) from December 2013 to October 2016. A novel LAMS used in this study was designed to have bilateral flare ends, 4 anti-migration flaps (at each side) and a pair of 2 anti-reflux valves (inside the lumen). Technical success was defined as a successful placement of the stent. Clinical success and clinical success is defined as a resolution of the PC/WON and disappearance of the symptoms.

Results: Among 10 patients treated with LAMS, 4 patients had complicated PC and 6 patients had WON. In plastic stent group, 15 patients had complicated PC and 3 patients had WON. The median size of fluid collection before treatment was 69.5 mm (range, 48-214 mm) in LAMS group and 92.0 mm (56-253 mm) in plastic stent group. Median duration of stent placement was 47 days (1-355 days) in LAMS group and 55 days (1-216 days) in plastic stent group. Treatment outcomes of the LAMS group were not inferior despite the significantly higher proportion of WON patients in the LAMS group compared to the plastic stent group. There were no statistically significant differences in the technical success rate (100% vs. 94.4%; p = 0.959), clinical success rate (70% vs. 77.8%; p = 0.491), resolution rate (76.8% vs. 80.7%; p = 0.705), complication rate (40% vs. 50%; p = 0.456). In LAMS group, 3 patients experienced mild fever and 1 patient showed peritonitis due to immediate stent migration. In plastic stent group, mild fever was developed in 4 patients, all amount of pneumatic peritonitis was in 1 patients, self-migration of stent (after resolution of fluid collection) was in 2 patients. 3 patients showed serious adverse events - 1 patient in each group experienced peritonitis due to immediate stent migration and 1 patient with plastic stent group developed active bleeding. Procedure time (30.7 minute) vs. 41.2 minutes; p = 0.106) and fasting period after treatment (3.1 days vs. 2.1 days; p = 0.344 were also not different between two groups.

Conclusion: For EUS-guided drainage, LAMS showed acceptable treatment outcome compared to the rate in conventional drainage even in relatively small amount of pancreatic fluid collection. And no additional fasting period was required in the LAMS group compared to the plastic stent group. Further well-designed prospective studies are needed to validate these findings.

Disclosure of Interest: All authors have declared no conflicts of interest.
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An attack is lower than patients without cholecystectomy, and the difference was
5.35–16.30); 30.6% (26/85), 6.18 (IQR 2.60–9.07). To biliary AP, the recurrence

Aims & Methods: This study aimed to retrospectively correlate the clinical char-
acteristics of the necrotic cavity with the extent of endoscopic transmural drainage: 49
patients (38 males; mean age 60.79 ± 13.44) with symptomatic WON treated by
an attempted EUS-TD initially were enrolled in this study. The relationship
between the outcome of treatment and the clinical characteristics including morpho-
logical and endoscopic characteristics of WON was assessed.

Results: The mean size of WON was 126.63 ± 46.79 mm. EUS-TD was techni-
cally successful in 48/49 (97.9%) patients and 26 (54.2%) improved with EUS-
TD alone while step up approach was needed in 19 patients. DEN, percutaneous
necrosectomy may be required. The factors

Introduction: Endoscopic ultrasound-guided transmural drainage (EUS-TD) has
been shown to be a safe and effective minimally invasive treatment for walled-off
necrosis (WON). However, in some cases, simple drainage is not sufficient to manage
the symptoms of WON and step up approaches such as direct endoscopic
necrosectomy (DEN) and surgical necrosectomy may be required. The factors
associated with the outcome of endoscopic treatment for WON remain unclear.

Aims & Methods: This study aimed to retrospectively correlate the clinical char-
acteristics of the necrotic cavity with the extent of endoscopic transmural drainage: 49
patients (38 males; mean age 60.79 ± 13.44) with symptomatic WON treated by
an attempted EUS-TD initially were enrolled in this study. The relationship
between the outcome of treatment and the clinical characteristics including morpho-
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TD alone while step up approach was needed in 19 patients. DEN, percutaneous
necrosectomy may be required. The factors

Disclosure of Interest: All authors have declared no conflicts of interest.

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MPA.0000000000000364.
admission to European hospital. A receiver operating characteristic (ROC) analysis was built up to classify patients of severe AP. Later, a multiple discriminant analy-sis was performed, using the Wilks lambda test, to identify the variables that differ most between patients with mild AP and moderate/severe AP. A ratio calculated using the most discriminant cytokines was studied in relation to sever-ity and mortality.

**Results:** ROC curves showed that TH1 cytokines IL6, IFN-γ and TNF-α can be measured for the prediction of severe AP, while TH2 cytokines IL4, IL13, GM-CSF, for the prediction of a mild or moderate condition. A stepwise analysis showed that IL13 and IFN-γ were the biomarkers which contributed most to the discrimination between mild and moderate/severe AP (Wilks’ lambda = 0.855, p < 0.0001; Wilks’ lambda = 0.747, p < 0.0001, respectively). We calculated the IL13/IFN-γ index. This ratio was significantly higher in patients with mild AP with respect to patients compared between groups (p = 0.025). This difference was also observed between severe AP and the rest of the patients (p = 0.007). The ROC curve was also modified, increasing the area under the curve (AUC), the sensitivity and the specificity, in relation to AP severity.

Comparing an IL13/IFN-γ ratio that could be of great interest in the assessment of prognosis in AP. A high value of the IL13/IFN-γ ratio at hospital admission is associated with a good prognosis of AP.

**Disclosure of Interest:** All authors have declared no conflicts of interest.
Diameter (cm) 9(4.5)
Location 13(28.3)
Body/tail 31(67.4)
Whole 2(4.3)
Features
Poorly-defined wall 4(8.7)
Loculation 11(23.9)
Lumpy/mass content 18(39.1)
Organism
Gram positive 7(15.2)
Gram negative 4(8.7)
Mixed 15(32.6)
Unknown 20(43.5)
Site of cyst enterostomy
Stenting a 36(78.3)
Duodenal bulb 10(21.7)
Necrosectomy
Patient (n, %) 28(60.9)
Number of Necrosectomy (n, IQR) 1(2)
Nasocystic drainage (n, %) 15(32.6)
Technical success 45(97.8)
Stent revision 12(26.1)
Spontaneously migration 8
Dislodged during necrosectomy 2
Ineffective drainage 2
Adverse events 20(43.5)
Bleeding 9
Mortality 10
Outcomes
Duration of hospital stay (days) 64(33)
Duration of stent insertion (week) 10(4.5)
Clinical success 43/93(46)
Recurrence 3(6.5)

Data are either median (IQR) or no. (%) of patients, unless otherwise indicated.

Introduction: Post-endoscopic retrograde cholangiopancreatography (ERCP) pancreatitis (PEP) is a common and serious adverse event following ERCP, with a reported incidence of 9.7% in unselected patients [1]. Given huge economic and clinical burden, effective approaches for post-ERCP pancreatitis prophylaxis remains a major priority for research. Nonsteroidal anti-inflammatory drugs (NSAIDs) have also been shown the potential efficacy in prophylaxis PEP across high-risk patients, especially for diclofenac or indomethacin [3–5]. Recently, a prospective, double-blind, controlled trial conducted by Levenick [6] and colleagues in the USA showed that the reduction in PEP using indomethacin was not as significant as previously reported. In fact, even more cases of pancreatitis occurred in indomethacin group compared with placebo group. Subsequently, a high-quality meta-analysis also concluded that there is no prophylaxis for the prevention of PEP among average-risk patients[7]. These findings raised the question that whether administration of rectal indomethacin should be recommended in average-risk patients.

Aims & Methods: We aimed to determine the beneficial effect of rectal indomethacin in the prevention of post-ERCP pancreatitis in average-risk of patients. We systematically searched for Medline and EMBASE, Web of science, and Cochrane library before October 2016. Studies that evaluated rectal administration of indomethacin in the prevention of post-ERCP pancreatitis were included in the analysis. We adopted a random-effects model to calculate overall relative risk (RR) and 95% confidence interval (CI).

Results: We identified ten randomized clinical trials from initial search and finally included in the meta-analysis. Administration of rectal indomethacin significantly reduced the incidence of PEP in combined population (RR, 0.63; 95% CI, 0.50–0.77). There was no significant heterogeneity across included studies (I² = 14.2%, P = 0.31). In subgroup analysis, rectal indomethacin was effective in both high-risk (RR, 0.49; 95% CI, 0.35–0.71) and average-risk (RR, 0.69; 95% CI, 0.55–0.86) patients and reduced the risk of mild and moderate to severe pancreatitis. The overall results remained unchanged and robust in sensitivity analysis. There was no evidence of significant publication bias among this meta-analysis.

Conclusion: Rectal administration of indomethacin is an effective approach to prevent the incidence of post-ERCP pancreatitis both in high-risk and average-risk population undergoing ERCP. However, more high-quality randomized controlled trials are needed to further investigate the optimal timing for administration of indomethacin.

Disclosure of Interest: All authors have declared no conflicts of interests.

References

P0766 THE IMPACT OF THE SPECIALISTIC GAS TROENTEROLOGICAL UNIT ON THE OUTCOME OF ACUTE PANCREATITIS (AP) IN THE VENETO REGION (NORTH-EAST OF ITALY)

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Introduction: Acute pancreatitis (AP) is one of the most common gastrointestinal diseases requiring hospitalization with an annual incidence of 13–50 cases per 100,000 persons. It is a potentially fatal disease with an overall mortality ranging from 2 to 8%. Both epidemiology and outcomes are variables according to the different hospitals. Furthermore, few studies have evaluated the impact of the hospital units on AP outcomes.

Aims & Methods: To evaluate both the trend and outcomes of acute pancreatitis according to the admitting hospital units: Surgery, Internal/General Medicine, Gastrointestinal (GI) Unit, Intensive Care Unit (ICU). This is a retrospective
cohort study based on the anonymous computerized database of hospital discharge (Veneto Region, North-East of Italy). The principal diagnosis of AP according to the International Classification of Diseases 9th revision, Clinical Modification (ICD 9-CM, code 577.0) of the hospital discharges was selected. The period from January 2001 to December 2015 was analysed. Veneto population was considered as the reference population (in the period, it varied from 4,529,823 to 4,927,527 inhabitants, with 51% females). Hospitalization, Length of stay (LOS), in-hospital mortality, need for surgery (according to the DRG 191–194, 199–201 which identified bila-pancreatic surgery) were reported according to hospital Units. Statistics: Chi squared for trend and Odds Ratio (OR) were applied.

Results: During the analysed period, 23,389 overall hospitalizations for AP, annual hospitalizations of 32 patients/100,000 inhabitants and in-hospital mortality of 3.2% were observed. Characteristics of the patients were: mean age: 62.2 ±/−19.3y, 54% Males (M); Female (F) mean age: 65y/+/−19.3ys, male mean age: 59.4y/+/−19.3ys (p < 0.05). Hospitalizations was higher in males (M: 35.4: F: 28.4, OR 1.24 (95% CI: 1.20–1.27, p < 0.001). On comparison to General Medicine Units, GI units were associated with a low in-hospital mortality (OR: 0.37, CI 95%: 0.28–0.49, p < 0.05) and an high NFS (OR: 2.88, CI 95%: 2.18–3.81, p < 0.05).

Admitting Hospital Unit: Number of In-Hosp. Lengths of stay (%) Mortality (%)
(2001–2015) cases (%) (days) General Medicine (Non GI) 6, 980 (30%) 13.5 ± 10.7 4.3% 88 (1.3%)
Gastrointestinal (GI) Units 3, 797 (16%) 12 ± 11.2 1.7% 135 (3.6%)
Surgical Units 12, 112(52%) 13 ±/−13.6 2.7% 443 (3.7%)
Intensive Care Unit 52 (2%) 17.2 ± 21.8 12.9% 42 (8.1%)

**Conclusion:** During the last 15 years in the Veneto Region, hospitalization rate, in-hospital mortality rate and need for surgery of acute pancreatitis significantly decreased. Conversely, admissions in both General Medicine and GI units increased. Management of AP in GI units seems to be related with a best outcome: lower in-hospital mortality and probably, more eligible patients for surgical treatment.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**References**

P0768 ACUTE PANCREATITIS IN PATIENTS WITH IPMNS: RETROSPECTIVE STUDY OF 346 PATIENTS OBSERVED FROM 2009 TO 2016
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Introduction: In literature the frequency of acute pancreatitis (AP) in patients with IPMNs varies between 12 and 65%, but most of studies are from surgical series and often pancreatitis occurred after surgery was included. Furthermore, most of the studies includes in the dictum of "symptomatic IPMNs" the presence of less severe disorders, such dyspeptic symptoms, making series unclear.

Aims & Methods: The aim of this study was to investigate the correlation between the severity of IPMN and acute pancreatitis and his disease severity. A retrospective analysis was performed on all observed patients with IPMN-MD, IPMN-BD and mixed type at Gastroenterology Unit in the period between January 2009 and March 2016. In the study patients with an instrumental or histological diagnosis of IPMNs were included.

Results: A total of 346 patients (164 males and 182 females, mean age at the first report 61.6 ± 12.2 years). At the time of radiological diagnosis, 45% were asymptomatic, 51% had had symptoms, while 4% of the data were missing: the frequency of AP (excluding biliary etiology) of all 346 patients with IPMN was 26%. AP was edematous in 85% of patients and necrotic in 15%. We found increased frequency in patients with PA with IPMN of the main pancreatic duct (MD and mixed), and unfocal type. The localization to the body seems to more be correlated with the presence of AP. The number of cysts (for IPMN-BD and mixed type) was significantly lower in patients who have had AP.

Conclusion: Our medical extraction series confirms that the PA is an event that occurs in 26% of patients with IPMN, with a prevalence of the male sex, it is associated with a IPMN central and mixed type, predominantly located in the head to the body. The pancreatitis is not associated with malignancy in resected patients.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0769 APOLIPOPROTEIN B AND A-I RATIO PREDICTS SEVERE ACUTE PANCREATITIS
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Introduction: Severe acute pancreatitis (SAP) has a considerable mortality and morbidity rate. Although many indices have been developed to classify the severity of acute pancreatitis (AP), there is no ideal method for predicting SAP. The ratio of apolipoprotein B to A-I (apoB/A-I) is associated with metabolic syndrome and inflammatory status.

Aims & Methods: This study aims to investigate the association between severity of AP and serum apoB/A-I ratio. Patients with AP were prospectively enrolled at Yonsei University Wonju College of Medicine from March 2015 to August 2016. The severity of acute pancreatitis was assessed according to the revised Atlanta classification criteria (Atlanta 2012).

Results: Of 191 patients with AP, 134 (70.2%) were classified as mild AP, 42 (22.2%) as moderately severe AP, and 15 (7.9%) as SAP. The apoB/A-I ratio was highest in patients with SAP compared with those with mild and moderately severe AP (p<0.001). The apoB/A-I ratio positively correlated with Atlanta classification, computed tomography severity index, and Bedside index for severity of AP. The apoB/A-I ratio showed the highest ability to predict SAP in patients with AP compared with apolipoprotein B or apolipoprotein A-I alone.

Conclusion: Serum apoB/A-I ratio appears to have value in predicting SAP in patients with AP.

Disclosure of Interest: All authors have declared no conflicts of interest.
P0770 IMAGING IN CHRONIC PANCREATITIS – DATA FROM THE SCANDINAVIAN-BALTIC PANCREAS CLUB DATABASE

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Introduction: The Scandinavian-Baltic Pancreas-Club database collects data from patients with chronic pancreatitis (CP) in Nordic countries. Grading of structural changes is important in the description of a CP cohort.

Aims & Methods: We aimed to characterise structural changes of the pancreas in patients with CP. Subjects with definitive or probable CP according to the M-ANNEHIM diagnostic-criteria were included. Structural changes were graded according to the M-ANNEHIM-classification. A subgroup was also scored by the modified Cambridge score. Clinical data on disease-duration, nutrition, exocrine function, pain, alcohol/smoking habits and frequencies of malnutrition and diabetes were collected. A grouping of the M-ANNEHIM score (A: Normal = 0, B: Minimal change = 1 to 2 and C: Moderate/marked = 3–4) was performed for correlation to the clinical data.

Results: The database contains 932 patients (623 men). The M-ANNEHIM-score was present from 446 subjects and both imaging scores from 93 subjects. According to M-ANNEHIM subjects were graded as 0: Normal (8,1%), 1: Equivocal (22,9%), 2: Mild (12,1%), 3: Moderate (17,9%) and 4: Marked (39,0%). Correlation of the imaging scores: The imaging-scores demonstrated acceptable correlation (ρ = 0.75, p < 0.001) and good agreement (ICC = 0.71 (0.59, 0.8), p < 0.001). Agreement was best for groups with marked changes. The clinical parameters divided by M-ANNEHIM groups are presented in the table.

<table>
<thead>
<tr>
<th>Clinical parameter</th>
<th>A: Normal</th>
<th>B: Minimal change</th>
<th>C: Marked</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disease duration (Years)</td>
<td>3.6(5.2)</td>
<td>4.6(5.8)</td>
<td>5.0(6.4)</td>
</tr>
<tr>
<td>Pain (VAS 0–100)</td>
<td>38.3(39.2)</td>
<td>39.4(36.5)</td>
<td>35.5(35.3)</td>
</tr>
<tr>
<td>Nutrition (BMI kg/m²)</td>
<td>24.2(5.0)</td>
<td>24.7(5.5)</td>
<td>23.7(4.7)</td>
</tr>
<tr>
<td>Malnutrition (%)</td>
<td>4</td>
<td>10</td>
<td>11</td>
</tr>
<tr>
<td>Diabetes (%)</td>
<td>37</td>
<td>43</td>
<td>39</td>
</tr>
<tr>
<td>Smoke (Pack years)</td>
<td>0(0–20)</td>
<td>0(0–25)</td>
<td>17(0–37)*</td>
</tr>
<tr>
<td>Alcohol (Lifetime years &gt; 0.5units/day)</td>
<td>0(0–18)</td>
<td>0(0–18)</td>
<td></td>
</tr>
</tbody>
</table>

*p < 0.05 (Kruskal-Wallis). No other differences reached significance. Values: mean (SD) or median [IQR-range]. Malnutrition: BMI < 18.5.

Conclusion: Subjects with marked structural changes had the highest lifetime smoke-doses. There was poor correlation of structural changes to the clinical features. The two imaging scores demonstrated acceptable correlation and agreement. Poor agreement in normal/minimal-change groups may reduce the value of the scores where they are most needed. The results are presented on behalf of the SBPC study group.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P0771 OSTEOPATHY IS COMMON IN PATIENTS WITH CHRONIC PANCREATITIS, BUT IS NOT RELATED WITH VITAMIN D AND FECAL ELASTASE LEVELS (P-BONE STUDY)

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Introduction: In patients with chronic pancreatitis (CP) malabsorption of vitamins D and K, alcoholism, smoking and inflammatory status contribute to low bone mineral density (BMD). A recent meta-analysis estimated the prevalence of osteoporosis (25%) and osteopenia (40%) in CP and highlighted limitations of the reviewed studies.

Aims & Methods: To evaluate the prevalence of osteoporosis and osteopenia in patients with CP and to investigate the correlation between BMD and CP features, and vitamin D and PEI. This is a multicentre cross-sectional study (P-BONE, A Pancreas 2000 project) on prevalent CP patients. The Diagnosis and severity of the disease was defined according to the M-ANNEHIM classification. Clinical information and biochemical variables were recorded: PEI was assessed by fecal elastase. Standardized dual-energy X-ray absorptiometry was performed by dual energy x-ray absorptiometry (DEXA). Categorical variables were analysed by means of Fisher’s exact test, and continuous variables by t-test. A logistic regression analysis was performed to identify risk factors for osteoporosis or osteopenia. The relationship between continuous variables was assessed with Pearson correlation coefficient.

Results: 211 consecutive CP patients were enrolled at 6 Centres (67% M; mean age 60 ± 13 years). Osteopenia was diagnosed in 42% and osteoporosis in 22% of cases. Aetiology was alcoholic in 43%, and 18% had severe CP. 56% of patients had PEI. The mean value of vitamin D was 20ng/ml and 56% of cases had vitamin D insufficiency. There was no correlation between vitamin D levels, or elastase levels and t-score at either spine or femur. Alcoholic aetiology was associated with higher risk of osteoporosis at low levels of fecal elastase (p 0.02) and with lower level of vitamin D (p 0.001) but not with osteoporosis or osteopenia. Female sex and older age seems to be associated with a higher risk of developing osteoporosis (OR 4.595%CI 2.98–9.001; OR 1.09 95% CI 1.30–1.50) while a higher BMI is associated with a reduced risk of its occurrence (OR 0.89 95%CI 0.77–0.94 p 0.001).

Conclusion: The present data confirm a high rate of osteopathy in CP patients. However, there was apparently no correlation between BMD, pancreatic exocrine function, severity of the disease or vitamin D levels. Other factors, such as vitamin K might deserve investigation for their possible relationship with bone mineral density in CP patients.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
Cancer screening should be discussed especially in case of pancreatitis with calcifications.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0773 EXOCRINE FUNCTION, NUTRITION AND ENZYME TREATMENT IN THE SCANDINAVIAN BALTIC PANCREAS CLUB DATABASE - PRELIMINARY DATA

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Introduction: The Scandinavian-Baltic-Pancreatic-club database collects patients with chronic pancreatitis (CP) from Nordic countries. Description of exocrine pancreatic insufficiency (EPI) and consequences is important in characterization of CP cohorts.

Aims & Methods: Characterise EPI from CP in a Northern European cohort. Patients with definitive or probable CP (M-ANNHEIM diagnostic criteria) were included from nine centres. Demographic data, body-mass index (BMI), faecal elastase (FE), enzyme-doses and lab-parameters were collected. Values: Mean (SD) unless otherwise stated. EPI-classification grouped patients as follows: A: Normal, B-Mild: EPI not requiring enzymes, C-Proven: EPI requiring enzymes.


Clinical parameter (A) Normal (B) Mild insufficiency (C) Proven insufficiency

Exocrine pancreatic function (%)

33 16 51

Faecal Elastase (µg/g) (mean (SD)) p < 0.001

368 (161) 128 (144) 51 (69)

Nutrition: (kg/m²) (mean (SD)) p < 0.005

24.6(4.9) 23.7(4.3) 22.6(4.3)

Frequency BMI > 25 (%)

5 16

Vitamin D: Frequency BMI < 18.5 (%)

5 23.7 17.6

Enzyme Treatment (lipase-units/day) (median [IQ range])

0[0–7500] 120000

Hemoglobin: (median [IQ range]) p < 0.05

11.8(2.7–3.0) 10.7(2.8)

Faecal Elastase and disease duration (years)**

<10: 143(175) >10: 91(18)

*p < 0.001. 9% received <5000 lipase-units/day. 14 subjects having FE > 200 received enzymes, 48 subjects with FE < 100 received no enzymes. **no age/sex differences in EPF

Conclusion: In our material frequency of EPI is higher than reported in the NAPS2 study (31%). Consequences of EPI were lower BMI, underweight, higher enzyme-doses and lower haemoglobin. Need for vitamin D supplements was highest in the group with mild EPI not receiving enzymes.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0774 FLUID AND HCO3− SECRETION AND CFTR ACTIVITY IS INHIBITED BY CIGARETTE SMOKE EXTRACT IN GUINEA PIG PANCREATIC DUCTAL CELLS

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Introduction: Smoking represents an independent risk factor for the development of chronic pancreatitis (CP). It is well documented that secretion of pancreatic ductal alkaline fluid (which is regulated mostly by the anion exchanger and CFTR) is diminished in CP.

Aims & Methods: In this study we would like to understand whether smoking has any effects on pancreatic ductal fluid and HCO3− secretion. Guinea pigs were exposed to cigarette smoke four times a day for 30 min for 6 weeks. The CFTR expression was analysed by immunohistochemistry. Pancreatic ducts were isolated from guinea pig pancreas. Cigarette smoke extract (CSE) was prepared by smoking of 15 cigarettes into 10 ml distilled water by a smoking machine. Intracellular Ca2+ concentration and pH were evaluated by microfluorometry. Fluid secretion was measured by video microscopy. CFTR currents were detected by whole cell configuration of patch clamp technique.

Results: Cigarette smoking significantly diminished the expression of CFTR and the fluid and HCO3− secretion in guinea pig pancreas. CSE dose dependently decreased fluid and HCO3− secretion in guinea pig pancreatic ducts via inhibition of anion exchanger, Na+/H+ exchanger and Na+/HCO3− cotransporter and also forskolin-stimulated Cl− current of CFTR Cl− channel. CSE incubation altered the pattern of carbazochrome-induced Ca2+ signal in pancreatic ducts suggesting that some of the inhibitory effects may be regulated by calcium signalling.

Conclusion: Tobacco smoking and CSE inhibits pancreatic ductal fluid and HCO3− secretion and the activity of the CFTR which may play role in the smoke-induced pancreatic damage. This study was supported by OTKA, MTA, SZTA and UNKP.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0775 HISTOLOGICAL DIAGNOSIS WITH RAPID ON-SITE EVALUATION IN ENDOSCOPIC ULTRASOUND-GUIDED FINE-NEEDLE ASPIRATION OF PANCREATIC SOLID LESIONS

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Introduction: Rapid on-site cytologic evaluation (ROSE) for determining the suitability of a specimen often provides high efficacy of endoscopic ultrasound-guided fine needle aspiration (EUS-FNA). In our center, we propose an additional role of ROSE in histological diagnosis aimed at improving diagnostic accuracy.

Aims & Methods: From January 2009 and December 2015, 215 patients were evaluated who underwent both endoscopic ultrasound-guided fine needle aspiration (EUS-FNA) for pancreatic solid lesions and surgery. We retrospectively compared the diagnostic performance of ROSE during EUS-FNA with the final diagnosis confirmed by surgically resected specimens. Diagnosis by ROSE using Diff-Quik was carried out by both a cytopathologist and an endoscopist.

Results: The median of needle passes required for ROSE was 1 (range, 1–5). Final diagnoses for the 215 lesions were pancreatic ductal adenocarcinoma (PDAC; n = 102), pancreatic ductal adenocarcinoma (PDAC; n = 9), pancreatic neuroendocrine tumor (pNET; n = 30), solid pseudopapillary neoplasm (SPN; n = 9), metastatic tumors (n = 4), and acinar cell carcinoma (ACC; n = 1). Primary lesions for metastatic tumors in the pancreas were renal cell cancer (RCC; n = 2), small cell lung cancer (SCLC; n = 1), and colon cancer (n = 1). When adenocarcinoma (including suspicious cases) was suspected by ROSE, ROSE diagnosed 94.6% (159/168) of adenocarcinomas. When special type tumor (pNET, SPN, RCC, SCLC) was suspected by ROSE, ROSE diagnosed 96.4% (27/28) of special type tumor.

Conclusion: All adenocarcinomas suspected by ROSE were malignant tumors. When special type tumor (pNET, SPN, RCC, SCLC) was suspected by ROSE, Diagnostic accuracy of ROSE was 96.4%. Diagnostic accuracy using ROSE is high agreement in final histological diagnosis. It is suggested that ROSE may also be useful for diagnosis of special type tumor.

Disclosure of Interest: All authors have declared no conflicts of interest.

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P0777 THE NOVEL ROLE OF GASTROKINE, A GASTRIC TUMOR SUPPRESSOR PROTEIN, IN PANCREATIC CARCINOGENESIS

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Introduction: Pancreatic ductal adenocarcinoma (PDAC) has one of the most dismal prognoses of all cancer types. Diagnostic techniques for early malignant lesions are limited, which shows an evident need to understand the pathomechanism leading to PDAC and find a suitable marker for early detection. Initial processes in PDAC development involve acinar to ductal metaplasia (ADM) with further neoplastic progression into four pancreatic intraepithelial neoplastic (PanINs) stages. After accumulation of mutations, these lesions will further evolve into PDAC. Gastrokin 1 & 2 (GKN1 & GKN2) are secreted proteins found in the stomach where they are involved in gastric epithelial homeostasis. While current research focuses on the exploration of tumor-suppressive properties of GKN1 in gastric tumors, nothing is known about GKN function in other organs. A whole genome microarray of KRAS, Tp53, Cdkn2a, Cdkn2b and macroautophagy (hereafter referred to as autophagy) has been implicated in some of human diseases, lesions in vitro was tested.

Results: GKNs were upregulated during early stages of pancreatic carcinogenesis in mouse and human tumor-suppressive properties of GKN1 in gastric tumors, nothing is known about GKN function in other organs. A whole genome microarray of KRAS, Tp53, Cdkn2a, Cdkn2b and macroautophagy (hereafter referred to as autophagy) has been implicated in some of human diseases, lesions in vitro was tested.

Conclusion: We identified for the first time specific gastrokine expression in pancreatic ductal adenocarcinoma (PDAC) in human and mouse pancreatic tissue. The secretion into pancreatic juice. Preliminary results from the first timepoint of analysis showed accelerated tumor development in GKN1+ve KC mice. Wild type acinar cells transdifferentiated in vitro only in the presence of TGFa. On the contrary, GKN1+ve acinar cells transdifferentiated spontaneously, and resulted in higher number of ADMs.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0778 AUTOPHAGY IS ESSENTIAL FOR PANCREATIC CANCER DEVELOPMENT IN A NEW HUMANIZED GENETICALLY-MODIFIED ADULT MOUSE MODEL

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Introduction: Pancreatic ductal adenocarcinoma is one of the deadliest malignancies and there are no effective therapies for it. According to a search of The Cancer Genome Atlas (T-CGA) project (release 8.0), pancreatic cancer has one of the highest numbers of deleterious mutations in human cancers. TCGA, alterations in Kirsten rat sarcoma (KRAS), Tumour protein (TP)53, Cdkn2a and Cdkn2b genes. Besides, increased autophagy was observed in the lenti- and shRNA-KTCC infected primary cells. This finding provides considerable insight into the role of autophagy in pancreatic cancer and autophagy inhibition might be a potential target in treating pancreatic cancer.

Aims & Methods: Our aim was to analyse gastrointestinal cancer cell response to various hyperthermia levels, accompanied by chemotheraphy, in a manner of cell cytotoxity, apoptosis and intracellular cisplatin concentration. Cancer cell lines of gastric (AGS), pancreatic (T4M4) and colorectal (Caco-2) origin were exposed to cisplatin and different temperature regimens (37°C to 45°C) either in isolated manner, or in combination. Cells were treated for one hour, mimicking HIPEC timing in clinical setting. The intracellular concentration of cisplatin was measured immediately after experiment by mass spectrometry. 48 hours later changes of cell viability and apoptosis rates depending on temperature in addition to cisplatin treatment were evaluated by MTT and Annexin-V/AAD flow cytometry respectively.

Results: Response of AGS to hyperthermia was as implied. Viability of the cells was gradually decreasing by raising the temperature. CACO-2 cells had no significant response to temperature rise up to 42°C, but at 43°C viability dropped by 14% constantly remaining at higher temperatures. T4M4 cells acted in an unexpected manner, whereas decreasing viability by 30% in the interval between 37°C to 42°C and 20% increase at 43°C was observed. Following simultaneous exposure to hyperthermia and cisplatin we observed no additive temperature alteration in the cell survival. However, at particular temperature regimens, we observed temporary proliferation increase: AGS – at 42°C (33%); T4M4 – at 43°C (32%). Higher temperatures dramatically inhibited AGS – by 70%; T4M4 - by 76%. There was the linear pattern of slight decrease (up to 26% at 45°C) of viability in CACO-2 cells. Isobologram analysis of combined hyperthermia and cisplatin treatment revealed strong antagonism of hyperthermia and chemotherapy in all analyzed cell lines. Nevertheless, hyperthermia of 43°C in addition to cisplatin promoted apoptosis of AGS cells by 33%, CACO-2 by 26%, T4M4 by 19%. Moreover, application of hyperthermia (43°C) could contribute to increase of intracellular cisplatin concentration by 30%, 20% and 18% AGS, CACO-2 and T4M4 cells respectively.

Conclusion: Our results indicate that there is no linear contribution of hyperthermia to chemotherapy in all analyzed cell lines. Therefore, in clinical setting it should be applied individually, regarding cancer type. Moreover, particular temperatures can worsen the treatment and increase cancer cell growth.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0779 HIPEC IN GI CANCERS. IS HYPERTHERMIA FRIEND OR FOE?

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Introduction: Hyperthermia as a positive additive to chemotherapy is described in multiple studies. Despite controversial results hyperthermic intraperitoneal chemo-therapy (HIPEC) is a standard treatment option for some types of gastrointestinal cancer that invades peritoneum. However, the results of clinical data and basic research are uneven. Moreover, there is a lack of fundamental knowledge on additive cytotoxic effect of hyperthermia on cancer cells of different origin.

Aims & Methods: We aimed to analyse gastrointestinal cancer cell response to various hyperthermia levels, accompanied by chemotherapy, in a manner of cell cytotoxity, apoptosis and intracellular cisplatin concentration. Cancer cell lines of gastric (AGS), pancreatic (T4M4) and colorectal (Caco-2) origin were exposed to cisplatin and different temperature regimens (37°C to 45°C) either in isolated manner, or in combination. Cells were treated for one hour, mimicking HIPEC timing in clinical setting. The intracellular concentration of cisplatin was measured immediately after experiment by mass spectrometry. 48 hours later changes of cell viability and apoptosis rates depending on temperature in addition to cisplatin treatment were evaluated by MTT and Annexin-V/AAD flow cytometry respectively.

Results: Response of AGS to hyperthermia was as implied. Viability of the cells was gradually decreasing by raising the temperature. CACO-2 cells had no significant response to temperature rise up to 42°C, but at 43°C viability dropped by 14% constantly remaining at higher temperatures. T4M4 cells acted in an unexpected manner, whereas decreasing viability by 30% in the interval between 37°C to 42°C and 20% increase at 43°C was observed. Following simultaneous exposure to hyperthermia and cisplatin we observed no additive temperature alteration in the cell survival. However, at particular temperature regimens, we observed temporary proliferation increase: AGS – at 42°C (33%); T4M4 – at 43°C (32%). Higher temperatures dramatically inhibited AGS – by 70%; T4M4 - by 76%. There was the linear pattern of slight decrease (up to 26% at 45°C) of viability in CACO-2 cells. Isobologram analysis of combined hyperthermia and cisplatin treatment revealed strong antagonism of hyperthermia and chemotherapy in all analyzed cell lines. Nevertheless, hyperthermia of 43°C in addition to cisplatin promoted apoptosis of AGS cells by 33%, CACO-2 by 26%, T4M4 by 19%. Moreover, application of hyperthermia (43°C) could contribute to increase of intracellular cisplatin concentration by 30%, 20% and 18% AGS, CACO-2 and T4M4 cells respectively.

Conclusion: Our results indicate that there is no linear contribution of hyperthermia to chemotherapy in all analyzed cell lines. Therefore, in clinical setting it should be applied individually, regarding cancer type. Moreover, particular temperatures can worsen the treatment and increase cancer cell growth.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0780 CACHEXIA INVOLVEMENT IN THE LOCAL SPREAD OF PANCREATIC DUCTAL ADENOCARCINOMA

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THE INTRACELLULAR CYTOSKELETON MARKER IS OVEREXPRESSED IN PANCREATIC DUCTAL ADENOCARCINOMA

Aims & Methods: Our goal was to assess the significance of activin protein expression in PDAC related to the clinical stage and survival. There were included patients with histological proven of adenocarcinoma (n=115) and a median follow-up of 24 months (SD 124). The plasma levels of activin were analyzed using western blot. The t test was used to determine the difference between the two groups, Kaplan-Meier curve and log-rank tests were used to determine the differences in survival curves of studied patients.

Results: Activin was overexpressed more frequently in PDAC compared to controls (p=0.001), and has been closely related to advanced clinical stage (stage III-IV), tumor size, location and with the presence of metastasis (p<0.05). Activin expression was higher in patients with type 2 diabetes (p=0.04). No relationship between activin level and the patients age, sex or tumor size, was noted. Patients with activin high expression had a shorter survival time than PDAC patients with activin low expression (Log-rank = 4.35; p=0.03).

Conclusion: Activin pathway is related to cachexia and the local spread of PDAC, the presence of diabetes and survival.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0782 QUALITY OF LIFE DURING CHEMOTHERAPY IN JAPANESE PATIENTS WITH UNRESECTABLE ADVANCED PANCREATIC CANCER

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Introduction: This study is to assess QoL during chemotherapy in patients with advanced pancreatic cancer. Twenty-one Japanese patients with unresectable advanced pancreatic cancer and performance status 0–1 were included in this study. All patients were treated with FFX or Gn as first-line chemotherapy. QoL was assessed using the Japanese Organization for Research and Treatment for Cancer Quality of Life Core Questionnaire (EORTC QLQ-C30), and anxiety and depression were measured using the Hospital Anxiety and Depression Scale (HADS) at baseline and 2 weeks and every month after initiation of chemotherapy. Changes between score at baseline and median score after chemotherapy were compared using Wilcoxon signed-rank test. Continuous variables are presented as median (range).

Results: Thirteen male and 8 female patients were included, with a median age of 65 (59–75) years and BMI of 21.3 (16.0–26.2) kg/m2. The chemotherapy regimens were FFX in 5 men and 2 women, modified-FFX in 4 men and 4 women, and Gn in 4 men and 2 women. Eight patients took opioids for pain, and 4 received celiac plexus neurolysis. Regarding global health status (GHS) and functional scales in QLQ-C30, baseline scores were: GHS, 50 (17–92)%; physical, 87 (53–100)%; role, 83 (33–100)%; emotional, 67 (33–100)%; cognitive, 83 (33–100)%; and social, 67 (11–100)%.

Conclusion: Pain as well as QoL factors should always be considered to manage chemotherapy properly in patients with advanced pancreatic cancer. Disclosure of Interest: All authors have declared no conflicts of interest.

References

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treated by EUS-CPN. Clinical information was obtained retrospectively from the medical report. The follow-up was associated with the patient died or was lost to follow-up. Between November 2014 and March 2017, 70 patients with PC pain were enrolled. We performed EUS-CPN by injection of 5 ml of bupivacaine mixed with 15 ml of pure ethanol on the celiac axis and normally occluded pancreatic duct by an endoscopic ultrasound-guided fine needle aspiration needle. Treatment response was assessed by self-reported pain relief and change in the daily dose requirement of morphine. Treatment response was defined as or decrease or stay of the same amount of morphine consumption after EUS-CPN, or achieve morphine dosage level within 4 weeks after EUS-CPN if morphine consumption temporarily elevated because of the delayed response of EUS-CPN. Pain evaluation was conducted at 1 week, 4 weeks after EUS-CPN and tumor disease progression.

Results: The pain relief rate was 81.4% (57/70). The median duration of pain relief was 4 months. 10 patients required a second EUS-CPN due to pain relapse, and 90% (9/10) showed response to the repeat procedure. Of the 44 patients who showed response to the initial EUS-CPN during chemotherapy, the response is related to the diagnosis of metastasizing in 18% of cases compared to 45% of other presentations (P = 0.017). Between the response group and no-response group, there were significant differences in the prevalences of liver metastasis (47 vs. 92%, P < 0.001), lower metastasis (12 vs. 38%, P = 0.02) and lymph node metastasis (56 vs. 92%, P < 0.015), and in the serum levels of CEA (median: 6.7 vs. 17.1 mg/ml, P = 0.017), CA19-9 (median: 617.2 vs. 3519 U/ml, P = 0.009), CRP (median: 0.61 vs. 1.91 mg/dl, P = 0.029) and albumin (median: 3.4 vs. 3.8 g/dl, P = 0.029). Univariate analysis revealed a significantly smaller percentage of patients with CRP level elevation over 3.0 mg/dl from baseline within 4 weeks after EUS-CPN (11 vs. 38%, P = 0.01). The overall survival after EUS-CPN was also significantly longer in the response group as compared to the no-response group (median: 5.8 vs. 1 month, P = 0.03).

Conclusion: Our study demonstrated that EUS-CPN had therapeutic effect on intractable pain in unresectable PC in the long follow-up. Repeat EUS-CPN was also effective in patients who showed a treatment response to the first EUS-CPN. Positive benefit from EUS-CPN had strong cancer inflammation and aggressiveness, indicative of higher CRP, CA19-9 and lower albumin levels, and the higher frequencies of liver metastasis.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0784 PRESENTATION SYMPTOMS AND RISK FACTORS ARE ASSOCIATED WITH DIAGNOSTIC DELAY AND DISEASE STAGE BUT NOT WITH PROGNOSIS OF Pancreatic CANCER

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Introduction: Pancreatic ducal adenocarcinoma (PDAC) 5-year survival rate is only 6% as only 20% of patients are eligible for surgery at diagnosis, due to distant metastases, and chemotherapy is often only palliative. Given the highly accurate assay, risk assessment of the IPMN cases was tested. At present, 92 PDA and 145 IPMN patients with either benign or malign disease stage at diagnosis. However, symptoms and delay do not seem to affect disease stage at diagnosis. However, symptoms and delay do not seem to affect prognosis. These results suggest that diagnosis at the preclinical stage is necessary to change disease prognosis.

Disclosure of Interest: All authors have declared no conflicts of interest.
P0786  TREATMENT EFFICACY AND ADVERSE EVENTS OF GEMCITABINE PLUS NAB-PACLITAXEL USED FOR METASTATIC PANCREATIC CANCER: A RETROSPECTIVE COHORT STUDY
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Introduction: Pancreatic cancer is a lethal disease and the fifth most common cause of cancer-related death in Korea. Pancreatic cancer patients show dismal prognosis with a 5-year survival rate less than 10%, because the majority of patients are diagnosed in advanced stage. Since the late 1990s, gemcitabine-based chemotherapy has been used as a mainstay of metastatic pancreatic cancer (mPC) treatment and various combination therapies (such as combination with capetibafone or erlotinib) had been attempted to improve the patients’ survival, so far. Recently, MPACT trial, a randomized phase III trial showed that combination of gemcitabine and nab-paclitaxel had statistically significant survival benefit compared with gemcitabine monotherapy. Based on the results of this trial, gemcitabine with nab-paclitaxel combination therapy is currently being used as a standard therapy for pancreatic cancer patients. However, only 2% of the MPACT trial study population was Asian, and other researches on Asian population group are also lacking. Therefore, we investigated treatment efficacy and safety of gemcitabine plus nab-paclitaxel combination therapy for mPC treatment in Korean population.

Aims & Methods: Total 66 metastatic pancreatic cancer patients treated with gemcitabine (1000mg/m²) and nab-paclitaxel (125mg/m²) regimen (on day 1, 8, 15 of a 28-day cycle) as the first line chemotherapy from February 2016 were identified using the Severance Hospital Pancreatic Cancer Cohort Registry. Treatment efficacy (overall survival (OS), progression-free survival (PFS), objective response rate) and treatment-related adverse events (AE) of patients (occurrence rate, severity grade and dose-intensity) were analyzed.

Results: The median follow-up period was 7.4 months (range 1.5–14.9 months); during this period, 21 (31.8%) patients died. Median cumulative dose of gemcitabine was 685.5mg/m² (range 251.9–1070.8mg/m²) and nab-paclitaxel was 3021.4mg/m² (range 1095.8–6031.3mg/m²). Grade 3/4 neutropenia was the most common AE (59.1%) followed by general weakness (48.5%), alopecia (48.5%), nausea (45.5%), and nausea and vomiting (42.4%). The incidence of neutropenia was 54.5% and 12 (18.2%) patients experienced grade 3 neutropenia. 30 (45.5%) patients showed grade 3 neuropathy and 10 (12.2%) patients had febrile neutropenia. Grade 3 gastrointestinal AE was observed in 11 (16.7%) patients and 26 (42.4%) patients experienced dermatologic AE such as alopecia and skin eruption. About 59% of patients experienced treatment delays due to adverse events. Dose reduction was performed in 39 (59.1%) patients and 14 patients experienced treatment cessation due to severe AE.

Table 1: Treatment efficacy and treatment-related adverse events of gemcitabine with nab-paclitaxel

<table>
<thead>
<tr>
<th>Variables</th>
<th>Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of chemotherapy</td>
<td>Cycles (28-day schedule) 5 (2–12)</td>
</tr>
<tr>
<td></td>
<td>Duration, days 141 (32–435)</td>
</tr>
<tr>
<td>Efficacy of Chemotherapy</td>
<td>Overall survival - months (95%CI) 12.0 (9.515–14.485)</td>
</tr>
<tr>
<td></td>
<td>Progression-free survival - months (95%CI) 7.8 (5.021–10.579)</td>
</tr>
<tr>
<td>Adverse events</td>
<td>Peripheral neuropathy 36 (54.5%)</td>
</tr>
<tr>
<td></td>
<td>Grade ≥ 3 neuropathy 12 (18.2%)</td>
</tr>
<tr>
<td></td>
<td>Grade ≥ 3 Neutropenia 30 (45.5%)</td>
</tr>
<tr>
<td></td>
<td>Febrile Neutropenia 10 (15.2%)</td>
</tr>
<tr>
<td></td>
<td>Administration of G-CSF 14 (21.2%)</td>
</tr>
<tr>
<td></td>
<td>Grade ≥ 3 adverse event 11 (16.7%)</td>
</tr>
<tr>
<td></td>
<td>General weakness 32 (48.5%)</td>
</tr>
<tr>
<td></td>
<td>Dermatologic adverse event 28 (42.4%)</td>
</tr>
<tr>
<td></td>
<td>Dose reduction due to AE 21 (31.8%)</td>
</tr>
<tr>
<td></td>
<td>nab-paclitaxel 39 (59.1%)</td>
</tr>
<tr>
<td></td>
<td>Delay of administration due to AE n (%) 39 (59.1%)</td>
</tr>
<tr>
<td></td>
<td>Cessation of administration due to AE n (%) 14 (21.2%)</td>
</tr>
</tbody>
</table>

Conclusion: These results suggest that gemcitabine and nab-paclitaxel combination therapy is effective for metastatic pancreatic cancer treatment in East-Asian population group. Similar to previous studies, this combination therapy showed remarkable neurotoxicity and myelosuppression. Careful monitoring and proper management during chemotherapy is required.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P0787  IMPACT OF PREOPERATIVE EUS-FNA ON PERITONEAL RECURRENT AND SURVIVAL IN PATIENTS WITH PANCREATIC CANCER
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Introduction: Endoscopic ultrasound-guided fine needle aspiration (EUS-FNA) is a useful and safe method for tissue confirmation of malignancy. This method has the risk of tumor cell dissemination along the needle track or within the peritoneum by preoperative EUS-FNA.

Aims & Methods: The aim of our study was to estimate the risk of peritoneal recurrence and the impact on long-term outcomes by preoperative EUS-FNA in resected pancreatic cancer. The records of patients diagnosed with pancreatic cancer who underwent curative resection between 2009 and 2013 were reviewed retrospectively. A total of 394 patients were included: 78 patients with preoperative EUS-FNA (EUS-FNA group) and 316 without preoperative EUS-FNA (Non-EUS-FNA group). Peritoneal recurrence was diagnosed based on image findings.

Results: Median length of follow-up was 23 months (range 1~94 months). A total of 82 patients had peritoneal recurrence: 34.6% (27/78) in EUS-FNA group vs. 28.2% (89/316) in Non-EUS-FNA group (P=0.20). Cancer-free survival and overall survival were not different between the groups: median cancer-free survival in EUS-FNA group was 10.8 months compared with 10.6 months in Non-EUS-FNA group (P=0.83), and median overall survival in EUS-FNA group was 56.4 months compared with 56.7 months in Non-EUS-FNA group (P=0.93).

Conclusion: Preoperative EUS-FNA for pancreatic cancer was not associated with an increased rate of peritoneal recurrence and mortality. Our study suggests that EUS-FNA is a safe method for obtaining tissues of pancreatic masses.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P0788  HENTI & PDPI EXPRESSION IN EUS-FNAB SAMPLES OF PanIN-3: EPIDEMIOLOGICAL, CLINICAL FEASIBILITY AND PROGNOSTIC SIGNIFICANCE OF GEMCITABINE-β-SI-BASED CHEMORADIOThERAPY
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Introduction: Gemcitabine (Gem) therapy had been the standard treatment for advanced pancreatic ductal adenocarcinoma (PDAC) for long time. Even though FOLFIRINOX, a combination of fluorouracil, oxaliplatin and irinotecan, and gemcitabine-nab-paclitaxel (GnP) therapy are currently recommended as first-line drugs, Gem is still one of the important options. Efficient permeation of Gem into cells requires specialized integral membrane transporter proteins to cross plasma membranes. Among these transporters, the major mediators of Gem uptake into human cells are the human equilibrative nucleoside transporter 1 (hENT1). In the previous study started since 2005, we found hENT1 expression in endoscopic ultrasonography-guided fine-needle aspiration biopsy (EUS-FNAB) samples to be a useful prognostic marker of Gem-based chemoradiotherapy (Gem-CRT) for pancreatic ductal adenocarcinoma (PDAC) (Pancreas 2016). Since November 2011, our institution has replaced Gem + tegafur/gimeracil/oteracil (S-1) (GS-CRT) with Gem-CRT in an attempt to improve clinical response and prognosis. Aggregate median survival time (MST; months) of GS-CRT was compared with previous Gem-CRT result, and the superior efficacy of GS-CRT was observed (MST: 16 versus 20, respectively), particularly in hENT1-negative patients (MST: 9 versus 14, respectively). However, there were no differences in
Six were excluded (4 with IPMN without worrisome features nor surgical indication were considered. A further assessment of DPD expression was carried out in those samples determined to have sufficient material remaining (n = 58). This is the first meta-analysis showing that statins exert a protective effect on the incidence of PDAC. Future studies taking into account statin dose, duration and subgroup of patients are needed in order to clarify the association.

Disclosure of Interest: All authors have declared no conflicts of interest.
Aims & Methods: In this study, we aimed to overcome the subsampling issue and to establish a more reliable framework for quantification of rare tumor cell-derived mutant alleles for non-invasive diagnosis of gastrointestinal cancer. To establish more reliable ddPCR protocol for quantification of low-frequency alleles within a limited cfDNA pool, two-step multiplex ddPCR targeting eight KRAS-gene-relevant mutant KRAS variants was examined using a Bio-Rad QX200 droplet digital PCR platform. Plasma samples from patients with colorectal cancer (n = 10) and pancreatic cancer (n = 9) were evaluated, and cfDNA from healthy volunteers (n = 30) was utilized to calculate reference intervals.

Results: Limited cfDNA yields in patients with resectable colorectal and pancreatic cancers did not meet the requirement for efficient capture and quantification of rate mutant alleles by ddPCR. To overcome the subsampling issues and achieve better assay specificity, we attempted pre-amplification of plasma cfDNA using primers flanking KRAS exon 2 as the first-step PCR. Eight pre-amplification cycles followed by a second-run ddPCR were sufficient to approximate 5000–10,000 target alleles/ng cfDNA, resolving the subsampling issue; furthermore, the signal-to-noise ratio for rare mutant alleles against the massive background was present by the wild-type allele was significantly enhanced. The cut-off limit of reference intervals for mutant KRAS was determined to be ~0.09% based on samples from healthy individuals.

Conclusion: The modification introduced in the ddPCR protocol facilitated the quantification of low-copy alleles carrying driver mutations, such as oncogenic KRAS, in localized and early-stage cancers using small blood volumes, thus offering a minimally invasive modality for timely diagnosis.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

P0792 ANALYSIS OF CLINICAL PREDICTIVE FACTORS AFFECTING THE OUTCOME OF FIRST-LINE CHEMOTHERAPY FOR THE PATIENTS WITH ADVANCED Pancreatic CANCER

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Introduction: Benefit of second line chemotherapy (SL) after failed first-line chemotherapy (FL) for advanced pancreatic cancer has not yet been established. We intend to identify prognostic factors and ultimately devise a model of clinical parameters for decision of SL versus basic supportive care (BSC) after failure of FL chemotherapy.

Aims & Methods: 408 patients who received gemcitabine-based first-line chemotherapy for advanced pancreatic adenocarcinoma at Yonsei University Hospital between January 2010 and December 2014 were retrospectively reviewed. Significant clinical parameters regarding second line related survival were identified using a stepwise predictive factor analysis.

Results: 161 of 408 (39.5%) received SL therapy. Median overall survival from the beginning of SL (OS2) was 20.0 weeks (14.0 ~ 34.0). Significantly more SL patients presented higher body mass index (BMI) (p=0.001) and ECOG 0–1 (p=0.003) at diagnosis, lower rate of lung metastasis (p<0.001) and longer duration of FL (p<0.001). More SL patients had received gemcitabine-based concurrent chemo-radiation therapy (CCRT) (p=0.029) compared to FL only patients. Presence of liver metastasis was significant to OS2 were BMI at diagnosis (p=0.019, HR=0.870), duration of FL therapy (median duration 16weeks (8.0-28.00)) (p=0.004, HR=0.986), presence of peritoneal metastasis (p=0.002, HR=1.732) at diagnosis, malignant thrombosis during firstline chemotherapy (p=0.001, HR=0.428). Experience of CCRT was also a significant prognostic factor (p=0.001, HR=2.245); initial staging of the CCRT group was TNM stage3, which might be the ultimate factor impacting OS2.

Conclusion: Study suggests that SL chemotherapy may be beneficial for patients with longer duration of FL chemotherapy, higher BMI at diagnosis, patients without peritoneal metastasis at diagnosis, no malignant thrombosis event during chemotherapy and patient initially TNM stage3, who received Gemcitabine based CCRT.

Disclosure of Interest: All authors have declared no conflicts of interest.

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8. Kim ST, Choi YJ, Park D, Ewha Womans University Medical School, Seoul/Korea, Republic of

P0793 RAPID ON SITE EVALUATION (ROSE): AN ESSENTIAL TOOL IN ECHO-ENDOSCOPIC (EUS) STUDY OF SOLID LESIONS OF THE PANCREAS

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Introduction: Rapid on site evaluation for endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) of the pancreas provides immediate information regarding cellular adequacy, avoiding repeated procedures.

Aims & Methods: The aim of this study was to evaluate the impact of ROSE in EUS-FNA of solid pancreatic lesions. Retrospective study of consecutive EUS-FNA of solid pancreatic lesions, in a tertiary center, between 2012 and 2016. A total of 259 EUS-FNA was performed on 197 patients with mean age of 63.4 (+/− 12.8) years. The anatomical distribution of the lesions was: 56.4% in the head, 17% in the body, 10% in the uncinate process and 5.8% in the tail. The mean number of passes was 3.3 (+/−1.4) and the needle size was 25G in 60.8% and 22G in 23.8%. ROSE was performed 34.7% of the punctures (23.6% along with the initial EUS-FNA), with a mean number of passes 3.4 (+/−1.9). The diagnostic yield of initial EUS-FNA without ROSE was 44.8% vs 83.6% when ROSE was performed (p < 0.001). When not conclusive, there was no significant differences in the diagnostic yield of the repeated EUS-FNA with (with and without ROSE). Beyond ROSE in the first puncture, higher levels of Ca 19.9 (199 vs 10ng/mL, p = 0.001), size of the lesion (31.6 vs 29.8 mm, p < 0.001), invasion of adjacent structures (64.6% vs 47.5%) and malignancy (73.2% vs 25.4%, p < 0.001) were associated with EUS-FNA diagnostic accuracy. In multivariate analysis, ROSE (p = 0.001) and the size of the lesion (p = 0.023) were independent predictors of adequate diagnostic samples. In this study, ROSE was able to improve the diagnostic yield in solid pancreatic lesions and should be considered whenever possible in the first procedure, until an overall adequate diagnostic yield (>70%) is achieved.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0794 ESOPHAGEAL FISTULA HEALING BY MESENCHYMAL STEM CELL-DERIVED EXTRACELLULAR VESICLES IN A THERMORESPONSIVE GEL: A PRE-CLINICAL PORCINE STUDY

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Introduction: Postoperative digestive fistula remain a challenging condition associated with a high morbidity-mortality, unsatisfactory healing rates and high refractoriness. The limitation of current approaches highlights the need for a better therapeutic strategy in terms of both long-lasting efficacy and safety. Mesenchymal stem cell (MSCs) are strongly involved in tissue injury repair. MSCs feature an immune-privileged status while displaying pro-angiogenic,
and antifibrotic properties. Increasing evidences point out MSC action via sub-cellular extracellular vesicles (EVs), MSC EVs recruit or reprogram the therapeutic properties of their cellular counterparts while offering remarkable advantages in terms of safety (no proliferation, no differentiation, no vascular occlusion following administration) and shelf life stability. Herein, we evaluated, in vivo, the role of the healing potential of MSC EVs delivered through a thermoresponsive gel (Pluronic F127) allowing the administration in a sol state through a catheter and gelation in situ at body temperature to retain EVs at fistula site.

Aims & Methods: Seventeen esophageal fistulas were surgically created by placing two plastic stents during 30 days into the neck of 9 pigs and randomized into control group (n = 6) and treated groups (gel alone n = 6 and gel-EVs n = 5). In the gel-EVs group, Pluronic F127 gel contained allogeneic EVs collected from the swine adipose stem cell conditioned medium, tested and radiological evaluation of fistula healing was performed at day 30 and day 45, before histological assessment.

Results: All fistulas were successfully induced at day 30. At day 45, the control group showed no improvement and external fistula secretion in all pigs. For this group, radiological evaluation showed open fistula tracts, which were confirmed by histology. In the gel group and gel-EVs groups, radiological examination showed a complete fistula closure in 67% (4/6) and 100% (5/5) of the animals, respectively. In the gel group, histological analysis confirmed a complete fistula for 3 from 6 cases while a partial closure was observed for 1 case from 6. In the gel-EVs group, histological complete fistula closure was reported for 4 from 5 cases while a partial closure was evidenced in 1 from 5 cases. In comparison with control group, treated fistulas showed a reduced inflammatory infiltrate and fibrosis and an enhanced angiogenesis, especially in the gel-EVs group.

Conclusion: This study provides the first evidence in the literature that MSC-EV's migration and angiogenic effect in a pre-clinical model. EVs were intravenously fully administered via a thermoresponsive Pluronic F127 hydrogel, gelling in situ to enable EV retention in the fistula tract. Besides, the gel further provided a pro-angiogenic and an anti-inflammatory effect. The combined action of MSC EVs and the pro-enhanced healing associated with EVs was confirmed by angiogenesis and fibrosis in the esophageal fistula model. This investigation paves the way towards a future sub-cellular localized fistula therapy merging safety and efficacy.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0795 REAL-TIME MULTIPHOTON MORPHOLOGICAL IMAGING FOR DIAGNOSING GASTRIC ATYPICAL HYPERPLASIA AND ADENOCARCINOMA

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Introduction: Compared with histopathology, real-time histology or virtual biopsy is important for clinical diagnosis, especially for endoscopic examination. Based on two photon fluorescence (TPF), multiphoton microscopy (MPM) imaging could demonstrate cell autofluorescence and second-harmonics generation (SHG) signal from collagen, which implied real-time information on tissue architecture and cellular morphology. More importantly, no contrast agent is needed for this live diagnosis. The aim of this study is to evaluate the feasibility of MPM to histologically diagnose gastric diseases, compared with other chromoendoscopy and H&E histopathology.

Aims & Methods: A pilot study was performed between March 2016 and August 2016. 30 gastric tissue slides (normal, low-grade dysplasia (LGD), high-grade dysplasia (HGD), and cancer) were examined under MPM. MPM and H&E images were compared by the experienced pathologist. Cellularity/nuclei ratio was analyzed to compare morphological features, while the major/minor axis was calculated to reveal cellular asymmetry.

Results: Near-infrared light (800 nm) was optimized and applied for multiphoton autofluorescence imaging in gastric tissue. Under MPM, gastric dysplasia tissue demonstrated enlarged, while cancer cells were characterized by irregular size and shape, enlarged nuclei, and increased nuclear-to-cytoplasmic ratio. All these were confirmed by H&E images. (Figure 1) The mean cellular/nuclear ratio for normal mucosa was 20.55±4.94, LGD 34.00±1.39, HGD 46.85±3.72, and cancer 56.80±3.37 (P<0.05). The mean major/minor axis ratio for normal mucosa was 1.31±0.09, LGD 2.02±0.16, HGD 1.70±0.18, and cancer 1.43±0.18 (P<0.05).

Conclusion: MPM-based optical biopsy was feasible and efficient to clinically diagnose gastric cancer. With miniaturization and integration of endoscopy, MPM can be applied to provide real-time histological diagnosis without invasive biopsy for gastric cancer in the future.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference
were compared between the rebamipide group and control group at 1 week and ulcer scarring by HE. The number of neutrophils and width of the fibrosis control group. One pig was sacrificed at 1 week after the ESD and the other two ulcer staging using the classification of Sakita and Miwa. A1 stage was defined as copist blinded to the test agents performed the ESDs with a 2% rebamipide diameter were performed at four sites in the stomachs of three pigs. An endoscopic findings were not present only in 21% gastric erosions 232/1034 (22.4%). The prevalence of gastric peptic ulcer was 2.9% (30/1034) and gastric scar 0.9% (9/1034), but duodenal ulcer 2.3% (24/1034) and duodenal scar 5.9% (62/1034). In addition, three gastric adenocarcinoma cases (0.29%) have been identified during the upper endoscopy. The study showed statistically significant difference between the groups of individuals with normal and decreased pepsinogen tests with gastric polyps 3.6% vs. 9.2%, p = 0.02, gastric erosions 23.6% vs. 11.2%, p = 0.04, duodenal ulcer (scar) 6.5% vs. 1%, p = 0.02, duodenal lymphangiectasia 1.9% vs. 6.1%, p = 0.02 and reflux esophagitis A–B 18%, reflux esophagitis B–6%, reflux esophagitis C–1, 3% and histologically confirmed Barrett’s esophagus-1.3%. The most common main endoscopic finding was noted gastric erosions 232/1034 (22.4%). The prevalence of gastric peptic ulcer was 2.9% (30/1034) and gastric scar 0.9% (9/1034), but duodenal ulcer 2.3% (24/1034) and duodenal scar 5.9% (62/1034). In addition, three gastric adenocarcinoma cases (0.29%) have been identified during the upper endoscopy. The study showed statistically significant difference between the groups of individuals with normal and decreased pepsinogen tests with gastric polyps 3.6% vs. 9.2%, p = 0.02, gastric erosions 23.6% vs. 11.2%, p = 0.04, duodenal ulcer (scar) 6.5% vs. 1%, p = 0.02, duodenal lymphangiectasia 1.9% vs. 6.1%, p = 0.02 and reflux esophagitis A–B 18%, reflux esophagitis B–6%, reflux esophagitis C–1, 3% and histologically confirmed Barrett’s esophagus-1.3%. The most common main endoscopic finding was noted gastric erosions 232/1034 (22.4%). The prevalence of gastric peptic ulcer was 2.9% (30/1034) and gastric scar 0.9% (9/1034), but duodenal ulcer 2.3% (24/1034) and duodenal scar 5.9% (62/1034). In addition, three gastric adenocarcinoma cases (0.29%) have been identified during the upper endoscopy. The study showed statistically significant difference between the groups of individuals with normal and decreased pepsinogen tests with gastric polyps 3.6% vs. 9.2%, p = 0.02, gastric erosions 23.6% vs. 11.2%, p = 0.04, duodenal ulcer (scar) 6.5% vs. 1%, p = 0.02, duodenal lymphangiectasia 1.9% vs. 6.1%, p = 0.02 and reflux esophagitis A–B 18%, reflux esophagitis B–6%, reflux esophagitis C–1, 3% and histologically confirmed Barrett’s esophagus-1.3%. The most common main endoscopic finding was noted gastric erosions 232/1034 (22.4%). The prevalence of gastric peptic ulcer was 2.9% (30/1034) and gastric scar 0.9% (9/1034), but duodenal ulcer 2.3% (24/1034) and duodenal scar 5.9% (62/1034). In addition, three gastric adenocarcinoma cases (0.29%) have been identified during the upper endoscopy. The study showed statistically significant difference between the groups of individuals with normal and decreased pepsinogen tests with gastric polyps 3.6% vs. 9.2%, p = 0.02, gastric erosions 23.6% vs. 11.2%, p = 0.04, duodenal ulcer (scar) 6.5% vs. 1%, p = 0.02, duodenal lymphangiectasia 1.9% vs. 6.1%, p = 0.02 and reflux esophagitis A–B 18%, reflux esophagitis B–6%, reflux esophagitis C–1, 3% and histologically confirmed Barrett’s esophagus-1.3%. The most common main endoscopic finding was noted gastric erosions 232/1034 (22.4%). The prevalence of gastric peptic ulcer was 2.9% (30/1034) and gastric scar 0.9% (9/1034), but duodenal ulcer 2.3% (24/1034) and duodenal scar 5.9% (62/1034). In addition, three gastric adenocarcinoma cases (0.29%) have been identified during the upper endoscopy. The study showed statistically significant difference between the groups of individuals with normal and decreased pepsinogen tests with gastric polyps 3.6% vs. 9.2%, p = 0.02, gastric erosions 23.6% vs. 11.2%, p = 0.04, duodenal ulcer (scar) 6.5% vs. 1%, p = 0.02, duodenal lymphangiectasia 1.9% vs. 6.1%, p = 0.02 and reflux esophagitis A–B 18%, reflux esophagitis B–6%, reflux esophagitis C–1, 3% and histologically confirmed Barrett’s esophagus-1.3%.
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Aims & Methods: To assess the influence of antithrombotic therapy on delayed bleeding rate after ESD, we prospectively investigated the delayed bleeding rate after ESD among the continuation of antithrombotic agents, the cessation of antithrombotic agents and heparin bridge therapy. 735 lesions in 665 patients were treated with ESD from January 2006 to December 2016. We compared the delayed bleeding rate in 153 patients receiving antithrombotic therapy with 512 patients without that. Furthermore, we compared the delayed bleeding rate in the patients continuing antithrombotic therapy with that in the patients with the cessation of antithrombotic therapy or with heparin bridge therapy. The patients who were taking two or more antithrombotic agents were treated with continuation aspirin or clopidogrel. The cessation period of antithrombotic therapy before ESD followed the guidelines for therapeutic endoscopy in antithrombotic agents-users from Japan Gastrointestinal Endoscopy Society. We defined delayed bleeding as hematemesis, a melena, or a decrease of Hb >2 g/dL.

Results: The delayed bleeding rate in the patients receiving antithrombotic therapy was 14.4% (22/153), which was significantly higher than that in the patients without antithrombotic therapy (5.7%: 29/512) (p=0.0007). The median timing of delayed bleeding in patients receiving antithrombotic therapy and that in patients without antithrombotic therapy were 5.7±4.6 days and 7.0±6.8 days, respectively, without significant difference (p=0.48). Of 153 patients taking antithrombotic agents continued and 38 discontinued antithrombotic therapy and resumed it after ESD (cessation group), 38 discontinued antithrombotic therapy and resumed it after ESD (cessation group), and 30 switched to heparin therapy before ESD (heparin bridge group). One patient was excluded because of uncertain about the period of cessation. The delayed bleeding rate of continuation group, cessation group and heparin bridge group were 13.2% (5/38), 13.1% (11/84) and 20.0% (6/30), respectively, without significant difference (p=0.63). The delayed bleeding rate of continuation group was 13.2% (5/38), 13.1% (11/84) and 20.0% (6/30), respectively, without significant difference compared to that of total number of cessation and continuation group (13.1% (16/122), p=0.24). Deep vein thrombosis was observed in one patient in the cessation group.

Conclusion: Antithrombotic therapy increased the delayed bleeding rate. However, the delayed bleeding rate in the patients continuing antithrombotic therapy during ESD was similar to that in the patients discontinuing antithrombotic therapy. Therefore, it is inappropriate that the patients with high risk of thrombosis continue antithrombotic therapy on gastric ESD, but the heparin bridge therapy requires a further examination.

Disclosure of Interest: All authors have declared no conflicts of interest.

References:

esophageal squamous cell carcinoma at the endoscopic center of Xinhua Hospital, Third Military Medical University (Chongqing, China) from January 2015 to February 2017, were enrolled in this study. We collected specimens of autologous esophageal mucosal tissue from these patients. After undergone ESD, these mucosal tissues were given via the “ulcer surface” by hemoclips and then fixed by means of a covered metal mesh stent. The stent was removed on post-procedure day 7. All patients were monitored by endoscopy.

Results: In our ESD was safely achieved in all cases. The overall longitudinal diameter of resected specimens was 117.8 mm (range, 70 to 150 mm). Autologous esophageus mucosa was successfully transplanted to “ulcer surface” using an endoscope. The number of mucosal patches ranged from 8 to 28. Complete re-epithelialization occurred within a median time of 8.6 days with a graft survival rate at 93.06%. Postprocedural sticture accompanied by dysphagia occurred in seven patients on post-procedure day 24.7 (range, 18–34 days). The median sessions of EBD and intraluminal steroid injection was 3.3 (range 1–6). No other serious complications occurred in these patients, such as immediate bleeding and perforation. Eight patients were still alive during the mean follow-up period of 11.6 months (range, 2.5 to 21 months). One patient developed lung metastasis and died of the disease 15 months after ESD.

Conclusion: Transplantation of autologous esophageus mucosa appears to be a safe means of relieving the severity of esophageal stenoses following Circumferential ESD.

Disclosure of Interest: All authors have declared no conflicts of interest.

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disclosure of interest: All authors have declared no conflicts of interest.

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was reached in 290/301 (96%) procedures. A perforation occurred in 3/301 ER patients (1% CI 0.21%–3.8%). Two perforations were closed with clips, all three patients received intra-venous antibiotics and were admitted to hospital for 2, 3 and 9 days. Bleeding requiring intraprocedural hemostasis occurred during 15% of procedures. Significant post-procedural bleeding requiring an intervention occurred in 5 cases (2%). Dysphagia requiring endoscopic dilatation occurred in 7 patients (3%), after ER with a mean number of 4 ± 2.9 resected pieces. Mean total procedure time for ER using the new MBM device was 33 ± 17.1 minutes.

**Conclusion:** The new MBM device used in this study proved to be effective for resection of early neoplastic lesions in BE: successful ER was achieved in 96% of procedures. Perforations were seen in 1% and significant post-procedural bleeding in 2%, complications were effectively managed endoscopically.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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**P0087 COST-EFFECTIVE ANALYSIS COMPARING STANDARD BIOPSY VS. DIGITAL BIOPSY BY CONFOCAL ENDOMICROSCOPY**


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**Introduction:** Endoscopy has greatly influenced gastrointestinal disease diagnosis. However, most lesions can be suspected but not certainly diagnosed only on the basis of endoscopic findings and therefore, histology is needed. On the other hand the reliability of detecting lesions histologically depends on the site, number, and size of biopsy (Bx) specimens with a 20–30% probability of sampling mistakes. Probe based Confocal Lumer Endomicroscopy (p-CLE) allows endoscopist to perform cellular evaluation of the gastrointestinal (GI) tract with a high (90%) diagnostic accuracy. It allows to perform target Bx. Moreover, the NPV is >98%. There is no information in the literature regarding the economic impact of performing digital biopsies (DBx) by p-CLE.

**Aims & Methods:** The aim of this study is to perform a cost-effectiveness analysis comparing the diagnosis of upper GI tract pathologies using only standard Bx following the literature recommendations (LR) vs. the diagnosis with DBx using p-CLE. This was a retrospective study with prospective collection data of patients included from Jan 2014 to Nov 2016. The pathologies included for p-CLE evaluation are summarized in Table 1. The diagnosis costs using standard Bx was calculated following the literature recommendations (Table 2). The standard Bx costs included the histological process and physician honoraria per Bx (USD 50.00), and one biopsy forceps per patient (USD 38.00). The DBx costs by p-CLE included the probe, the processor and the physician honoraria (USD 500.00). Baseline characteristics, p-CLE indications, the diagnostic accuracy of p-CLE and costs were described.

**Results:** 78 patients were included, 51.2% were female. The mean age was 50.18 years old. p-CLE indications distribution was: esophagus 29 (37.2%), stomach 46 (59%) and duodenum 3 (3.8%) subgroups. Biopsies were performed in 71/78 cases (91.0%). Table 1 shows the procedure cost reached with the different pathologies by following the LR for initial diagnosis and follow-up. The efficacy of p-CLE in our study was 91.7% sensitivity, 89.8% specificity, 90.1% NPV and 90.1% accuracy for the diagnosis of the malignant upper GI tract pathology, by Digital Biopsy with p-CLE. Finally, the cost-effective analysis comparing the diagnosis of upper GI tract pathologies using only standard Bx vs. the diagnosis with DBx using p-CLE is detected if more than 10 biopsies are attempted by procedure.

**Table 1:** Cost analysis following the Literature Recommendations (LR) for initial diagnosis and follow-up

<table>
<thead>
<tr>
<th>Pathology</th>
<th>No. of Bx</th>
<th>No. of Bx by LR</th>
<th>Updated Sydney System</th>
<th>Total cost of Bx (USD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Esophageal Tumor</td>
<td>8</td>
<td>8</td>
<td>438.00</td>
<td></td>
</tr>
<tr>
<td>Barrett’s Esophagus 1–3 cm</td>
<td>8</td>
<td>8</td>
<td>438.00</td>
<td></td>
</tr>
<tr>
<td>Barrett’s Esophagus ≥4 cm</td>
<td>8</td>
<td>8</td>
<td>438.00</td>
<td></td>
</tr>
<tr>
<td>Gastric Tumor</td>
<td>8</td>
<td>5</td>
<td>688.00</td>
<td></td>
</tr>
<tr>
<td>Gastric Atrophy and/or Metaplasia</td>
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<td>12</td>
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<tr>
<td>Gastric Ulcer</td>
<td>8</td>
<td>5</td>
<td>688.00</td>
<td></td>
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</tbody>
</table>

Bx: biopsies; LR: Literature Recommendations. a. For initial diagnosis. b. For follow-up. c. Cost includes histological process and physician honoraria per biopsy (USD 50.00), and the Bx forceps per patient (USD 38.00).

**Conclusion:** In our population, the digital biopsy by p-CLE proved to be more cost-effective, when ≥10 biopsies were indicated, like in cases of a Barrett’s Esophagus ≥4 cm, a Gastric Tumor, or in the context of two or more suspected pathologies (e.g.: esophageal and gastric disease).

**Disclosure of Interest:** C. Robles-Medranda: KOL for Pentax Medical, Boston Scientific Consulting. US Endoscopy Consulting. All other authors have declared no conflicts of interest.

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**P0088 GASTRIC PER-ORAL ENDOSCOPIC PYLOROMYOTOMY (G-POEM) IN THE TREATMENT OF REFRACTORY GASTROPARESIS: EXPERIENCE OF THE FIRST 9 CASES IN A MEXICO**

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**Introduction:** Gastroparesis is a syndrome characterized by a delayed gastric emptying, absence of a mechanical obstruction. Reduction in QOL scores has been observed. Etiologies include: idiopathic, diabetic, post-surgical. Diagnosis is based on the combination of symptoms and a delayed gastric emptying scintigraphy(GES) of >10% after 240 min. Multiple treatments have been used with temporary results or high morbidity, so new treatment options have been explored. G-POEM is a new endoscopic treatment which is based in the POEM treatment for achalasic patients and consist in a creation of a submucosal tunnel in order to perform an endoscopic pyloromyotomy. Initial results have been promising.

**Aims & Methods:** The aim of this study was to evaluate the safety and efficacy of G-POEM in a group of Mexican patients with refractory gastroparesis. This prospective study was carried out in a tertiary care center in Mexico city, between December 2016 and April 2017. We included patients with refractory gastroparesis defined as presence of symptoms such as: nausea, vomiting, early satiety with inability to finish a normal meal, bloating and upper gastrointestinal pain. These patients were on medical treatment and didn’t respond and have a positive gastroparesis cardiomagnetic index (GCSI) score combined with a >10% of retention at 240 min in the GES study. Exclusion criteria were malignancy, peptic ulcer disease, normal GES and coagulation disorders. Procedure steps were: performing a POEM procedure, beginning 5cms beyond pyloric arch with an longitudinal incision, then submucosal tunnel creation, myotomy of the pyloric arch up to the serosa and 2cms before this point and finally closure with clips. Follow-up included GCSI, endoscopy and GES at 3 months after procedure. Characteristics of procedure, and patients were documented. Stained pair-t test was used for comparisons between groups and p < 0.05 was considered as statistically significant.

**Results:** There were 9 patients included in this initial study, the mean age was 42.4 ± 8.5 years. 6 patients were female and 3 male. The most common etiology was posturgical 4/9 (44.4%), followed by diabetic 3/9(33.3%) and idiopathic 2/9 (22.2%). The mean G-POEM time was 61.4 ± 7.8 min, and complications were self-limited and presented in only 4 patients, the GCSI score decreased 68% between the pre-procedure levels as well as the GES which decreased 67% compared with levels at 3 months after G-POEM (34.3 ± 5.8 vs 13.1 ± 3.2 p = 0.003/ 20.74 ± 5.3 vs 6.83 ± 1.78 p = 0.001 respectively). 7/9 (77.7%) normalized the GES(<10% at 240 min). Endoscopy at 3 months after procedure didn’t show any complication (Table 1).

**Conclusion:** G-POEM is a safe and effective procedure in Mexican patients with refractory gastroparesis with a normalization of the GES in up to 77% of these patients.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**References**


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**Introduction:** Foreign body (FB) ingestion including food bolus impaction is frequently encountered in clinical practice. Few studies with large sample size
towards endoscopic management of FBs had been reported. No direct evidence has demonstrated the relationship between duration of FB impaction and outcomes of endoscopic management. Moreover, it remained unclear whether endoscopic management of FBs under general anesthesia could improve endoscopic outcomes when compared with topical pharyngeal anesthesia.

Aims & Methods: The aim of the present retrospective study is to analyze our endoscopic outcome and explores the best timing and anesthesia methods of endoscopic intervention in FB ingestion with FB ingestion. All consecutive patients suspected of FB ingestion were enrolled. The demographic, clinical and endoscopic data were collected and analyzed.

Results: Totally, 1294 cases were recruited in this retrospective research. The ages ranged from 7 months to 94 years, with a median age of 47.0 (31-63) years. The majority of patients (1191/1294 cases, 92.0%) presented with some symptoms after FB ingestion, in order of frequency odynophagia (415 cases, 26.3%), foreign body sensation (340 cases, 23.6%) and sore throat (267 cases, 20.1%). The duration of FB impaction ranged from 4 hours to more than 2 years with a median time of 1.063-3 days. Bony FBs, jujube pit, food bolus and dental prosthesis were the most frequent FBs in population. Anatomically, FBs were mostly impacted in the oesophagus (n=1025, 68.9%), especially in the upper oesophagus (n=523, 32.5%), followed by stomach (n=95, 6.1%), duodenum (n=36, 3.0%) and pharynx (n=24, 2.0%). Nearly half of the patients (49.9%) developed FB-related complications, mainly including mucosal injuries (356 cases, 27.5%) and ulcers (210 cases, 16.2%). The most common underlying pathologies were oesophageal stricture (35 cases, 39.3%) and oesophageal cancer (11 cases, 15.5%). As the duration of FB impaction increased, positive finding and successful removal of FB by endoscopy significantly decreased (p < 0.001). Furthermore, complication rate significantly increased with time (p < 0.001). Age (OR=1.15, 95%CI: 1.20-1.91, p < 0.001), type and location of FBs (OR=4.51, 95%CI: 2.95-6.90, p < 0.001; OR=2.26, 95%CI: 1.48-3.46, p < 0.001), anaesthesia methods (OR=1.35, 95%CI: 1.05-1.75, p = 0.02) and duration of FB impaction (OR=1.74, 95%CI: 1.50-2.00, p < 0.001) were verified as risk factors for development of FB-related complication by logistic regression analysis. General anaesthesia could not improve FB detection (p = 0.181) or success rate of endoscopic management of FBs (p = 0.135), as well as decrease the complication rate when compared with topical pharyngeal anaesthesia (52.3% VS 47.5%, p = 0.033).

Conclusion: FB-related complication rate increased with time, endoscopic management under general anaesthesia could not improve therapeutic effects when compared with problem in endoscopic ESD. Patients suspected of FB ingestion should receive endoscopic management as soon as possible.

Disclosure of Interest: All authors have declared no conflicts of interest.

**P0810 CLINICAL OUTCOMES AFTER ENDOscopic RESection FOR ESOPHAGUSQUAMOUS CELL CARCINOMA COMPARING THE CASES WITH MM AND SM1 INVASION**

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Introduction: Recent advances in endoscopic resection (ER) provide us increasing chances for resecting esophageal squamous cell carcinoma (ESCC) with muscularis mucosae (MM) and SM1 invasion as MM/SM1 invasive cancer is reported to have 8-20% of metastatic risks and is defined as relative indication for ER in guideline by Japan Esophageal Society. For them, we perform additional laparoscopic surgery such as chemo radiotherapy (CRT) or operation considering the risk of metastasis and patients’ condition.

Aims & Methods: To know the difference of metastatic risk and local outcome, we retrospectively studied 121 cases of ESCC with pathological MM/SM1 invasion (MM/SM1:97/24) resected by ER from 2003 to 2013 in Cancer Institute Hospital. After pathological diagnosis of resected lesions, we performed additional therapy such as CRT, radiation therapy (RT) or operation, to the cases with lymphovascular invasion (LVI) or droplet infiltration (DI). Median observation period was 48 months.

Results: Enrolled cases included 112 males and 9 females and their median age was 66 (39-86). We resected ESCC by ESD in 71 cases and by EMR-C in 50 cases and their median size was 27 mm. Local recurrence was observed in 6 cases which were all after EMR (12%). As for local recurrence 5 cases were treated by resection and 1 case by APC, resulting in no re-recurrence. Of 97 cases of MM, 15 cases (15.5%) had LVI, 10 cases (10.3%) had DI. We recommended additional therapy in 21 cases (21.6%). Additional therapy was performed in 15 cases (15.5%) (ope/CRT/RT/9/5/1). No case died of ESCC and 22 cases (22.7%) died of other diseases. Of 24 cases of SM1, 9 cases (37.5%) had LVI, 5 cases (20.8%) had DI. We recommended additional therapy in 12 cases (50.0%). Additional therapy was performed in 9 cases (37.5%) (ope/CRT/RT/chemotherapy: 3/4/1/1). Three cases died of ESCC and 5 cases (20.8%) died of other diseases. Comparing both groups, tumor size and local recurrence rate were not different each other. The frequency of LVI was significantly higher in SM1 than in MM (p = 0.05) and the frequency of DI was higher in SM1, although not significant (p = 0.161). The metastatic recurrence was observed significantly frequent in SM1 than MM (16.7% vs 2.1%; p < 0.01). The 5-year overall survival (OS) did not different each other, but CSS in MM was significantly lower than in SM1 (p < 0.01).

Conclusion: ESCC with MM invasion was superior in metastatic recurrence and CSS than ESCC with SM1 invasion, although we treat MM/SM1 in the same way. Additional therapy should be considered more positively in cases of SM1 than in cases of MM, considering metastatic risk and patients’ conditions.

Disclosure of Interest: All authors have declared no conflicts of interest.

**P0811 GASTRIC ESD IN AN ANIMAL SURVIVAL MODEL USING THE ANUBIS-SYSTEM**

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Introduction: ESD is generally still under evaluation. The one-piece resection of lesions larger than 2 cm has many advantages against piece meal resection. One advantage of flexible preparation in ESD is to lift and prepare the specimen simultaneously. We used the ANUBIS-system for intragastric ESD.

Aims & Methods: The experimental study was conducted in a porcine model in general anesthesia. We started the study with 7 pigs in a survival model using the Anubusscope (Carl Storz, Germany). After insertion of the scope insufflations of the stomach was done using CO2. After the opening of the valves at the tip of the scope, an area of 5 cm in diameter was selected for resection. Injection was done with the two arms of the scope using a grasping and a hook-knife. Also the grasper could use for coagulation. The specimen was removed with the scope after closing its valves.

Results: The procedure was successful in all animals with operation time ranging from 102 to 189 minutes with a learning curve. After weight gain in all cases, the animals were sacrificed after postoperative day 2 and the workup showed competent healing with a star-like scar.

Conclusion: The use of an operating platform like the Anubuscope has the advantages of flexible preparation in opposite position of the instruments in ESD. The disadvantages are the only two degrees of freedom of the flexible instruments and the rotation-like movements. Also, it is not possible to reach all regions of the stomach.

Disclosure of Interest: All authors have declared no conflicts of interest.

**P0812 USEFULNESS OF NARROW BAND IMAGING WITH MAGNIFYING ENDOSCOPY AS A SCREENING TEST FOR GASTRIC CANCER**

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Introduction: Narrow band imaging with magnifying endoscopy (NBI-ME) is used for gastric cancer; however, whether NBI-ME is useful as a screening test for gastric cancers has not yet been determined. Additionally, it is important to consider the impact on the atrophy of the background gastric mucosa in gastric cancer screening because the incidence of gastric cancer depends largely on the degree of atrophy noted in the background gastric mucosa.

Aims & Methods: We aimed to determine the usefulness of NBI-ME as a screening tool for gastric cancer. We retrospectively studied 3515 patients who had undergone screening upper gastrointestinal endoscopy between April 2013 and March 2014. We excluded patients with advanced gastric cancer and those who had undergone gastrectomy. Thus, we studied 1080 patients who received NBI-ME and 2435 patients who had undergone conventional endoscopy. We classified the degree of atrophy of the background gastric mucosa using the Kimura-Takemoto classification. Severe atrophy was noted in 1620 patients (Group S), and mild atrophy in 1895 patients (Group M). We evaluated the biopsy rate, the detection rate of gastric neoplasms, and the accuracy of biopsy using NBI-ME compared to conventional endoscopy.

Results: The biopsy rate of NBI-ME and conventional endoscopy in Group M was 5.4 and 7.7%, respectively, while in Group S it was 14.9 and 14.8%, respectively. The biopsy rate did not differ significantly between those who received NBI-ME and those who had undergone conventional endoscopy. The detection rate of gastric neoplasms using NBI-ME and conventional endoscopy in Group M was 0 and 0.2%, respectively, while in Group S it was noted to be 4.2 and 1.8%, respectively. Thus, the detection rate of NBI-ME was significantly higher than that of conventional endoscopy in Group S (p < 0.01). The accuracy of biopsy with NBI-ME and conventional endoscopy in Group M was 0 and 3.2%, respectively, but in Group S it was noted to be 36.4 and 14.1%, respectively. Thus, the accuracy of biopsy using NBI-ME is significantly superior to conventional endoscopy in Group S (p < 0.01).

Conclusion: NBI-ME as a screening test for gastric cancer is useful for patients with severe atrophy of the background gastric mucosa because this technique has shown a higher detection rate of gastric neoplasms and better accuracy of biopsy.

Disclosure of Interest: All authors have declared no conflicts of interest.
cardiovascular diseases [3]. Thus, the verified risk prediction model of post-ESD bleeding may enable to determine preventive therapeutic options and restarting date of antplatelet agents.

Aims & Methods: The aim of this study is to develop the predictive risk model of post-ESD bleeding. A total of 3574 patients, who were taken ESD from January 2007 to November 2016 in a Korean tertiary hospital, were included in this retrospective study. To avoid overfitting of the prediction model, we divided the patients randomly into two groups, either a derivation group or a validation group. Preoperative and procedural-related variables were selected via univariate and multivariate analysis. A risk score was calculated to assess the bleeding prediction model of a patient in the derivation group and was discriminated in the validation group.

Results: Post-ESD bleeding occurred in 248 patients (6.4%). In the derivation group, multivariable logistic regression revealed renal disease or on diabetes (odds ratio [OR], 3.90; 95% confidence interval [CI], 1.48–9.09; P = 0.0029), anti-platelet agent (OR, 3.07; 95% CI, 1.44–6.05; P = 0.0002), and en-bloc resection (OR, 3.83; 95% CI, 1.34–9.34; P = 0.0059) as significant risk factors (C-statistic = 0.607; 95% CI, 0.52–0.61; P = 0.0054). In the validation group, the model also showed significantly discriminatory power (C-statistic = 0.580; 95% CI, 0.53–0.627). Based on the scoring system of odds ratio, bleeding risk was 4.1% in the low risk set (score ≤ 4), 7.0% in the high risk set (score > 4, P = 0.0003) (validation set).

Conclusion: Our study investigated a prediction scoring system of estimating the bleeding risk, including the patient, endoscopist factors. A risk score can be calculated before the procedure and the endoscopists can predict bleeding potency before the gastric ESD. Based on the scoring system, endoscopists may offer therapeutic plans such as prolongation of admission dates or medication schedules.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P0816 USEFULNESS OF DUAL RED IMAGING IN ESOPHAGEAL AND GASTRIC ENDOSCOPIC SUBMUCOSAL DISSECTION


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Introduction: Endoscopic submucosal dissection (ESD) remains difficult procedure due to bleeding and perforation. One of the reasons that these complications are occurred is unclear visibility of submucosal layer. Dual red imaging (DRI) is a new endoscopic imaging technique which is focused on deeper layer by using narrow long wavelength light than white light imaging(WLI). Therefore, DRI improves the visibility of vessels and demarcation line between the submucosal and muscle layers for colorectal ESD. The aim of this study is to evaluate the usefulness of DRI for esophageal and gastric ESD.

Aims & Methods: A retrospective analysis was performed on patients who underwent ESD for esophageal or gastric cancer in our institution. ESD was performed by circumferential incision using WLI at first. Submucosal dissection was performed using DRI in principle, and Ulcer bed was observed with DRI after resection. Total resection time (from incise to complete resection), perforation rate, and hemostasis rate after procedure were recorded. These parameters were compared with our matched previous procedures using propensity score (1: 2). We recorded paired endoscopic images using DRI and WLI at the same time during the dissection, then estimated the visibility of vessels and submucosa by using visual scale (0–100) by 5 endoscopists. We compared the visibility of DRI with WLI followed by the estimation.

Results: Twenty lesions (esophagus: 3, stomach: 17) of 18 patients were enrolled for this study. Total resection time was 67.0 ± 27.9 min, and was shorter than matched data (141.7 ± 113.5 min) significantly (p = 0.0054). Hemostasis rate after resection and perforation rate were not different significantly. The score of vessels visibility using DRI and WLI were 68.6 ± 17.5 and 62.3 ± 19.6, respectively. The score of submucosal visibility using DRI and WLI were 70.0 ± 18.0 and 64.9 ± 19.0, respectively. DRI was superior to WLI in both scores significantly (p < 0.0001).

Conclusion: Though our study is preliminary, DRI improves total resection time, visualisation of vessels and demarcation line between the submucosal and muscle layers significantly as previous study showed on colorectal ESD. DRI uses narrow long wavelength light. The light reaches slightly deeper layer than WLI. Therefore, we can see not only clear vessels but intact submucosa with this technique. Endoscopic procedure is done clearer by blood, fat, and fibrosis. We named this effect "noise cancelling effect" by DRI. This effect gets better the visibility better, therefore the esophageal and gastric ESD makes easier and safer.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference
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P0818 RISK FACTORS OF COMPLICATION RELATED TO ENDOSCOPIC MANAGEMENT OF FOREIGN BODIES IN THE ESOPHAGUS: A PROSPECTIVE STUDY IN 595 CASES FROM MULTIPLE CENTERS IN CHINA

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Introduction: Foreign bodies (FBs) ingestion is a common medical emergency accounting for 4% of all emergency endoscopies, secondary only to the G1 bleeding.1-3 75% - 78% of FBs are located in the esophagus4,5. The need of endoscopic management reached up to 63 - 76%4,5,6 3% - 20% of incidence of complications.7 According to the latest guidelines from ESGE, emergent endoscopy is recommended for the impaction of sharp-pointed objects within 24 hours.8 However, there were still different opinions on the endoscopic methods with different FBs.

Aims & Methods: The study was performed from October 2015 to August 2016 among 595 patients with clinical suspicion of foreign body ingestion from 18 general hospitals in China. The patient data including age, gender, clinical features, and data about endoscopic management including types and locations of foreign bodies, retrieval devices, outcomes and complications were collected and analyzed.

Results: 1) The most common types of foreign bodies were fish bones (34.0%), chicken bones (22.1%), fruit nuclei (11.7%) and food bolus (14.6%). The majority of them were short objects (< 2.5 cm, 74.0%), subsequently followed by middle objects (2.5 - 6.0 cm, 24.5%) and long objects (> 6.0 cm, 1.5%). Most objects were lodged in the proximal esophagus (75.9%), followed by the middle segment (17.0%) and distal segment (6.9%) of esophagus. 2) 96.3% of all cases had obvious clinical symptoms. Clinical symptoms occurred more often in the proximal segment of the esophagus (98.1%) than any other segments of the upper gastrointestinal tract (92.6%) (P < 0.001). 3) The successful retrieval rate through endoscopy was 94.5%. It was even higher with general anesthesia (99.3%) than without it (92.7%) (P < 0.01). 4) Complication rate was as high as 34.0%, which was increased with long retention time and sharp objects (P < 0.001). The rate was increased by 2.2- and 6.1-folds after impacted for over 48 hours as compared to less than 24 hours. Logistic regression analysis indicated that sharp objects had obviously more complications than non-sharp ones (OR 3.36, 95% CI: 1.97-5.74). In particular, the incidence of perforation was 5.6%, which was strongly related with long retention time and sharp objects (P < 0.03), but not with locations or lengths of the objects (P > 0.05).

Conclusion: General anesthesia could largely improve the retrieval rate through endoscopy. Foreign bodies, especially sharp ones, should be removed as soon as possible within 24 hours, to further decrease severe complications.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P0819 BIOPSY STRATEGIES FOR ENDOSCOPIC SCREENING OF PRE-MALIGNANT GASTRIC LESIONS

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Introduction: AG and IM are detectable precursor lesions of most gastric carcinomas. Early endoscopy examination may potentially result in early detection and treatment of advanced precursor lesions and cancer. The annual incidence of GA and IM among the general population in Europe, for GA was 0.1% and for IM was 0.25%. The histological assessment and biopsy sampling protocol has been standardized in the updated Sydney system and the recommended five gastric biopsies were widely applied in the staging system for gastric cancer risk stratification.1,2 Some believe that the GA risk screening requires consideration of the cost - suffering of patients as well as rational utilization of medical resources, so adopt five biopsy may be presumably less inappropriate in large-scale population gastric cancer risk screening. In this study, we evaluated the OLGA and OLGIM staging in a standardized five biopsy protocol through screening patients underwent endoscopy with abdominal pain and discomfort. In order to identify a more optimal biopsy strategy with quite high consistence with the standardized five biopsy protocol in OLGA and OLGIM staging and less number of biopsies during cancer risk assessment, we re-evaluated OLGA and OLGIM staging adopting different biopsy combinations (evaluated the appropriate biopsy locations and number of biopsies).

Aims & Methods: Gastric atrophy (GA) and intestinal metaplastic (IM) are precursor lesions of gastric cancer (GC), the extent and severity of which was intimate correlated with the occurrence of GC. Operative Linkon Gastritis Assessment (OLGA) and Operative Linkon Gastric Intestinal Metaplasia Assessment (OLGIM) with five biopsy samples are superordinate stages system during Gastric risk stratification. We analysis the degree of GA and IM in these five locations and screen out an more representative, simple and convenient biopsy samples composition for gastric risk screening.

Methods: 368 patients with abdominal pain and other discomfort undergoing endoscopy were enrolled in the study. Five biopsy pieces (two from antrum, namely lesser to the later curvature and corpus, one from corpus, larger and lesser curvature and one from incisura angularis) were acquired and graded by senior gastrointestinal pathologists according to the updated Sydney system. Gastric risk stratification was calculated by adopting OLGA and OLGIM staging system.

Results: GA and IM are respectively acquired in the incisura angularis mucosa than the both lesser and larger curve of antrum and corpus respectively (P<0.05), especially the moderate and severe degree. More GA and IM alternations happened in the lesser curve of the antrum and corpus than in the corpus and proximal corpus (P<0.05). The composition of the incidence anguish mucosa than the both lesser and larger curve of antrum and corpus, angularis biopsy) with quite accurate consistence with five biopsy pieces protocol using OLGA and OLGIM staging (94.0% and 92.9%), together with a rather low omission diagnostic rate of OLGA and OLGIM HI + N (5.8% and 7.2%).

Conclusion: The incisura angularis with more moderate and severe GA and IM should be recommended as conventional biopsy site during endoscopy. The three biopsies (corpus, larger curve of antrum and corpus) with more encouragement and more cost accuracy than five biopsy pieces protocol using OLGA and OLGIM staging system, and thus could be recommend in the further gastric risk screening applying OLGA and OLGIM staging.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
Aims & Methods: patients. However, very few studies concentrated on the symptoms and similar manometric findings compared with younger patients. (LES). The Elderly patients have longer courses of disease, less perception of esophageal aperistalsis and incomplete relaxation of lower esophageal sphincter.

MYOTOMY FOR ACHALASIA IN PATIENTS OLDER THAN 70

PO821 GASTROINTESTINAL STROMAL TUMOURS SHOULD BE REJECTED EVEN IN A SMALL SIZE – A RETROSPECTIVE ANALYSIS IN 33 CASES

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Introduction: In gastrointestinal stromal tumors (GISTs) without a risk of metastasis to other organs, local resection is acceptable. In small GISTS, however, it is controversial whether surgical resection is necessary because a risk of recurrence/metastasis in these tumors are considered to be quite low. Laparoscopic endoscopic cooperative surgery (LECS) is a promising surgical technique as one of minimally-invasive, function-preserving surgeries. By using this technique, we are aggressively resecting gastric SMTs including relatively small ones.

Aims & Methods: To investigate necessity of surgical resection for small GISTS, we retrospectively assessed a malignant potential of these tumors which were resected nonexposed endoscopic wall-inversion surgery (NEWS) (nonexposure LECS technique) as well as feasibility and safety of this technique. Between August 2013 and October 2016, NEWS was conducted in 33 consecutive SMTs which met all of following conditions: possible GIST which was preoperatively diagnosed by histology or imaging modalities, less than 3 cm in size and inaccessible-growing type. NEWS was feasible, safe and therefore recommended for these tumors including Eckardt score, lower esophageal sphincter pressure, adverse events and recurrence.

Results: All patients underwent POEM successfully. Mean procedure time was 13.7 years-old and 23.3±8.4 mm, respectively. The procedure was successfully completed in all cases in a mean procedure duration of 206±43 min. The patients were discharged without severe adverse events 7.3±1.5 days after the procedure. The first endoscopy after the procedure was performed 5.8 months after discharge in 22 cases, which showed no residual food in the remnant stomach in all cases. Neither apparent impairment of food intake nor disease-related death occurred and a body weight loss was 0.9±2.3 kg during the mean observational period of 13.7 years.

Conclusion: Some small GISTS which could be retrieved transorally had a high malignant potential, NEWS was feasible, safe and therefore recommended for these tumors including ulcerated GISTs as a minimally-invasive surgical option to avoid an additional surgical scar for the retrieval of the specimen and a risk of intragastric tumor cell seeding into the peritoneum during the procedure.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference


PO822 LONG-TERM OUTCOMES OF PERORAL ENDOSCOPIC MYOTOMY FOR ACHALASIA IN PATIENTS OLDER THAN 70 YEARS

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Introduction: Achalasia is a rare esophageal motor disorder characterized by esophageal aperistalsis and incomplete relaxation of lower esophageal sphincter (LES). The Elderly patients have longer courses of disease, less perception of symptoms and similar manometric findings compared with younger patients. Peroral endoscopic myotomy (POEM) is a novel endoscopic therapy which recently has been described as an incisionless and less invasive scarless myotomy alternative for treating achalasia. However, very few studies concentrated on the long-term outcomes of POEM for achalasia patients, especially for elderly patients.

Aims & Methods: Peroral endoscopic myotomy (POEM) is a minimally invasive endoscopic myotomy for achalasia. But the long-term outcomes of POEM for achalasia in elderly patients are unclear. We therefore aim to evaluate the efficacy and safety of POEM for achalasia in patients older than 70 years. A total of 33 consecutive patients aged ≥70 years were enrolled in this study, who had undergone POEM for achalasia from May 2011 to March 2016 in the Endoscopy Center of Zhongshan Hospital. We retrospectively assessed the short and long term outcomes of these procedures including Eckardt score, lower esophageal sphincter pressure, adverse events and recurrence.

Results: All patients underwent POEM successfully. Mean procedure time was 50.7±22.0 mm and postoperative hospital stay was 2.8±1.5 days. No severe complications related to POEM were encountered. The mean follow-up period of 40.5±19.1 months (range from 12.2 to 70.9 months), the therapeutic success rate was 90.9% (30/33). Mean Eckardt score was 7.6±2.0 and 1.4±1.3 before and after POEM, respectively (P<0.001). Mean LES pressure decreased from 38.4±13.5 mmHg to 32.3±9.9 mmHg after POEM (P<0.001). Clinical gastroesophageal reflux occurred in 11 cases (33.3%) after the procedure which was successfully resolved by proton pump inhibitors.

Conclusion: POEM can be a safe and effective treatment option for achalasia in elderly patients older than 70 years with significant improvement in symptoms.

Disclosure of Interest: All authors have declared no conflicts of interest.

References


PO823 POST-POEM ESOPHAGITIS – REAL REFLUX ESOPHAGITIS OR JUST A HEALING PROCESS?

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Introduction: POEM has become a standard treatment of achalasia based on its excellent efficacy and safety. However, unlike in laparoscopic myotomy, POEM is not accompanied by an antireflux procedure and thus the rates of both clinically relevant post-POEM reflux (measured by symptoms and/or 24 h pH monitoring) and post-POEM esophagitis are key questions of long-term POEM safety. Several studies have reported the rates of post-POEM reflux and post-POEM esophagitis being as high as 30–40%. The aim of this retrospective analysis was to analyze whether esophageal erosions, detected endoscopically early after POEM, represent real reflux esophagitis or rather signs of still ongoing healing process after POEM.

Aims & Methods: A single-center retrospective analysis of 192 patients who underwent POEM in our institution. Three months after POEM, 162 patients underwent both pH monitoring and endoscopy and treatment with PPIs was assessed. At 24–36 months, a control endoscopy was performed in 41 patients to screen for esophagitis. We reviewed all available video recordings of POEM procedures and subsequent control endoscopies to analyze whether the localization of erosions was limited to the site of submucosal tunneling (e.g. between 2–4 o'clock in patients after anterior POEM) or also outside this area (real reflux erosions). We also analyzed evolution of esophagitis in time and correlated it with pH monitoring and intake of PPIs.

Results: At 3 months, esophagitis was present in 64 out of 162 patients (39.6%). Of those, 21 (33%) were on PPIs by the time of endoscopy and 43 (67%) were not. Among 43 patients with esophagitis and available video recording, 29 (67.4%) had erosion(s) only on the site of submucosal tunnel and 14 (32.6%) had erosions also elsewhere. Among patients with erosion(s) only on site of the tunnel, 13 (44.8%) had normal acid exposure time (assessed by pH monitoring.
performed off PPIs). At 24–36 months, esophagitis was present in 9 out of 41 patients (p < 0.04 vs. 3.5 months). In 6 out of 10 patients with esophagitis present at 3 months, who underwent control endoscopy at 24–36 months, esophagitis resolved completely even though only 2 patients had been treated by a PPI.

Conclusion: After POEM, the majority of patients with esophagitis had erosions on site of submucosal tunnel and early esophagitis often occurred in patients without an abnormal acid exposure. These findings suggest that an ongoing healing process after POEM might interfere in findings of presumed post-POEM reflux esophagitis. Thus, the rate of real post-POEM reflux esophagitis may be lower than previously thought.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0824 ENDOSCOPIC SUBMUCOSAL TUNNEL DISSECTION FOR LESSER GASTRIC CURVATURE SUPERFICIAL NEOPLASMS

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Introduction: Endoscopic submucosal dissection (ESD) has been widely used for resection of gastrointestinal neoplastic lesions, but there are still technical challenges in treating large ones especially located in lesser gastric curvature. In the Endoscopic submucosal dissection (ESD) has been widely used for Gastroenterology, the First Affiliated Hospital of Soochow University, Suzhou/D. Shi,

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REFERENCES


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P0826 ENDOSCOPIC SUBMUCOSAL DISSECTION FOR UPPER GI SUBMUCOSAL TUMOURS


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Introduction: Submucosal tumours (SMT) in the upper gastrointestinal tract (UGI) impose diagnostic and therapeutic challenges. They may have malignant potential and endoscopic ultrasound (EUS) guided diagnosis is often inadequate. A substantial proportion may not involve the muscularis propria (MP) and thus may be amenable to endoscopic excision. Snare-based techniques are usually unable to completely excise such lesions, though without complete excision ongoing endoscopic surveillance may be necessary. Endoscopic submucosal dissection (ESD) offers the possibility of complete resection and definitive...
P0827 COMPARING APPROACHES TO SELF-EXPANDING METALLIC STENTS INSERTION

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Introduction: The incidence of oesophageal cancer has increased significantly over the past two decades. The majority of these cancers are incurable at diagnosis. Therefore, the management is aimed at maintaining quality of life by ensuring adequate nutrition and palliation of symptoms, mainly dysphagia. Self-expandable metallic stents (SEMS) have a well-recognised role in the palliative management of patients with oesophageal cancer. These stents are inserted endoscopically, under direct vision (EC) or with fluoroscopic assistance to endoscope (FAE). There is little evidence to compare outcomes between these approaches.

Aims & Methods: The objective of this study was to compare the outcomes, using various performance indicators, in patients who underwent SEMS for palliation in oesophageal cancer via different approaches (EC or FAE) at the Royal Infirmary of Edinburgh (RIE). A retrospective observational study was conducted between May 2014 to April 2016; a total of 62 SEMS. The approach to stent insertion was subject to operator choice and availability of fluoroscopic assistance, and as such can be akin to randomized study. We compared early and late complications associated with two techniques. Early complications included pain, vomiting, bleeding, perforation and tachycardia. Late complications included tumour growth, oesophageitis, stent migration and stent malposition.

Results: Forty-seven stents were inserted by EC and fifteen by FAE. The mean age was 62 years with 19 male patients (63%). Mean lesion size was 18 mm. Twenty-five patients (83.3%) had completely resected lesions. Four patients (13%) had involvement of the MP which was identified during the resection, and one patient (3%) had MP injury which precluded complete resection. Three of five lesions of the incompletely EC procedures were in the proximal body of the stomach, however only two lesions of the completely resected lesions were in the proximal body (P=0.004). Otherwise, there were no significant differences between the patients and lesions characteristics. The histology of the SMT lesions were 9 NET, 6 leiomyoma, 5 Granular cell tumours, 4 inflammatory fibroid polyposis, 2 GIST, 2 dysplastic Lipoma, one myofibroblastic tumour and one Warthin’s like tumour. Nineteen patients had completed surveillance endoscopy (SE) without an endoscopic and histological recurrence (Median follow up 18 months). Six patients are pending SE. The four patients with deep MP involvement were referred for surgery.

Conclusion: EC for selected UGI SMT is an effective treatment. Long-term endoscopic follow-up confirmed the absence of recurrence endoscopically and histologically. MP involvement cannot be reliably excluded by prior EUS. This technique should be considered for UGI SMT lesions without MP involvement in experienced centres.

Disclosure of Interest: All authors have declared no conflicts of interest.

Variable | EC (47) | FAE (15)
---|---|---
Male (%) | 33 (70) | 10 (67)
Location of tumour Upper | 32 (9) | 40 (6)
Limit (IQR) Lower | 37 (5.1) | 38 (7)
Limit (IQR) | 2 (1.8) | 3 (2.5)
Sedation and analgesia use | 50 (100) 100 (0) | 75 (50)
Midazolam dose (mg) | 100 (0)

(continued)
P00829 NOVEL IMAGE ENHANCEMENT TECHNOLOGY USING LINKED COLOR IMAGING WITH ACETIC ACID INDIGOCARMINE MIXTURE FOR DIAGNOSIS OF EARLY GASTRIC NEOPLASM Y. Kawahara1, H. Kanazaki2, S. Kawano2, M. Iwamuro2, Y. Kom0, T. Gotoda2, H. Sakae2, Y. Bab2, Y. Obayashi2, Y. Okamoto1, H. Okada1
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Introduction: A value of the combination of magnifying endoscopy of and image enhancement endoscopy (IEE) technology (e.g. NBI, BLI) is reported in a diag-nosis for the early gastric neoplasm. That method is useful, but in order to master it it is necessary to learn and familiarize complex classifications. Therefore, this diagnostic method is still more difficult for general endoscopists. Linked Color Imaging (LCI) was recently developed using a laser endoscopic system (Fujifilm Co., Tokyo, Japan). LCI acquires images by simultaneously using narrow-band short wavelength light and white light in an appropriate balance. This combina-tion of light provides more information about the vascular architecture and the mucosal surface than that obtained with typical white-light imaging. When we use acetic acid indigocarmine mixture (AIM) with LCI mode, we reported that the magnifying images of early gastric cancer are very clear, three-dimensional and near to real histology. So, we examined the examined the utility of this method.

Aims & Methods: This was a prospective observational study performed at a single tertiary referral center. The subjects are 120 lesions of 115 patients with gastric neoplasm. We are indicated the endoscopic submucosal dissection (ESD) and were given preoperative endoscopy in our hospital from September 2014 to February 2017. Firstly we observed the lesions by magnifying endoscopy with the BLI mode and diagnosed using VS classification system. Secondly we observed the lesions by magnifying endoscopy with LCI+AIM method and diagnosed using VS classification system. Furthermore, we classified tumor differ-entiation into high differentiation, moderately differentiated, and poorly differ-entiated by its surface pattern. Finally, we classified the visualization ability of the surface fine structure in Clear, Visible, and Invisible and evaluated it. We carried out ESD and compared the image with the histopathology.

Results: By the results, 92 lesions (79.1%) were gastric adenoma and 28 lesions were gastric adenoma. The differentiation ability of a cancer and the non-cancer (adenoma) did not have the significant difference between the BLI mode and the LCI+Aim methods. Diagnosis of differentiation of gastric cancer was correct in 87 of 92 cases (94.6%). In the classification of visualization ability, 32 lesions were Clear, 44 lesions were Visible, 44 lesions were Invisible by BLI mode, On the other hand, 45 lesions were Clear, 64 lesions were Visible, 11 lesions were Invisible by BLI mode. In the visualization ability of the surface fine structure, LCI+Aim method is significantly clearer than BLI mode (p < 0.001).

Conclusion: When we use AIM, indigocarmine accumulates in pit of the duct, and duct structures become clear by the acetic acid. By LCI mode, we can observe the vascular pattern of the lesion clearly. So by the combination of AIM and LCI, we can observe the endoscopic images closer to actual histological images. By this method, we can compare histopathology with an endoscopic image intuitively, so we believe that a magnifying endoscopy diagnosis of the gastric cancer is enabled even if we do not use various confusing classifications.

Disclosure of Interest: All authors have declared no conflicts of interest.

P00831 RESULTS FROM THE FIRST UK VIRTUAL COMPLEX POLYP MD M. Chatterjee, M. Rutter
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Introduction: Data from the UK Bowel Cancer Screening Programme (BCSP) has established that the assessment and management of large non pedunculated colocolar polyps (LNPCPs) varies markedly, leading to variable and often suboptimal outcomes, especially for the most complex lesions1. A multicentre complex polyp multidisciplinary team meeting was created within the North East of England BCSP with the aim of ensuring more robust decision making and managemment of complex LNPCPs.

Aims & Methods: A virtual multicentre MDM was conducted via audioteleconferencing within the North East of England between 2014-6 to discuss complex LNPCPs (LNPCPs with increased risk of malignancy or complexity associated with endotherapy, as defined in BSG/ACPGBI guidelines2). Non-complex LNPCPs were not discussed. Patient data was distributed securely via NHSmail. Outcomes were assessed prospectively using key performance indicators (KPIs) from the BSG/ACPGBI guidelines2.

Results: 61 complex LNPPC cases were managed via the MDM with 8 excluded from analysis (7: managed prior to MDM referral, 1: MDM advice not fol-lowed), 27 lesions were managed with primary endotherapy, 23 with primary surgery and 3 cases conservatively. Of the endoscopic cases, 2 required surgery and 2 endotherapy to a finding and 1 to a follow up. 12 month recurrence was 8.7% with no reported complications. The rate of surgical man-agement using the BSG/ACPGBI KPI (including only surgically managed benign lesions or lesions subject to failed endotherapy) was 39.5%. The en-bloc resection

Disclosure of Interest: All authors have declared no conflicts of interest.

References
Ninez O, et al. Estudio de los factores predictivos de lesiones digestivas graves tras la ingestión de ácidos. Med Clin (Barc) 2004;123(16):611-4

**Disclosure of Interest:** All authors have declared no conflicts of interest.**
rate of complex LNPPCs with features suggestive of increased malignancy risk was 27.1% (SD 14.69) in low-ADR group vs. 20.22% (SD 9.55) in high-ADR group.

### Breakdown via High risk features of malignancy

<table>
<thead>
<tr>
<th>Size Range</th>
<th>Low-ADR Group Mean SD</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1–2 cm</td>
<td>≥20% 34.09 15.46</td>
<td>2.029</td>
</tr>
<tr>
<td>&gt;2 cm</td>
<td>&lt;20% 4.04 3.69</td>
<td>0.470</td>
</tr>
</tbody>
</table>

### Conclusion

Endoscopists with higher ADR tend to detect significant more SSA and adenomas with 1–2 cm in size, but have lower proportions of pedunculated adenomas than those with a low ADR. In our study cohort no significant differences in flat shape or diminutive size was measurable.

### Disclosure of Interest

All authors have declared no conflicts of interest.

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### References


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Introduction: Patients of endoscopists with high (≥20%) adenoma detection rate (ADR) have less risk for interval cancer than those of low ADR (<20%). Lesion-related-factors, such as size, shape and histology influence the detection rate of physicians with high ADR tend to detect more full and spattered adenomas than those with low ADR.

Aims & Methods: Our study aim is to investigate the differences of size, shape and serrated histology of adenomas between low- and high-ADR group in our screening cohort. We analyzed 22,534 screening colonoscopies performed by 261 endoscopists between 2007 and March 2017 within the austrian certificate of screening colonoscopy. T-Test was used to assess differences.

Results: 39.1% of endoscopists were categorized in the ADR low- and 60.9% in the high-ADR group. Overall, mean ADR was 23.06% (SD 0.55) with a minimum of 0.39% and a maximum of 48.72%. In the low-ADR-group mean ADR was 14.56 (SD 0.42) and 28.51 (SD 0.50) in the high-ADR group. Regarding to size, there was a significant difference (p = 0.029) in detection of adenomas of 1–2 cm with a mean of 8.44% (SD 6.02) in low- vs. 10.22% (SD 6.64) of all adenomas in high-ADR group but no differences between adenomas <0.5 cm, 0.5–1 cm and those bigger than 2 cm. Regarding shape, proportion of pedunculated adenomas in low-group-ADR differ significantly higher (p = 0.002), with a mean of 19.36% (SD 14.60) vs. 17.40% (SD 9.55) but there were no differences between flat and sessile adenomas. With a mean proportion of 4.43% (SD 5.61) vs. 6.64% (SD 5.97), the proportion of sessile serrated adenomas (SSA) differ significantly between low-ADR vs. high-ADR group (p < 0.01).

Disclosure of Interest: All authors have declared no conflicts of interest.

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Introduction: ESD is a complex procedure, mainly in non-Asian countries where the learning process is not well established. Results may be improved in Western countries with a careful selection of lesions for ESD and avoiding those with greater chance of technical difficulty. Factors predicting technically difficult ESD when it is performed by non-Asian endoscopists should be clarified.

Aims & Methods: We aimed to identify the potential risk factors that are associated with a higher technical difficulty during ESD in a Western European setting where there are no available Asian experts. We prospectively recorded consecutive ESD cases performed by members of the ESD Working Group of the Spanish Society of Digestive Endoscopy. Demographic and clinical characteristics of the patients, location and morphology of the lesions, and technical factors were collected. We defined difficult ESD as those aborted procedures, time-consuming (duration >180 min.) or when changing the technique to piecemeal resection was needed to remove the tumor. Analyses were carried out using IBM SPSS software for Windows (IBM Corp., Armonk, NY, USA). Parametric continuous variables are reported as the mean ± standard deviation (SD). A Kolmogorov-Smirnov test was used to evaluate normal distribution. Categorical variables are reported as either frequencies or percentages. Statistical differences between the groups were analyzed using a chi-squared test for categorical data. The meaningful variables with a p value <0.1 in the univariate analysis were included in the logistic regression model. Multivariate analysis was performed using binary logistic regression methods. Odds ratios (ORs) and 95% confidence intervals (CI) were calculated to assess the strength of the influence of each individual variable.

Results: We included 265 lesions in 265 patients [mean age ± SD: 69 ± 10; 150 males (56.6%)]. They were recruited in 15 Spanish University Hospitals between January 2016 and March 2017. Location of the lesions were: esophagus (n = 7; 2.6%), cardiac (n = 5; 1.8%); stomach (n = 48; 18.1%); duodenal bulb (n = 1; 0.3%); colon (n = 144; 54.3%) and rectum (n = 60; 22.6%). Mean lesion size was 38.8 ± 18.5 mm. Median duration of the procedure was 105 min. (8–375). In 73 cases (27.5%) criteria for difficult ESD were fulfilled. Endoscopic resection was aborted in 7 cases (2.6%). When endoscopic resection was achieved (n = 258; 97.3%), both situations, duration >3 h and a piecemeal resection, were noted in 21 (8.1%) patients. Duration >3 h in 25 cases (9.7%) and unsuccessful en bloc...
resection in 20.7% were observed in isolation, respectively. Table 1 shows the univariate and multivariate analysis of factors regarding technically difficult ESD.

### Table 1: Univariate and multivariate analysis of possible factors related to technically difficult ESD.

<table>
<thead>
<tr>
<th>Variables</th>
<th>UNIVARIATE ANALYSIS</th>
<th>MULTIVARIATE ANALYSIS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Procedure</td>
<td>OR (C.I. 95%)</td>
<td>p</td>
</tr>
<tr>
<td>Case load &lt;10</td>
<td>0.8 (0.4–1.6)</td>
<td>0.5</td>
</tr>
<tr>
<td>2 endoscopists vs. 1 operator</td>
<td>20.6(5.9–72.6)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Location</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Colorectal</td>
<td>2.6 (1.2–5.7)</td>
<td>0.01</td>
</tr>
<tr>
<td>Stomach</td>
<td>0.5 (0.2–1.0)</td>
<td>0.06</td>
</tr>
<tr>
<td>Lesion</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Size &gt;30mm</td>
<td>2.4 (1.3–4.4)</td>
<td>0.004</td>
</tr>
<tr>
<td>Recurrent tumour</td>
<td>3.2 (1.3–8.1)</td>
<td>0.008</td>
</tr>
<tr>
<td>Protruded morphology</td>
<td>0.9 (0.5–1.9)</td>
<td>0.9</td>
</tr>
<tr>
<td>Depressed component</td>
<td>0.6 (0.2–1.7)</td>
<td>0.4</td>
</tr>
<tr>
<td>Poor manoeuvrability</td>
<td>3.5 (1.7–7.5)</td>
<td>0.001</td>
</tr>
<tr>
<td>Previous biopsy</td>
<td>1.0 (0.6–1.8)</td>
<td>0.9</td>
</tr>
<tr>
<td>Submucosal invasion</td>
<td>1.3 (0.3–3.7)</td>
<td>0.6</td>
</tr>
<tr>
<td>Severe submucosal fibrosis (F2 vs. F0/F1)</td>
<td>3.3 (1.7–6.4)</td>
<td>0.0002</td>
</tr>
<tr>
<td>Complications</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intraprocedural bleeding</td>
<td>4.1 (1.9–8.7)</td>
<td>0.0003</td>
</tr>
</tbody>
</table>

### Conclusion
The factors independently associated with technically difficult ESD (abortive procedures, time-consuming or finished with a piecemeal resection) were: lesion size >30mm, poor manoeuvrability, recurrent lesions and intraprocedural bleeding. Except for the last one, the remaining factors can be identified during the first diagnostic endoscopy. Endoscopists who will start performing ESD should try to avoid these difficult procedures in the early part of their learning curves.

### Disclosure of Interest
All authors have declared no conflicts of interest.

### References

**P0834 EPOCH-MAKING TECHNIQUE OF FULL-THICKNESS RESECTION FOR THE COLORECTAL TUMOR BY USING LAPAROSCOPY ENDOSCOPIC COOPERATIVE SURGERY (LECS)**

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**Introduction:** We established the Laparoscopy Endoscopy Cooperative Surgery (LECS) procedure to overcome the limitation of colorectal endoscopic submucosal dissection (ESD). This procedure is a local full-thickness resection of the combined procedure of laparoscopy assisted colectomy (LAC) and ESD procedure. Also, it is the method that is epoch-making for minimal invasive treatment that kept an intestinal function.

**Aims & Methods:** The aim of this study was to investigate the feasibility and safety of LECS procedure applied with endoscopic submucosal dissection (ESD) technique obtained adequate surgical margin. We performed ESD on 1376 colorectal tumors in 1341 patients (male: female = 777:564; mean age, 66.1years). Among these cases, six cases had perforation (0.4%), and three of six cases required emergent surgery. We examined the cause of perforation and the limit of ESD from the view point of safety. We performed one-piece resection for 11 cases (male: female = 7:4; mean age, 63.5years) of colorectal tumors using LECS procedure. In the first, the indication of LECS is at high risk of the perforation by the treatment of ESD and EMR and is the lesion that safety cannot secure. In addition, the indication is the lesion which is curable by the local excision without lymph node dissection. Therefore, submucosal invasive (T1) cancer with the risk of lymph node metastasis does not become the indication for this full-thickness resection technique. From the above-mentioned basic concept, indications of the LECS procedure for colorectal tumors were thought to be: 1) Intramucosal carcinoma (Tis) and adenoma with high-grade atypia involved appendix or diverticulum. We examined the clinical pathological outcomes of 11 cases.

**Results:** Four of six cases that caused perforation in ESD were cases with fibrosis in the submucosal layer. Three cases of those were moderate to severe degree fibrosis cases, and a limit of ESD seemed to exist in these lesions from the viewpoint of safety and curability. We accomplished full-thickness resection successfully for 11 cases using LECS procedure as follows: 5 cases of Tis cancer, 4 cases of adenoma, 1 case of schwannoma, and 1 case of GIST. The reasons as we judged that the indication of LECS procedure were as follows: three cases accompanied by severe degree fibrosis, 2 cases involved diverticulum, 3 cases involved appendix, 2 cases of submucosal tumor, and 1 case of poor endoscopic operability. These cases were considered a limitation of ESD due to the high risk of perforation. An operative time was an average of 195.8 minutes (127 to 332), and the perioperative bleeding was an average of 8.9g (3 to 20). We experienced no complications, and average post-operative hospital stay was 7.7(6 to 12) days. Histological examination of the resected specimens revealed negative lateral and deep margins. The postoperative follow-up was carried out first a half year later, and it was every one year subsequently. In the above-mentioned follow-up schedule, blood examination, colonoscopy, CT scan were performed for clinical evaluation. The residual/local recurrence case was absent for 31.6 months (range 10-60 months) for the mean follow-up period. Also, without complications such as postoperative anastomotic stricture or adhesive ileus, we followed favorable course.

**Conclusion:** We developed a LECS procedure to overcome the limit of ESD, and completed full-thickness one-piece resection of the tumors considered as high risk of perforation in the endoscopic treatment.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**Reference**

**P0836 HIGH INCIDENCE OF MINOR ADVERSE EVENTS AFTER ENDOSCOPIC MUCOSAL DISSECTION FOR COLORECTAL NEOPLASMS**

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**Introduction:** Endoscopic mucosal resection (EMR) and submucosal dissection (ESD) are effective procedures for reducing the need for colorectal surgery. Many studies have focused on major adverse events related to EMR and ESD such as bleeding and perforation. However, data on structured assessment of minor post-procedural adverse events remain scarce. We therefore evaluated the incidence of major and minor adverse events within 30 days of EMR or ESD.

**Aims & Methods:** We prospectively performed a single-center study on consecutive patients who underwent colorectal EMR or ESD between April 2014 and April 2016. We asked for permission to interview the patients 1 day, 14 days, and 28 days after their procedure. Four gastroenterologists performed all procedures. The assigned nurse performed the data and interviewed the patients in person on day 1 and day 14 ± 2 days, and via phone on 28 ± 2 days after their respective EMR/ ESD procedure. A standardized interview form was developed to assess the occurrence of (i) major adverse events (hospital visit required), (ii) minor adverse events, and (iii) working days lost due to adverse events. The primary outcome was the occurrence of all adverse events, which were classified as either “major” or “minor”.

**Results:** We enrolled 630 patients who underwent EMR or ESD. 615 (97.6%) (499 EMR, 116 ESD) were contacted. Male comprised 68.5% (n = 415), and the mean age was 57.9 years (±1.3). Major adverse events occurred in 31 (5%), 16 (2.5%), and 1 (0.2%) patients on days 1, 14, and 28, respectively. Minor adverse events occurred in 284 (46.1%), 344 (55.9%), and 25 (4.1%) patients on days 1, 14, and 28, respectively. Bleeding was the most common major event on days 1 and 14 ± 2 days, and abdominal bloating and bowel habit change were the most common minor events on days 1 and day 14, respectively. 11 (1.8%) and 20(3%) patients took leaves of absence due to adverse events on day 14 and 28, respectively. The detailed events are listed in Table 1.

**Conclusion:** Although the number of major adverse events was small, nearly half of the patients reported minor adverse events on 14 days following colon EMR/ ESD. Most minor adverse events subsided by the day 28.

**Disclosure of Interest:** All authors have declared no conflicts of interest.
Table 1: Number of Patients with Adverse events on Day 1, 14, and 28.

<table>
<thead>
<tr>
<th>Event</th>
<th>Day 1 N = 315(51.2%)</th>
<th>Day 14 ± 2 days N = 360(58.5%)</th>
<th>Day 28 ± 2 days N = 264(42.2%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>EMR ESD</td>
<td>EMR ESD</td>
<td>EMR ESD</td>
<td>EMR ESD</td>
</tr>
<tr>
<td>Minor 284(46.1%)</td>
<td>Minor 344(55.9%)</td>
<td>Minor 25(4.1%)</td>
<td></td>
</tr>
<tr>
<td>Bowel habit change</td>
<td>217(43.5%)</td>
<td>267(53.5%)</td>
<td>19(3.8%)</td>
</tr>
<tr>
<td>Abdominal bloating</td>
<td>112(28)</td>
<td>30(14)</td>
<td>156(41)</td>
</tr>
<tr>
<td>Minor bleeding</td>
<td>36(25)</td>
<td>45(22)</td>
<td>156(41)</td>
</tr>
<tr>
<td>Mild abdominal pain</td>
<td>42(16)</td>
<td>54(24)</td>
<td>156(41)</td>
</tr>
<tr>
<td>Dizziness</td>
<td>33(13)</td>
<td>25(10)</td>
<td>156(41)</td>
</tr>
<tr>
<td>Headache</td>
<td>26(7)</td>
<td>19(6)</td>
<td>156(41)</td>
</tr>
<tr>
<td>Back pain</td>
<td>17(3)</td>
<td>16(3)</td>
<td>156(41)</td>
</tr>
<tr>
<td>Easy fatigability</td>
<td>10(1)</td>
<td>65(21)</td>
<td>156(41)</td>
</tr>
<tr>
<td>General Myalgia</td>
<td>4(2)</td>
<td>26(8)</td>
<td>156(41)</td>
</tr>
<tr>
<td>Nausea/vomiting</td>
<td>3(3)</td>
<td>8(2)</td>
<td>156(41)</td>
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<tr>
<td>Tenesmus</td>
<td>3(3)</td>
<td>18(9)</td>
<td>156(41)</td>
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<tr>
<td>Fecal sosense</td>
<td>2(1)</td>
<td>7(4)</td>
<td>156(41)</td>
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<tr>
<td>Voiding difficulty</td>
<td>1(1)</td>
<td>5(3)</td>
<td>156(41)</td>
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<tr>
<td>Dry mouth</td>
<td>1(1)</td>
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<td>156(41)</td>
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<tr>
<td>Epigastric pain</td>
<td>2(1)</td>
<td>3(1)</td>
<td>156(41)</td>
</tr>
<tr>
<td>Leg pain</td>
<td>1(1)</td>
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<td>156(41)</td>
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<tr>
<td>Urticaria</td>
<td>1(2)</td>
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<td>Indigestion</td>
<td>1(23)</td>
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<td>Drowsiness</td>
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<td>Herpes zoster</td>
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<td>Flank pain/proctalgia</td>
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<td>156(41)</td>
</tr>
<tr>
<td>Sleep disturbance</td>
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</tbody>
</table>

**P0837 DEVELOPING PATIENT-REPORTED EXPERIENCE MEASURES FOR GI ENDOSCOPY: RESULTS OF PATIENT INTERVIEWS**

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**Introduction:** Patient experience is increasingly recognised as a key measure of quality of care. Ensuring positive experience is important to patients and fundamental in maximising participation in screening programmes and re-attendance for surveillance procedures. Current measures of patient experience of gastrointestinal (GI) endoscopy are clinician derived. Patient Reported Experience Measures (PREMs) should be patient derived and incorporate pre-and post-procedure experience. We aimed to identify themes considered as important to patients undergoing GI procedures as a basis for developing PREMs.

**Aims & Methods:** We aimed to identify themes important to patients undergoing GI investigations, to enable questionnaire development. Patients who had undergone upper or lower GI investigations (gastroscopy, colonoscopy and CT pneumocolon) were invited to attend for a semi-structured interview. 32 interviewees were purposefully sampled to ensure diversity. Interviews were conducted by a research fellow trained in qualitative methods and were audio recorded and transcribed verbatim. Recruitment continued until saturation was achieved. Analysis used qualitative thematic methods focusing on anticipated and emergent themes, using constant comparison to ensure that all perspectives were included in the explanation of the data.

**Results:** 168 patients were approached. 32 interviews were completed (12 gastroscopy, 10 colonoscopy and 10 CT pneumocolon), with a male:female ratio of 18:14. The time interval from examination to procedure ranged from 5 to 44 days. Mean age was 63.1 years (SD 11.5) days. Mean age was 63.1 years (SD 11.5)

**Conclusion:** Despite heterogeneity between procedures consistent themes related to patient experience emerged. This work will be used to develop PREMs for Gastrointestinal Endoscopy.

**Disclosure of Interest:** L.J. Neilson: Research post previously funded by Aquilant endoscopy

C.J. Rees: Colin Rees has received research grants from ARC medical, Olympus Medical, Aquilant endoscopy, Norgine, travel grants from Boston scientific and Cook medical and speaking grants from Norgine and Olympus All other authors have declared no conflicts of interest.

**Reference**


**P0838 RANDOMIZED CONTROLLED TRIAL OF ABDOMINAL VIBRATION STIMULATION AND WALKING EXERCISE FOR BOWEL CLEANSING PRIOR TO COLONOSCOPY**


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**Introduction:** Adequate bowel preparation is important to perform colonoscopy for accurate mucosa examination, lesion detection and treatment. Walking exercise is known to be effective for colon cleansing. However, it is difficult for patients with uncomfortable walking to improve the status of bowel cleansing.

**Aims & Methods:** Therefore, we prospectively evaluated the clinical feasibility and clinical validity of the abdominal vibration stimulation for bowel
preparation. In this randomized, prospective, investigator-blind study and single center setting, 141 inpatients for elective colonoscopy were randomized to two groups. PEG solution was used for bowel cleaning in all patients. The one is walking over 3000 steps and the other is having abdominal vibrator more than 30 minutes before colonoscopy. After examination we recorded procedure results, sedation information, patient's satisfaction and adequacy of bowel preparation by using the Boston Bowel Preparations Scale (BBPS).

**Results:** There were no significant differences between vibrator group (n=75) and walking group (n=66) in bowel preparation quality (Total BBPS 7.40 vs 7.23, p=0.519), withdrawal time (30.40 vs 30.03 mins, p=0.829), number of polyps (4.09 vs 3.17, p=0.085), patient satisfaction (4.39 vs 4.12, p=0.249) and number of diarrhea after taking PEG (11.49 vs 11.42, p=0.903). vibrator group was superior than walking group in time of first defecation after taking PEG (112.9 vs 123.42 mins, p=0.005) andecal intubation time (6.23 vs 8.52 mins, p=0.011).

**Conclusion:** Bowel preparation accompanied with abdominal vibration stimulation showed almost similar results to a walking group which was conventional methods for adequate bowel preparation. The patients with the condition which cause uncomfortable gait such as old age, CVA, Parkinsons, or joint disease, bowel preparation with abdominal vibrator is expected to help in proper bowel cleansing for therapeutic colonoscopy.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**References**

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**References**
THE INCIDENCE OF SYNCHRONOUS ADVANCED NEOPLASIA OF RECTAL LATERALLY SPREADING TUMORS WITH A SKIRT

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Introduction: A "skirt" is a slightly elevated flat lesion with wide pits occasionally observed at the margin of laterally spreading tumors (LSTs), and rectal LSTs had significantly more skirt lesion in comparison to colonic LSTs. Although the clinicopathological, endoscopic, and molecular characteristics of LSTs with a skirt have been reported [1], there are no reports concerning the incidence of synchronous neoplastic lesions of rectal LSTs with a skirt.

Aims & Methods: The aim of this retrospective study was to clarify the incidence of synchronous advanced neoplasia (AN) of rectal LSTs with a skirt. A total of 13,116 cases underwent colonoscopy in our hospital between January 2012 and June 2016. Of these, 101 consecutive rectal LSTs were examined to assess the incidence of synchronous AN detection rate and the number of AN according to the location of AN lesion; divided into the right colon, left colon and rectum. A skirt was defined on the basis of the following endoscopic findings: spreading across the margins of the LST, consisting of a slightly elevated flat lesion, and containing wide pits. AN was defined as the presence of any of the following features: adenomas larger than 10 mm, adenomas with villous histology or high-grade dysplasia including intra-mucosal carcinoma and invasive cancer.

Synchronous advanced neoplasias of rectal LSTs with and without skirts

<table>
<thead>
<tr>
<th></th>
<th>Rectal LSTs with skirts</th>
<th>Rectal LSTs without skirts</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with advanced neoplasia</td>
<td>(n=25)</td>
<td>(n=76)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>5 (20.0%)</td>
<td>36 (47.4%)</td>
<td>0.02</td>
</tr>
<tr>
<td>Right colon</td>
<td>2 (8.0%)</td>
<td>23 (30.3%)</td>
<td>0.03</td>
</tr>
<tr>
<td>Left colon</td>
<td>1 (4.0%)</td>
<td>21 (27.6%)</td>
<td>0.01</td>
</tr>
<tr>
<td>Rectum</td>
<td>3 (6.0%)</td>
<td>5 (6.6%)</td>
<td>0.41</td>
</tr>
</tbody>
</table>

Number of advanced neoplasia

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>Right colon</th>
<th>Left colon</th>
<th>Rectum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>5 (20.0%)</td>
<td>2 (8.0%)</td>
<td>1 (4.0%)</td>
<td>3 (6.0%)</td>
</tr>
</tbody>
</table>

Results: A skirt was observed in 25 of 101 rectal LSTs (24.8%). Rectal LSTs with a skirt (median age 69 years, 52% female, mean size 51.7 ± 21.1 mm) had 22 high-grade dysplasia and 3 submucosal carcinomas, and rectal LSTs without a skirt (median age 72 years, 34% female, mean size 24.7 ± 16.0 mm) had 8 low-grade dysplasia, 45 high-grade dysplasia, and 23 submucosal carcinomas, respectively. The overall AN detection rate in rectal LSTs with a skirt (20.0%) was significantly higher than in rectal LSTs without a skirt (6.0%).

Discussion: Endoscopic shielding technique with the combination of PRP and TriBio in a rat model of thermal injury. Thermal injury was obtained according to our rat model [3]. Lesions were performed in male Sprague-Dawley rats (400–450 g) under general anesthesia. Animals were randomized to receive one of the following shields onto the lesions: PRP + TriBio and PRP + TriBio. Rats underwent endoscopic follow-up at 7 days and 2 weeks. Afterwards, animals were sacrificed and ulcers sites were macroscopically and histopathologically evaluated.

Disclosure of Interest: R. Bartoli: Authorship of the patent J. Boix: Authorship of the patent V. Lorenzo-Zúñiga: Authorship of the patent All other authors have declared no conflicts of interest.

References


EFFECTIVE LOCAL THERAPY FOR TREATMENT OF THERMAL INJURY

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Introduction: Endoscopic resection of large lesions leads to extensive mucosal defects and submucosal exposure, with a substantial risk of adverse events. The prevention of these complications is inefficient with current methods. Endoscopic shielding, as a simple and safe technique, has been proposed to improve mucosal restoration, and therefore, the incidence of these events. Previous reports have confirmed the efficacy of the placement of hydrogels based on platelet-rich plasma (PRP) (1) or hialuronic acid with other substances (TriBio) (2), but never the combination of both hydrogels, in the prevention of delayed complications after mucosal damage.

Aims & Methods: To assess the efficacy of endoscopic shielding with the combination of PRP and TriBio in a rat model of thermal injury. Thermal injury was obtained according to our rat model (3). Lesions were performed in male Sprague-Dawley rats (400–450 g) under general anesthesia. Animals were randomly assigned to receive one of the following shields onto the lesions: PRP + TriBio and PRP + TriBio. Rats underwent endoscopic follow-up at 7 days and 2 weeks. Afterwards, animals were sacrificed and ulcers sites were macroscopically and histopathologically evaluated.

Results: Animals treated with PRP + TriBio obtained the best results in comparison with other hydrogels (PRP and TriBio). Mucosal healing rate (percentage of mucosal restoration) at 14 days was significantly higher with PRP + TriBio (100% vs 82% and 90%; p < 0.05). Histological study confirmed these data, showing total restoration of mucosal layer with PRP + TriBio

Conclusion: The use of a combination of the two covering agents (TriBio and PRP) is the best approach to obtain mucosal healing in a rodent model of endoscopic thermal injury in colon

Disclosure of Interest: R. Bartoli: Authorship of the patent J. Boix: Authorship of the patent V. Lorenzo-Zúñiga: Authorship of the patent All other authors have declared no conflicts of interest.

References

Results: Intratumoral injection was feasible in all animals with no adverse events. Biopsies obtained size of tumors ranged from 6 to 8 mm. Anti-VEGF in comparison with anti-EGF obtained the best results (significantly reduction in size and cell necrosis). However, only alfobceptor showed total acute tumoral necrosis.

Conclusion: Intratumoral injection of anti-VEGF in a drug-eluting platform is able to produce tumoral necrosis in an experimental model of CRC. This technique could open a new way to manage CRC.

Disclosure of Interest: R. Bartoli: Authorship of the patent
J. Boix: Authorship of the patent
V. Lorente: Authorship of the patent
All other authors have declared no conflicts of interest.

P0844 A THREE-DIMENSIONAL IMAGING SYSTEM IMPROVES THE ENDOSCOPIC VISIBILITY OF NON-POLYPOID COLORECTAL NEOPLASMS

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Introduction: Three-dimensional (3D) imaging techniques have been developed in the medical field. Previous research reports that simulated 3D colonoscopy improves the detection of colorectal lesions [1]. A novel 3D imaging system has been recently developed, which can create 3D virtual video images from conventional two-dimensional (2D) endoscopic images [2]. However, actual cases have not been studied.

Aims & Methods: This study aimed to investigate whether the 3D system can improve the visibility of colorectal neoplasms compared with conventional 2D endoscopy. We examined non-polypoid colorectal neoplasms and recorded their videos using conventional 2D endoscopy and the 3D system. The movies were evaluated by 8 endoscopists (4 experts and 4 non-experts) and 4 medical students. Each neoplasms was assigned a visibility score between 4 (excellent visibility) and 1 (poor visibility).

Results: The mean visibility scores were 3.35±0.58 for 2D endoscopy and 3.75±0.44 for the 3D system. The score was significantly higher for the 3D system than for 2D endoscopy (p<0.01). When comparing the evaluations by the experts, non-experts, and medical students, the differences in the scores by the non-experts and medical students were noted to be higher (p<0.05). In contrast, the scores by the experts were also higher for the 3D system, but no statistical difference was observed (3.50±0.53 for 2D endoscopy and 3.87±0.35 for the 3D system, p=0.08). As a result, 10 out of 12 observers noted that the 3D system had better visibility than conventional 2D colonoscopy, and none of the observers noted deterioration in visibility with the 3D system.

Conclusion: The present findings suggest that the 3D imaging system improves the visibility of non-polypoid colorectal neoplasms, and this is more effective for non-experts. Our findings would contribute to improvement in the detection of these neoplasms. Disclosure of Interest: All authors have declared no conflicts of interest.

References

P0845 PAIN DURING COLONOSCOPY: DIFFERENCES BETWEEN PATIENTS’ EXPERIENCES AND CAREGIVERS’ ASSESSMENT

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Introduction: Pain is a subjective perception, which contributes to difficulties to provide adequate pain relief according to every patient’s needs. Colonoscopy is by many patients considered as a painful and strenuous procedure. Aims & Methods: To investigate congruence and differences between patients’ and caregivers’ report of pain during colonoscopy. Patients (≥18 years) undergoing an outpatient colonoscopy (all indications) have consecutively been included (n=862). Before the procedure the patients completed questionnaires regarding sociodemographic information and anxiety. After the colonoscopy the patients registered their pain experience on a six-grade scale, ranging from “no pain” to “extremely severe pain”. Caregivers (physicians and endoscopy nurses) estimated patient’s pain using the same scale.

Results: Data from 785 patients has been collected, mean age 52 (18–90) years; 486 (62%) were female and 51% of patients reported “moderate pain”, and a sub-group of 14% were not adequately relieved. These subgroup reported severe, very severe or extremely severe pain. 90% of the patients were given analgesics and sedation during the investigation. For patients who reported, “severe, very severe or extremely severe pain” (n=111), pain was underestimated by physicians and nurses in 58% of all assessments. This was most commonly seen among the youngest patients, 18-29 years (n=99), where pain was underestimated in 25.5% among the group. There was also a difference according to gender; physicians underestimated pain in 60% of men who reported “moderate pain” (n=66) while the nurses underestimated pain in 27% among the same group of men. Women’s pain was overestimated by caregivers in 26% (n=188) of all cases with mild pain. Patients undergoing colonoscopy for the first time (n=331), and reporting “moderate pain”, were underestimated by physicians in 58% and by nurses in 25%. 58% of the patient reports that they were anxious before the procedure. This group reported more pain than the group without anxiety (p<0.001). Presence of anxiety and a high level of anxiety among the group correlated better with the patient’s report and the patient’s pain report. The agreement between pain reports from patients and caregivers were poor to fair, with slight differences between nurses (Kappa =0.37; p<0.000) and physicians (Kappa =0.29; p<0.000) in total, congruent pain reports between patients and caregivers were seen in 36% of all assessments.

Conclusion: Agreement between caregivers’ and patients’ pain reports is far from perfect, and the agreement is influenced by several factors such as the profession of the caregiver, as well as patient factors including pain severity, anxiety, age, gender and previous experience of colonoscopy. The goal for the future should be to individualize the use of analgesics based on every patient’s needs, which seems to be of special importance in specific groups of patients.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0846 DEVELOPMENT OF A NEW ENDOSCOPIC CLASSIFICATION SYSTEM AND INTER-ONLINE VALIDATION (FACILE GROUP) OF COLONIC LESIONS USING ADVANCED IMAGING MODALITIES IN IBD PATIENTS

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Introduction: The SCENIC consensus proposed recommendations for optimal detection and management of dysplasia during colonoscopic surveillance for IBD. Characterization of colonic lesions in IBD remains challenging even when using advanced endoscopic imaging modalities (high definition [HD], virtual chromoendoscopy [VCE] dye chromoendoscopy [DCE]). Aims & Methods: We aimed to develop a unified endoscopic classification of advanced imaging to predict histology of colonic lesions, and to validated by international experts (Frankfurt Advanced Chromoendoscopy IBD LESions-FACILE Group). We developed an endoscopic classification of IBD lesions, based on morphology, colour, demarcation, surface pattern, vessel pattern, sign of inflammation (table). A library of 60 colon lesions, including dysplasia, sessile serrated adenomas/polyps, invasive cancer and pseudopolyps collected at surveillance colonoscopy by using HD, DCE and VCE with i-scan or NBI were assessed. The diagnostic performance of the score was tested based on the final histopathology and the inter-observer variability of the eight examiners. The examiners have had to perform a pre-test (45 minutes) before analyzing the colonic lesions. Multivariate analysis with bootstrapping, of characteristics of the classification was performed to determine the strength of endoscopic predictors of dysplasia.

Results: Of the 60 IBD lesions, 33 (55%) were dysplasia, 6 (10%) cancer, 9 (15%) SSA/Ps and 12 (20%) pseudopolyps. Across the experienced academic raters sensitivity, specificity, PPV, NPV and accuracy in predicting histology, were 72%, 79%, 91%, 40%, 72%. Individual rater accuracy ranged from 66% to 77%. Sensitivity, specificity, PPV, NPV, accuracy, for predictions made with perfect, and the agreement is influenced by several factors such as the profession of the caregiver, as well as patient factors including pain severity, anxiety, age, gender and previous experience of colonoscopy. The goal for the future should be to individualize the use of analgesics based on every patient’s needs, which seems to be of special importance in specific groups of patients. Disclosure of Interest: All authors have declared no conflicts of interest.

References
OR 0.31 (95% CI:0.17–0.54), vessel architecture OR 5.1 (95% CI: 2.7–10.2), sign of inflammation within the lesion OR 0.39 (95% CI: 0.18–0.85) were independent predictors of dysplasia, with vessel architecture and morphology being the best predictors. The sensitivity, specificity, PPV, NPV and accuracy at the multivariate analysis stage were 94% (95% CI: 90–96%), 51% (95% CI: 43–58%), 88% (95% CI: 82–92%), 69% (95% CI:62–75%), 85% (95% CI: 79–90%). Inter-rater agreement of the raters improved from the pre-test (Kappa = 0.27.95% CI: 0.19–0.38) to post test (Kappa = 0.34.95% CI: 0.23–0.45;P = 0.02) but was moderate.

Conclusion: We developed and validated the first endoscopic classification using all imaging modalities (HD, VCE, DCE) to characterize and differentiate dysplastic from non-dysplastic lesions in IBD. Non polypoid lesions, irregular surface and vascular pattern as well as inflammation within the lesions were predictive of dysplasia. The inter-observer variability of the score was moderate. The classification will be further refined based on the multivariate analysis and a prospective study is ongoing.

Table 1: Advanced endoscopic classification of IBD lesion

<table>
<thead>
<tr>
<th>Morphology (mm):</th>
<th>Endoscopic inflammatory activity (within the lesion)</th>
<th>Endoscopic inflammatory activity (surrounding area)</th>
<th>Demarcation</th>
<th>Colour of the lesion (relative to the background)</th>
<th>Vessel architecture</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polypoid/non polypoid</td>
<td>No ulcerations</td>
<td>Yes</td>
<td>No</td>
<td>Paler</td>
<td>Non visible</td>
</tr>
<tr>
<td>Paris Classification (fp, Is, Ha, Ib, Ic, II)</td>
<td>Ulceration</td>
<td></td>
<td></td>
<td>Same intensity</td>
<td>Regular</td>
</tr>
<tr>
<td>Endoscopic inflammatory activity</td>
<td>No ulcerations</td>
<td></td>
<td></td>
<td>Darker</td>
<td>Irregular</td>
</tr>
<tr>
<td>(within the lesion)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Regular/non-structural</td>
</tr>
<tr>
<td>No ulcerations</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Villo–irregular</td>
</tr>
<tr>
<td>Ulceration</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Villo–regular</td>
</tr>
<tr>
<td>Endoscopic inflammatory activity (surrounding area)</td>
<td>No ulcerations</td>
<td></td>
<td></td>
<td></td>
<td>No visible</td>
</tr>
<tr>
<td>Demarcation</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Regular</td>
</tr>
<tr>
<td>Yes</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Irregular</td>
</tr>
</tbody>
</table>

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference


P0048 THE ROLE OF PROBE CONFOCAL LASER ENDOMICROSCOPY WITH IMAGE ENHANCED ENDOSCOPY IN CHARACTERISATION AND ENDOSCOPIC RESECTION OF DSYPOLYIC LESIONS IN INFLAMMATORY BOWEL DISEASE PATIENTS

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Introduction: Detection, characterization and therapeutic management of flat dysplastic lesions during surveillance colonoscopy in inflammatory bowel disease (IBD) can be a challenge. The recent SCENIC consensus has introduced a new terminology and concept “endoscopically resectable” when the distinct margins of a detected lesion could be identified. New endoscopic techniques and skills are required to recognize the margins reliably and assess the surrounding mucosa to plan endoscopic removal successfully and organ sparing. We report our experience of the use of probe confocal endomicroscopy (pCLE) combined with selective electronic virtual (VCE) and dye chromoendoscopy (DCE) for management of challenging dysplastic lesions during surveillance in IBD.

Aims & Methods: IBD patients underwent surveillance colonoscopy using high-definition (HD)-iSCAN (Pentax EC-3940F; Japan) VCE and DCE in combination with pCLE (Cellvizio, Paris, France). pCLE was applied following IV injection of fluorescein 5% 10 ml to assess the histological features of the lesion, the margins and the mucosa surrounding the visible colonic lesion. Biopsies eventually proved dysplasia or SSA of the colonic lesions. The study was approved by the Calgary Conjoint Health Services Research Ethics Board of the University of Calgary. All patients gave informed consent.

Results: Seven patients with IBD and disease duration of ≥8 years and in clinical remission [Eaden, 2001 #2] (mean age 55 years; 6 male, UC = 4 CD = 3) were prospectively included. They underwent surveillance colonoscopy using HD-iSCAN (Pentax EC-3940F; Japan). When a colonic lesion was detected, selective iSCAN - VCE was performed with or without DCE (five out of seven had DCE)

Abstract No: P0048

<table>
<thead>
<tr>
<th>UC/CD</th>
<th>Kudo Paris Border</th>
<th>Endoscopy Findings</th>
<th>Endomicroscopy Findings</th>
<th>Histology</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left sided UC</td>
<td>IIH/IV</td>
<td>Ib Size &gt; 2.5 cm</td>
<td>distinct</td>
<td>Villiform appearance of the crypts with stellar opening. The colonic mucosa surrounding the lesion was normal.</td>
<td>SSA</td>
</tr>
<tr>
<td>Crohn’s colitis</td>
<td>IIH/JII</td>
<td>Ib Size &gt; 2.5 cm</td>
<td>indistinct</td>
<td>Villiform elongated appearance of the crypts with dark epithelium, decreased number of the</td>
<td>LGD</td>
</tr>
</tbody>
</table>

P0048 THE ROLE OF PROBE CONFOCAL LASER ENDOMICROSCOPY WITH IMAGE ENHANCED ENDOSCOPY IN CHARACTERISATION AND ENDOSCOPIC RESECTION OF DSYPOLYIC LESIONS IN INFLAMMATORY BOWEL DISEASE PATIENTS (continued)
with methylene blue 1% to characterize the surface, vascular pit pattern and the margins of the lesion. Each of the 7 patients had non polypoid colonic lesions, 4 were sessile (Paris Is) and 3 flat (IIa/IIb). Four of them were amenable to endoscopic therapy and were successfully removed using endoscopic mucosal resection (EMR) en-block or piecemeal technique. Interestingly, one patient with multiple scattered ‘pseudopolyps’ had a 8 mm sessile pseudopolypoid lesion with a suspicious areas of SSA in the midst that was confirmed by real pCLE.

The endoscopic, endomicroscopic and histological findings of all the lesions were described in Table 1.

**Conclusion:** This case series highlights the first successful use of pCLE in combination with VCE and DCE to predict, characterise and treat colonic neoplasia in IBD. pCLE may be an additional tool to aid the endoscopist in therapeutic management by deciding endoscopic resectability versus colectomy.

**Disclosure of Interest:** All authors have declared no conflicts of interest.
P0850 THE SAFETY AND EFFECTIVENESS OF COLORECTAL ENDOSCOPIC SUBMUCOSAL DISSECTION USING A SCISSORS-TYPE KNIFE IN ELDERLY PATIENTS

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Introduction: Endoscopic submucosal dissection (ESD) is one of the most useful methods for treating early colorectal neoplasms and conventionally utilizes an IT, hook, or needle knife. However, because these devices are used without fixation to target, it confers a potential risk of complications due to unexpected incision. To reduce the risk of complications from ESD performed using a conventional knife, we used a scissors-type knife (SB Knife Jr) in elderly patients. In the previous study, we reported that ESD performed using SB Knife Jr is a technically efficient and safe method for treating early colorectal neoplasms. However, the efficacy and safety of colorectal ESD using SB Knife Jr in elderly patients remain unclear.

Aims & Methods: The aims of our study were to evaluate the efficacy, safety, and clinical outcomes of colorectal ESD using SB Knife Jr in patients aged ≥75 years in comparison with those in younger patients. We evaluated 291 lesions in 271 patients (male-to-female ratio, 148:123; median age, 70 years) treated with ESD using SB Knife Jr between October 2010 to March 2017 at Kure Municipal Medical Center and Chugoku Cancer Center. The patients were divided into two groups, an elderly group (A: age >75 years; 95 patients, 97 lesions) and a non-elderly group (B: age <75 years; 176 patients, 194 lesions). We evaluated the en block resection rate, complete resection rate, curative resection rate, resected tumor size, procedural time, complications, and long-term outcomes, including survival rate. The 3-year overall survival and tumor-specific survival rates were analyzed in the entire study cohort, and the local and distant recurrence rates were analyzed in the cohort with curative resection and observationally managed with non-curative resection.

Results: The mean age was 80.0 years in group A and 64.3 years in group B. The male-to-female ratios were 45:50 and 103:73 in groups A and B, respectively. Regarding histopathological findings, the prevalence rates of tubular adenoma were 37.1% (36/97) and 36.1% (70/194); T1a, 39.2% (38/97) and 44.8% (87/194); T1b, 10.3% (10/97) and 10.3% (20/194); and T1b, 13.4% (13/97) and 8.8% (17/194). The mean follow-up period: group A, 523 days; group B, 582 days. The 3-year overall survival and tumor-specific survival rates were 94.8% (89/95) and 94.4% (184/194); and the curative resection rates, 93.3% (91/97) and 93.8% (171/194) in groups A and B, respectively, showing no significant difference. The mean resected tumor size was 33.9 ± 16.6 mm in group A and 34.7 ± 15.2 mm in group B, and the median procedural time was 75.6 min (range, 10-420 min) in group A and 75 min (range, 10-533 min) in group B, showing no significant difference. The en bloc resection rates were 96.9% (94/97) and 99.0% (192/194); the complete resection rates, 94.8% (92/97) and 94.8% (184/194); and the curative resection rates, 83.5% (81/97) and 88.1% (171/194) in groups A and B, respectively, showing no significant difference. Regarding complications, no perforation during the procedure occurred in any of the cases. The delayed bleeding rate was 1.0% (1/97) in group A and 2.6% (5/194) in group B. Delayed perforation and delayed bleeding occurred in one patient each in group A and were treated conservatively. Regarding long-term outcomes, the local recurrence rate was 1.0% (1/97) in group A and 0.5% (1/194) in group B, and no distant recurrence was observed in the recurrence analysis cohort. Regarding survival analysis (mean follow-up period: group A, 523 ± 469 days; group B, 628 ± 582 days), the 3-year overall and disease-specific survival rates were respectively 98.8% and 100% in group A, and 93.3% and 98.3% in group B. One patient (0.5%, 1/194) died of colorectal cancer 26 months after ESD for other diseases in group B, while one patient (1.1%, 1/95) died of other diseases in group A.

Conclusion: ESD performed with SB Knife Jr is a technically efficient and safe method associated with favorable long-term outcomes in cases of early colorectal neoplasms in elderly patients.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P0851 DETECTION AND CHARACTERIZATION OF SSA/PS DURING SURVEILLANCE COLONOSCOPY IN LONG STANDING ULCERATIVE COLITIS: THE ROLE OF ADVANCED ENDOSCOPY TECHNIQUES


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Introduction: Sessile serrated polyps (SSA/Ps) are pre-malignant lesions that may lead to colorectal cancer in accelerated manner. These lesions are easily missed by endoscopists as these are difficult to detect in IBD patients. We aimed to assess the prevalence, detection rate and endoscopic findings of SSA/Ps in long standing IBD patients prospectively undergoing surveillance colonoscopy using dye (DCE) or virtual electronic chromoendoscopy (VCE) or high definition white light imaging (HD-WLE) colonoscopy. SSA/Ps are not an infrequent finding at surveillance colonoscopy in IBD patients. There was no difference in detection rates of SSA/P using HD-WLE, DCE or VCE. Endoscopic features were recorded in each group with regard to location, morphology (polypoid/non polypoid), size and mucosal pit pattern, and these were characterized using the Kudo modified classification and Paris classification. The histology was reported by modified Vienna classification.

Results: Thirty-three SSA/Ps were detected in 20 (11UC, 9 CD; 11 female, age range 34-72 y, median age 61 years) patients out of the 270 patients with IBD (median duration of the disease 14 years) undergoing surveillance colonoscopy were assessed by HD-WLE (n = 90), VCE (n = 90) or DCE (n = 90). Surveillance colonoscopy with HD imaging (High Definition) alone, or with iSCAN VCE or DCE was performed. Endoscopic features were recorded in each group with regard to location, morphology (polypoid/non polypoid), size and mucosal pit pattern, and these were characterized using the Kudo modified classification and Paris classification. The histology was reported by modified Vienna classification.

Conclusion: SSA/Ps are not an infrequent finding at surveillance colonoscopy in IBD. There are prevalent in the right colon location and these generally have Kudo pattern of IHO. SSA/Ps can be recognized endoscopically by Kudo pit landmarks or terminal ileum while the European and American guidelines suggest available photo documentation probably a panoramic view of the ileocecal valve and caecum. In this retrospective study we aimed to assess colonoscopists’ practice in photo documentation of colonoscopy completion.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

Abstract: P0851

<table>
<thead>
<tr>
<th>Age</th>
<th>F</th>
<th>M</th>
<th>Mean</th>
<th>UC/CD</th>
<th>Localization &amp; Size</th>
<th>Paris classification</th>
<th>Kudo pit pattern</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right</td>
<td>Left</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;5mm</td>
<td>≥5mm</td>
<td>I/p</td>
<td>Hb/Ha</td>
<td>E/H</td>
<td>IHO</td>
<td>IHO-IV</td>
<td></td>
</tr>
</tbody>
</table>

Serrated adenoma n = 33

11 | 61 | 11/9 | 29 | 4 | 16 | 17 | 16 | 17 | 1 | 26 6
pattern even in IBD patients. Further studies are needed to evaluate the natural history and clinical impact of the SSA/Ps pathways in IBD patients.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0852 IN VIVO HISTOLOGICAL PREDICTION OF COLORECTAL POLYPS USING FICE TECHNOLOGY

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Introduction: The histological characterization of colorectal polyps using FICE (Fujinon Intelligent Color Enhancement) technology presents high diagnostic accuracy. However, the excellent results in histological prediction are a reflection of the clinical practice by trained endoscopists, and their application remains to be confirmed outside this context.

Aims & Methods: To evaluate the in vivo histological prediction accuracy of colorectal polyps <10 mm in size using FICE technology and compare with histopathology. We propose this tool for daily practice, involving all the endoscopists of our endoscopy unit.

Disclosure of Interest: All authors have declared no conflicts of interest.
null
Results: 1382 LSL in 1243 patients were analysed. 1155/1243 (92.9%) patients had a solitary LSL. The majority of patients with multiple LSL had two (77.3%) or three (15.9%) lesions. 889/1382 (64.3%) of LSL were G. G LSL were more likely to be solitary (87.0%) than NG LSL (77.5%, p < .001). G LSL were more commonly large (>40 mm in size) (49.5%) than NG LSL (26.0%, p < .001) and were more commonly found in the right colon (proximal to transverse colon) (54.2% versus 48.3%, p = .034). In 88 patients with multiple LSL the dominant LSL was G (49/88 (55.7%). A dominant G LSL was associated with fewer other LSL than a dominant NG LSL, p = .029.

Table 1: The morphology of the dominant (largest) laterally spreading lesion (LSL) predicts the presence and number of synchronous LSL. Morphology of the dominant lesion did not predict the others would be of the same morphology (p = .697). The dominant LSL was large in 43.2% of cases. Size of the dominant LSL predicted size of the other LSL (p < .001). 58.6% of dominant LSL were located in the right colon. In 65.9% patients all LSL were in the same colonic segment; this was not predicted either by the location of the dominant LSL (p = .860) or its morphology (p = .228).

### Dominant LSL Morphology

<table>
<thead>
<tr>
<th>Solitary (n = 1155)</th>
<th>Multiple (n = 227)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Granular (n = 889)</td>
<td>737 (87.0)</td>
<td>116 (13.0)</td>
</tr>
<tr>
<td>Non-granular (n = 493)</td>
<td>382 (77.5)</td>
<td>111 (22.5)</td>
</tr>
</tbody>
</table>

### Dominant LSL Morphology

<table>
<thead>
<tr>
<th>Number of synchronous LSL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Granular (n = 49)</td>
</tr>
<tr>
<td>Non-granular (n = 29)</td>
</tr>
</tbody>
</table>

Conclusion: 7% of patients will have more than one LSL. In these patients the dominant lesion morphology predicts the presence and number of additional LSL (the Colonic Mucosal Phenotype). More than 20% of NG LSL are associated with an additional LSL whereas G LSL are predominantly large and solitary. Practitioners of endoscopic resection should be aware that NG LSL may be multiple and ensure full examination of the colonic mucosal surface, particularly since they are higher risk for MC than G LSL.

Disclosure of Interest: All authors have declared no conflicts of interest.

### P0860 WIDE-FIELD PIECEMEAL COLD SNARE POLYPECTOMY OF LARGE SESSILE SERRATED POLYPS WITHOUT A SUBMUCOSAL INJECTION IS SAFE

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Introduction: Large series suggest endoscopic mucosal resection is safe and effective for the removal of large sessile serrated polyps ≥10mm (large SSP) but it exposes the patient to the risks of electrocutery, principally delayed bleeding.

Aims & Methods: We aimed to examine the feasibility and safety of piecemeal cold snare polypectomy (pCSP) for the resection of large SSP. Over 12 months sequential large SSP without endoscopic evidence of dysplasia referred to a tertiary endoscopy centre were considered for pCSP. The technique for pCSP was standardised. The lesion and its margins were assessed using high definition endoscopic imaging. Snare resection commenced at one margin including a 2–3mm rim of normal tissue. A thin-wire snare was used in all cases. Firm downward pressure and suction of luminal gas aided tissue capture. Subsequently the assistant closed the snare until resistance was felt, and then completely once the endoscopist was satisfied with the amount of captured tissue. If transection did not occur within five seconds gentle traction was exerted on the snare catheter against the tip of the colonscope. If transection still did not occur, the snare placement was revised. The mucosal defect was then expanded with a flushing pump containing 0.9% saline. Further resections were then performed aligning the snare with the cut edge of the expanding mucosal defect. Once the resection was completed the mucosal defect was inspected for residual serrated tissue. If residual was detected further generous snare resection was performed. Oozing of blood from the resection site was common and was not actively treated. Submucosal injection was not performed. High-definition imaging of the defect margin was used to ensure the absence of residual serrated tissue. Adverse events were assessed at 2 weeks and surveillance was planned between 6 and 12 months.

Results: 41 SSP were completely removed by pCSP in 34 patients. 7 patients had two lesions removed. The median size of SSP was 15mm (IQR 14.5–20), range 10–35mm. The median duration of procedures was 4.5 minutes (IQR 1.4–6.3). There was no evidence of perforation or significant intra-procedural bleeding. There were no significant adverse events at 2 week follow up including delayed bleeding and post polypectomy syndrome. 8/41 lesions underwent first follow-up at median 6 months with no evidence of recurrence.

### Table 1: Baseline characteristics and outcomes of the 34 patients and 41 SSP that underwent piecemeal cold snare polypectomy (pCSP).

<table>
<thead>
<tr>
<th>pCSP (n = 41)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient</td>
</tr>
<tr>
<td>Age, mean (standard deviation)</td>
</tr>
<tr>
<td>Sex, female (%)</td>
</tr>
<tr>
<td>Lesion</td>
</tr>
<tr>
<td>Size, median (IQR)</td>
</tr>
<tr>
<td>Location, proximal to transverse colon (%)</td>
</tr>
<tr>
<td>Paris classification (%)</td>
</tr>
<tr>
<td>0-IIa</td>
</tr>
<tr>
<td>0-IIb</td>
</tr>
<tr>
<td>Endoscopic evidence of dysplasia (%)</td>
</tr>
<tr>
<td>Kudo, highest (%)</td>
</tr>
</tbody>
</table>

Procedure

Duration, median minutes (IQR) 4.5 (1.4 to 6.3)

Piecemeans, median (IQR) 3.0 (3–5)

Protrusion within defect (%) 9 (22.0)

Intra-procedural bleeding requiring intervention (%) 0 (0)

Histopathology, serrated adenoma (%) 41 (100)

Low grade cytological dysplasia (%) 3 (7.3)

Outcomes

pCSP (n = 41)

Adverse events

Clinically significant post endoscopic bleeding (%) 0 (0)

Delayed perforation (%) 0 (0)

Post procedural pain (%) 0 (0)

Admission to hospital for related complication within 2 weeks 0 (0)

Follow up

Months to SC1, IQR 6 (5–7)

Reurrence at SC1, 0 (0)

Histologic recurrence at SC1, 0 (0)

Conclusion: There is potential for pCSP to become the standard of care for non-dysplastic large SSP. This may reduce the burden on patients and healthcare systems of removing SSP, particularly by avoidance of delayed bleeding.

Disclosure of Interest: All authors have declared no conflicts of interest.

### P0861 THE PROSPECTIVE OBSERVATION STUDY FOR OVER 10MM COLORECTAL LESIONS ENDSOCOPICALLY RESECTED USING BIPOLAR SNARE

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Introduction: Polypectomy of adenomas reduces death due to colorectal cancer; therefore colonscopy is the gold standard to detect and treat adenomatous lesions. Most adenomatous lesions are less than 20mm in size. Therefore, these are not indication for endoscopic submucosal dissection (ESD). Recently, there are some reports about cold snare polypectomy (CSP). CSP is effective and easy to remove lesions of less than 5–10mm in size. On the other hand, in over 10mm lesions, many endoscopists would remove it by endoscopic mucosal resection (EMR) with monopolar snare. It is expected that the bipolar snare would decrease the incidence of perforation because of electric current flow peculiar to bipolar snare that does not flow through the wall of colon. So, by using bipolar snare, hot snare polypectomy (HSP) that can be easily resected in a short time may be safely performed for over 10mm colorectal lesions. However, there is no report about them.

Aims & Methods: We aimed to clarify removal method, procedure time and complications for over 10mm colorectal lesions endoscopically resected using bipolar snare. Consecutive patients with over 10mm colorectal lesions endoscopically resected using bipolar snare in National Cancer Center Hospital East between September 2016 and March 2017 were enrolled in this study, prospectively. The removal method rate of these lesions, each procedure time, complete resection rate, bleeding rate and perforation rate, and pathological finding were assessed.

Results: A total 92 lesions in 67 patients were analyzed. 47 patients (70%) were male, and the median age was 67 years (range: 44–88). The median lesion size was 15mm (range: 10–30). The macroscopic type was 33 (36%) polypoid lesions and 59 (64%) flat lesions. The location was 55 (60%) lesions in right colon, 31 (34%) lesions in transverse colon and 16 (18%) lesions in left colon.
in left colon and 6 (6%) in rectum. Pathological diagnosis was 22 (24%) hyperplastic polypl or SSA/P, 42 (46%) low grade dysplasia (LGD), 23 (26%) high grade dysplasia (HGD), and 1(1%) submucosal invasive cancer. In the removal methods, HSP was 71 (77%) lesions and EMR was 21 (23%). The median procedure time of HSP and EMR was 37 seconds (range: 7–430) and 167 (range: 60–450) (p < 0.001). The median lesion size of was HSP and EMR was 12 mm (range: 10–30) and 20 (range: 10–26) (p < 0.001). The immediate bleeding of HSP and EMR occurred in 7 (10%) lesions and 6 (3.3%) (p = 0.009). The delayed bleeding of HSP and EMR occurred in 2 (3%) lesions and 0 (p = 0.143). Perforation was not occurred. No tumors were horizontal and vertical margin positive. In the pathological diagnosis, 86% of hyperplastic polypl or SSA/P, 86% of LGD, and 57% of HGD was resected by HSP, and submucosal invasive cancer was resected by EMR.

**Conclusion:** Of over 10 mm colorectal lesions was resected by using bipolar snare, 77% were resected by HSP. The procedure time of HSP was significant shorter than EMR.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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**P0862 THE SMSA POLYP SCORE RELIABLY PREDICTS ROBUST ENDPOINTS OF ENDOscopic MUCOSAL RESECTION OF COLORECTAL LATERALLY SPREADING LESIONS**

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**Introduction:** The SMSA polyp scoring system is an objective method of stratifying the difficulty of polypectomy based on expert consensus opinion. The score is simple, intuitive and has previously not been evaluated in a large multicentre setting.

**Aims & Methods:** We aimed to determine the ability of the SMSA polyp score to predict robust endpoints after endoscopic mucosal resection (EMR) of colorectal laterally spreading lesions (LSL). The SMSA polyp score was applied to a prospectively collected multicentre database of LSL resected by EMR over eight years. This score describes the complexity of polypectomy with respect to four major domains (table 2) and is subsequently divided into four levels. Standard inject and resect EMR procedures were performed with detailed patient, procedural and outcome data recorded prospectively over the study period including all features of the SMSA. In patients who had multiple lesions resected the largest lesion was retained for analysis. The primary endpoints were correlation of SMSA score with completion rate, adverse event rate and adenoma recurrence.

**Results:** 2305 lesions in 2305 patients (47.4% M, 45%, 2% right colon) underwent EMR. The majority of lesions were SMSA 4 (50.2%) with a median lesion size of 30 mm (range 20–160 mm). Failed single session EMR occurred in 97 (4.2%) and this was predicted by increasing SMSA (p < 0.001). Intra-procedural bleeding was significantly more common with increasing SMSA (2, 19/229 (8.3%) versus SMSA 4 291/1158 (25.1%), p < 0.001). Clinically significant post EMR bleeding (CSPEB) was more common as SMSA increased with 17% in the SMSA 2 group and 90 (7.8%) in the SMSA 4 group, p < 0.001. Intra-procedural perforation and delayed perforation were no different between the groups. After EMR surgery at two weeks was more common in the SMSA 4 group (p < 0.001). Of those patients that underwent their first surveillance colonoscopy (SC1), endoscopic recurrence (EDR) was more common in the SMSA 4 group than the SMSA 2 group, 206 (23.7%) as compared to 9 (5.4%), p < 0.001. This was also the case for histologic recurrence (p < 0.001). The difference in EDR persisted to the second surveillance colonoscopy (SC2) with no recurrences in the SMSA 2 group versus 9.1% in the SMSA 4 group.

**Table 1:** Outcomes after endoscopic mucosal resection at the initial procedure, 2 weeks and subsequent surveillance procedures.

<table>
<thead>
<tr>
<th>SMSA 2</th>
<th>SMSA 3</th>
<th>SMSA 4</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>229 (9.9)</td>
<td>918 (39.8)</td>
<td>1158 (50.2)</td>
</tr>
<tr>
<td>Successful EMR (%)</td>
<td>226 (98.7)</td>
<td>894 (97.4)</td>
<td>1088 (94.0)</td>
</tr>
<tr>
<td>Duration - min (median IQR)</td>
<td>10 (5–15)</td>
<td>15 (10–20)</td>
<td>20 (20–45)</td>
</tr>
<tr>
<td>IPB (%)</td>
<td>19 (8.3)</td>
<td>115 (12.5)</td>
<td>291 (25.1)</td>
</tr>
<tr>
<td>Deep injury * (%)</td>
<td>11 (4.8)</td>
<td>33 (3.6)</td>
<td>54 (4.7)</td>
</tr>
<tr>
<td>CSPEB (%)</td>
<td>4 (1.7)</td>
<td>11 (4.7)</td>
<td>3 (5.4)</td>
</tr>
<tr>
<td>Delayed Perforation (%)</td>
<td>0 (0)</td>
<td>2 (0.2)</td>
<td>5 (0.4)</td>
</tr>
<tr>
<td>Surgery at 2w (%)</td>
<td>20 (8.7)</td>
<td>50 (5.4)</td>
<td>117 (10.1)</td>
</tr>
<tr>
<td>Underwent SC1 (%)</td>
<td>88</td>
<td>326</td>
<td>462</td>
</tr>
<tr>
<td>EDR SC2 (%)</td>
<td>0 (0)</td>
<td>21 (6.4)</td>
<td>42 (9.1)</td>
</tr>
<tr>
<td>Surgery SC2 (%)</td>
<td>0 (0)</td>
<td>1 (0.3)</td>
<td>3 (0.6)</td>
</tr>
</tbody>
</table>

**Conclusion:** SMSA is a simple readily applicable clinical score that identifies a subgroup of patients who are at increased risk of EMR related complications including CSPEB and recurrence. This information is useful for planning EMR lists with respect to time and resource allocation. Moreover SMSA could have a major impact on training, both in identifying appropriate training cases and providing an objective benchmark against which to assess the progress of trainees in EMR.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**References:**


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**P0863 USE OF ACETIC ACID FOR EVALUATING SESSILE SERRATED ADENOMA/POLYP: A PILOT STUDY**

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**Introduction:** Sessile serrated adenoma/polyp (SSA/P) has been accumulated increasing attention since its risk for developing to cancer had been clarified. These polyps are difficult not only to detect but also to determine their precise margin after detection especially in right side colon. Such a difficulty leads high recurrence rate after endoscopic resection. Magnifying function and narrow band imaging (NBI) is reported to be useful for evaluation of SSA/P but it needs special equipment, extra time, and expertise. Easier, uncomplicated, and non time consuming method is desired. The use of acetic acid or acetic acid-indigo carmine mixture have been introduced into endoscopic diagnosis in Barrett’s esophagus, early gastric cancer, and colorectal early cancer. However, there have been no reports on using this agent as aid for the optimal diagnosis of the margin of SSA/P. If this rather cheap agent were helpful for realizing the precise margin of SSA/P, it could decrease insufficient removal of the polyp and recurrence after that.

**Aims & Methods:** The aim of this pilot study is to assess whether the acetic acid could facilitate the recognition of the margin of SSA/P. We used acetic acid as a mixture with indigo carmine and compared it to conventional evaluating methods; narrow band imaging (NBI) and indigo carmine. From December 2016 to February 2017, patients in whom SSA/P more than 10 mm were found in right side colon in daily practical colonoscopy by single endoscopist in our institute were included. We used the standard scope without magnifying function. First we observed lesions with conventional white light and NBI. Second, we recorded pictures with indigo carmine (IC) spray alone on it. Finally, we sprayed the mixture of acetic acid and indigo carmine mixture (AIC) directly through the endoscopic working channel without using catheter onto lesion. Using recorded pictures during these procedures, ability for recognizing the margin of polyps were compared between IC and AIC, or NBI and AIC by 3 endoscopists, and the concordance rate of diagnosis among these three were assessed as Kappa statistics.

**Results:** 9 SSA/P lesions in 7 patients were investigated. In all cases, AIC was helpful to recognize the margin of polyps without causing any obstructive effect. We also observed disappearance of mucous on the surface, dilated crypts caused by acid contact, and aceto-whishit reaction on the surgical glands in all lesions. In comparing the ability for recognizing the margin of the lesions, 6.3 in 9 lesions (mean among 3 practitioners) were thought to be as AIC better than IC, and...
similarly 7.3 in 9 were better than NBI. Kappa value among participants was 4.8; moderate agreement (p = 0.0016). All polyps were removed endoscopically after evaluation. All lesions were histologically diagnosed as SSA/P without dysplasia.

**Conclusion:** Acetic acid was useful and promising to facilitate the endoscopic recognition of the precise margin of SSA/P in right side colon. Strength of this method is that it is very simple and needs no special equipment nor skill.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

References

**Aims & Methods:**

From February 2016, all patients who required localization of a target lesion before colorectal surgery underwent endoscopic tattooing using autologous blood. A total of 80 patients who underwent endoscopic tattooing using India ink or autologous blood were included in this study. From February 2016, all patients who required localization of a target lesion before colorectal surgery underwent endoscopic tattooing using autologous blood at a single tertiary medical center, and the outcomes were collected prospectively. As a comparison, we retrospectively reviewed the medical records of a further 40 consecutive patients who underwent endoscopic tattooing using India ink before February 2016. The primary outcomes were the visibility of the tattooing in the peritoneal cavity and related adverse events.

**Results:** Endoscopic tattoos produced using India ink were visible in 38 (95%) patients, and tattoos created using autologous blood were visible in 36 (90%) patients. In the autologous blood group, the tattoo could not be identified in four patients due to excessive peritoneal fat, bleeding tendency, congenital anomaly, and tattooing to an inadequate depth. Eight (20%) patients in the India ink group and four patients (10%) in the autologous blood group experienced endoscopic tattooing-related adverse events.

**Conclusion:** Preoperative endoscopic tattooing using autologous blood is a feasible and safe modality for the preoperative localization of colorectal lesions.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**Rate of adenomatous or submucosal invasion for each type of LST**

<table>
<thead>
<tr>
<th>LST Type</th>
<th>Number (%)</th>
<th>Cancer (%)</th>
<th>T1sm (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LST G</td>
<td>102/27</td>
<td>0</td>
<td>5/4</td>
</tr>
<tr>
<td>LST-G with large nodule</td>
<td>07/28, 4</td>
<td>134/35, 5</td>
<td>9/17, 5</td>
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<td>LST-NG</td>
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<td>11/8, 2</td>
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<td>LST-NG with type Ia</td>
<td>34/9, 0</td>
<td>34/9, 0</td>
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</table>

**Conclusion:** Our western series confirm similar rates of submucosal adenocarcinoma according to the type of LST as compared to Asian series. LST-G with large nodule, and LST-NG with depression were associated with a higher risk of submucosal invasion and invasive pit pattern was the stronger predictor of malignancy. Endoscopic submucosal dissection should be systematically performed in these cases.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

References
Introduction: Endoscopic submucosal dissection represents the standard of care for large superficial colo-rectal neoplasms in Japan. In Europe, only few studies reported diagnostic results, essentially in the rectal location. Colonic ESD is more technologically challenging because of the colonic loops, intestinal motility, the folded anatomy, problems caused by inconstant gravity, and submucosal fibrosis. Colonic ESD is although more risky because perforations are most often non-clinically apparent in the rectal location (under peritoneal reflection) contrary to the colonic location. Here we reported our results of two years of colonic ESD performed by two French expert teams that began colonic ESD after a strong animal training and a strong experience in rectal and upper-digestive tract ESD.

Aims & Methods: Retrospective bicentre study of all cases of colonic ESD performed between 01/2016 and 03/2017 for superficial pre-cancerous or cancerous neoplasms. Primary Endpoint was to evaluate the En bloc, R0, curative resection rate and extended curative resection rate (Curative resection + non-curative due to positive horizontal margins and without recurrent disease on endoscopic control). Secondary endpoints were to compare these results with results of rectal ESDs performed during the same period.

Results: 2674 cases were performed in two French centers between 01/2015 and 03/2017 for superficial pre-cancerous or cancerous neoplasms. During the same period 93 rectal ESDs were performed for superficial pre-cancerous or cancerous neoplasms. Descriptive results: male 54 (61%), mean size of the specimen: 49 mm, mean duration of procedure 125.1 min, mean speed of ESD: 18.9 mm²/min, perforation rate: 9 (10.3%), post procedural bleeding rate: 2.3%, secondary endpoints were compared with those of rectal ESDs performed during the same period.

Conclusion: Colonic ESD could be performed with similar results than rectal ESD in French expert teams with prior strong experience in animal ESDS and rectal ESDs. It allows en bloc resection of large superficial colorectal neoplasms with a very low risk of recurrence. RTs comparing colonic ESD to piece-meal EMR are needed to determine the appropriate place of each technique in Europe.

Disclosure of Interest: All authors have declared no conflicts of interest.
needed. We recorded endoscopic diagnostic accuracy according to Baron criteria, time to reach the caecum, and the patient’s pain/discomfort and operator’s difficulty.

Results: We studied 12 patients (7M/5F), mean age 41 yrs and disease duration 5.33 yrs. 53 colonic segments out of the 54 evaluated had the same assessment of disease activity (absent = 0 points, mild = 1 pt, moderate = 2 pts and severe = 3 pts) with a mean difference score with 0.3 pts (SD 0.33 pts) (SD 0.60) with S, without significant difference. The caecum was reached in 11/12 cases by S in an average of 29.42 min (SD 28.94), and in 10/12 cases by R, in an average of 46.67 min (SD 24.98 min), with a mean difference of 17, 25 min., not statistically significant. Incomplete colon explorations with R clustered in Milan, probably because of smaller experience. An average of 1.45 (SD 0.79) mg of midazolam were used during S while 0.41 (SD 0.38) mg during R. Mean pain/discomfort on a 0–10 scale was 2.08 (SD 1.67) for R and 4.17 (SD 1.74) for S, with a statistically significant difference (p = 0.006) favouring R. Mean perceived operator’s difficulty on a 0–10 scale was 4.44 (SD 1.78) for R, and 4.08 (SD 1.44) for S, with a mean difference of 0.42 pts favouring S, not statistically significant.

Conclusion: R appears to be a promising method for disease staging in patients with ulcerative colitis, because of comparable accuracy and reduction in pain and discomfort. A tool channel to obtain biopsies and perform therapeutic endoscopy, together with images of higher definition (CMOS digital Camera HD ready) and virtual chromo-endoscopy, useful for follow-up and screening for dysplasia in patients with long duration of disease are now available in the latest version of R. The “column” connected to the latest version of the robot is the size of a portable suitcase, and suitable for remote operation. Further studies with newer versions of R are needed to assess the role of this technology from an economic point of view and in special settings like failed colonoscopies, dysplastic lesions in UC, bed-side colonoscopy, colonoscopy in rural areas.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P0870 WHAT IS THE CONCORDANCE FOR THE DIAGNOSIS OF LATERALLY SPREADING-TYPE LESIONS (LST) AMONGST WESTERN AND JAPANESE EXPERT ENDOSCOPISTS?


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Introduction: The LST classification and Paris classification systems are internationally used to describe polyp morphology. Differences between Japanese and Western endoscopists in the use of classification systems, have been observed. We aimed to evaluate the inter-observer agreement of LST classification amongst Western & Japanese experts.

Aims & Methods: A total of 40 endoscopic video clips depicting LSTS (10% minor LST) were sent by 6 expert endoscopists: 3 from Japan and 3 from the West. Assessments included LST classification (LST-G homogeneous, LST-G mixed, LST-NG flat, LST-NG pseudodepressed), Paris classification, invasiveness, treatment suggestion and mean size of lesion. We calculated the interobserver agreement with weighted kappa and Chi square.

Results: Japanese endoscopists diagnosed more lesions as LST-G than Western (62.7 vs. 45.4%), Western diagnosed more LST-NG than Japanese (54.6 vs. 37.3%; p = 0.007). The interobserver agreement of the LST classification amongst all six experts was good according to the weighted Kappa of 0.61 (IC 95% 0.45–0.78) for Japanese, and moderate at 0.45 (IC95% 0.27–0.64) for Western. Difference in concordance between the two cohorts was not statistically significant (p = 0.22). When only two categories were considered (LST-G vs NG), agreement was very good according to Japanese (weighted Kappa of 0.81; 95% CI 0.65–0.97) and good for Western endoscopists (0.65; 95% CI 0.46–0.85). Again, difference in concordance was not statistically significant (p = 0.22).

Piecemeal Endoscopic Resection was suggested in 34, 7% cases by Western, but never by Japanese endoscopists, whereas Endoscopic Submucosal Dissection was recommended in 50.4% and 16.1% cases by Japanese and Western experts respectively (p < 0.0001).

Conclusion: This study is the first to validate the LST classification system comparing East and West. There were significant differences in the types of LST diagnosed, and concordance was good in the Japanese cohort and moderate in the Western, but not significantly different. The recommendations for treatment were also different. We suggest a modification of the classification system to enable a more unanimous diagnosis and therapeutic strategy.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

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Introduction: A scoring system based on size, morphology, site and access (SMSA score) was established for determining the complexity of polypectomy and endoscopic treatments. It could predict outcome of endoscopic interventions.

Aims & Methods: The aim of this study was to assess the usefulness of the SMSA scoring system relating the difficulty level with outcomes and complications of EMR and to compare it with a subjective classification of difficulty. We conducted a prospective multi-center study with 1997 consecutive patients with large (>20mm) non-pedunculated colorectal lesions (LNPLC) treated by EMR (n = 2198) at 23 hospitals belonging to the Spanish Endoscopy Society Endoscopic Resection Group, from January 2013 to October 2016. We
calculated the SMAS score of difficulty and assessed the ability of SMAS to identify 5 outcomes: 3-months recurrence, 1-year recurrence, global recurrence (endoscopy not effective after 2 or more treatments), delayed bleeding and perforation. We compared results with those obtained using a subjective classification of difficulty: easy or medium vs difficult. Comparisons were conducted using chi-squared tests and complemented with logistic regression models.

Results: The SMAS scoring system classified 690 polyps (39%) as level 4 and 1098 (61%) as level 3, whereas the subjective classification system classified 392 (22%) as difficult and 1389 (78%) as easy or medium. The agreement between measures of difficulty was weak (k = 0.33). 255 patients (19.9%) had recurrence 3 months after EMR, 84 (11.6%) had recurrence at 1 year, 78 (3.5%) suffered delayed bleeding and 5 (1.6%) perforation. Using the subjective indicator of difficulty, recurrence was also delayed bleeding (p = 0.001) but not for perforation.

Conclusion: The SMAS grading tool is a predictor of outcomes or recurrences and bleeding following resection of LNPLC. However, in our multi-center sample, it does not appear to overcome the ability of a subjective indicator of difficulty. This was evidenced during the EMR. It seems that this score can be used to facilitate planning, training or competency assessment, but efforts should be focused on validating the scoring system in a real situation, adjusting the score of variables or including new ones.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

P0872 NARROW BAND IMAGING GUIDED BIOPSY IMPROVES THE YIELD OF HISTOLOGY FOR THE DIAGNOSIS OF GASTROINTESTINAL TUBERCULOSIS (GITB)
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Introduction: Accurate diagnosis of gastrointestinal tuberculosis (GITB) is challenging due to pauci-bacillary nature of disease and poor sensitivity of histopathology. Role of tissue acquisition using narrow band imaging magnification (NBI-M) to improve yield of histopathology over high-definition white light endoscopy (HD-WLE) has not been assessed. Aim: We aimed to test the utility of narrow band imaging with magnification versus high-definition white light imaging guided endoscopic biopsy for diagnosis of gastrointestinal tuberculosis. In this prospective study from July 2015 to November 2016, adult cases of clinically suspected GITB were recruited. All patients underwent randomised test, contrast enhanced computed tomography of abdomen, esophagogastroduodenoscopy and/or colonoscopy using both HD-WLE and NBI-M and guided biopsies using both were taken. Histopathological examination was done by two independent pathologists. A final diagnosis of GITB was made if acid-fast bacilli were seen in tissue or grown in culture, histopathology showed caseous necrosis with granulomatous inflammation or clinical/radiological and endoscopic features were suggestive of tuberculosis and clinical response to antitubercular therapy. Results: A total of 35 cases of clinically suspected GITB were recruited. A final diagnosis of tuberculosis was made in 32 cases (daedalor n = 4, ileocolic n = 28). Concomitant evidence of active or healed pulmonary tuberculosis was seen in 21% of cases. The mean age, haemoglobin and erythrocyte sedimentation rate of patients with tuberculosis were 36.4±14.6 years, 10.2±2.4 g/dl, 37.8±15.3 mm/hour respectively. The mean duration of symptoms was 10.9 months. The most common symptoms were pain abdomen (78%), weight loss (62.5%), and loss of appetite (40.6%), fever (37.5%), vomiting (34%) and diarrhea (22%). Mantonius test was positive in 40.6% cases. The most common endoscopic findings were ulcerations (75%), nodularity (46.8%), distorted ileocecal valve (28%) and strictures (21.8%) (Table 1). The most common radiological findings were mural wall thickening (65.6%), mesenteric lymphadenopathy (56%) and strictures (40%) (Table 1). NBI-M guided biopsy confirmed the diagnosis of GITB in 46.88%, while HD WLE guided biopsy confirmed diagnosis of GITB in 28.12% (P = 0.04). The two sets of biopsies together confirmed diagnosis of GITB in 53.1%. The area under curve for NBI-M plus HDWLE, NBI-M alone and HDWLE alone were 0.770 (63.87–0.73) (0.60–0.85) and 0.64 (0.50–0.77) respectively. Patients were started on anti-tubercular therapy for nine months. Four patients underwent surgery for intestinal obstruction while on anti-tubercular therapy. Twenty eight completed full therapy and improved.

Conclusion: NBI-M guided biopsy improved the yield of histology for diagnosis of GITB.

Disclosure of Interest: All authors have declared no conflicts of interest.

Abstract: P0871. Outcome by SMAS grade. Odds ratios and 95% CI ROC Curves by SMAS using the score in the continuous format.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>N (%)</th>
<th>Parameter</th>
<th>N (%)</th>
</tr>
</thead>
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<td>Mesenteric lymphadenopathy</td>
<td>18 (56)</td>
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<td>Nodularity</td>
<td>15 (46.8)</td>
<td>Mural thickening</td>
<td>21 (65.6)</td>
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<td>13 (40)</td>
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<td>Ascites</td>
<td>5 (15.6)</td>
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<td>Intussusception</td>
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<td>Psoas abscess</td>
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Endoscopic findings

Radiological findings

P0873 EFFICACY AND SAFETY OF ENDOSCOPIC RESECTION OF LARGE COLORECTAL ADENOMAS – CLINICAL EXPERIENCE OF A TERTIARY REFERRAL CENTER
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Introduction: Colorectal cancer is a leading cause for cancer related mortality. Adenomatous poly, the precursor lesion, can usually be endoscopically resected to prevent cancer. Currently, there are no criteria for surgical vs. endoscopic resection and decision is individually made by the treating physician.

Aims & Methods: We aimed to evaluate factors associated with short-term efficacy and safety of endoscopic resection of large ≥20 mm and giant (≥40 mm) adenomas. Consecutive cases that underwent endoscopic resection of adenomas larger than 20 mm were included. Endoscopic, clinical and histological details of polyps and of the endoscopic procedure were recorded as well as the need for further surgery.

Results: Total of 351 resections were included. Average diameter was 30.34 ± 10.66 mm. Surgery was indicated in 21 (5.98%) cases. In a multivariate analysis for efficacy, two variables were independent risk factors for surgery: adenoma size (OR 95%CI 1.08 (1.04–1.12) and cecal location (OR 95%CI 5.97 (1.60–22.33)). Post-polypectomy complications were documented in 85 cases (24.2%): bleeding - 69 (19.7%, 54/69 managed during procedure), perforations - 8 (2.3%) and significant discomfort up to early termination of procedure - 15 (4.3%). Only 21 (6.0%) developed serious complications requiring further hospitalization. In multivariate analysis for safety, independent risk factors for post-polypectomy complications were: adenoma size (OR 95%CI 1.04 (1.01–1.06), poly morph morphology (sexile OR 95%CI 2.55 (1.45–4.51), flat OR 95%CI 2.40 (1.04–5.52) and submucosal adrenaline injection (OR 95%CI 1.87 (1.11–3.20)). Every increment of 1 mm in adenoma diameter above 20 mm, increased the need for surgery by 8% and the risk for complications by 4%.

Conclusion: Resection of large or giant adenomas is generally a safe procedure when performed by an experienced endoscopist. Although adenoma size is the most significantly related to efficacy and safety, each case of giant adenoma should be evaluated in a referral center for feasibility of endoscopic resection.

Disclosure of Interest: All authors have declared no conflicts of interest.
**P0874 COLORECTAL MUCOSAL DEFECT CLOSURE FOLLOWING ENDOSCOPIC MUCOSAL RESECTION: A SYSTEMATIC REVIEW AND META-ANALYSIS**

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Introduction: Clinical delayed bleeding is the most frequent adverse event following endoscopic colorectal mucosal resection. Observational and interventionist studies on the efficacy of prophylactic closure (PC) following endoscopic mucosal resection (EMR) showed conflicting results.

Aims & Methods: The primary objective of this review is to evaluate the effectiveness in preventing bleeding and post-polypectomy syndrome (PPS) or perforation of PC of colonic mucosal defects following endoscopic resection. We performed a systematic review and meta-analysis of randomized controlled trials (RCTs) from MEDLINE.

Results: 269 articles were initially screened: 5 were RCTs, 4 of them were pooled in the quantitative analysis. A total of 555 patients and 557 resection lesions (proximal colon: 220; distal: 337) were included. Endoscopic procedures: 459 loop polypectomies and 98 submucosal dissections. A total of 298 lesions were randomized to PC versus 259 to non-closure (NC). Number of events on PC group: delayed bleeding (n = 3), PPS and perforation (n = 61). Number of events on NC group: delayed bleeding (n = 13), PPS and perforation (n = 14). Prophylactic mucosal defect closure was effective in reducing delayed bleeding risk (OR: 0.206, 95%CI 0.045-0.77; p = 0.020; I² = 0.0%; 2 RCT and 452 lesions included). There was a non-significant trend for PPS/perforation risk reduction after PC (OR: 0.349, 95%CI 0.114-1.070, p = 0.066; I² = 0.0%; 2 RCT and 374 lesions included).

Conclusion: Prophylactic closure of mucosal defects after EMR of flat or sessile colorectal lesions ≥ 10 mm reduces the risk of delayed bleeding. Further studies are needed to evaluate the effect on PPS/perforation prevention.

Disclosure of Interest: All authors have declared no conflicts of interest.

**P0875 RECTAL ESD IN VERY OLD PATIENTS (>80 YEARS): A FRENCH MULTICENTER RETROSPECTIVE STUDY**

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Introduction: Endoscopic Submucosal Dissection has become the standard of care for large superficial rectal precancerous and cancerous lesions. It allows an en-bloc resection of large superficial lesions that increase the quality of pathologic staging. Endoscopic Submucosal Dissection has become the standard of care for large superficial rectal precancerous and cancerous lesions. It allows an en-bloc resection of large superficial lesions that increase the quality of pathologic staging.

Results: 58 rectal ESDs were performed in four French centers between 06/2010 and 12/2016 for superficial pre-cancerous or cancerous neoplasms in patients older than 80 years. Four French teams that performed more than 150 ESDs in the last 5 years. Primary Endpoint was to evaluate the ESD. R0, curative resection rate and complications in patients older than 80 years. Secondary endpoints were to compare these results with rectal ESDs performed during the same period for patients younger than 80 years.

Conclusion: ESD is feasible and efficient in very old patients. However, ESD resection and R0 resection are less frequent than in younger patients probably due to more challenging lesions (more frequent cancer on the pathological analysis). ESD should be the treatment of choice for large rectal superficial neoplasms of the rectum in very old patients in view of its oncological efficiency and its safety in comparison to the surgical alternative.

Disclosure of Interest: All authors have declared no conflicts of interest.

**P0876 COLONOSCOPY SPLIT-DOSE PROTOCOL IMPLEMENTATION: A SINGLE-CENTRE EXPERIENCE**

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Introduction: Split-dose bowel preparation (SD) is more effective in bowel cleansing quality in patients from a district hospital. The implementation of a split-dose bowel preparation protocol in bowel cleansing quality in patients from a district hospital.

Aims & Methods: The main objective of the study was to explore the impact of a SD protocol in bowel cleansing quality in patients from a district hospital. This was an exploratory observational study of patients who underwent total colonoscopy between Jun/2016-Mar/2017 with polyethyleneglycol bowel preparation before and after SD protocol implementation. Bowel cleansing quality was assessed prospectively (using Boston Bowel Preparation Score) and compared between SD and PD groups. Tolerance was assessed using a patient questionnaire.

Results: A total of 344 patients were included, 53% were male, mean age of 61.8 ± 13.6 years. Bowel preparation: 66% SD and 34% PD. Overall, 72% of colonoscopies occurred in morning shifts. Mean interval between finishing bowel preparation and colonoscopy was 4h50 (SD) and 8h09 (PD). Adequate bowel cleansing was found in 51% of patients (SD 83% vs. PD 79%; p = 0.34). There was an association between adequate bowel cleansing and a shorter interval between finishing preparation and colonoscopy (5h40 vs. 7h15; p = 0.010). Split-dose preparation was associated with a better cleansing in the right colon (2.17 ± 0.69 vs. 2.03 ± 0.65; p = 0.047) and a trend for better overall cleansing (6.70 ± 1.87 vs. 6.32 ± 1.90; p = 0.067). On morning shifts, there was a significant association between SD prep and better overall cleansing (p = 0.030) and also right colon cleansing (p = 0.034). After adjusting for morning shifts, we found an association between SD preparation and better bowel cleansing (risk difference 0.406; 95%CI – 0.023–0.834; p = 0.063). There was no difference between groups on bowel urgency (SD 2.6% vs. PD 1.7%; p = 0.718). SD preparation was associated with worse sleep quality (SD 25% vs. DA 7%; p = 0.004).

Conclusion: The implementation of a split-dose bowel preparation protocol in our hospital was associated with better bowel cleansing, especially on the right colon. Split-dose preparation was not associated with higher bowel urgency, although there was a worse sleep quality.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference
P0877 EQUAL ADENOMA DETECTION RATE IN COLON PATIENTS WITH SPINAL CORD INJURY AND CONTROLS – A CASE-CONTROL STUDY
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Introduction: Spinal cord injury (SCI) is a devastating event that occurs with a discharge incidence of 199 per million, which results in an estimated prevalence of up to 2525 per one million [1]. Cancer is a major cause of death in patients with spinal cord injury (SCI) [2]. Preventive strategies claim increasing attention, but must deal with special problems. Most SCI patients suffer from neurogenic bowel abnormality, a loss of bowel control, sweats, reduced skin sensibility, constipation or evacuation difficulties. Therefore, bowel preparation requires modified and intensified regimens and more intensive care to prevent pressure ulcers and optimum skin management [3, 4, 5]. Colonoscopy itself may be associated with increased morbidity in SCI patients, since a poorer quality of bowel cleansing or failure to reach the caecum could diminish adenoma detection rates (ADR) [6, 7], while complication rates could increase due to severe morbidity.

Aims & Methods: The primary objective was to determine the adenoma detection rate (ADR) in general, right and left hemicolectomy. Secondary objectives were polyp, advanced adenoma and carcinoma detection rates, size of adenomas and polyps in either localization, intensity and effect of bowel preparation, rate of complete colonoscopies, need for re-endoscopy, duration of colonoscopic procedures, deepest point of insertion and complication rates. We reviewed retrospectively consecutive SCI patients who underwent colonoscopy from 2003 to 2013 and assigned an age-, gender- and year of performance-matched control group.

Results: In 236 SCI, compared to 414 control patients, bowel preparation lasted longer (3.57 ± 1.5 vs. 1.15 ± 0.6 days, p < 0.001), achieved insufficient cleansing rate more often (23.7 ± 3.6%) and caused more adverse events (OR: 0.37 ± 2.6). Colonoscopy needed longer time (36.9 ± 25.0 min, p < 0.001), remained incomplete more often (24.6 ± 4.6%), resulting in more re-colonoscopies (14.8 vs. 4.3%), and caused more adverse events. Colonoscopy itself might achieve a comparable quality.

Disclosure of Interest: None declared.

P0879 CONTRIBUTION OF COLONOSCOPY IN ELDERLY PATIENTS OLDER THAN 70 YEARS
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Introduction: The elderly patients are considered as a particular population. Colonoscopy has an important place at this population because of the limited number of normal paraclinic examinations and the high incidence of tumor disease, specially the colo rectal cancer.

Aims & Methods: The aim of this study was to determine the indications and results of colonoscopy in people older than 70 years We performed a retrospec- tive descriptive study over a period of 2 years from the beginning of the endo- scopic unit until February 2017, conducted in the department of hepatogastroenterology of our university hospital. All patients over the age of 70 years who have underwent colonoscopy have been included.

Results: A total of 1095 colonoscopes were performed, 10.3% were indicated for people older than 70 years. The mean age was 74.15 years with a median age of 75 years and a maximum age of 91 years. The prevalence of males was 51%, 10.5% of cases (n = 10) were diabetic, 12.6% (n = 12) hypertensive, 12.6% (n = 12) with ischemic heart disease 8.4% (n = 8) had cardiac insufficiency and 9% (n = 9) had a digestive neoplasia. Colonoscopy was indicated for hematochezia 40% (n = 38), transit disorders in 33.6% (n = 32), abdominal pain in 14.7% (n = 14), IBD in 3.1% (n = 3), radiographic abnormalities in 13.6% (n = 13), iron defi-
cency anemia in 4.2%, and for patients with a family history of colorectal cancer in 1% of cases. Colonoscopy was abnormal in 83% (n = 93), with polyps in 48.3% (n = 45), suspected lesions of malignancy in 16.1% (n = 15), Diarrhea in any culture positive results (n = 15), cirrhosis in 19.3% (n = 18), IBD in 3.7% (n = 3). There were two recurrences (13.3%) at 3-months within the 15 cases with piecemeal resection, treated endoscopically, which were noted in en-bloc (ESD or EMR) resection patients (p = 0.044). Three (7.7%) and one (1.3%) patients had an indication for surgery in case-control groups (p = 0.107).

Conclusion: The presence of certain factors should be assessed during the procedure to identify patients who are high-risk for ESD conversion regardless of size or location, particularly the duration of the dissection.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P0878 RISK FACTORS AND PRACTICAL CONSEQUENCES OF COLORECTAL ESD CONVERSION TO EMR AT A WESTERN REFERRAL CENTER IN DAILY PRACTICE
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Introduction: There are limited data concerning risk factors and consequences of colorectal endoscopic submucosal dissection (ESD) conversion to mucosal resection (EMR) in western centers.

Aims & Methods: Hospital-based frequency-matched case-control retrospective study. All patients were identified from a database of 223 consecutive dissections between 2013 and 2017. The cases were those with ESD conversion to EMR for a >20 mm colonic lateral spreading tumor (LST). The controls were randomly selected by frequency 1:2 matching for tumor size (±0.5mm) and location (rectum/non-rectum). The presence of different factors were evaluated to deter-

P0880 ENDOSCOPIC CLOSURE OF ACUTE IATROGENIC PERFORATIONS OF THE GASTROINTESTINAL TRACT AND PREDICTORS OF NEED FOR EARLY SURGERY: A SYSTEMATIC REVIEW AND META-ANALYSIS
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Introduction: Acute iatrogenic perforations are one of the recognized complications of both diagnostic and therapeutic gastrointestinal endoscopy. For decades, surgical treatment has been the standard of care, but endoscopic closure has become a more popular approach, due to feasibility and the reduction of the
burden of surgery, combined with the availability of various endoscopic closure devices.

Aims & Methods: To assess the technical and clinical success and safety of endoscopic closure, in total, and for each endoscopic device used. Also, to identify factors predicting success as a first line treatment, and failure of endoscopic treatment.

References:
2. Voemans, R., Moine, O., and Von Rentlen, D. (2012). Efficacy of endoscopic closure (NBI) allows, after training, "in-vivo" classification of colorectal polyps. Recent guidelines propose a "do not resect" strategy. However, the results may have been affected by the addition of an additional category (1s) to the NICE classification.

Disclosure of Interest: All authors have declared no conflicts of interest.

References:

P0882 “O-RING SIGN” AS A NOVEL COLONOSCOPIC FINDING WITH NARROW-BAND IMAGING FOR DETECTING DEPRESSED-TYPE COLORECTAL LESIONS
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Introduction: In recent years, colorectal cancer (CRC) has become a focus of attention as likely representing “missed” or “rapidly-growing” lesions in colorectal screening for colorectal cancer (CRC). Currently, lesions thought responsible for CRCV (carcinoma including neoplastic colorectal polyps) and flat lesions occurring on the right side of the colon, and there is an increasing need for endoscopic modalities to prevent overlooking these lesions. Colorectal screening using narrow-band imaging (NBI) during colonoscopy withdrawal from the cecum, which was started at our clinic since November 2008, suggested that the NBI colonoscopy was superior to white-light imaging (WLI) colonoscopy in detecting flat and depressed-type lesions (1). With NBI, the depressed area of a lesion is recognized as “whitish” and the surrounding ring-like mucosa as “brownish”, which constitutes the “O-ring sign”.

Aims & Methods: We aimed to evaluate the incidence and characteristics of the “O-ring sign” in depressed-type colorectal lesions. A total of 227 endoscopically resected and histologically confirmed depressed lesions (375 156, 71) were included for analysis. The colorectal lesions of these were retrospectively examined for “O-ring sign” positivity and intensity (grade 0, negative; grade 1, mildly to moderately positive; and grade 2, highly positive). Of these, 16 were included as evaluable and a total of 211 evaluable lesions were analyzed. Results: Of the 211 lesions (IIa + Hc; 40, IIc; 71 analyzed, 84 (Hc + Hc; 60, Hc; 24), 105 (IIa + Hc; 69, IIc; 36), 22 (IIa + Hc; 12, IIc; 10, found to be in grades 0, 1, and 2, respectively, with 60.2% of these shown to be “O-ring sign”-positive (127,211), with IIa + Hc and IIc accounting for 57.4% (81,141) and 65.7% (46,70), respectively, of these lesions. While an examination by tumor size and location revealed no clear tendency in “O-ring sign” positivity, an examination by grade revealed a higher “O-ring sign” positivity rate among those with high-grade dysplasia (84.6%; 11,13) than those with low-grade dysplasia (59.2%; 116,196).

Conclusion: NBI colonoscopy screening for the “O-ring sign” as an index appears to improve the detection of depressed-type colorectal lesions.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference
1. Fuji T. Gastrointest Endosc 2010; W1480

P0883 THE LEARNING CURVE FOR COLORECTAL ENDOSCOPIC SUBMUCOSAL DISSECTION (ESD) BETWEEN EXPERT AND TRAINEE ENDOSCOPIST
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Introduction: Endoscopic submucosal dissection (ESD) has been acceptable as a minimally invasive therapy and providing en-bloc resection for early malignant and pre-malignant lesions of gastrointestinal cancer. Colorectal ESD has some difficulties such as a risk of perforation and its severity compare to gastric ESD. Hence, Colorectal ESD is more challenging than gastric ESD in endoscopic technique. In Japan, where has high incidence of gastric cancer, endoscopists

References:
1. Fuji T. Gastrointest Endosc 2010; W1480

P0888 REAL-TIME HISTOLOGICAL CHARACTERIZATION OF COLORECTAL POLYPS: THE IMPACT OF TRAINING
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Introduction: Narrow-band imaging (NBI) allows, after training, "in-vivo" classification of colorectal polyps. Recent guidelines propose a "do not resect" strategy for rectosigmoid hyperplastic polyps with a degree of confidence, with >90% negative predictive value (NPV) for adenoma.

Aims & Methods: We aimed to evaluate the impact of the training for the simulta-
neous evaluators (International Colorectal Endoscopic Classification) and WASP (Workgroup Serrated Polyps and Polyposis) classifications. Prospective, single-center study of patients undergoing elective colonoscopy (colonscropy-CF-H1908, Olympus, in two periods: P1: January-February/ 2016 and P2: January-February/2017. Endoscopists had no prior experience in NBI in P1, except for an interactive session of 20 minutes, and after P1 applied the technique during 2016 at their discretion. Polyps were assessed for its location, size and morphology (Paris classification); NICE/WASP. 1 (hyperplastic), 2 (serrated), 3 (adenoma), 4 (deep submucosal invasive cancer); confidence level (low: <90% vs high: >90%) of the predictions. NICE/WASP classifications were compared with histology. Learning impact evaluated by P1 and P2 comparison. Statistics: Software-R (version 3.1.2).

Results: 95 patients were selected (P1: n = 192; P2: n = 98), average size 6.4 mm (2.5 mm), 60% located in the left colon, 71.0% 0h. No difference in size, location, morphology and histology between P1 and P2 groups. An improvement of global accuracy in the application of NICE/WASP classification (P1: 72.5% vs P2: 75.5% of the predictions: 78.5% (95% CI: 71.1%–84, 8%) vs 90.5% (95% CI: 81.5%–96.1%) (p = 0.044). In the P2 data subanalysis, NICE/WASP classification for adenoma showed specificity, sensitivity, positive predictive value and NPV of 82% (70–99%), 94% (80–99%), 96% (87–100%) and 72% (56–85%), respectively; for rectosigmoid polyps ≥5mm, with high confidence level (n = 35), NPV for adenoma was 80% (59–93%).
could have many experiences of gastric ESD that may be beneficial for the future work of the new trainee. Little knowledge about the learning curves of the young endoscopists who perform the colorectal ESD first.

Aims & Methods: We conducted multi-center retrospective observational study to elucidate the safety and learning curve of the trainee who perform the colorectal ESD. Trainee endoscopists were comprised of 261 cases of colorectal ESD performed by three endoscopists in Nippon Medical School Hospital and Machida Icho Hospital from 2010 to August 2016. The ESD devices were Flush knife BT (Fujifilm), Dual knife (Olympus), Hook knife (Olympus) or a combination by operator’s discretion. The endoscopist A and B, who had over 10000 examinations of colonoscopy and experiences of gastric ESD as (expert group), and endoscopist C had about 1000 colonoscopies and 200 large bile duct stones was accepted by the trainee endoscopist who had no experience of gastric ESD.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0884 LARGE BALLOON DILATION VERSUS MECHANICAL LITHOTRIPSY AFTER ENDOSCOPIC SPHINCTEROTOMY IN MANAGEMENT OF LARGE COMMON BILE DUCT STONES AMONG CIRRHOTIC PATIENTS

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Introduction: Removal of large common bile duct (CBD) stones is one of the challenges during ERCP and it seems more difficult in cirrhotic patients due to superstition of the complications in cirrhotic patients under ERCP because of liver cirrhosis can tolerate ERCP to treat their biliary tract or pancreatic diseases. Patients with liver cirrhosis are three times more susceptible to cholelithiasis, than the non-cirrhotic population and liver cirrhosis is an independent risk factor for cholecystitis and other diseases and that is why ERCP is increasingly performed for patients with cirrhosis. Endoscopic sphincterotomy (EST) has become a standard step in the management of CBD stones and introduction of both mechanical lithotripsy (ML) and large balloon dilation (LBD) facilitated extraction of the large CBD stones. Despite the increasing use of both techniques, a head-to-head comparison of the two groups was not reported. Therefore, the aim of this study was to evaluate the efficacy of large balloon dilation group showed more success in stone retrieval rate, the difference was statistically significant (P value 0.04).

Conclusion: The training of colorectal ESD first was acceptable by the trainee endoscopist, who had no experience of gastric ESD.

Disclosure of Interest: All authors have declared no conflicts of interest.
PO886 A NOVEL METHOD OF PREVENTING DUODENOBILIARY REFUX BY MEANS OF SUSPENDED OVERLENGTH BILIARY STENTS IN PATIENTS WITH BILIARY STRICTURE

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Introduction: Endoscopic insertion of plastic or metal stents is a well-established treatment for malignant or part of benign biliary obstruction. The major limitation of this technique is stent occlusion. Duodenobiliary reflux has been considered as a key contributor to stent occlusion. No appropriate method can so far prevent duodenobiliary reflux. Different strategies to prolong the patency of plastic stents included changing stent size, stent design, but stent sludge due to duodenal biliary reflux remains an unsolved problem. We have been using a novel suspended overlength biliary stents (reformed with nasobiliary tube) as substitution for ordinary biliary plastic stent to prevent the reflux from January 31, 2016. To December 31, 2016.

Aims & Methods: The aim of the study is to evaluate the efficacy and patency of the suspended overlength biliary stents. The suspended overlength biliary stents (SOBS) were placed in intrahepatic bile duct in 61 patients with extrahepatic bile duct strictures who were followed up at least three months from January 1, 2016, to December 31, 2016. Nasobiliary tube of 7.5Fr or 8.5Fr with multiple side holes were cut 30 cm with operation knife from the top on sterile operating table. The purpose of the set of 30 cm length is to ensure the tail reaches the duodenal horizontal part. The SOBS were placed in the intrabiliary hepatic duct by using conveyer under the fluoroscopic guidance at the end of ERCP. Radiography of the Meglumine Diatrizoate was performed in each patient of SOBS group to evaluate the existence of duodenal biliary reflux. 74 patients who were performed at least two or more ERCP with extrahepatic bile duct strictures treated with ordinary plastic stents (OBS group) from last ten years were compared with SOBS group.

Results: (1) The mean age of SOBS and OBS were 68.8±15.6yrs and 60.4±14.7yrs (P = 0.002), respectively. (2) 35 (57.4%) and 34 (45.9%) patients were malignant biliary obstruction in SOBS and OBS group, respectively (P = 0.227). Malignant obstruction included bile duct cancer and biliary duct invasion of pancreatic cancer. Benign obstruction included autoimmune pancreatitis, chronic pancreatitis, post operation stenosis, inflammatory stenosis due to cholelithiasis. (3) The mean first and second patency was 4.5 months and 5.6 months in OBS groups. All the patients in OBS group experienced at least three months to 15 months (mean patency was 5.2 months). The mean follow-up was 80 days to 12 months (mean patency was 5.2 months). The mean follow-up period of the other 50 patients in SOBS groups was 6.5 months. (range from 3 months to 15 months). No evidence of duodenal biliary reflux were detected in SOBS group.

Conclusion: Suspended overlength biliary stents can prolong the patency and reduce the occlusion rate effectively due to duodenobiliary reflux in both malignant and benign biliary stricture.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
Primary analysis: success defined as score of 1 or 2 (no assistance/minimal verbal cues), Acceptable failure rate - p0

Overall Cognitive Success 20 2268 12 (60) 5 (25)

- Logical plan based on cholangiogram 20 2220 19 (95) 10 (50)
- Demonstrated clear understanding of indication 20 2264 20 (100) 14 (70)
- Stent insertion 17 1029 14 (82.3) 3 (17.6)
- Balloon sweep 19 1062 18 (94.7) 3 (5.3)
- Stone clearance 14 697 9 (90) 3 (30)
- Stricture dilation 10 432 9 (90) 3 (30)
- Cannulation: native papilla 17 1041 3 (17.6) 0 (0)
- Overall cannulation 19 2075 13 (68.4) 6 (31.5)

Cognitive Aspects
- Demonstrated clear understanding of indication
- Appropriate use of fluoroscopy
- Proficient use of real time
- Logical plan based on cholangiogram
- Demonstrated understanding of use of indomethacin

Overall Technical Success

<table>
<thead>
<tr>
<th>Basic Technique</th>
<th>No. of evaluations</th>
<th>No. of AETs achieving competence (%)</th>
<th>No. of AETs achieving competence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intubation</td>
<td>20</td>
<td>2239</td>
<td>20 (100)</td>
</tr>
<tr>
<td>Achieving short position</td>
<td>20</td>
<td>2226</td>
<td>19 (95)</td>
</tr>
<tr>
<td>Identifying the papilla</td>
<td>20</td>
<td>2223</td>
<td>19 (95)</td>
</tr>
</tbody>
</table>

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Introduction: To analyze the frequency of probable causes of asymptomatic hyperamylasaemy and acute pancreatitis after ERCP and their prevention. Two groups of patients were covered: a retrospective (340) and prospective (154) group. Patients had evidence of bile ducts impaired passability of varying etiology. In these cases ERCP is the final stage in the diagnostic and therapeutic algorithm. All ERCPs were carried out by one expert endoscopist. Patients from the prospective group were administered intramuscularly with Diclofenac (75 mg) before and after the manipulation. The methods used in the study were: demographic data; history and physical examination; laboratory data; imaging methods; ERCP; clinical course and statistical methods for processing data received.

Results: The most common indication for ERCP in all patients was cholestasis constellation (88.1%). In a minority of patients ERCP was purely diagnostic (6.1%), while at 93.9% it was also therapeutic. Of all patients at 47 of cases (9.5%) hyperamylasaemy was observed, and at 12 or 2.4% - acute pancreatitis was observed. Patients who developed acute pancreatitis often have acute calculous cholecystitis. Due to the small number of patients with acute pancreatitis, however, these results should be carefully commented. Patients who developed acute pancreatitis were found to have a lower level of alkaline phosphatase and ES and higher values of leukocytes on the 72nd hour. The univariant logistic regression analysis identified the following risk factors for developing hyperamylasaemy: cholethiasis; sclerosing papilloiditis of ERCP; normal values of serum total bilirubin and elevated CRP levels in receiving. In order to establish a predictive model a multiple logistic regression analysis was performed. The model includes: average total bilirubin at entry and cannulation of the pancreatic duct more than 3 times. The estimated true percentage for predicting lack of hyperamylasaemy with this predictive model is very good - 97%. Univariate logistic regression analysis identified the following risk factors for the development of acute pancreatitis: cannulation of the pancreatic duct and the presence of calculous cholecystitis when entering.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0889 ACUTE PANCREATIS AND HYPERAMYLASAEMY DEVELOPMENT AFTER ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY – CHALLENGES AND PREVENTION

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Introduction: Endoscopic retrograde cholangiopancreatography (ERCP) is one of the most technically complex procedures performed by gastroenterologists. After a significant increase in the indications for implementing ERCP, gastroenterologists began to pay greater attention to complications identification and prevention. Despite the widespread improvement of endoscopic techniques and increased experience of endoscopists, the rate of complications has not declined significantly.

Aims & Methods: To analyze the frequency of probable causes of asymptomatic hyperamylasaemy and acute pancreatitis after ERCP and their prevention. Two groups of patients were covered: a retrospective (340) and prospective (154) group. Patients had evidence of bile ducts impaired passability of varying etiology. In these cases ERCP is the final stage in the diagnostic and therapeutic algorithm. All ERCPs were carried out by one expert endoscopist. Patients from the prospective group were administered intramuscularly with Diclofenac (75 mg) before and after the manipulation. The methods used in the study were: demographic data; history and physical examination; laboratory data; imaging methods; ERCP; clinical course and statistical methods for processing data received.

Results: The most common indication for ERCP in all patients was cholestasis constellation (88.1%). In a minority of patients ERCP was purely diagnostic (6.1%), while at 93.9% it was also therapeutic. Of all patients at 47 of cases (9.5%) hyperamylasaemy was observed, and at 12 or 2.4% - acute pancreatitis was observed. Patients who developed acute pancreatitis often have acute calculous cholecystitis. Due to the small number of patients with acute pancreatitis, however, these results should be carefully commented. Patients who developed acute pancreatitis were found to have a lower level of alkaline phosphatase and ES and higher values of leukocytes on the 72nd hour. The univariant logistic regression analysis identified the following risk factors for developing hyperamylasaemy: cholethiasis; sclerosing papilloiditis of ERCP; normal values of serum total bilirubin and elevated CRP levels in receiving. In order to establish a predictive model a multiple logistic regression analysis was performed. The model includes: average total bilirubin at entry and cannulation of the pancreatic duct more than 3 times. The estimated true percentage for predicting lack of hyperamylasaemy with this predictive model is very good - 97%. Univariate logistic regression analysis identified the following risk factors for the development of acute pancreatitis: cannulation of the pancreatic duct and the presence of calculous cholecystitis when entering.

Conclusion: We detected a low incidence of asymptomatic hyperamylasaemy (9.5%) and acute pancreatitis (2.4%) in the group of patients which were subjected to ERCP. Clinical and laboratory parameters characterizing the patients who developed these complications, and risk factors for acute pancreatitis and asymptomatic hyperamylasaemy were determined. The effect of intramuscular Diclofenac administered before and after ERCP has no effect.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0890 MOST ADVANCED ENDOSCOPY TRAINEES DO NOT MEET COMPETENCE FOR NATIVE PAPILLAE CANNULATION IN ERCP: RESULTS FROM A PROSPECTIVE MULTICENTER STUDY

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Introduction: Advanced endoscopy trainees (AETs) achieve ERCP competency at variable rates and specific case volumes do not ensure competence. However, training and credentialing guidelines continue to utilize an absolute procedure volume to determine competence. There are limited data on whether current training composition and volumes ensure ERCP competence in the US.

Aims & Methods: (i) To define ERCP learning curves, utilizing a centralized database, with a focus on cannulation rates using a large national sample of AET programs (AETPs). (ii) To critically examine the composition of current ERCP training in AETPs. ASGE-recognized AETPs were invited to participate and AETs were graded on every ERCP after completion of 25 hands-on ERCP exams. Grading was performed using our previously developed and validated tool [The EUS and ERCP Skills Assessment Tool (TEESAT)] which assesses technical and cognitive competence in a continuous fashion. Grading for each skill was done using a 4-point scoring system: 1-no assistance, 2-minimal verbal cues, 3-multiple verbal cues or hands-on assistance and 4-unable to complete. A comprehensive data collection and reporting system was built using REDCap, a web-based data collection software, and SAS to create learning curves using cumulative sum (CUSUM) analysis for overall and individual technical and cognitive components of ERCP. Individual results and comparison to peers were sent to AETs and trainers quarterly. Acceptable and unacceptable failure rates were set a priori. AETs with <20 evaluations were excluded and success was defined as a skill score of 1 or 2. Individual and combined graphs to assess change in cannulation success rates were constructed and the Cochran-Armitage trend test was used to assess improvement in success rates.

Disclosure of Interest: No conflicts of interest.
Results: Of the 62 programs invited, 20 AETPs participated and 20 AETs were included in the final analysis. At the end of training, median numeric of ERCPs performed/AET was 350 (15–500). Overall, 2649 ERCP exams were graded; the rates of PERCPP in E1 and A1 were 2.3% (3 patients) and 1.7% (2 patients) respectively. One 84-year-old patient of E1 with a presumed malignant common bile duct (CBD) stricture had PERCPP and died 17 days after ERCP, having opted for palliation. The remaining 4 patients had uneventful conservative management of PERCPP. E1 had one patient with immediate bleeding post-sphincterotomy controlled with a CBD stent whilst A1 had 2 patients requiring adrenaline injection for haemostasis. In addition, E1 had one patient with retroduodenal perforation managed conservatively and A1 had one patient with CT evidence of intramural duodenal haematoma which was uneventful. Both E1 and A1 had one case each of uncomplicated hyperamylasaemia. A summary of complications, with patient and procedural characteristics, is listed in Table 1.

Conclusion: In our observational study, which was not intended or powered for statistical analysis, there was no overt difference in the rates of PERCPP when comparing between endoscopist- or assistant-controlled wire-guided CBD cannulation. The overall complication rate was similar and although there were some differences in procedural characteristics between the two endoscopists, there were no characteristics predisposing to PERCPP overtly skewed towards either endoscopist’s case load. Furthermore, randomised trials, or a crossover study, provided the endoscopists and assistants are equally competent in both methods of wire cannulation, are needed to clarify the safety profile of either technique.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

P0892 CONFIRMATION OF THE EFFECT OF AN ANTAGONIST TO CONSCIOUS SEDATION ON THE PREVENTION OF ASPIRATION PNEUMONIA AFTER ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY

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Introduction: Most endoscopic retrograde cholangiopancreatography (ERC) -related procedures are performed under “conscious sedation”, a drug-induced depression of consciousness during which patients are comfortable and able to maintain purposeful responses to verbal or tactile stimulation, and cardiorespiratory function generally remains intact 1. Meanwhile, we sometimes observe adverse events related to conscious sedation after ERC such as aspiration pneumonia 2. So far, it is unknown whether immediate recovery from conscious sedation with antagonists is necessary or not.

Aims & Methods: We aimed to reveal the efficacy of flumazenil, an antagonist to benzodiazepines, on the prevention of adverse events, especially, aspiration pneumonia related to conscious sedation which is most frequent after ERC. One hundred ninety patients who underwent ERC between January to December

P0891 SIMILAR POST-ERCPT PANCREATITIS RATES IN ENDOSCOPIST- VS ASSISTANT-CONTROLLED WIRE-GUIDED BILE DUCT CANNULATION: A SINGLE CENTRE OBSERVATIONAL STUDY

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Introduction: A recent randomised study by Buxbaum et al1 demonstrated a significantly lower rate of post-endoscopic retrograde cholangiopancreatography (ERC) pancreatitis (PERCPP) in endoscopist- versus assistant-controlled bile duct cannulation. We set out to audit the rates of PERCPP at our centre based on this finding.

Aims & Methods: All ERCPs performed by two endoscopists between April 2015 and March 2016 were audited retrospectively. The two endoscopists practiced endoscopist- (E1) and assistant-controlled (A1) wire-guided cannulation exclusively. Both E1 & A1 had access to the same medications, sphincterotomes, equipment, and teams. Data was obtained and anonymised from electronic patient records and endoscopy reporting software. PERCPP was defined as abdominal pain with hyperamylasaemia at least three times the upper limit of normal (ULN) 24–48 hours after ERCP with or without corresponding imaging findings within 7 days; or abdominal pain with a further rise in pre-existing hyperamylasaemia to at least three times ULN 24–48 hours after ERCP with or without corresponding imaging findings within 7 days. Additional data was collected for CT evidence of post-ERCPP complications, hyperamylasaemia without pancreatitis, bleeding, and post-ERCPP cholangitis. Patient and procedural characteristics predisposing to pancreatitis were also recorded.

Results: A total of 250 procedures were audited. E1 performed 132 procedures (54% female; median age 63.5) and A1 performed 118 procedures (67% female; median age 63). The rates of PERCPP in E1 and A1 were 2.3% (3 patients) and 1.7% (2 patients) respectively. One 84-year-old patient of E1 with a presumed malignant common bile duct (CBD) stricture had PERCPP and died 17 days after ERCP, having opted for palliation. The remaining 4 patients had uneventful conservative management of PERCPP. E1 had one patient with immediate bleeding post-sphincterotomy controlled with a CBD stent whilst A1 had 2 patients requiring adrenaline injection for haemostasis. In addition, E1 had one patient with retroduodenal perforation managed conservatively and A1 had one patient with CT evidence of intramural duodenal haematoma which was uneventful. Both E1 and A1 had one case each of uncomplicated hyperamylasaemia. A summary of complications, with patient and procedural characteristics, is listed in Table 1.

Conclusion: The results of this study confirm the substantial variability in learning curves and competence among AETs in ERCP validating the shift away from threshold numbers to determine competence. We report the feasibility of establishing a centralized national database to report individualized ERCP learning curves using a novel web-based comprehensive data collection and reporting system. Using strict definitions, a minority of AETs achieved competency in native papilla cannulation which may, in part, be due to limited cannulation time provided to AETs. Selective native papilla deep cannulation needs to be an important benchmark for assessing competence. Methods to improve native papilla cannulation rates and strategies to increase AET exposure to advanced ERCP techniques are required.

Disclosure of Interest: S. Wani: Consultant for Boston Scientific. Medtronic All other authors have declared no conflicts of interest.

Reference
The aim of this study was to evaluate the impact of this hydration protocol (AHP) for patients undergoing ERCP in order to prevent pancreatitis (PEP). In our department we implemented an aggressive retrograde cholangiopancreatography (ERCP). Some studies have shown that the distributions of used b-blockers (midazolam/diazepam) were 64/8/17/26 in the F group and 30/11/16/18 in the non-F group. There was no significant difference of patients' characteristics between both groups. The mean procedure times were 36.7 minutes in the F group and 30.3 minutes in the non-F group, respectively. There was no significant difference between the incidence and severity of PEP. Our AHP didn't reduce the incidence of PEP or its severity. Indeed, the non-F group had a lower incidence of PEP (4.1% vs. 6.7%) and a lower severity of PEP (3 cases Vs. 5 cases). Conclusion: Flumazenil did not have any preventive effect on the occurrence of aspiration pneumonia related to conscious sedation after ERCP.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
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Introduction: Pancreatitis is the leading complication of endoscopic retrograde cholangiopancreatography (ERCP). Some studies have shown that the distributions of used b-blockers (midazolam/diazepam) were 64/8/17/26 in the F group and 30/11/16/18 in the non-F group. There was no significant difference between both groups. Conclusion: Flumazenil did not have any preventive effect on the occurrence of aspiration pneumonia related to conscious sedation after ERCP.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
1. Committee AsO, Chandrasekhar V, Khashab MA, Multiusam VR, Acosta RD, Agrawal D, Bruining DH, Eloubeidi MA, Fanelli RD, Fockens P, Galloway DS, Acosta RD, Agrawal D, Bruining DH, Eloubeidi MA, Fanelli RD, Fockens P, Galloway DS. Endoscopy introduced the Infinity brush was used in all cases of ERCP cytology. These were compared with historical controls, where a classical 8Fr biliary cytology brush was used. In both groups, at least two passages were made, with transfer to a thin prep solution, as per prior protocol. Follow-up data, namely clinical course, radiological data or other histological results were collected for a definitive diagnosis.

Results: Thirty-five new brush cases were compared with 52 historical controls. There was no significant difference between the incidence and severity of PEP. Pancreatitis was significantly associated with the use of an AHP, intravenous aggressive hydration may have a role in PEP prophylaxis. Further studies are needed to establish its true value.

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Results: Thirty-five new brush cases were compared with 52 historical controls. There was no significant difference between the incidence and severity of PEP. Pancreatitis was significantly associated with the use of an AHP, intravenous aggressive hydration may have a role in PEP prophylaxis. Further studies are needed to establish its true value.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
P0895 PROSPECTIVE STUDY OF EARLY PRECUT VS. UTMOST PRECUT PANCREATIC STENT IN INITIAL PANCREATIC DUCT CANNULATION
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Introduction: In biliary access, repeated biliary cannulation attempts are a risk factor for post-ERCP pancreatitis (PEP). Early precut is an effective technique for success of biliary cannulation and can significantly reduce the incidence of PEP. The aim of this study was prospectively to evaluate clinical efficacy the performance of utmost early precut with pancreatic stent in the patients whom pancreatic duct cannulation was performed initially.

Aims & Methods: When guidewire was placed in the pancreatic duct initially by chance, the patients were randomized into early precut (Group A) or utmost early precut sphincterotomy with pancreatic stent (Group B). In Group A, pancreatic duct cannulation within 5 times and attempted precut papillotomy with outstanding difficulty. In Group B, from the first, pancreatic stent was inserted and then precut with an incision over a pancreatic stent was done. Main outcome measurements were frequency of successful CBD cannulation and post-procedure related complications.

Results: From January 2015 to August 2016, the two groups were similar with regard to patient demographics. A total of 50 patients were enrolled. 26 patients were assigned to the Group A and 24 to the Group B. Successful CBD cannulation was achieved in 23 of 26 (88.5%) patients in the Group A and 23 of 24 (95.8%) patients in the Group B. The mean cannulation time was 16 minutes in the Group A and 14.8 minutes in the Group B. Post-procedure hyperamylasemia was significantly higher in Group A. The overall incidence of post-procedure pancreatitis was 11.5% (3/26) in the Group A and 4.2% (1/24) in the Group B (P < 0.05).

Conclusion: In patients with pancreatic duct cannulation initially by chance, compare to early precut group, utmost early precut with pancreatic stent over the guidewire can easily facilitate biliary cannulation and the success rate but also promise low incidence of post-ERP pancreatitis. In experienced hands, utmost early precut technique can dramatically reduce the trauma of ampulla and risk of PEP compared with conventionally persistent cannulation attempts.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P0896 POST-ERCP BLEEDING IN THE ERA OF MULTIPLE ANTIPLAQUE AGENTS
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Introduction: Antithrombotic therapy with antiplatelet agents (APA) has been increasingly utilized during the last few decades. This study aimed to determine the risk of post-ERCP bleeding among those patients who are taking APAs, especially in the era of multiple agents.

Aims & Methods: From July 2012 to May 2016, the patients who underwent 1st therapeutic ERCP were identified from the ERCP database of 3 institutions in USA and Korea. The primary outcomes were the frequency, type, and severity of ERCP-related bleeding according to the use of APA.

Results: The frequencies of post-ERCP bleeding among the four different groups were 16 of 203 (8.0%) in No drug group, 12 of 256 (4.7%) in Aspirin group, 3 of 48 (6.3%) in Single APA group, and 4 of 48 (8.3%) in Multiple APA group (p < 0.001). Most cases of post-ERCP bleeding were mild (29/35, 88%). In the univariate analysis, post-ERCP bleeding was associated with age, pull-type sphincterotomy, and APA, and inversely associated with balloon dilatation of the biliary papilla. In the multivariate analysis, pull-type sphincterotomy odds ratio [OR] 7.829, 95% confidence interval [CI] 1.41–43.453, p = 0.019) and country (Korea; OR 0.124, 95% CI 0.042–0.361, p < 0.001) were associated with post-ERC bleeding.

Conclusion: The frequency of post-ERCP bleeding was statistically higher in patients on any APAs within 6 days prior to ERCP. However, in the multivariate analysis, APA use was not associated with post-ERCP bleeding. Until a large study is sufficiently powered to show differences in bleeding rates, caution is recommended when considering invasive procedures during ERCP in patients on APAs.

Disclosure of Interest: All authors have declared no conflicts of interest.

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P0897 PROSPECTIVE COMPARISON OF DIGITAL SPYGLASS DIRECT VISUALIZATION SYSTEM VS DIRECT PERORAL CHOLANGIOSCOPY USING A MULTIBENDING ENDOSCOPE AS A SINGLE-OPERATOR CHOLANGIOSCOPY FOR MANAGING BILARY LESIONS
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Introduction: In a recent, a digital version of single-operator cholangioscope (SpyGlass DS) and direct POC (DPOC) using a multibending ultrasound endoscope were introduced as improved forms of each POC, especially in image quality and technical difficulty, respectively.

Aims & Methods: In this study, we prospectively compared the procedure success rates of SpyGlass DS and DPOC for diagnosis and treatment of BD lesions. A total of 15 patients with BD lesions (diameter of CBD >8mm) requiring evaluation or treatment using POC were enrolled prospectively. All patients received POCs using SpyGlass DS and multibending ultrasound endoscope for DPOC. According to the presence of obstructive lesion, all patients were classified as obstructive type or non-obstructive type, respectively. Procedural success defined as an ability to advance the cholangioscope to the desired target and get adequate cholangioscopic visualization for the targeted lesion.

Results: The overall technical success rates of SpyGlass DS and DPOC were 100% and 93.3%, respectively (P = 0.5). In DPOC, 1 patient was failed to insert the endoscope into the CBD. In SpyGlass DS, 2 patients were failed to visualize the targeted lesion. The procedural success rates of SpyGlass DS and DPOC according to the type of lesion were not different in 9 obstructive type (100% vs. 88.9%, P = 0.5) and 6 non-obstructive type (66.7% vs. 100%, P = 0.227). The successful diagnostic and therapeutic procedures by DPOC and SpyGlass DS were observed in 8 of 8 patients (100%) and 7 of 9 patients (77.8%) (P = 0.265), respectively.

Conclusion: Both advanced image quality of SpyGlass DS and improved technical difficulty of DPOC by a multibending ultrasound endoscope showed comparable and high procedure success rates in patients with dilated BD. Future prospective studies focused on overall cost savings and long-term clinical outcomes are seems to be required for deciding adequate indications of each POC systems.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P0899 THE DILEMMA OF MANAGEMENT BORDERLINE COMMON BILE DUCT STONE. DOES STONE SIZE MATTER?: A PROSPECTIVE RANDOMIZED STUDY
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Introduction: Management of common bile duct stones (CBDs) in patients with borderline CBD presents a surgical challenge. The aim of this study was to compare conservative treatment with endoscopic stone extraction for the treatment of borderline CBD with stones.

Aims & Methods: This prospective randomized controlled trial includes patients with CBDs in borderline CBD (<10mm) associated with gallbladder stones who were treated with conservative treatment or endoscopic stone extraction followed by laparoscopic cholecystectomy (LC) and intraoperative cholangioscopy (IOC). The primary outcome was successful CBD clearance. The secondary outcomes were the overall complications, cost, and hospital stay.

Results: LC and IOC revealed complete clearance of CBDs in 48 (96%) cases in the endoscopic retrograde cholangiopancreatography (ERCP) group (52% of patients by ERCP, and 44% of patient passed the stone spontaneously), and in the remaining two patients, the CBDs was removed by transcytoscopy exploration. In the conservative group, LC and IOC revealed complete clearance of CBDs in 90% of cases, and in the remaining 10% of patients, the CBDs was removed by endoscopic sphincterotomy. Post-ERCP pancreatitis (PEP) is noticed significantly in the ERCP group (2% [4%] versus 8 [16%]; P = 0.04). The average net cost was significantly higher in the ERCP group. Recurrent biliary symptoms developed significantly in the ERCP group after 1 year (10% versus 0%; P = 0.02) in the form of recurrent cholangitis and recurrent CBDs.

Conclusion: Management of CBDs in patients with borderline CBD represents a surgical challenge. Borderline CBD increases the technical difficulty of ERCP and increases the risk of PEP. Conservative management of CBDs in borderline CBD not only avoids the risks inherent in ERCP and unnecessary preoperative ERCP, but it is also effective in clearing CBDs. The hepatobiliary surgeon
Aims & Methods: This study aimed to identify the incidence rate of and risk factors for PEP in a prospective large cohort study. This is a prospective multicenter study. In the present multicenter prospective study, SOSUI, we investigated the potential predictors of severity.

Aims & Methods: Of 2078 subjects who underwent ERCP between February 2015 and May 2016 at five high-volume centers, 1932, excluding those who were complicated by pancreatitis, undergone biliary tract reconstruction, or had papilla not reached, were included. Of the 1932 patients, 163 developed PEP were compared between the mild and severe cases to examine potential predictors of severity. PEP was diagnosed based on two or more of the following three conditions: (1) serum amylase elevation (above the upper limits of each center), abdominal pain lasting more than 24 hours, and (2) pancreatitis on CT. Severity was assessed based on the severity criteria of the Ministry of Health, Labour, and Welfare. Continuous variables, the Mann-Whitney U test was employed. For binomial comparison, univariate analysis was conducted using a chi-square test. Results: Twenty-five severe (1.3%) and 138 mild (7.1%) PEP patients were included. Patient and procedural factors were examined, demonstrating that the AMY values at 2 hours after ERCP were significantly higher in the severe cases than in the mild ones (P = 0.005). ROC analysis was conducted on the AMY values at 2 hours as a predictor of severe PEP, demonstrating that the cutoff value was 3.7 times higher than the upper limits of each center (sensitivity: 64%; specificity: 70%; and AUC: 0.65). In multivariate analysis using logistic regression by dividing the AMY values at 2 hours after ERCP into higher or lower than 3.7 times the reference value of each center, abdominal pain immediately after ERCP and AMY values at 2 hours after ERCP were identified as independent factors. Conclusion: Severe PEP should be diagnosed as early as possible for intervention. However, it may take a long time to assess clinical courses or examine images after examination. In the present study, abdominal pain immediately after ERCP and AMY values at 2 hours were identified as predictors of severity, being useful for facilitating early therapeutic intervention.

Disclosure of Interest: All authors have declared no conflicts of interest.

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5. Hall RC. Is natural orifice transluminal endoscopic cholecystectomy as safe and simple approach for performing an endoscopic cholecystotomy? Aims & Methods: The aim of this study was to evaluate the accuracy of T1 stage subdivision of ESCC by higher frequency EUS probe prior to ESD treatment. The overall 5-year survival rate of ESCC is 12–15%. It is import to diagnose ESCC in early stage and receive curative treatment. Endoscopic submucosal dissection (ESD) is a well-developed skill to complete resect gastrointestinal (GI) tract early cancer. The limitation of ESD is cancer invasion to submucosal layer and increasing the risk of lymph node metastasis (10–45%) of ESCC.\n
Reference: EUS-Endoscopic ultrasonography (EUS) is an examination for detecting the pancreas and other solid internal organs. EUS elastography was performed by 2 operators, using a linear echoendoscope. The mean SR value was significantly higher in the malignant tumors comparing with the benign tumors (55.56 vs 23.93, p=0.001). The sensitivity and specificity of SR for differentiation of pancreatic malignancy for a cut of 15.89 were, respectively, 95.45% and 87.5% (area under the curve of 0.89, 95% CI). The overall accuracy of the EUS elastography using the SR for the detection of pancreatic malignancy was 93%.

Conclusion: Quantitative EUS elastography presents good accuracy in the differentiation between malignant and benign pancreatic masses. It is a promising EUS technique in the diagnostic approach of solid pancreatic lesions, which may complement the study and characterization of the tumors, aiding in the diagnosis and follow-up of these patients.

Disclosure of Interest: All authors have declared no conflicts of interest.

References


P0903 ENDOSCOPIC ULTRASOUND-BASED TRANSUDODENAL CHOLECYSTOLOYTOMY VIA DOUBLE-FLANGED FULLY COVERED METAL STENT WITH HOT STENT DELIVERY S. Sun Endoscopy Center, Shengjing Hospital of China Medical University, Shenyang/China Contact E-mail Address: sunsiyuncu@aliyun.com

Introduction: Laparoscopic cholecystectomy (LC) has become the 'gold standard' for the treatment of symptomatic gallstones. However, before clinical implementation, instruments still need modification, and a more convenient treatment is still needed.

Aims & Methods: The aim of this study was to evaluate the transudodenal tractcholecystectomy technique in the treatment of gallbladder disease without cholecystectomy, being patient with cholesterol gallstones and high surgical risks were enrolled between January 2015 and March 2017. Endoscopic ultrasound (EUS)-guided cholecystostudodenotomy by deploying a double-flanged fully covered metal stent with hot stent delivery was performed and endoscopic sphincterotomy (EST) was also performed during this procedure for those patients with accompanying common bile duct stones. One or two weeks later an forward-viewing endoscope was advanced into the gallbladder via the stent, and cholecystolithotomy or polypectomy was performed. After the stents were removed, a pigtail-type naso-cholecystic drainage catheter was inserted into the gallbladder over the guide wire and removed 2 days later. Four weeks later gallbladder was assessed by abdominal ultrasound.

Results: EUS-guided cholecystostudodenotomy with double flanged metal stent deployment was successfully performed in all of 26 patients (Male/Female, 11/15; mean age, 61 ± 16.19ys). After the procedure, fistulas had formed in each of the patients and the stones of 7 patients expelled themselves completely. Endoscopic ultrasound (19) and polyectomy (2) were successfully performed through the stents, and then the stents were removed. Common bile duct stones were also successfully removed in 6 patients. EGD showed all the fistula closed completely after 3 days. The ultrasound examination of the gallbladder 4 weeks later showed no stones remaining and also showed satisfactory functioning of the gallbladder. The mean follow-up period was 11 months (range: 1–27months). Cholesterol gallstones recurrence were not detected in any patient during follow-up.

Conclusion: The EUS-guided placement of a novel metal stent with hot stent delivery is a safe and simple approach for performing an endoscopic cholecystostudodenotomy, which can subsequently allow procedures to be performed for treating biliary disease, including cholecystolithotomy.

Disclosure of Interest: All authors have declared no conflicts of interest.

References


P0904 QUANTITATIVE ENDOSCOPIC ULTRASOUND ELASTOGRAPHY IN THE DIFFERENTIAL DIAGNOSIS OF PANCREATIC SOLID TUMORS H. Ribeiro1, C. Leita2, J. Pinto2, R. Azevedo1, F. Pereira1, R. Sousa1, A.L.L. Pires Caldeira3, E. Pereira1, A. Banduoso1 1Gastroenterology, Amato Lusitano Hospital, Castelo Branco/Portugal 2Gastroenterology, Unidade Local de Saúde de Castelo Branco, Castelo Branco/Portugal

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Introduction: Quantitative second generation endoscopic ultrasound (EUS) elastography allows the quantitative analysis of tissue stiffness and can be a useful auxiliary tool in the differential diagnosis of pancreatic solid tumors (1)(2).

Aims & Methods: The aim of this study was to evaluate the accuracy of the quantitative EUS elastography in the differential diagnosis of pancreatic solid masses, discriminating malignant from benign masses, using strain ratio (SR) analysis. A prospective study was performed for 15 months and included 29 consecutive patients who underwent EUS for the evaluation of solid pancreatic masses. EUS elastography was performed by 2 operators, using a linear echoendoscope. The mean of 3 measures was considered as the SR final result for each lesion. EUS-fine-needle aspiration of the lesions was performed after SR assessment and the final diagnosis was based on the cytology or histology results. Accuracy of the elastography was obtained by the analysis of ROC curves.

Results: Included 29 patients in a total of 30 lesions with conclusive histological/cytologic diagnosis (8 inflammatory masses, 19 adenocarcinomas, 2 neuroendocrine tumors and 1 undifferentiated carcinoma). The mean SR value was significantly higher in the malignant tumors comparing with the benign tumors (55.56 vs 23.93, p=0.001). The sensitivity and specificity of SR for differentiation of pancreatic malignancy for a cut of 15.89 were, respectively, 95.45% and 87.5% (area under the curve of 0.89, 95% CI). The overall accuracy of the EUS elastography using the SR for the detection of pancreatic malignancy was 93%.

Conclusion: Quantitative EUS elastography presents good accuracy in the differentiation between malignant and benign pancreatic masses. It is a promising EUS technique in the diagnostic approach of solid pancreatic lesions, which may complement the study and characterization of the tumors, aiding in the diagnosis and follow-up of these patients.

Disclosure of Interest: All authors have declared no conflicts of interest.
**P0906 COMPARISON OF DIAGNOSTIC PERFORMANCES FOR THE EVALUATION OF SUSPECTED MALIGNANT BILIARY STRICTURE AMONG SOME SIMILAR SESSION EUS-AND ERCP-GUIDED TISSUE SAMPLING**

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**Introduction:** Determining the cause of suspected biliary strictures is always a difficult problem in clinical practice. Although EUS-guided tissue sampling (EUS-TS) revealed a better diagnostic yield in suspected malignant biliary obstructive lesions compared to ERCP-guided tissue sampling (ERC-P-TS), there was few studies for which techniques are better dependent on primary tumor. Aim of our study is to compare the diagnostic yields between EUS-TS and ERC-P-TS in patients with suspected malignant biliary obstructive lesion according to primary tumor sites. By reviewing medical records, we enrolled patients who underwent same-session examination of EUS and ERC-P for the evaluation of suspected pancreatobiliary obstructive lesion.

For cytopathologic diagnosis, endoscopic ultrasound-guided fine needle aspiration (EUS-FNA) or biopsy (EUS-FNB) and ERC-P-TS using brush cytology and/or forceps biopsy were performed. The diagnostic performances were compared between two techniques according to primary tumor sites.

**Results:** From January 2011 to September 2016, we enrolled 125 patients and 32 patients were excluded due to the following reasons: loss of follow up in 8, ERC-P-TS of pancreatic duct in 23, and ERC-P-TS from peripancreatic biopsy in 4. Among the enrolled patients (93 patients; 62 males, mean age 65.8 years, 86 (92.5%) had malignant tumor such as cholangiocarcinoma in 39, pancreatic cancer in 37, and other malignant tumors in 10 patients. And 7 (7.5%) patients had benign lesion. EUS-TS revealed higher rate of overall diagnostic accuracy comparing to ERC-P-TS (82.8% vs. 60.2%, p = 0.001). Depending on primary lesions, the diagnostic accuracy for pancreatic lesions was statistically higher in EUS-TS than ERC-P-TS (84.4% vs. 51.1%, p = 0.003). Conclusion: EUS-TS is superior to ERC-P-TS for the evaluation of suspected malignant pancreatobiliary obstructive lesions. Especially, if the biliary obstruction was caused by pancreatic cancers, EUS-TS would need to be a priority for cytopathologic diagnosis.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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**P0907 PREVALENCE OF POSTERIOR MEDIASTINAL LYMPHADENOPATHIES IN PATIENTS UNDERGOING ENDOSCOPIC ULTRASOUND-INDUCED MALIGNANT INDICATIONS: A PORTUGUESE SINGLE-CENTRE PROSPECTIVE STUDY**

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**Introduction:** Significant heterogeneity in geographic distribution in the prevalence of mediastinal lymphadenopathies have been documented in CT studies. Awareness of the geographic prevalence and characteristics of lymphadenopathies will be relevant when performing endoscopic ultrasonography (EUS) for malignant neoplasia. EUS is considered the gold standard method for the evaluation of suspected malignant lymphadenopathy and frequently follow-up. Endoscopic ultrasound with fine-needle aspiration is the most accurate diagnostic method in these lesions. The role of repeated EUS-FNA with cystic fluid analysis in follow-up of PCNs is not clear.

**Aims & Methods:** 1. To document the prevalence and characteristics of mediastinal lymphadenopathies in patients submitted to EUS for non-malignant extra-thoracic disease. 2. To identify predictive factors for the presence of mediastinal lymphadenopathies. A prospective, unicentric study was performed between July and December 2016. Mediastinal stations 9, 8, 7, 6, 5, 4L and 2 were systematically evaluated using a linear echoendoscope in all patients undergoing EUS due to benign extra-thoracic pathology, without history of oncologic disease. Demographic, clinical and EUS features were analysed, including location, number, shape, dimensions and echogenicity of the lymphadenopathies.

**Results:** We analysed 75 patients: M/F; 32/43; Mean age; 63. The majority (72%) of the patients presented lymphadenopathies in at least one mediastinal station and 59% in 2 or 4L. Only 6% of these had short axis diameter >10 mm, most were oval (59%) or triangular (37%) and 40% had a hyperechogenic center. The prevalence of lymphadenopathies was higher in smoker patients (83% vs 64%, p=0.024), with a higher average number of lymphadenopathies per patient in this group (2.1 vs 1.6; p=0.017). Similar findings were documented in patients with relevant occlusational or environmental respiratory exposure (prevalence 83% vs 71%; average number 3 vs 1.7). By logistic regression analysis, none of the variables addressed was associated with the presence of mediastinal lymphadenopathies.

**Conclusion:** This prospective Portuguese study documented a higher prevalence of mediastinal lymphadenopathies than previously reported in northern Europe, in smokers and in patients with relevant occupational exposure, may negatively influence the specificity and positive predictive value for malignancy of mediastinal lymph node (N) staging by EUS, with particular relevance in esophageal and pulmonary cancer staging.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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**P0908 ACCURACY OF ENDOSCOPIC ULTRASOUND IN GASTRIC ADENOCARCINOMA PATIENT SELECTION FOR NEOADJUVANT THERAPY**

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**Introduction:** Recent studies demonstrated the positive impact of neoadjuvant treatment for gastric adenocarcinoma T ≥ 2 and/or N+. Aims & Methods: We aimed to assess the accuracy of endoscopic ultrasound in the selection of patients with gastric adenocarcinoma for neoadjuvant therapy. A unicentric retrospective analysis of patients with the anatomicopathological diagnosis of gastric adenocarcinoma between 2011 and 2016, who performed endoscopic ultrasound for staging and underwent surgery without prior neoadjuvant treatment. The concordance (kappa) and accuracy [sensitivity (S) and specificity (E)] of the endoscopic ultrasound for T ≥ 2 and/or N + (criteria for neoadjuvant treatment) were assessed using the anatomicopathological staging of the resected surgical specimen.

**Results:** The final sample included 144 patients (64.6% male) with a median age of 68.5 ± 12.2 years. In most cases (80.6%), the neoplasia was distal (antrum, incisura angularis and body). The neoplasia was of the intestinal type, diffuse and mixed in 63.5%, 18.8% and 16% of the cases, respectively. After examination of the resected surgical specimen, 53.5% of patients had criteria for neoadjuvant treatment (T ≥ 2 and/or N+). The overall kappa, specificity and sensitivity of the endoscopic ultrasound for T ≥ 2 and/or N + were 0.720 (p < 0.001), 85.2% (95% CI: 75.6-92.1%) and 87.3% (95% CI: 76.5-94.4%), respectively. The overall kappa, sensitivity and specificity of the endoscopic ultrasound for T ≥ 2 and/or N + were higher in proximal lesions (cardia and JEG) (k = 0.924, 94.4% and E-100%) compared with distal lesions (k = 0.671, 82.5% and E-84.9%) and in intestinal type lesions (k = 0.765, 84.9% and E-92.7%) compared with diffuse type lesions (k = 0.682, 88.4% and E-80%) or mixed (k = 0.566, 81.8% and E-75%).

**Conclusion:** In one of the largest series of patients, we showed that endoscopic ultrasound was an overall high agreement and accuracy in the selection of gastric adenocarcinoma patients for neoadjuvant therapy, although they higher for proximal and intestinal lesions.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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**P0909 IS IT USEFULL TO REPEAT ENDOSCOPIC ULTRASOUND WITH FINE NEEDLE ASPIRATION OF PANCREATIC CYSTIC LESIONS? A RETROSPECTIVE STUDY**

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**Introduction:** Pancreatic cystic neoplasms (PCNs) require initial imaging characterization and frequently follow-up. Endoscopic ultrasound with fine-needle aspiration (EUS-FNA) for CEA measurement and cytology of cystic fluid is the most accurate diagnostic method in these lesions. The role of repeated EUS-FNA with cystic fluid analysis in follow-up of PCNs is not clear.

**Aims & Methods:** To determine if patients with pancreatic cysts with a second repeated EUS-FNA for cystic fluid analysis for CEA and cytology had a change in cyst classification or on clinical decision. Retrospective analysis of a EUS FNA database, with 284 patients who had EUS-FNA for pancreatic cyst evaluation from 2007–16, of which 35 had 2 EUS procedures, and of these, 22 had 2 consecutive EUS-FNA procedures.

**Disclosure of Interest:** All authors have declared no conflicts of interest.
Aims & Methods: We enrolled in the study all the patients who underwent and avoid unnecessary surgery. Recently intracystic fluid glucose has been proposed as a pancreatic cyst marker. Some pancreatic cysts still remain challenging. There has been an increasing interest in non-mucinous cysts (7.7 mg/dl vs 95.7 mg/dl, p < 0.0001). In the diagnosis of cystic pancreatic neoplasms, mucinous cystadenomas; 12 intraductal papillary mucinous neoplasms (SCN) in five cases, mass-forming pancreatic cysts in four cases, and autoimmune pancreatitis (AIP) in 40 cases. Just after EUS-FNA, tissue sample in the FNA needle was flushed out into petri dish with saline. The specimen was carefully examined to ensure diagnostic criteria were met. Histology was assessed using formalin-fixed and processed for pathological evaluation. All residual liquid specimen in whole was immediately immersed in liquid-based fixation medium (CytoRichTM Red) at the bedside. The liquid was centrifuged and processed for LBC in pancreatic cell samples obtained by EUS-FNA. Sufficient material rate of cytology was retrospectively evaluated in all cases, and diagnostic yield between cytology and histology in patients with malignant diseases was compared. In addition, availability of immunohistochemistry (IHC) and ICC was assessed retrospectively.

Results: Sufficient material rate in cytological evaluation was 96.6% in all enrolled specimens (282/292). 10 insufficient materials were obtained from PC in 4 cases, and AIP in 3. In the diagnostic cytology between the two groups. The mean time between the two EUS-FNA procedures was significantly shorter in the surgical patients group. Diagnostic cytology was not confirmed using rapid onsite evaluation. Accuracy of cytology, histology, and combination of cytology and histology were 84.4%, 72.9%, and 90.0%, respectively. In the study of samples with mucinous cystic neoplasms, sufficient material rate of cytology and histology were 99.1% (223/225) and 98.3% (201/205). Positive predictive values of cytology and histology were 81.7% (184/225) and 67.6% (152/225). 65.8% (48/73) of pathologically non-diagnosed cases could be diagnosed as malignant cystic neoplasms. In 26 specimens where IHC was needed, IHC was available in 23 of the 26 specimens (88.5%) and ICC was available in all specimens. In the three specimens, ICC was not available owing to pathological insufficiency. Cytology in pancreatic cystic lesions obtained by EUS-FNA may be useful for reducing insufficient material rate and conducting ICC as well as in samples in other medical fields.

Disclosure of Interest: All authors have declared no conflicts of interest.

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Disclosure of Interest: All authors have declared no conflicts of interest.

References
Conventional EUS-guided fiducial placement requires back-loading each fiducial through the tip of the FNA needle. Thus, delivery of multiple fiducials can be cumbersome and time-consuming.

Aims & Methods: We aimed to evaluate the feasibility, safety, and performance characteristics of fiducial deployment in PC patients using a novel exchangeable FNA system with pre-loaded 22-gauge EUS fiducial needles. This was a single-center pilot study of 10 consecutive PC patients undergoing EUS-guided fiducial placement for SBRT. The fiducial delivery system contains a 22-gauge EUS needle pre-loaded with 2 gold markers with knurled design. After the 2 markers were deployed, the EUS fiducial needle insert was exchanged out for a second pre-loaded EUS fiducial needle insert through the exchangeable FNA system for total deployment of 4 markers in each patient. All patients underwent CT after fiducial placement as part of SBRT to evaluate successful deployment and complications. The primary endpoint was procedure success, defined as deployment of at least 3 fiducials into the desired target area. Secondary endpoints were total procedure time, fiducial delivery time, and safety.

Results: Fiducial placement was attempted in 10 consecutive patients with PC (mean age 61.7 years, males 60%). The tumor was located in the head (n = 6), neck (n = 2), and the body (n = 2) of the pancreas. Mean size of the tumor was 2.7 cm (range 1.6–5.3). Procedure success was achieved in all 10 (100%) patients. All 10 patients successfully received fiducials. Mean total procedure time was 12.2 minutes (range 5–18). By comparison, using historic controls of the first 10 patients who underwent conventional EUS-guided fiducial placement, the mean total procedure time was 26 minutes (range 16–44, p < 0.002). Mean fiducial delivery time was 4.2 minutes (range 1–8). There were no immediate or delayed (7 days) complications.

Conclusion: EUS-guided fiducial placement with a novel exchangeable FNA system and pre-loaded 22-gauge EUS fiducial needle is quick, technically feasible and safe. This system may theoretically decrease the risk to the clinical staff by eliminating the need for back-loading fiducials through exposed needle tip and handling of potentially dirty needles. Given the potential safety and time advantages, further prospective studies are warranted for validation.

Disclosure of Interest: E. Shin: Consultant, C2 Therapeutics No conflict of interest relevant to the abstract.
M.A. Kashab: Consultant, Boston Scientific No conflict of interest relevant to the abstract.
M.I. Canto: No conflict of interest relevant to the abstract.
All other authors have declared no conflicts of interest.

P0918 AGE AND GASTRIC EMPTYING TIME ARE PREDICTIVE FACTORS FOR INCOMPLETE CAPSULE ENDOSCOPY: RESULTS OF A MULTIVARIATE ANALYSIS IN A LARGE STUDY POPULATION

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Introduction: Capsule endoscopy has been demonstrated to be a first-line tool for small bowel visualization. However, it has some limitations such as incomplete examinations - i.e. the capsule does not reach the cecum - leading to missing lesions.

Aims & Methods: To evaluate those factors that can predict incomplete examinations, to identify those patients at risk for incomplete procedures and to define those approaches that may improve the efficiency of the examination reducing the time of the diagnostic process as well as the need to repeat procedures. A total of 1918 patients who underwent capsule enteroscopy at our center between 2008 and 2015 were retrospectively analyzed. We evaluated variables such as age, sex, anthropometric parameters, comorbidity, drugs, outpatient care, analytical parameters, indication of the test and transit times. Initially, a univariate analysis and then, a multivariate analysis using a logistic regression model were carried out.

Results: In the univariate analysis, the following variables showed a statistically significant association with the rate of incomplete examinations: age, gender, indication of procedure, outpatient care, history of abdominal surgery, heart disease, capsule ingestion posture, hematoglobin levels, renal failure and both gastric and small bowel transit times. These variables were included in the multivariate analysis and less than 286 minutes (OR = 1.78, 95% CI: 1.72–3.93) and small bowel transit time > than 286 minutes (OR = 3.52 95% CI: 2.26–5.48) showed a statistically significant association with the risk of incomplete examination.

Conclusion: Complete capsule endoscopy is predictable. Patients older than 65 years and/or a gastric emptying time greater than 42 minutes are independent predictive factors for incomplete procedures. In these clinical scenarios, pharmacological preventive measures or endoscopic introduction should be taken into account to avoid incomplete examinations.

Disclosure of Interest: All authors have declared no conflicts of interest.

A482 United European Gastroenterology Journal 5 (S1)

Abstract: P0917

P0917 DEVELOPMENT AND VALIDATION OF A HIGHLY SENSITIVE AND SPECIFIC AUTOMATED ALGORITHM TO EVALUATE THE ABUNDANCE OF BUBBLES IN SMALL BOWEL CAPSULE ENDOSCOPY

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Introduction: Bubbles can impair the visualization of the small bowel (SB) mucosa during capsule endoscopy (CE).

Aims & Methods: Our aim was to develop and to validate a computed algorithm, with the purpose to evaluate the abundance of bubbles in SB-CE. Two sets of 200 SB-CE normal still frames were extracted from 45 complete third-generation SB-CE videos. Two experienced SB-CE readers analyzed both sets of images twice, in a random order. Each still frame was categorized as "scarce in" or "abundant in" bubbles (random order. Each still frame was categorized as "scarce in" or "abundant in" bubbles). Two experienced SB-CE readers analyzed both sets of images twice, in a random order. Each still frame was categorized as "scarce in" or "abundant in" bubbles. Two sets of 200 SB-CE normal still frames were extracted from 45 complete third-generation SB-CE videos.

Validation step
Algorithm 1: GLCM 94.38 93.58 95.32 92.31 0.9852 0.040
Algorithm 2: Fractal dimension 84.27 82.57 86.54 79.78 0.9269 10.1
Algorithm 3: SURF 94.74 94.23 95.15 93.75 1.45
Algorithm 4: SURF 94.74 94.23 95.15 93.75 1.45

Conclusion: GLCM detector strategy had the best diagnostic capabilities, with Se and Sp over 90%) and a perfect reproducibility (coefficient), sensitivity (Se), specificity (Sp), Receiver operating characteristic (AUROCC) of four algorithms for evaluation of bubble abundance in small bowel capsule endoscopy still frames (development step).

Disclosure of Interest: X. Dray: Xavier Dray has received consultation fees from Covidien GI solutions All other authors have declared no conflicts of interest.

P0919 A NOVEL CAPSULE TECHNOLOGY PLATFORM FOR SPECIFIC LOCALIZED COLON DRUG DELIVERY

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2Rambam Health Care Campus, Haifa/Israel
3Borow Medical Center, Bnei Shearim/Israel
Poor cases had significantly lower CCE sensitivity compared with fair, good and excellent cases, for 6 mm polyps (P-value = 0.007). When stratifying cases based on the current adequacy cutoff, sensitivity for 6mm polyps was considered a match, if the size measured by the capsule (≥50%) range overlapped the size measured by the colonoscopy (≥50%) range, and polyp location estimates by the 2 methods were in the same or adjacent segments[2]. Results: The mean age of the analyzed cohort was 57.1 (SD 5.8) with 342 males (44.6%).

Conclusion: This analysis indicates, that when utilizing 4 liter PEG and oral suflate solutions for CCE procedure preparation, current cleansing assessment scale and methodology may need to be re-evaluated - to better correlate with polyp detection. Currently, “fair” cleansing may not indicate inadequate cleansing for polyp detection.

Disclosure of Interest: S. Perek: Employee of Medtronic
S. Farkash: Employee of Medtronic
N. Schwartz: Employee of Medtronic

References

P0921 COLON CAPSULE ENDOSCOPY MAY REDUCE COLONOSCOPY MISS RATE – A MULTICENTER STUDY
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Introduction: Colonoscopy miss rate is an area of intense focus, as it directly correlates with colorectal cancer incidence rate. Previous studies reported a colonoscopy miss rate of 2%–22%, depending on polyp size and histology [1]. Colon Capsule Endoscopy (CCE) is a visualization diagnostic modality of the colon mucosa, which has demonstrated high sensitivity for polyps and adenomas [2]. Determining the nature of polyps detected by CCE but missed by the imperfect gold standard (colonoscopy), may facilitate both optimization of CCE application (potential CCE additive value) and increase colonoscopy polyp detection.

Aims & Methods: Characterize polyps detected by CCE, which were missed by colonoscopy. 695 screening population participants, from 17 sites in the United States and Israel, underwent CCE procedure followed by a blinded colonoscopy. The overall colonoscopy adenoma detection rate in this study was very high – 39% [2]. Following the blinded colonoscopy, the patient’s CCE report was assessed. Based on the findings in this report, the colonoscopy performing physician decided whether or not to immediately follow up with a second colonoscopy. 70 of the CCE findings were detected by the second colonoscopy. These 70 polyps were compared with 683 polyps detected by blinded colonoscopy, using logistic regression model. Adjusted Odds Ratios (Adj.OR) and corresponding Confidence Intervals (CI) were estimated.

Results: Of the 70 polyps missed by first colonoscopy and detected by second colonoscopy, 20 (29%) were 6mm or larger (based on colonoscopy size estimation). 19 (27%) were either adenomatous or sessile serrated lesions and 16 (23%) were described as either flat or sessile-flat by colonoscopy performing physician. Stratification of polyps based on location:

<table>
<thead>
<tr>
<th>Detected by blinded colonoscopy (n = 683)</th>
<th>Detected after CCE and unblinding (n = 70)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cescum</td>
<td>64 (84%)</td>
</tr>
<tr>
<td>Ascending</td>
<td>181 (94%)</td>
</tr>
<tr>
<td>Transverse</td>
<td>98 (46%)</td>
</tr>
<tr>
<td>Descending-Sigma</td>
<td>243 (90%)</td>
</tr>
<tr>
<td>Rctum</td>
<td>97 (85%)</td>
</tr>
</tbody>
</table>

Colon cleansing

<table>
<thead>
<tr>
<th>Sensitivity (≥6 mm); n = 272</th>
<th>Specificity (≥6 mm); n = 495</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adequate cleansing</td>
<td></td>
</tr>
<tr>
<td>153/195 = 78.5% (72.2%–83.7%)</td>
<td>308/350 = 88.0% (84.2%–91.0%)</td>
</tr>
<tr>
<td>Inadequate cleansing</td>
<td></td>
</tr>
<tr>
<td>54/77 = 70.1% (59.1%–79.2%)</td>
<td>130/145 = 89.7% (83.5%–93.7%)</td>
</tr>
<tr>
<td>P-value</td>
<td>0.147</td>
</tr>
<tr>
<td>Poor cleansing</td>
<td>3/9 = 33.3% (11.7%–64.9%)</td>
</tr>
<tr>
<td>15/16 = 93.8% (69.7%–100%)</td>
<td></td>
</tr>
<tr>
<td>P-value</td>
<td>0.007</td>
</tr>
<tr>
<td>Fair, good and excellent</td>
<td>204/263 = 77.6% (72.1%–82.2%)</td>
</tr>
<tr>
<td>423/479 = 88.3% (85.1%–90.9%)</td>
<td></td>
</tr>
</tbody>
</table>

Poor cases had significantly lower CCE sensitivity compared with fair, good and excellent cases, for 6 mm polyps (P-value = 0.007). When stratifying cases based on the current adequacy cutoff, sensitivity for 6mm polyps is similar in inadequate (“poor” + “fair”) cases compared to adequate (“good” + “excellent”) cases (70.1%, 78.5% respectively; P-value = 0.147).
Multivariate logistic regression revealed that after adjusting to polyph’s size, cecal and rectal segments were associated with increased chance of CCE additive value to colonooscopy (cecum vs. ascending or transverse colon: Adj.OR = 3.2 [95% CI: 1.3–7.6] and Adj.OR = 4.3 [95% CI: 1.4–14.6] respectively; rectum vs. ascending or transverse colon: Adj.OR = 2.6 [1.1–5.8] and Adj.OR = 3.6 [95% CI: 1.2–11.4] respectively). There were 59 patients (8.49% of study population), with at least one CCE additive value to colonooscopy event.

Conclusion: CCE has the ability to detect polyps missed by traditional colonooscopy, especially lesions in the cecum and rectum.

Disclosure of Interest: S. Perek: Employee of Medtronic N. Schwarz: Employee of Medtronic

References
Conclusion: Among the three types of stents, the 7Fr soft tip was suitable for ECPC. The ideal stent in the phantom and animal models was the fully covered self-expandable metallic stent (cSEMS). The ideal stent needs to be technically feasible and safe for EUS-BD and possibly reduce adverse events.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

Disclosure of Interest: All authors have declared no conflicts of interest.
Aims & Methods: We examined six type II perforations associated with ERCP. We retrospectively evaluated the clinical findings, the length of hospital stay, the need for surgery and death.

Results: Of the 3250 ERCP procedures performed from March 2010 to November 2016, only six (0.18%) resulted in perforations (male/female, 2/4; median age: 69 years; age range: 54–80 years). ERCP procedures were performed with carbon dioxide insufflation. Five patients underwent ERCP for biliary stenosis due to pancreatic or duodenal strictures and one patient was being evaluated for clinical. Successful closure of persistent sphincterotomy-related duodenal perforation using FCSEMS was obtained in all patients. One patient developed ERCP-related pancreatitis, successfully treated with medical therapy. Three FCSEMS were successfully removed after a median of 18 days, the remaining three fell out spontaneously. The median length of hospital stay was 8.5 days (range 4–20 days). There were no deaths or need for surgery.

Conclusion: The placement of FCSEMS is easy, safe and quick. In our cohort of patients, FCSEMS is the effective endoscopic approach for management of type II perforations recognized during ERCP.

Disclosure of Interest: All authors have declared no conflicts of interest.

References:

P0929 EFFICACY AND ONCOLOGIC SAFETY OF ENDOSCOPIC DUODENAL STENTING IN PATIENTS WITH ADVANCED PANCREATIC CANCER
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Introduction: Duodenal obstruction is often seen in patients with advanced pancreatic cancer. Endoscopic duodenal stenting (DS) has become increasingly popular due to its less invasiveness compared with surgical gastrojejunostomy. With recent new advances in chemotheray and radiation therapy, conversion surgery after neoadjuvant therapy are performed in some cases with APC.

Aims & Methods: To evaluate the efficacy and safety of DS as palliative treatment and bridge to surgery in patients with APC. We retrospectively analyzed patients who received DS placement between March 2012 and March 2017. Twenty-three patients (11 men/12 women median age, 65.6; 46–82 years) with APC. GOO scoring system (GOOSS) was used as an index of clinical success.

Results: A total of 23 Patients consisting of 6 patients treated with chemotherapy and 11 patients treated with neoadjuvant chemoradiotherapy were included in this study. Obscrted parts of the duodenum were D1 in 2, D2 in 5, D3 in 12, and D4 in 5 patients. Technical success of DS was achieved for all patients. The mean GOOSS before DS and after DS were 0.5 and 2.6 respectively (p < 0.001). The median time to restart solid meal after DS was 2.9 days. Biliary obstruction was seen in 13 patients and managed with endoscopic biliary stenting. Adverse events occurred in 6 patients, including 1 with cholangitis, 1 with bleeding and 3 with stent occlusion. The intervention technical and clinical success rates were 100% (5/5) and 80% (4/5), respectively. The median survival time after DS was 159 days. In neoadjuvant chemoradiotherapy patients, 4 patients were performed surgery for APC.

Conclusion: DS in patients with APC was effective and safe. The findings of this study suggest that DS is worth considering as the bridge to surgery in patients receiving neoadjuvant therapy.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0930 CLINICAL FAILURE IN COLONIC STENTING FOR MALIGNANT LARGE BOWEL OBSTRUCTION: OUTCOMES AND RISK FACTORS IN 172 PROCEDURES
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Introduction: Endoscopic stenting with self-expandable metallic stents (SEMS) has become widely accepted for an alternative to emergency surgery in the management of malignant large bowel obstruction (LBO) after the initial introduction of SEMS in 1991. Recent years, advance in procedural equipment and accumulation of experience have improved technical success rate in colonic stenting for malignant LBO. However, there is still a divergence in the success rate of SEMS.

Aims & Methods: The aim of this study is to clarify the factors that reduce clinical success rate of stent placement. This study was conducted by a retrospective chart review at a single center. The endoscopy database and clinical records from the University of Tokyo Hospital, Tokyo, Japan, were reviewed retrospectively between May 2007 and February 2017. Patient’s symptoms, characteristics, clinical data were obtained from electronic medical record. The obstructions were diagnosed clinically and radiologically and were evaluated by the colorectal surgeons. The Clinical and Endoscopic Scoring System (CROSS) was used for the assessment of clinical success. The technical success was defined as deployment of a stent across the entire length of the stricture on the first attempt. Clinical success was defined as resolution of symptoms and radiological relief of the obstruction within 24 hours, as confirmed by radiographic observations.

Results: A total of 172 patients (91 males, 81 females; mean age 68 years) underwent colorectal stenting for malignant LBO. This procedure was performed to 80 colorectal cancer (CRC) patients (48%) and to 92 patients (52%) with cancer of other etiology. Stenting was performed as a bridge to surgery (BTS) therapy in 33 patients (19.2%), whereas stenting was planned palliative. Technical and clinical success rate was 98.8% and 89.5%, respectively. Clinical success rate dropped from 98.9% (91/92) to 78.8% (71/90) when the patient had obstruction of distal colon or rectum vs in 139 patients (80.8%). Sixty-seven patients (39%) had a tumor causing obstruction in the proximal colon, and 105 patients (61.0%) in the distal colon or rectum. The mean length of obstruction was 6 cm, and obstruction of 60 patients (34.9%) longer than 6 cm. The clinical and technical success rate was 98.3% and 89.5%, respectively. Clinical success rate dropped from 98.9% (91/92) to 78.8% (63/80) when the obstruction caused by extra-colonic malignancy (ECM) (p < 0.05). The clinical success rate of colonic stenting was 85.7% (90/105) and 95.5% (64/67) (p < 0.05) when the patient had obstruction of distal colon or rectum vs in proximal colon. In multivaria analysis, placement in distal colon or rectum, obstruction by ECM, and obstruction longer than 6 cm were independent risk factors associated with lower clinical success rate (odds ratio [OR] 3.19; 95% CI 0.96–10.6, [OR] 24.5; 95% CI 3.19–189.3, [OR] 31.7; 95% CI 3.22–223.7).

Conclusion: The placement of SEMS for malignant LBO is safe and effective, but clinical success rate drops in the cases with obstructions of distal colon or rectum, longer than 6 cm, or caused by ECM. Considering the indication of colonic stenting for malignant LBO, these factors should be evaluated before procedure.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0931 THE CLINICAL Efficacy OF MITOMYCIN-C injection Therapy in Refractory benign esophageal Stenosis: A Preliminary Study
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Introduction: Refractory Esophageal Stenosis (RES) definition differs among studies. Unresolved benign esophageal stenosis even after 5 or more sessions of endoscopic dilation therapy in most studies. Until now, there have been no treatment showing the satisfactory results. Mitomycin C (MMC) inhibits DNA synthesis reduces fibroelastic collagen formation. Tried in RES in several studies. The meta-analysis about treatment of refractory gastrointestinal stenosis with MMC in total 24 studies. The most commonly reported site esophagus (79%). Only 9 recruited adult patients (n = 98). Of these, 23 patients were RES.
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OF COMPLETE AND PARTIAL LOWER GI ANASTOMOSIS

P0932 TREATMENT WITH MULTIPLE REABSORBABLE STENTS

1 colorectal surgery. Colostomy or ileostomy and later redo anastomosis or Hartmann’s procedure are the mainstay of therapy, but edema and inflammation (median 6.7 months). Presence of adhesions can prevent adequate management, and therefore alternative salvage repair methods may be required. Reabsorbable polydioxanone stents are a proposed method but with still debatable results in terms of correct placement, clinical success, early and late stenosis, stent migration, perforation, bleeding, fecal incontinence and local pain.

Aims & Methods: We report here on the use of reabsorbable polydioxanone stents (RPS) in colorectal anastomotic stenosis or dehiscence. We treated with RPS placement, endoscopic dilation and daily mesalazine enemas and/or suppos-

Table 1: Outcomes of MMC injection therapy

<table>
<thead>
<tr>
<th>Variables</th>
<th>values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of Bougie dilation before MMC injection</td>
<td>5/6/7/8/9</td>
</tr>
<tr>
<td>The number of session of MMC injection 1/2</td>
<td>3/5</td>
</tr>
<tr>
<td>Mean GOO score before MMC injection</td>
<td>2.5</td>
</tr>
<tr>
<td>Mean score of GOOSS after final MMC injection</td>
<td>0.29</td>
</tr>
<tr>
<td>Mean diameter of stenosis before MMC injection, mm</td>
<td>5.2</td>
</tr>
<tr>
<td>Mean diameter of stenosis 3 month after final MMC injection, mm</td>
<td>8.9</td>
</tr>
<tr>
<td>Clinical success rate (%)</td>
<td>87.5</td>
</tr>
<tr>
<td>Complications (N, %) perforation bleeding requiring transusion of other interventions others</td>
<td>0(0) 0(0) 0(0)</td>
</tr>
</tbody>
</table>

Conclusion: In our study, the mitomycin injection therapy was effective in patients who had retractable benign esophageal stenosis. The mitomycin injection therapy could be considered as an alternative for retractive benign esophageal stenosis. A large-scale prospective studies are required in future.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P0933 EVALUATION OF FACTORS ASSOCIATED TO A SUCCESSFUL DILATION IN POST-ESD STRICTURES

E. Perez-Cuadrado-Robles1, H. Pieseux2, T. Moreels1, R.C.P. Yeung1, E. Dancé2, P.H. Deprez1

Aims & Methods: We report here on the use of reabsorbable polydioxanone stents (RPS) in colorectal anastomotic stenosis or dehiscence. We treated with RPS placement, endoscopic dilation and daily mesalazine enemas and/or supp-

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Introduction: The prevalence of post-ESD esophageal strictures is non-negligible, with a critical impact on the patients’ quality of life. Balloon-dilation may be the first-line therapy. However, factors associated to a successful dilation in post-ESD strictures remain unclear.

Aims & Methods: This is an observational and analytical retrospective study. Sixty-eight consecutive patients (mean age: 65±11, 76.5% men) who underwent endoscopic dilation because of post-ESD symptomatic esophageal strictures between 2006 and 2016 were included. They had Barrett’s esophagus (n=46, 67.6%), epidermoid carcinoma (n=21, 30.9%) and other (n=1). Patients with a critical impact on the patients’ quality of life. Balloon-dilation may be the first-line therapy. However, factors associated to a successful dilation in post-ESD strictures remain unclear.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
P0934 EFFECTIVENESS OF REPEATED DILATIONS IN THE MANAGEMENT OF ESOPHAGEAL BENIGN STRICTURES

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Introduction: Refractory or recurrent esophageal benign strictures (REBS) are frequent, and defined as the impossibility to reach or maintain a diameter of 14 mm after 5 sessions of endoscopic dilation (ED). Because of a lack of guidelines, their management remains challenging, sometimes leading to radical surgical procedure.

Aims & Methods: The aim of this study was to define the efficacy of long-term and repeated ED in the management of REBS. This was a monocentric retrospective study involving patients managed in our tertiary center between January 2002 and April 2017 for REBS. All the endoscopic dilations were performed using Savary bougies or hydraulic balloons, depending on the operator’s choice. Demographical and clinical data were recorded for each patient. The endoscopic management was detailed with the number of procedures, the endoscopic device used, the diameter of dilation, and potential concomitant treatment (as self-expanding metal stent, steroid injection or incisional therapy). The primary endpoint was the efficacy of sustained and recurrent ED, defined as the absence of further dilation within 3 months of the last procedure or an interval between the 2 last ED greater than 3 months. A failure was considered in case of death, need for surgery, permanent enteral feeding tube or an interval between the last 2 procedures lower than 3 months. The secondary endpoints were to document the characteristics of dilation procedures and concomitant treatments, the decreasing of the number of dilations per trimester, and to elucidate potential predictive factors for success of ED.

Results: A total of 39 patients (23 men) with a mean age of 47.5 ± 20.7 years were included. The etiologies of strictures were anastomotic (46.1%), caustic (28.2%), peptic (10.3%) or other etiologies (radiation injuries, esophageal diverticuloty, severe viral esophagitis, 15.4%). A clinical success of repeated ED was achieved in 27 patients (69.2%). Twelve patients (30.8%) experienced failure, among them seven (17.9%) required frequent dilations, two (5.1%) underwent surgery, two (5.1%) maintained an enteral feeding tube, and one patient (2.6%) died consecutively to inhalation pneumonia. A mean of 9.4 ± 4.2 ED sessions were performed per patient, with a mean treatment duration of 22.6 ± 20.1 months. Regarding concomitant treatments, 16 patients (41%) had at least one fully-covered metallic stent implantation, incisional therapy was performed in 11 patients (28.2%), and 3 patients (7.7%) received corticosteroid injections. The number of dilations per trimester gradually decreased over time. No significant predictive factor of success was found, such as etiology of stricture or the use of concomitant treatment, particularly. Nevertheless, an greater number of dilations during the first trimester could promote the success of the management (3.2 ± 2.2 dilations in the success group vs 2.2 ± 0.8 in failure group, p = 0.056).

Conclusion: Repeated and maintained endoscopic dilations are effective (70%) in the management of REBS, regardless of the etiology of stricture. A prolonged management up to 2 years, and the initial rhythm of endoscopic procedures may favor the final success. A systematic schedule for ED would improve the efficacy of this management.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0935 EFFICACY AND SAFETY OF NEWLY DEVELOPED ENDOSCOPIC COLONIC STENTS WITH AN INCREASED EXPANDABLE FORCE: A RETROSPECTIVE COMPARISON WITH CONVENTIONAL COLONIC STENTS

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Introduction: Endoscopic stenting with self-expandable metallic stents (SEMSs) is a widely accepted procedure for treating malignant colonic obstruction. This procedure was covered by the National Health Insurance of Japan in January 2012, and the WallFlex colonic stent and Niti-S colonic stent can currently be used in Japan. In the previous study, we reported that the WallFlex colonic stent has more expanded force than the Niti-S colonic stent. On the other hand, the risk of stent-related perforation was lower when using the Niti-S stent due to its structure. Currently, we newly developed an SEMS (Niti-S structure, with 18-mm diameter with increased expanded force compared with the conventional type), which comprised the benefits of both WallFlex and Niti-S. In this study, we compared the efficacy and safety of the newly developed colonic stent with the conventional colonic stents.

Aims & Methods: This study aimed to compare the efficacy and safety of the newly developed colonic stent with the conventional colonic stents (the WallFlex colonic stent and the Niti-S colonic stent). Overall, 91 patients (96 lesions, male/female: 48/43, average age: 73.2 years) underwent endoscopic SEMS placement between November 2012 and March 2017 at Kure Medical Center and Chugoku Cancer Center. The WallFlex colonic stent was used in 36 patients (38 lesions: Group W), the Niti-S colonic stent in 51 patients (53 lesions: Group N), and the newly developed colonic stent in 5 patients (5 lesions: Group D). Stratified analysis of the clinical background, technical success rate, procedure time, clinical success rate, and complications was performed to compare Group W, Group N, and Group D.

Results: Endoscopic SEMS placement was attempted in 96 lesions as a bridge to surgery (BTS) in 52 lesions (54%) and as palliative therapy (PALT) in 44 lesions (46%). In Group W, SEMS was placed in 19 lesions (50%) as BTS and in 19 lesions (50%) as PALT; in Group N, SEMS was placed in 32 lesions (60%) as BTS and in 21 lesions (40%) as PALT; and in Group D, SEMS was placed in 1 lesion (20%) as BTS and in 4 lesions (80%) as PALT. The technical success rate was 100% in all groups. The overall clinical success rate was 93.7% (90/96): 89.5% (34/38) in Group W, 96.2% (51/53) in Group N, and 100% (5/5) in Group D. Complications within 7 days included abdominal pain (3/38, 8%), poor
expansion (1/38, 3%), and lever (1/38, 3%) in Group W and perforation due to overdistension (2/35, 6%) in Group N. In Group N after the surgery, the integrated stent-related perforations (4/38, 11%) and stent occlusion (1/38, 3%) in Group W and stent occlusion (2/35, 4%) in Group N. All 4 patients with stent-related perforations had undergone palliative stenting with the WallFlex colonic stent, and the stent-related perforation rate in Group W was significantly higher than that in Group N (P < 0.05). In Group D, there were no complications and no stent occlusion.

Conclusion: The technical and clinical success rates were extremely high in all groups. The details of the stent-related perforations were also retrieved. Multiple regression models were fitted to the data to test the association between potential predictors and preoperative lymphoma and lymphopenia on POD1 as parameters of immune suppression.

Results: The preoperative lymphocyte count was 1, 240/ml (IQR: 0.895–1.700) in the POEM group. The lymphocyte count on POD1 was 0.670/ml (IQR: 0.500–0.982), p < 0.001; on POD3, it was 0.800/ml (IQR: 0.580–1.070), p < 0.001; and on POD7, it was 0.825/ml (IQR: 0.550–1.180), p < 0.001. In a model that also included the interval between the end of neoadjuvant therapy and the esophagectomy, the number of surgical access (laparotomy, thoracotomy and cervicotomy) and the number of nodal metastasis, only the final dose of radiotherapy resulted to be an independent predictor of lymphocytes count on POD1.

Conclusion: Patients with esophageal and esophagogastric junction cancer present a significant postoperative immunosuppression that lasts at least for the first postoperative week. The total amount of radiation received by the mediastinum is the only predictor of the preoperative and postoperative lymphocyte count.

Disclosure of Interest: All authors have declared no conflicts of interest.
Aims & Methods: The aim of this review was to determine the optimum choice and the route of conduit after oesophagectomy in adults. PubMed, MEDLINE and the Cochrane Library (January 1985 to January 2017) were systematically searched for studies which reported outcomes of colonic interposition after oesophagectomy in adults. The primary outcome measure was overall morbidity and secondary outcome measure was operative mortality.

Results: Twenty-seven studies, involving 1849 patients (median age 60 years, 1177 males, 697 malignant disease) who underwent colonic interposition were analysed. The overall pooled morbidity rate of left vs. right colonic conduit was 9.6% [95% CI (6.24-12.87), p < 0.0001] vs. 16.5% [95% CI (11.07-22.02), p < 0.0001] respectively. The overall pooled mortality rate of left vs. right colonic conduit was 5.6% [95% CI (3.59-7.60), p < 0.0001] vs. 10.3% [95% CI (7.23-13.27), p < 0.0001] respectively. Retrosenal route placement was associated with the lowest overall pooled morbidity of 9.2% [95% CI (6.48-11.99), p < 0.0001], and lowest overall pooled mortality of 4.8% [95% CI (3.74-5.89), p < 0.0001]

Conclusion: Left colon is the conduit of choice for colonic interposition after oesophagectomy in adults and the retrosternal route should be favoured.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
CS group, 16 patients had unresectable disease (due to lack of remnant liver volume or hilar biliary area, or both) and 7 to three hepatic segments and 9 initially had unusable disease (progressive primary disease or suspicion of other distant metastasis); therefore, upfront chemotherapy was selected.

**Results:** The frequency of adverse prognostic factors tended to be higher in the CS and S groups (mean ± SD: 3.7 ± 1.7 and number of metastatic lymph nodes (4.2 ± 6.3 vs 2.7 ± 2.3). Nevertheless, overall survival (OS) in the CS and S groups since primary tumor resection was equivalent (3-year survival rate: 43.1% vs 54.1%, Log-rank P = 0.14) and much better than that in the C group (3-year survival rate: 40.2%). Although liver-limited relapse-free survival (RFS) since hepatectomy tended to be worse in the CS group than in the S group (3-year survival rate: 45.5% vs 62.7%, Log-rank P = 0.14), RFS after hepatectomy was equivalent in the C group and S group (3-year survival rate: 33.3% vs 21.6%, Log-rank P = 0.97). Early tumor shrinkage (ETS) was found to be a stronger prognostic factor for liver resection after chemotherapy than existing prognostic factors in univariate and multivariate analyses, and RFS was much better in patients with ETS than in those with non-ETS (3-year survival rate: 62.5% vs 77.5%, Log-rank P = 0.05).

**Conclusion:** OS and RFS in the CS group compared favorably with those in the S group despite the high frequency of poor prognostic factors; patients with ETS had a better prognosis after liver resection. Liver resection after chemotherapy revealed comparatively favorable prognosis in well-selected patients with cSCLM, and early responsiveness to chemotherapy was useful in determining the indication for liver resection in patients receiving chemotherapy for cSCLM.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**Reference**

**P0943 PERIOPERATIVE ADMINISTRATION OF BROAD SPECTRUM ANTIBIOTICS REDUCES THE INCIDENCE OF SURGICAL SITE INFECTION FOLLOWING PANCREATODUODENECTOMY**


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**Introduction:** Pancreatoduodenectomy (PD) is one of the operations associated with high risk of surgical site infection (SSI). The one of the reasons is said that SSI is associated with the preoperative biliary infection caused by preoperative examinations or drainage of biliary tract. In our clinical trial [1]; SSF after pancreatoduodenectomy could be decreased by using the perioperative selective antibiotics based on preoperative biliary culture. The bacteria cultured from SSI were Enterobacteriaceae such as Enterococcus and Enterobacter species with high frequency.

Recently, however, most of the patients who had planned to undergo PD received internal biliary drainage preoperatively. It means preoperative collection of the bile juice is hard for the patient with internal biliary drainage. In order to solve this problem, we compared the conventional perioperative prophylactic antibiotics (Cefmetazole: CMZ) and the broad-spectrum antibiotics covering the Enterobacteriaceae (Piperacillin/Tazobactam + Vancomycin: PIPC/TAZ + VCM), retrospectively. The aim of this study is to assess the impact of two types of perioperative antibiotics usage in patients undergoing PD.

**Aims & Methods:** Sixty-nine patients underwent PD at Hokkaido University Hospital (Japan) between April 2015 and March 2016, when prospective surgical site infection surveillance was performed. Thirty-eight patients were administered CMZ as perioperative prophylactic antibiotics from April 2015 to March 2016, and 31 were PIPC/TAZ + VCM from April 2016 to March 2017. CMZ was injected intravenously every three hours from the start of operation, and once after the operation. PIPC/TAZ was injected intravenously every three hours from the start of operation and twice three times on the next day after the operation, whereas CMZ was injected intravenously in the morning of operation (20 mg/kg) and just after the operation (15 mg/kg).

Comparison between CMZ group and PIPC/TAZ + VCM group was performed by chi-square test, Student t-test, unpaired t-test, nonparametric test and contingency coefficient, and each of them was performed in terms of case series of a single surgeon at three Japanese tertiary referral centers.

**Results:** There were no significant differences in clinical features and operative outcomes between the two groups. The patients with PIPC/TAZ + VCM received significantly shorter duration of postoperative antibiotics administration than the patients with CMZ (5.9 ± 8.5 vs. 13.0 ± 18.2 days; p = 0.048). Significantly lower incidence of SSI was revealed in patients with PIPC/TAZ + VCM (9/31(29.0%) vs. 3/16 patients in CMZ group) (p = 0.048). Especially, significantly lower incidence of incisional SSI was revealed in patients with PIPC/TAZ + VCM (23/316.5%) than in those with CMZ (14/38(36.8%) (p = 0.004). The redneck syndrome as one of the side effects of CMZ was observed in 5/31 patients (16.1%). No multifocal recurrence of bacteria were identified. The occurrence of multifocal recurrence of bacteria were investigated, as well.

**Conclusion:** The broad-spectrum perioperative antibiotics covering Enterobacteriaceae such as Enterococcus and Enterobacter species could decrease the incidence of SSI and duration of postoperative antibiotics administration compared to CMZ. More strict indication to select the patients who should be administered VCM, because the occurrence of side effects of VCM was relatively high.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**Reference**

**P0944 PARADIGM SHIFT? SHOULD A LYMPHADENECTOMY ROUTINELY BE PERFORMED ALSO AMONG GALLBLADDER CANCER PATIENTS WITH T1A DISEASE?**

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**Introduction:** Gallbladder cancer is the most frequent malignant tumor of the biliary tract. The most frequent symptomatic form of gallbladder cancer is a symptomatic gallstone disease. The prevalence of gallbladder cancer is up to 0.3% worldwide with a median age at the time of diagnosis of 70 years. The 5-years survival rate is approximately 20% (up to 40% in T1a). Therefore, gallbladder cancer is currently considered as a curable disease. The mainstay of treatment is complete removal of the diseased gallbladder with lymphadenectomy. The treatment of choice for small gallbladder cancer (T1a) is minimally invasive surgery. The question of whether to perform a lymphadenectomy in patients with T1a is a matter of debate.

**Aims & Methods:** Sixty-five T1a patients underwent gallbladder cancer with lymphadenectomy were identified. The group was divided into two groups (with/without lymphadenectomy). The groups were compared in terms of clinicopathological characteristics, surgical outcome. The SPECTRUM ANTIBIOTICS COVERING ENTEROBACTERIACEAE

**Results:** The redneck syndrome as one of the side effects of VCM was observed in 5/31 patients (16.1%). No multifocal recurrence of bacteria were identified. The occurrence of multifocal recurrence of bacteria were investigated, as well.

**Conclusion:** The broad-spectrum perioperative antibiotics covering Enterobacteriaceae such as Enterococcus and Enterobacter species could decrease the incidence of SSI and duration of postoperative antibiotics administration compared to CMZ. More strict indication to select the patients who should be administered VCM, because the occurrence of side effects of VCM was relatively high.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**Reference**

**P0944 PARADIGM SHIFT? SHOULD A LYMPHADENECTOMY ROUTINELY BE PERFORMED ALSO AMONG GALLBLADDER CANCER PATIENTS WITH T1A DISEASE?**
Introduction: Pancreatic cancer is the fifth most common gastrointestinal malignancy and the most common of all biliary tract cancers. Overall, it is associated with a poor prognosis. Consensus guidelines suggest that patients with T1a cancers can be observed with cholecystectomy alone while patients with T1b or greater lesions should undergo lymphadenectomy in the hepatoduodenal ligament. Extent of surgery is especially important for those patients given efficient systemic therapy is lacking.

Aims & Methods: The aim of this study was to critically explore whether those surgical and patient population-based factors that given that current evidence is mainly based on small patient series. Especially we assessed the rate of T-stage specific lymph node positivity and the impact of lymphadenectomy on long-term outcomes. The National Cancer Data Base of the United States was reviewed from 2004 to 2012 to identify non-metastatic gallbladder cancer patients with T1a, T1b, or T2 stage primary tumors. Patients were grouped by whether a dedicated lymphadenectomy was performed or not while those with missing information were excluded. Groups were compared for baseline characteristics. Pathologic lymphadenectomy was defined by univariate and multivariable adjusted logistic regression with adjustment for important patient- and tumor characteristics. Overall survival was assessed using Cox proportional hazard regression analyses before and after full bivariate pairwise propensity score matching.

Results: Of the 3879 patients included, 287 (7.4%) had T1a, 661 (17.0%) T1b, and 2931 (75.6%) T2 gallbladder cancer. Most patients were female (n = 2751, 70.9%), median age was 72 years (range 21–90). Among patients with T1a, T1b, and T2 disease, 102 (35.5%), 278 (42.1%), and 1526, (52.1%) underwent a dedicated lymphadenectomy, respectively. Over the study period, the rate of lymph node excision increased from 43% to 58% (p for trend = 0.005). The rates of positive lymph nodes were 11.8%, 16.2%, and 42.5% for T1a, T1b, and T2-stage, respectively. 5-year overall survival rate was 31.6% for patients without and 44.6% for patients with a dedicated lymphadenectomy and 58.6%, 43.9%, and 34.5% for T1a, T1b, and T2-stage, respectively. After multivariable adjustment, the risk of longer lymphadenectomy increased with tumor stage compared to T1a disease (vs. T1b: OR: 1.37; CI: 1.01–1.86, vs. T2: OR: 1.95; CI: 1.48–2.57). Compared to their counterparts, patients who underwent lymphadenity for gallbladder cancer were more likely to have had an R0 resection status or radiation therapy, were diagnosed in later years, were younger, had a lower Charlson-Deyo-comorbidity score, were operated in high volume centers and traveled a longer distance to the treatment facility. In univariate analysis, no survival benefit of lymphadenectomy was found for T1a disease (HR 1.04, 95%CI 0.70–1.54) while lymphadenectomy improved overall survival in T1b (HR 0.72, 95%CI 0.58–0.90) and T2 stage (HR 0.59, 95%CI 0.53–0.65). Given significant bias of undergoing lymphadenectomy, full pairwise propensity-score matching was performed. A trend towards overall survival benefit was also found for T1b disease (HR 0.44, 95%CI 0.25–0.79). Overall survival benefit remained for T1b (HR 0.68, 95%CI 0.51–0.91) and T2-stage (HR 0.63, 95%CI 0.55–0.71).

Conclusion: Our results support current consensus guidelines that T1b and T2 gallbladder cancer patients should undergo LA. However, based on the high rate of nodal positivity among patients with T1a disease and the trend towards overall survival improvement among T1a patients who underwent lymphadenectomy, we suggest to rethink this dogma and advocate to perform lymphadenectomy also in surgically fit patients with T1a disease.

Disclosure of Interest: All authors have declared no conflicts of interest.

References


P0945 RECTAL SWAB CULTURE CAN DIRECT ANTIMICROBIAL PROPHYLAXIS AND PREDICT THE RISK OF INFECTIONAL COMPLICATIONS AFTER PANCREATICO-BILIARY SURGERY: A PROSPECTIVE SCORING SYSTEM MATCHING RETROSPECTIVE STUDY

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Introduction: Surgical site infections (SSIs) after gastrointestinal surgery cause significant morbidity, prolong hospitalisation and increase health care costs. Thus, SSI prevention is critical. To prevent bacterial colonisation in suture material, which disables local mechanisms of wound decontamination, triclosan-coated sutures were developed. We retrospectively analysed the efficacy of triclosan-coated polydioxanone sutures in abdominal fascia and skin closure using a propensity score matching analysis.

We further analysed the surgery types for which these sutures are best suited.

Aims & Methods: The study protocol followed the principles of the Declaration of Helsinki and received ethical approval from the Ethics Committee of the Fukuoka University (approval no. 12-7-96). At our department, we used conventional abdominal closure methods during gastrointestinal surgery before August 2012. Thus, we retrospectively collected surveillance data over a 1.5-year period for the control group. From September 2012, we began using triclosan-coated sutures for closure. Here, we collected data for the study group from September 2012 to September 2013. In total, we included 1768 patients (control group, n = 640; study group, n = 1128) who underwent gastrointestinal surgery. Baseline differences and selection bias were adjusted using propensity score matching.

Results: Before matching, the SSI incidence differed significantly between the control and study groups for all gastrointestinal surgeries [12.4% (140/1128) vs. 5.7% (28/455); p = 0.001] and hepato-biliary-pancreatic [16.4% (11/64) vs. 4.3% (5/116); p = 0.045]. In hepato-biliary-pancreatic surgery, 18.2% (40/220) vs. 7.8% (5/64) (p = 0.045) for hepato-biliary-pancreatic procedure, 12.7% (26/204) vs. 10.5% (12/114) (p = 0.347) for upper gastrointestinal (GI) surgery, 14.6% (43/294) vs. 5.3% (10/190) (p = 0.001) for lower GI surgery, 8.8% (24/274) vs. 4.1% (7/169) (p = 0.045) for hepato-biliary-pancreatic surgery, 18.2% (40/220) vs. 7.8% (5/64) (p = 0.030) for emergency surgery and 5.1% (7/136) vs. 1.0% (1/103) (p = 0.074) for others. Of 1768 cases, 483 pairs were matched using propensity score matching. No parameter used for the propensity score differed between the groups. After matching, a significant difference in the SSI incidence between the control and study groups for all gastrointestinal surgeries [9.7% (47/436) vs. 5.7% (28/455); p < 0.001]. We found a significant difference in the SSI incidence between the control and study groups for lower GI [17.0% (168/878) vs. 14.3% (21/149); p = 0.018] and hepato-biliary-pancreatic [16.4% (11/64) vs. 4.3% (5/116); p = 0.049] surgeries. No significant difference was found between the groups for upper GI surgery, emergency surgery and others. Multivariable logistic regression analysis showed that triclosan-coated suture use for lower GI surgery was the independent factor affecting the SSI incidence (p = 0.017). The sutures demonstrated a significant efficacy in lower GI surgery.

Conclusion: Few studies have focussed on the types of surgery best suited for triclosan-coated sutures. Our findings suggest that abdominal fascia and skin closure using these sutures reduces the SSI risk, particularly for lower GI surgery.

Disclosure of Interest: All authors have declared no conflicts of interest.

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**P0947 COMPARISON OF POSTOPERATIVE CONDITIONS BETWEEN OPEN-PROSTAPLE IN THE DOUBLE-FLAP TECHNIQUE AND THAT WITH A CIRCULAR STAPLER IN LAPAROSCOPIC PROXIMAL GASTRECTOMY**

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**Introduction:** In recent years, laparoscopic proximal gastrectomy (LPG) has been actively performed in our institution to reduce invasiveness. However, proximal gastrectomy is sometimes followed by reflux. Until February 2015, we performed esophagogastrosentery with a circular stapler (CS) accompanied by fundoplication in LPG. However, in March 2015, to avoid the postoperative complication, we have been using esophagogastrosentery with the double-flap (DF) technique. This DF technique in LPG for gastric cancer. Aims & Methods: We conducted this study to examine whether DF can reduce the reflux and eliminate reflux ulcers and thus be possible to reduce postoperative complications. From February 2012 to February 2017, 47 LPGs were performed at Keio University Hospital.  

First, surgical time, bleeding, incidence of postoperative complication, postoperative hospital stay, and incidence of Anastomotic stenosis were examined as surgical factors and compared between the DF and CS groups. Second, gastroesophageal reflux finding on endoscopy, condition of the remnant stomach according to residue, gastritis, bile (RGB) classification at postoperative 6 months and 1 year, and proton pump inhibitor (PPI) intake were examined as postoperative factors. Finally, albumin and hemoglobin levels at postoperative 6 months and 1 year were examined as nutrient factors. Gastroesophageal reflux was assessed with scores of 0–5 in accordance with the Los Angeles (LA) classification.  

**Results:** Twenty-three LPGs with DF and 24 LPGs with CS were performed during the period. Compared with the CS group, the DFT group had a significantly longer surgical time (272.3 ± 55.5 vs 241.1 ± 26.7 min, p < 0.01). Other surgical factors showed no statistically significant differences between the two groups. For as postoperative factors, although no significant differences in PPI intake, LA classification, and RGB classification were found, the DFT group showed a significantly lower score than the CS group (p < 0.01). Postoperative nutrition scores showed no significant differences between the two groups. Conclusion: Although LPG with DF required a longer surgical time than LPG with CS, DF is thought to be a safe reconstruction method in LPG. In addition to its safety, DFT can reduce postoperative reflux in patients who undergo LPG.  

**Disclosure of Interest:** All authors have declared no conflicts of interest.  

**References:**  

**P0948 NOVEL ENDOSCOPIC REPAIR TECHNIQUE FOR GASTROINTESTINAL LEAKS AND PERFORATIONS USING NEGATIVE PRESSURE THERAPY WITH OPEN-PORE POLYURETHANE-FOAM AND FILM DRAINAGE**

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**Introduction:** Gastrointestinal (GI) leaks and perforations are difficult to manage and often mandate laparotomy and extensive surgical interventions for their treatment. Endoscopic Negative Pressure Therapy (ENPT) has been developed to treat leaks such as fistula and perforations. However, ENPT has only been utilized in the management of rectal and esophageal leaks. By modifying the delivery catheter we were able to adapt ENPT to treat duodenal defects, that otherwise would have required surgery or more invasive methods to be used.  

**Aims & Methods:** Herein, we report ENPT using open-pore Polyurethane-foam and Film Drainage in a series of 10 patients with duodenal leakages. This is an innovative variant of ENPT. In 7 patients we used the OPD device, in one patient OFD, and in two patients OPD and OFD. All leakages (100%) were successfully closed after a treatment period of 11 days in median (range 7-19 days). Nine patients were treated with intraluminal and one patient with intracavitary variant of ENPT. In 7 patients we used the OPD device, in one patient OFD, and in two patients OPD and OFD. All leakages (100%) were successfully closed allowing early enteral feeding and thus reducing hospital stay.  

**Conclusion:** ENPT using small diameter tube with open-pore film was effective to treat duodenal leakages. Advantage of OFD is the small diameter which allows easy endoscopic placement through small openings and nasally insertion. OPD and OFD are placed accurately at the site of leakage and perforations using common endoscopic techniques and thus represent a potential addition to the armamentarium to treat these difficult lesions.  

**Disclosure of Interest:** G. Loske: Gunnar Loske is a consultant for Lohmann & Rauscher, Medical Clinic, Westküstenkliniken, Heide/Germany. All other authors have declared no conflicts of interest.

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**P0949 INFLUENCE OF THE HYBRID METHOD OF DETOXICATION ON BLOOD CLARIFICATION EFFECTIVENESS AT PATIENTS WITH THE MULTIFACIAL FAILURE**

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**Introduction:** The main relesser for development of multifacile failure syndrome is multivital organ failure, which often occur after surgical complications and more than in 70% of cases leads to lethal outcomes. Increase of an endotoxemia leads to development of the expressed pathological processes and to a fast descomposition of bodies of natural detoxication system at the subsequent development of a multifacile failure. Increase in detoxication ability of sorbents can happen due to change of chemical composition, or due to collimating of padding properties to them by their modification by various agents by means of an immunization on their surface of endotoxine. In this plan especially important role is got by the researches directed to development of sorbents with oxidizing activity.  

**Aims & Methods:** Aim of study is to estimate effectiveness of the modified hae-mosorbtor application for patients about the MOFS. The experimental part of work was conducted on 14 not purebred dogs with the acute liver failure modelled by bandaging of distal department of the CBD. After development of pathological process animals were divided into 2 groups. To the first group of animals the procedure of a haemosorbtion was carried out by a reference technique on use of a haemosorbtion of SKN-2K. To the second group of animals the haemosorbtion was carried out by the developed technique with the same sorbent, but the solution of a neutral anolyte subjected to oxidizing modification. For this purpose, in the flowing mode carried out a half-hour incubation of a sorbent from 2 l of solution of a neutral anolyte.  

**Results:** Results showed that at animals of the 2nd group in comparison with group of comparison improvement of a condition of an organism was expressed in a greater degree. After performing detoxication therapy by the developed technique a normalization of all studied parameters is registered. The same tendency is revealed also concerning nontoxic components. It is necessary to pay special attention to dynamics of a ratio of the common protein and an index average molecules/the common protein, pointing to synthesis process activation. The carried-out all-clincal blood test revealed the considerable improvement of indexes of white blood. In group of comparison it was not succeeded to achieve the complete normalization of the studied indexes. On the basis of what the conclusion was drawn on high effectiveness of the developed technique, and expediency of its introduction in clinical practice. Under our observation there were 45 patients needing carrying out getter detoxication in the postoperative period. The control group (25) was created by a random sample of case histories of patients with the MOFS who was earlier on treatment in our clinic and receiving a course of a haemo perfused therapy by a reference technique. The analysis of results of treatment of patients of a basic group showed that the positive dynamics of clinical indexes expressed in decrease of manifestations of an intoxication syndrome, improvement of health and labora-tory indexes is noted in earlier terms, and degree of expressiveness of positive changes at them was much higher. Dynamics of decrease in endogenic intoxica-tion is reflected by data of laboratory researches. We are showed that it is possible to increase quality of detoxication by a pretreatment of a haemo sorbent solution of a neutral anolyte. As a result of it the sorbent gains padding, oxidizing properties. At such modification there is an inclusion of oxygen-containing and acid groups in struc-ture of a sorbent, which besides the fact of sorbent protecive groups of carboylic and phenolic types thanks to which the oxidized coals gain the expressed cation-exchange ability are formed. Therefore, besides actually manifestations of an intoxication syndrome, improvement of health and labora-tory indexes is noted in earlier terms, and degree of expressiveness of positive changes at them was much higher. Dynamics of decrease in endogenic intoxica-tion is reflected by data of laboratory researches. We are showed that it is possible to increase quality of detoxication by a pretreatment of a haemo sorbent solution of a neutral anolyte. As a result of it the sorbent gains padding, oxidizing properties. At such modification there is an inclusion of oxygen-containing and acid groups in struc-ture of a sorbent, which besides the fact of sorbent protecive groups of carboylic and phenolic types thanks to which the oxidized coals gain the expressed cation-exchange ability are formed. Therefore, besides actually
References

Introduction: Laparoscopic cholecystectomy is the gold-standard for the treatment of gallbladder stone disease. Single-incision laparoscopic (SILS) cholecystectomy was introduced with the aim of reducing the invasiveness of classic laparoscopic surgery. Despite satisfactory cosmetic results of SILS cholecystectomy and its repute of a painless procedure, there are few published studies comparing early and long-term perioperative period of laparoscopic SILS cholecystectomy versus laparoscopic four-port cholecystectomy.

Aims & Methods: The aim of this study is the comparative evaluation of SILS cholecystectomy and laparoscopic four-port cholecystectomy. Early and long-term perioperative period has been analyzed in 240 patients who underwent laparoscopic cholecystectomy including 120 cases of single-port technique and 120 cases of four-port technique. Both groups were compared in surgical time, pain syndrome severity (visual analog scale), need for analgesics, postoperative complications, hospital-stay, daily activity recovery and return to physical work, patients' satisfaction of surgical results and their aesthetic effect.

Results: It was revealed that SILS cholecystectomy is associated with lower severity of postoperative pain, quick recovery of daily activity and return to physical work, high satisfaction rate of cosmetic results and significantly shorter hospital-stay as compared with four-port cholecystectomy. Disadvantages of SILS cholecystectomy include longer duration of surgery, high incidence of postoperative umbilical hernia. However, hernia was predominantly observed during the period of surgical technique development.

Conclusion: Further studies to standardize, evaluate the safety and benefits of SILS cholecystectomy are necessary.

Disclosure of Interest: All authors have declared no conflicts of interest.

References


Aims & Methods: We aim to present the experience using CSDCD for gastric leaks secondary to BS. In this retrospective study, patients with leaks secondary to gastric bypass (GBP) or sleeve gastrectomy (SG) from 4 centers were included. Data collected from november 2012 to january 2016 included sex, age, type of surgery, previous treatment, tract path, size of the leak opening and defect closure. Leaks were grouped according to the International Sleeve Gastroectomy Expert Panel Consensus in acute (post-operative days 1-7), early (1-6 weeks), late (after 6 weeks) and chronic (> 12 weeks). Biliary catheters were adapted to introduce the CSDCD through the gastroscopies working channels. Clinical success was defined as complete elimination of abdominal or thoracic drainage with imaging documentation of closure (CT with contrast or upper GI contrast study) after 2 months.

Results: 62 patients with leaks were included (31 SG, 11 GBP). Three acute leaks, 5 early, 2 late and 12 chronic. Prior failed therapies included: SEMS and enteral tube feeding (ETF), SEMS alone, SEMS and gastrostomy of excluded stomach, OTSC, ETF alone, jejunostomy and none (3 acute leaks had CSDCD as the primary treatment). Tract path was grouped as gastric-cutaneous (37), gastric-pleural (3) and gastric-bronchial (2). Median follow-up was 34, 8 weeks. All 3 patients with acute leak failed to close the defect. The CSDCD were removed within 7 days and SEMS were placed instead leading to defect closure. The 5 patients with early leaks had initial good response but within 30 days drainage recurred. The CSDCD were removed and replaced for a larger diameter device leading to permanent defect closure. Clinical success was achieved on 38 patients (90, 5%). In one patient with late leak the tract path was connected to an undrained cavity. Evolution was unsatisfactory and total gastrectomy accomplished.

Conclusion: CSDCD are effective to treat post bariatric surgery late and chronic leaks despite of the failed previous endoscopic treatment. Although early leaks finally healed it seemed advisable to maintain conservative treatment and wait for the leak to become late or chronic before CSDCD placement. Acute leaks must be managed with a combination of SEMS, ETF, OTSC as first step. 

Disclosed of Interest: All authors have declared no conflicts of interest.

References
Tuberculosis is still a problem of public health in Tunisia, which is a country of endemicity. The epidemiological situation of the disease is marked by the rise of the extrapulmonary forms especially abdominal tuberculosis.

Aims & Methods: The aim of this study was to analyze the epidemiologic, clinical, diagnostic, therapeutic and effective features of abdominal tuberculosis in a series of 150 patients. This was a descriptive and prospective monocentric study of 150 cases of abdominal tuberculosis conducted from 2004 to 2014 in a tunisian center. Diagnosis of tuberculosis was based on histological evidence or other on a biopsy of arguments.

Results: There were 150 patients enrolled. The mean age was 37.2 (17–72 years). Ninety seven (64.6%) were females. Symptoms were ascites 107 (71.3%), abdominal pain 28 (18.6%), weight loss and reduced appetite 80 (53.3%). Un tableau pathologique surgical was performed in one case. Patients (66.6%) had a lymph node involvement. Diagnosis of abdominal tuberculosis was histology and microbiology (surgical and biopsy).

Conclusion: Abdominal tuberculosis is one of the most common site of extra-pulmonary tuberculosis. No single test is adequate for diagnosis of abdominal tuberculosis. Therefore, in all patients an ongoing diagnostic dilemma requiring a high index of clinical suspicion.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
1. van Empel PJ et al. Mapping the Maze of Minimally Invasive Surgery Training. 48 medical students completed three tasks in a laparoscopic virtual reality simulator, a validated Minimally Invasive Surgical Trainer. Prior to the task, they performed a visuospatial test and answered questions regarding baseline characteristics (e.g. PC-gaming experience, age, gender, previous simulator experience). The data were analyzed regarding different parts of the simulation (time, economic value of carrying out radiological, endoscopic and histo-bacteriological investigations). The main operative findings in patients with coelioscopy or exploratory laparotomy were: Whist granulations (98%), adhesions (43.1%) and agglutination loops (1.5%). The presence of tuberculous granuloma was observed in 52 patients (81%). The course of treatment was as follows: cure in 50 patients (80.6%), recurrence in 6 patients (9.6%), relapse in 2 patients and 3 patients were lost to follow-up. The mortality in our series was 0%.

Disclosure of Interest: All authors have declared no conflicts of interest.

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TLR3-deficient and emulsifier-treated mice demonstrated that these models of gut injury characteristically depended on disruption of the epithelium that maintains microbiota dependency of intestinal inflammation reflects an inability to manage pathobiont bacteria, such as Adherent-Invasive E. coli (AIEC).

Aims & Methods: Our goal was to examine extent to which microbiota mismanagement and associated inflammation in TLR3-deficient and emulsifier-treated mice would manifest in a limited pathobiont-free microbiota. WT and TLR3-deficient mice were maintained in gnotobiotic isolators containing altered Schaedler flora (ASF), a community of eight bacterial species. Mice were treated with either WT or inoculated with AIEC LF82 [4]. Feces were assayed for bacterial loads, microbiota composition, and inflammatory marker lipocalin-2. Fecal LPS and flagellin bioactivity were measured via a cell-based reporter assay, and morphologic and metabolic parameters were determined.

Results: Neither CMC nor P80 induced evidence of intestinal inflammation nor metabolic syndrome in WT ASF animals. Analogously, relative to similarly maintained WT mice, loss of TLR3 did not result in low-grade intestinal inflammation or metabolic syndrome under ASF conditions. Concomitantly, the ASF microbiota community was not disturbed by CMC nor P80 and, moreover, was similar between WT and TSKO animals. Inoculation with AIEC strain LF82 resulted in profound alteration of the ASF community in TSKO mice compared to WT. Within an ASF LF82 inoculated in an ASF TSKO mouse model.

Conclusions: A limited complexity pathobiont-free microbiota, loss of the flagellin receptor TLR5 or emulsifier consumption does not impact microbiota composition nor its ability to promote inflammation. Addition of AIEC to this eutrophic microbiota composition, increases levels of lipopolysaccharide (LPS) flagellin, but only modestly promotes gut inflammation and adiposity, suggesting that the phenotypes previously observed require disruption of complex microbiota.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P0958 ISOLATION AND CHARACTERIZATION OF LAMINA PROPRIA MONONUCLEAR CELLS FROM HUMAN COLONIC MUCOSA

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Introduction: Lamina propria represents a thin layer of connective tissue rich in lymphoid cells and macrophages, underlying the epithelium of mucous membranes. Lamina propria mononuclear cells (LPMCs) are immune system’s first line of defense in the intestine characterized by the ability of differentiating invading pathogens from beneficial intestinal flora and swiftly removing them. Disrupted regulation of LPMCs is implicated in pathology of a group of diarrheal and inflammatory bowel disease (IBD). Two major types of IBD are ulcerative colitis, limited to the colon and chronic’s disease affecting any segment of the gastrointestinal tract. Chronic’s disease and ulcerative colitis were shown to be mediated by Th1-polarized helper (CD4+) T-cells, and Th2-polarized CD4+ T-cells. Conversely, while Th17-polarized cells are involved in pathogenesis of both diseases, therefore, research into biology and regulation of LPMCs is of essential importance for development of treatments for IBD symptoms.

Aims & Methods: The aim of this study was to develop a robust method for isolation and characterization of LPMCs from human colonic mucosa, compatible with further ex vivo cell culturing and research. Mucosal tissue samples contained the tissue not affected by tumor, removed during tumor surgery of patients consented to donation of tumor and the surrounding resected tissue. The tissue may be considered as healthy in terms of IBD. We have employed an isolation method consisting of disruption of epithelial cells by incubation of mucosa in a DTT and EDTA containing solution, followed by enzymatic and mechanical digestion of tissue and purification of mononuclear cells by density gradient centrifugation. Isolated cells were characterized by flow cytometry (FACS) detection of cell-type specific surface antigens and cytokine analysis.

To examine the plasticity of isolated cells in terms of polarization towards IBD-associated phenotypes, the cells were seeded at conditions mediating Th1, Th2 and Th17 differentiation of CD4+ T-cells and analyzed for activation of differentiation-specific gene expression and cytokine production by qPCR and ELISA assays. Aliquots of cells were cryopreserved and further analyzed for the effect of cryopreservation on distribution of surface antigens and CD4+ T-cell responses.

Results: Approximately 95% cell viability and 90% leukocyte (CD45+) cell purity was determined by FACS analysis of isolated LPMCs. According to cytokine analysis, CD45-negative cells may represent CD45-negative population of plasma cells: no contamination with epithelial cells was detected. Within CD45+ cell population, 26–47% T-lymphocytes, 17–24% B-lymphocytes, 8–17% macrophages and 21–46% monocytes were detected by FACS and cytokine analyses (N=3). Cryopreservation did not significantly affect cell viability and surface marker distribution. Isolated cells successfully polarized towards Th1, Th2 and Th17 CD4+ T-cell phenotypes, as confirmed by INF-γ gene expression and cytokine production for Th1, IL13 gene expression and IL5 cytokine production for Th2 and IL17 cytokine production for Th17 differentiated cells. Differentiation was confirmed via cryopreserved cells, with lower level of phenotype-specific cytokine production.

Conclusion: Method for LPMC isolation from human colonic mucosa tissue samples was successfully established with approximately 95% viability of isolated cell population. No detectable epithelial cell contamination was observed. Within CD45+ cell population, 26–47% T-lymphocytes, 17–24% B-lymphocytes, 8–17% macrophages and 21–46% monocytes were detected. Isolated cells were successfully polarized towards IBD-associated Th1, Th2 and Th17 CD4+ T-cell phenotypes, as confirmed by activation of phenotype-specific gene expression and cytokine production. Cryopreservation of isolated LPMCs did not significantly affect cell viability, distribution of cell-type specific surface antigens or polarization towards Th1, Th2 and Th17 CD4+ T-cell phenotypes.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

P0959 FACTORS ASSOCIATED WITH DISABILITY IN INFLAMMATORY BOWEL DISEASE: OUTPATIENT CROSS-SECTIONAL STUDY

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Introduction: The Inflammatory Bowel Disease-Disability Index (IBD-DI) has recently been validated to measure disability in IBD.

Aims & Methods: We aimed to assess disability in IBD outpatients using IBD-DI and to determine the sociodemographic, clinical and psychological factors that are associated with greater disability. Between August and October of 2016, patients with an established diagnosis of Crohn’s Disease (CD) or Ulcerative Colitis (UC) for at least 3 months and followed up at our outpatient clinic were invited to participate. Socio-demographic and clinical data were collected from electronic health record and interview. Optimism and disability were evaluated employing, personally or by phone, the validated Portuguese versions of the Revised Life Orientation Test (LOT-R) and IBD-DI, respectively. The association between sociodemographic, clinical and psychological variables (optimism) and IBD-DI (scale 0-100, proportional to the reported disability) was determined by univariate and multivariate analysis.

Results: A total of 143 patients (70 DC and 73 UC; 50.3% females) with a mean age of 38 ± 13 years were included. Most (85.5%) was in clinical remission. The mean IBD-DI-PT score was 17.9 ± 10.7, with a significant difference between DC and UC (p = 0.944). In univariate analysis, female gender, high level education, number of days off from work, articular manifestations, number of comorbidities, use of psychotropic drugs and pessimism (low LOT-R score) were significantly associated with higher disability (IBD-DI-PT score). In multivariate analysis, only female gender (β = 0.150), number of comorbidities (β = 0.186) and pessimism (β = 0.370) were significantly associated with higher disability. Clinical activity was associated with higher disability only for CD patients (β = 0.321).

Conclusion: IBD outpatients reported low levels disability associated with their disease, which can be explained by the high percentage of patients in clinical remission. Comorbidities and psychological factors (optimism) emerged as the main predictive factors of greater disability, reinforcing the importance of multidisciplinary approach to these patients. Clinical activity seems more important to CD than UC patients in terms of disability.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
P0960 BIOLOGIC THERAPY REDUCES T CELL ACTIVATION IN PATIENTS WITH CROHN’S DISEASE

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Introduction: Imbalance of immune bowel environment is associated with development of many diseases, such as Crohn’s disease (CD). Although the pathogenesis of CD remains unclear, a key feature of CD is dysregulation of immune responses and include, in addition to other cells, CD4+ and CD8+ T cells, which comprises adaptive phase and require proper inflammatory cues for their development. Corticosteroids are the mainstay of the abating phase. CD4+ T cells express markers that give them powerful functional abilities (Abbas et al., 1996). CD38 and HLA-DR besides being classically markers of cellular activation, are also known as markers of diseases progression (Lovealce et al., 2017). Some studies shows that CD4+ T cells play a key role in the immune inflammatory response leading to CD but this cells are poorly characterized in the blood of the patients.

Aims & Methods: This study aimed to characterized CD4+ and CD8+ T cells in the blood of patients with CD. The study was performed in individuals with CD (n = 40) and healthy controls (n = 38). Blood of healthy donors and patients with CD was collected in clinical laboratory from Hospital Albert Einstein. CD4+ and CD8+ T cells was quantified by multiparametric flow cytometry. Dosage of corticosteroid and ASCA was performed by commercial Elisa kit. The groups were compared for numerical measures using Student’s t-tests.

Results: The highest prevalence in both group was female, aged between 19 and 66 years with a median of 37.5 years. Among clinical exams, 61% of cases present a value greater than 200 in the dosage of Calprotectin, whereas in the control group this rate was 43.84% (p < 0.001) and IgA (p < 0.001) were also higher in age of cases when compared to control group. The population of CD3+ cells in peripheral blood of healthy controls and patients with CD was evaluated both in biological and corticoid treatment. A significant increase in the proportion of patients receiving corticosteroids (p = 0.02) compared to healthy controls. In the population of CD4+ a significant increase was observed in patients undergoing treatment with corticosteroids in relation to patients undergoing biological treatment (p = 0.0027). In CD4+ population, no statistical difference was observed between the groups. The markers CD38, CD62L and HLADR were also evaluated. In relation to CD38 (p = 0.0022) and CD62L (p = 0.015) in subpopulation of CD4+ T cells, a significant increase in the expressions was observed in the group of patients receiving corticosteroids in relation to the group receiving biological therapy. Regarding HLADR, statistical difference (p = 0.01) was observed between the group undergoing biological treatment and the group of healthy controls. In the subpopulation of CD8+ T cells, a significant increase (p = 0.02) was observed in the CD38 expression between the groups. Significant differences were recorded. In all experiments the levels of inflammation markers: myeloperoxidase (normalized number of reads in control samples reached 0.2 and was less than 0.06 in samples of patients with ulcerative colitis).

Conclusion: This study suggests that the use of biological therapy suppresses activated immune responses and include, in addition to other cells, CD4+ T cells, which comprises adaptive phase and require proper inflammatory cues for their development. Corticosteroids are the mainstay of the abating phase. CD4+ T cells express markers that give them powerful functional abilities (Abbas et al., 1996). CD38 and HLA-DR besides being classically markers of cellular activation, are also known as markers of diseases progression (Lovealce et al., 2017).

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P0961 CHANGES OF THE MUCOSAL COLON MICROFLORA ARE CAUSE OF INFAMMATION AT THE PATIENTS WITH ULCERATIVE COLITIS

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Introduction: Advancing of sequencing technologies in the first decade of the XXI century gives the opportunity to realization of large scale projects such as the 1000 human genomes project. This project provides enormous amount of the data for H.sapiens population genetics studies and different GWAS studies aimed to investigate connection of the human genetics variations with different diseases. It is especially interested to study the connection between the human genetics, the microbiome metagenomes of mucosa and different pathological conditions. Previously revealed, the size of the summary gut microbiome metagenome is on order more than the size of a human genome. The most of works devoted to the study of the connection between human and microbial genome changes with different pathological conditions based on the investigation of fecal samples. On our opinion, in the case of ulcerative colitis it is more effective to study the mucosal microbiome of the affected regions.

Aims & Methods: The aim of our work was to study the composition of mucosal microbiomes in the colon mucosa biopsies from patients with ulcerative colitis by using the target high throughput sequencing of bacterial 16S rRNA genes. Biopsies from four caucasoid race patients with left-sided ulcerative colitis in the abating activity. Meyo endoscopic index = 3, Rachmelevich clinical index = 4 and two patients from control group with irritable bowel syndrome were collected. The DNA was extracted from mucosal biopsies and 16S rRNA genes from it’s were target sequenced by using Illumina MiSeq sequencer. Sequencing reads were quality checked by the FastQC software and trimmed by using the trimmomatic software. To characterize the composition of the microbiota, trimmed reads were analyzed by the QIIME software. The obtained results were compared with the earlier published data: SRA Project - ERP001780 (96 samples from patients of control group, 44 samples from patients with ulcerative colitis)[1] and SRA Project - SRP056002 (703 samples from patients with ulcerative colitis).

Discussion: More than 124 bacterial genera were found in biopsies of four patients with ulcerative colitis. The analyzed samples of patients with ulcerative colitis were split in two groups by using the PCA analysis. The first group was characterized by decreasing of the concentration of the Firmicutes type bacteria (p-value <0.005) and increasing the concentration of Bacteroidetes (p-value <0.005). For the second group, It was founded decreasing of the concentration of the Actinobacteria type bacterias (p-value <0.05), 70-fold excess of Bacteroidetes vulgatus species bacteria concentration was revealed for one sample of the first group (normalized number of reads in control samples was less than 0.003, and reached 0.21 in samples of patients with ulcerative colitis). Additionally, the concentration of Escherichia coli species bacteria was increased in the 40 times for that sample (normalized number of reads in control samples was less than 0.003 in samples of patients with ulcerative colitis). Although, the predominance of Proteobacteria genus bacteria was not founded. The concentration of Faecalibacterium prausnitzii species bacteria was decreased by three orders of the magnitude for samples from the first group (normalized number of reads in control samples reached 0, 2 and was less than 0, 06 in samples of patients with ulcerative colitis).

Conclusion: The concentration increase of the conditional-pathogenic mucosal microflora (a mostly Bacteroidetes type bacteria) was discovered, which playing a prominent role in the development of ulcerative colitis and its pathological damage. Also, the deficiency of Faecalibacterium prausnitzii species bacteria was discovered, which decrease resistance of mucosa to the conditional-pathogenic microflora.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P0962 COLONIC INFLAMMATION DELAYS DEVELOPMENT OF STREPTOZOTOGEN-INDUCED DIABETES IN MICE THROUGH MODULATION OF ENDOGENOUS INCRETIN SYSTEM

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Introduction: The role of incretin hormone, GLP-1, in inflammatory bowel diseases (IBD) development and exacerbations is still poorly understood. GLP-1 decreases blood glucose levels and in patients with IBD delays the onset of pro-inflammatory cytokines and excessive administration of diabetogenic drugs. We hypothesize that the possible mechanism underlying this phenomenon is related to changes in the levels of incretin hormones.

Aims & Methods: The primary aim of this study was to investigate, in the mouse model of coexisting colitis and experimental diabetes, the role of incretin hormones as an underlying factor. Experimental diabetes was induced by administration of streptozotocin for 5 consecutive days (50 mg/kg, i.p.). Mice with experimental diabetes and receiving neither GLP-1, nor GIP were considered as diabetic. To develop a chronic and relapsing colonic inflammation, mouse model of colitis induced by intracolonic administration of TNBS (first dose: 150 mg/kg at day 1, booster dose: 75 mg/kg at days 12, 23, 34, 45, 56) was used. On day 60 mice were sacrificed and macroscopic score, ulcer score, colon length and bowel thickness were recorded. In all experiments the levels of inflammation markers: myeloperoxidase (MPO) activity, TNF-α and IL-1β expression were determined. The
**P0963 EOSINOPHIL-ASSOCIATED CYTOKINES AS INFLAMMATORY BOWEL DISEASE BIOMARKERS**

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**Introduction:** Pathogenesis of inflammatory bowel disease (IBD) is multifactorial and establishing diagnosis requires a performance of series of variable tests. The alternative, non-invasive, markers of IBD are intensively searched for. Eosinophils are acidophilic multifunctional granulocytes that remain outside the mainstream research on IBD. However, they are a rich source of cytotoxic proteins, pro- and anti-inflammatory cytokines, chemokines and growth factors and are likely to contribute to both inflammatory and regenerative phases of the disease. Accordingly, peripheral eosinophils of IBD patients are primed and pre-activated. They display increased responsiveness, adhesiveness, migration, and degranulation and are characterized by up-regulated secretion of their mediators. Locally, increased number and activation of eosinophils have been repeatedly observed in areas of active inflammation. Despite the acknowledged contribution of eosinophils to the disease pathogenesis, available data on cytokines closely related to the development and activity of peripheral eosinophils in IBD patients are either scattered or non-existent.

**Aims & Methods:** Aim of the study was assessment of the circulating eosinophil-associated cytokines and growth factors as differential markers and indicators of mucosal healing in inflammatory bowel disease. Study population consisted of 277 individuals: 101 patients with Crohn’s disease (CD), 77 with ulcerative colitis, 16 with irritable bowel syndrome (IBS) and 83 healthy controls. The disease severity was assessed using the Crohn’s Disease Activity Index (CDAI) for CD and the Mayo Disease activity index for UC. Results: The development of hyperglycemia in mice treated with TNBS was delayed compared to a non-inflected group, what was associated with significantly higher level of GLP-1 in blood. Surprisingly, the levels of GLP-2 were significantly reduced in diabetic mice with colitis, suggesting that two distinct mechanisms are involved in the regulation of the incretin hormones in response to intestinal inflammation. There were no significant differences in macropscopic score, colon length, and bowel thickness in diabetic mice with or without colitis. Nevertheless, significantly increased in diabetic mice with colitis compared to diabetic mice with no inflammation. No changes in MPO, TNF-α, IL-1β were observed between these groups.

**Conclusion:** We propose that GLP-1 production may be stimulated in response to colitis, contributing to the post-inflammatory regeneration phases of the disease.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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**P0964 MACROPAHGE IL10 SIGNALING IS REQUIRED FOR THE THERAPEUTIC EFFECT OF ANTI-TNF THERAPY IN INFLAMMATORY BOWEL DISEASE**

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**Introduction:** Interleukin(IL)10 is an important anti-inflammatory cytokine for the maintenance of gut homeostasis. Defects in the IL10 signaling pathway in macrophages leads to disregulation of regulatory (M2) type macrophages and subsequent inflammatory bowel disease (IBD). IBD patients are frequently successfully treated with anti-TNFα antibody therapy, although not all patients are responders.

**Aims & Methods:** We determined the effect of anti-TNFα therapy in both IL10 knock-out (KO) mice and in the CD4+CD45RBh high T-cell transfer model of colitis. Macrophage populations were quantified using qPCR analysis for CD206 and the macrophage marker F4/80 and flow cytometry for CD206. IL10 mRNA and protein levels were analysed with qPCR and ELISA.

**Results:** Colitis in the IL10 KO mice was completely resistant to anti-TNFα therapy, in sharp contrast to the colitis in SCID or Rag1 KO mice upon transfer with CD4+CD45RBh high T-cells, which was significantly reduced by anti-TNFα therapy. Successfull anti-TNFα therapy was accompanied by an increase of IL10 levels and an increase of regulatory (M2) type macrophages in the intestine. Blocking IL10 signaling, with an IL10 Receptor blocking antibody, diminished the therapeutic efficacy of anti-TNFα therapy. Anti-TNFα therapy was also unresponsive to anti-TNFα therapy upon receiving CD4+CD45RBh high T-cells. In these mice there was also no increase of intestinal M2 macrophages.

**Conclusion:** IL10 signaling in macrophages is pivotal for the therapeutic efficacy of anti-TNFα therapy in animal models for IBD. Defects in the IL10 pathway may also play a role in anti-TNFα non-responders which is subject of further investigation.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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**P0965 LONG-TERM CONSEQUENCES OF ANTIBIOTIC THERAPY: ROLE OF SCFAS AND INTESTINAL BARRIER INTEGRITY**

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**Introduction:** Epidemiological studies revealed that antibiotics exposure increases the risk of inflammatory bowel diseases (IBD) development (Hviid, 2011, Shaw, 2011, Kronman, 2012). However, mechanisms of this association are not fully understood. Recent studies revealed sustained alterations in gut microbiota after antibiotic treatment (Rashid, 2015, Dethlefsen, 2011), the full consequences of which remain unknown.

**Aims & Methods:** We investigated long-term effects of antibiotic treatment on gut microbiota, short-chain fatty acids (SCFAs) production, transport & sensing, mucosal and mucus layer functional state, surface mucus layer and epithelial barrier integrity. Male Wistar rats (n = 178, 140-160 g) were treated for 14 days with broad-spectrum antibiotic cefazolin (CT) (300 mg/kg, i.m.) or vehicle; euthanized in 1, 14 or 56 days after CT withdrawal. The fecal microbiota was analyzed by bacteriological culture methods; fecal SCFAs – by gas chromatography; colorectal localization and levels of FFAs & FFA3 receptors and MCT1, MCT4 & SMCT1 transporters of SCFAs – by immunohistochemistry; levels of FFAs, FF3, ERK1/2, p38, HIF1α proteins in colon mucosa – by Western blot analysis; reactive substances, mucus glycoproteins and their carbohydrate composition – by colorimetrically; epithelial permeability was evaluated by Evans blue permeation and bacterial translocation.

**Results:** CF injection leads to compositional changes of fecal microbiota which progress over time. In 56 days, we found increased level of Clostridium spp., E. coli, conditionally pathogenic and hemolytic bacteria. Levels of Bifidobacterium...
& Lactobacillus were unchanged during the study. Moreover, the concentrations of amino acids and short-chain fatty acids were decreased in UC mice, 0.4-, 8.5-, 4.8-fold (P < 0.05), respectively, the first day after Cf withdrawal. These changes were accompanied by decreased immunoreactivity for the FFA2, FFA3 receptors, SMCT1 and increase MCT1 & MCT4 transporters of SCFAs in colon mucosa. In 56 days, concentration of SCFAs and level of FFA3 was still below control values. These changes evoked a significant shift in colonic mucosal homeostasis. We revealed increased level of TBA-active substances, decreased the activity of SOD and catalase antioxidant enzymes with increased HIF1α, activation of P2Y2 receptor subtype P2Y2R, which are induced via α-defensin and oxidative stress development were associated with increased permeability of colon epithelium and bacterial translocation to blood in 56 days after Cf withdrawal. Moreover, the levels of mucus glycoproteins, hexoses and fucose decreased while sialation of mucus glycoproteins increased which is typical for IBD development. These changes were accompanied by increased activity of MMP-9 and decrease – MMP-2 in rats colon mucosa.

Conclusion: We showed for the first time that antibiotic treatment induced long-termed changes in SCFAs composition, levels of their receptors and transporters in colonic mucosa. It was associated with alterations in mucus composition, increased epithelial permeability that might increase susceptibility to IBD development.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

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Introduction: According to our previous report, the imbalance of Th17/Treg cells in the colonic tissue of IBD patients is related with the expression of CD45RA FoxP3foxp3 activated Treg(FrII) cells, which has the real function of immunosuppression, and with the elevation of CD45RA FoxP3foxp3 Treg(FrIII) cells, which provide FoxP3high Treg(FrIII) cells, which provide immunosuppressive activity.Activation of Toll-like receptor 2 (TLR2) leads to elevation of FrIII, which show FoxP3

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subsequently analyzed for STAT3 signaling (western blot), NFkB signaling (NFkB Transcription Factor Assay, western blot) and cytokine secretion (ELISA).

Results: Peripheral blood CD4+ T cells from IBD patients could be characterized by a significantly increased P2Y2R expression compared to healthy controls, with higher expression levels of the P2Y4 receptor subtype turned out to be comparable between both groups. Further subdividing the group of included IBD patients into Crohn’s disease and ulcerative colitis patients, we could not observe a significant difference in the P2Y2R levels between both disease entities. Interestingly, the increased P2Y2R expression in the lymphocyte compartment of IBD patients seemed to be limited to CD4+ T cells, as CD8+ T cells of those patients even showed decreased P2Y2R levels. Regarding potential regulators of P2Y2R expression in the context of IBD, our data identified IL-6 and TGF-beta as major inducers of P2Y2R expression in human CD4+ T cells. Interestingly, high extracellular UTP levels resulted in a decreased expression of the TGF-beta1 receptor on CD4+ T cells, implicating a potential negative feedback loop in which P2Y2R signaling might inhibit TGF-beta1 induced P2Y2R expression over time. However, the impact of P2Y2R on the pro-inflammatory capacity of human lymphocytes, our data indicate that the selective P2Y2R agonist 2-Thio-UTP is able mediate NFkappaB as well as STAT3 activation and to induce secretion of the pro-inflammatory cytokines IL-6 and IL-17 in stimulated human monocyte cell lines.

Conclusion: The observed increased expression of P2Y2R in CD4+ T cells of IBD patients together with the demonstrated pro-inflammatory effects of P2Y2R signaling in human T cells markedly strengthen the role of P2Y2R as a promising molecular target in IBD.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

P0969 HIF-1A STABILIZATION THROUGH HYDROXYLASE INHIBITION AMELIORATES DSS-INDUCED COLITIS AND INDUCES AUTOPHAGY

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Introduction: Environmental hypoxia has been increasingly recognized as an important environmental factor associated with Inflammatory Bowel Disease (IBD). Hypoxia allows the stabilization of hypoxia inducible factor (HIF) complexes and has been linked to the activation of autophagy. HIF-1a is induced in the inflamed mucosa from IBD patients and mouse models of colitis, but its role in intestinal inflammation is still controversial since both, positive and negative effects have been reported.

Aims & Methods: We aim to elucidate the effects of HIF-1a stabilization in autophagy and the development of intestinal inflammation in a murine model of colitis. Female C57BL/6J mice between 8-10 weeks of age were exposed to 2% O2 in drinking water for 7 days, and received 8 mg of the hydroxylase inhibitor dimethyloxaloylglycine (DMOG) intraperitoneally every second day. Mice were killed at day 9, mucosal damage was assessed by colonoscopy and mucosal endoscopic score of colitis severity (MEICS) was calculated. H&E staining was performed to analyze the histological damage. Expression of TNF, IL-6, IL-1β and Nlrp3 was analyzed by qPCR and protein expression of p-NFkB and Nrf2, as well as HO-1 by western blot. Chemoattractant C5a was measured with the ELISA.

Results: DMOG administration induced a significant lower reduction of body weight in DSS-treated mice compared to DSS-treated mice administered with vehicle. Furthermore, mice administered with DMOG presented less reduction of the colon length, a significant reduction in the MEICS and histological scores of colitis. The mRNA expression of the pro-inflammatory factors TNF, IL-6, IL-1β and Nlrp3 was significantly reduced in mice treated with DMOG compared to vehicle-treated mice. At a protein level, DMOG administration reduced the expression of NLRP3. DMOG-treated mice also showed activation of autophagy, as evidenced by a decrease in p-mTOR and p62 expression and an increase of LC3II. In vitro, hypoxia induced a significant accumulation of lysosomes, as measured by LysoTracker Yellow-HCK-123 to monitor lysosomal accumulation. Chromatin immunoprecipitation (ChIP) analysis was performed using an antibody against HIF-1a and pCR was performed using the promoter-specific primers for the p62 promoter binding sites of HIF-1a.

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P0972 THE PATHOGENIC MECHANISM OF ARYL HYDROCARBON RECEPTOR MEDIATED ABNORMAL DIFFERENTIATION OF INTESTINAL ILC3/ILC1 IN CROHN’S DISEASE

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Introduction: The abnormal differentiation of intestinal innate lymphoid cells ILC3 and ILC1 exist in autoimmune disease. ILC3 decreased and ILC1 increased in Crohn’s disease (CD) patients, suggesting that CD patients have abnormal intestinal ILC3/ILC1 alteration.

Aims & Methods: The present study investigated the aberrant colonic mucosal ILC3/ILC1 in active CD patients and 2, 4, 6-trimethylbenzene sulfonic acid (TNBS)-induced colitis mice. The expressions of aryl hydrocarbon receptor (AhR) in colon of active and quiescent CD patients were detected by western blot and immunofluorescence. The ILC3/ILC1 were investigated in CD patients and 2, 4, 6-trimethylbenzene sulfonic acid (TNBS)-induced colitis mice (AhR−/−, AhR+/+).

Results: Compared to quiescent CD patients, the expression of aryl hydrocarbon receptor (AhR) in the intestinal tissue in active CD patients was decreased. Meanwhile, the number of ILC3 in active CD patients and AhR knockout mice was decreased while ILC1 increased. The intestinal inflammation in AhR knockout mice given TNBS was more severe than wild-type mice.

Conclusion: These findings suggest that AhR may mediate abnormal differentiation of ILC3/ILC1, and the production of inflammatory cytokines, finally, promotes the pathogenesis of CD.

Disclosure of Interest: All authors have declared no conflicts of interest.

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P0973 PREVALENCE AND GENETIC DIFFERENCES IN ADHESION-RELATED GENES AMONG COMMENSAL AND ADHERENT-INVASIVE E. COLI STRAINS

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Introduction: Long polar fimbriae (Lpf(A)), FimH adhesion and ChiA chitinase have been related with adherent-invasive E. coli (AIEC) pathogenesis. Controversial results have been found regarding the prevalence of LpfA in AIEC vs non-AIEC (1, 2). Some FimH amino acid variants were reported to be specific for AIEC (3) whereas other variants were associated with phylogroup disease origin of the strains (4). Differences in the ChiA sequence were reported between LF82 and K-12 strains but this gene has not been studied in other AIEC yet (5).

Aims & Methods: The prevalence of LpfA and the distribution of FimH and ChiA variants in AIEC collection of AIEC and non-AIEC from different disease origins - Crohn’s disease (CD), ulcerative colitis (UC) and colorectal cancer (CRC) - was studied with the purpose to determine if these genes could be used as molecular markers for AIEC identification and disease diagnostics. In a collection of 7 AIEC and 29 non-AIEC isolated from CD, UC, CRC patients and controls, LpfA gene was PCR-amplified to assess its presence and fimh and chia genes were sequenced to identify point mutations. For comparison of FimH and ChiA protein sequences, UPGMA phylogenetic tree and allele identification was performed using MEGA5. The genetic differences were annotated as reference for the K-12 strain. Then, they were analysed statistically according to AIEC pathotype, phylogroup, and disease origin by the χ2 test and non-parametric tests were used to evaluate amino acid variability regarding the adhesion and invasion indices.

Results: Low gene frequency for lpfA1441 and lpfA1545 was reported (11.7% and 16.7% respectively). LpfA1545 was only found in strains from A (22%) and B1 phylogroup (86%) and no relation with AIEC phenotype or disease was observed. Two main clusters of FimH were obtained by phylogenetic analysis, classifying the strains according to the presence of S78N mutation. S78N and S78N variants were characteristic from strains of B2 and D phylogroups as none of the A or B1 strains presented it. Despite statistical significance was not observed, the strains with S78N, S78N, V163A, R166H mutations showed the highest adhesiveness. Regarding ChiA, two main clusters defined by the presence or absence of an insertion in 312–314 residues were observed. None of the five previously mutations found in FimH in LF82 strain were associated with AIEC strains whereas the V415A variant was found specifically in AIEC (20%) (p = 0.049). Of note, among the strains harbouring the 312–314 insertion, a subcluster that shared identical amino acid sequence included the LF82 strain and the 44% of AIEC strains but only the 10% of the non-AIEC (p = 0.019). No differences between FimH/ChiA variants and origin of isolation was observed.

Conclusion: In contrast with other studies, no relation of lpfA presence nor in FimH mutations with AIEC pathotype or disease was observed. Nonetheless, a variant in ChiA sequence more frequently found in AIEC isolates was reported being an interesting signature sequence for the detection of at least a subgroup of AIEC strains. Further confirmation in a wider strain collection would be required.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P0974 DISTINCT GUT MICROBIOTA PROFILES IN PATIENTS WITH PRIMARY SCLerosING CHOLANGITIS AND UCERATIVE COLITIS

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Introduction: Primary sclerosing cholangitis (PSC) is a progressive disorder of the biliary tree which can lead to end-stage liver disease, liver transplantation or even death1. Colitis accompanying PSC is considered to be a phenotype of IBD (inflammatory bowel disease) distinct from ulcerative colitis (UC) and is often referred to as "PSC-IBD"2.

Aims & Methods: Our aim was to compare the gut bacterial microbiota of patients with PSC and UC. Stool samples were prospectively collected and relevant clinical data obtained from 106 study participants, 43 PSC patients with (n = 32) or without (n = 11) concomitant IBD, 32 UC patients, and 31 healthy controls (HC). Sequencing of the 16S rRNA gene including the V3 and V4 regions was performed on Illumina MiSeq platform to cover low taxonomic
levels. Data were further processed in QIIME employing MoAsLin and LESe to generate final output data.

Results: Microbial profiles in both PSC and UC were characterized by low bacterial diversity and significant change in global microbial composition. *Rothia*, *Enterococcus*, *Streptococcus*, *Veillonella*, and three other genera were markedly overrepresented in PSC regardless of concomitant IBD. *Rothia*, *Veillonella* and *Streptococcus* were tracked to the species level to identify *Rothia mucilaginosa*, *Streptococcus infantis*, *S. acuclotylicus,* and *S. equil* along with *Veillonella parvula* and *V. dispar*. PSC was further characterized by decreased abundance of *Alistipes* and *Prevotella corpori*. Decrease in genus *Phascolarctobacterium* was linked to presence of colonic inflammation regardless of IBD phenotype. *Akkermansia muciniphila*, *Butyrivibrio plicatocororum* and *Clostridium colinum* were decreased in UC along with genus *Roseburia*.

Unclassified *Actinomyces* species were markedly increased in overlap syndrome of autoimmune hepatitis (AHI) and PSC. Low levels of serum albumin were significantly correlated with enrichment of order Actinomycetales. PSC–IBD. Several bacterial taxa clearly distinguished IBD phenotypes (PSC–IBD). Ulcerative colitis (UC) as well as PSC from PSC/AIH.

Disclosure of Interest: All authors have declared no conflicts of interest.

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2. Chapman RW, Arbogth BA, Rhodes JM, Summerfield JA, Dick R, Scheuer PJ, Sherlock S. Primary sclerosing cholangitis: a review of its clinical fea-
Results: 28 patients with Ulcerative Colitis, duration of disease 4 months to 31 years were included. 22 Healthy population were recruited to the study. Half of the patients had active disease as assessed by Ulcerative Colitis Severity Score. Disease severity positively correlated with frequency of mucosal TH17 (CD4+IL-17a+) and IL-17f. Breaches in tight junction protein expression were greater in severity: Claudin 1 (p < 0.006), Claudin 4 (p < 0.0016) and occludin (p = 0.03). The serum marker of bacterial translocation, lipopolysaccharide binding protein (LBP) was increased in UC compared to controls (p = 0.0078) and was positively correlated with breaches of Claudin 1 and Occludin (p = 0.018 and p = 0.012 respectively) Staining colon biopsies for the presence of lipopolysaccharide in the lamina propria demonstrated positive findings in healthy controls, supported by data from 16s rDNA analysis of blood from healthy controls. In the Ulcerative Colitis cohort in clinical remission the absence of lipopolysaccharide in the lamina propria was associated with elevated levels of LBP and increased breaches of Occludin (p = 0.0022).

Conclusion: Breaches of tight junction proteins in the colon of patients with stable clinical remission can be detected and are associated with perturbations of mucosal immunological function and markers of bacterial translocation. Lipopolysaccharide presence in the lamina propria of patients in remission appears to be associated with less tight junction breaches and reduced local and systemic evidence of bacterial translocation. These findings require further study, specifically to examine the role of mucosal immune tolerance to lipopolysaccharide and other bacterial cell products that may be present in the healed mucosa of ulcerative colitis.

Disclosure of Interest: All authors have declared no conflicts of interest.

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P9979 EFFECT OF FIBER AND FAT CONSUMPTION ON DISEASE ACTIVITY AND QUALITY OF LIFE IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE
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Introduction: Diet may influence intestinal inflammation via various pathways but the evidence regarding the role of fiber or fat intake in patients with inflammatory bowel disease (IBD) is controversial.

Aims & Methods: The aim of this study was to investigate the association between dietary fiber or total fat intake and disease activity or quality of life in Greek IBD patients. We prospectively collected food frequency questionnaires (FFQ) from consecutive IBD patients at outpatient visits. The European Prospective Investigation into Cancer and Nutrition (EPIC) Study FFQ for Greece population with the MAFF photographic food atlas were used in order to collect information for dietary habits of IBD patients. Moreover, disease activity with the simple colitis activity index (SCCAI) (for ulcerative colitis (UC)) and information for dietary fiber or total fat intake and disease activity or quality of life in Greek IBD patients diagnosed in 2010 in Eastern and Western European centres. Patients were followed prospectively for five years and clinical data were captured throughout the follow-up period. Disease behaviour was defined according the Montreal classification as B1: non-stricturing, non-penetrating, B2: stricturing; B3: penetrating based on endoscopy, cross-sectional imaging or surgery. The risk of surgical resection was analysed by Cox regression analyses using the proportional hazard assumption including multiple covariates (age, gender, disease location, diagnostic delay, smoking status, change in behaviour, geographic region and treatment with biologics within 6 months from diagnosis).

Results: A total of 488 incident CD patients were included in the study, of which 347 (71%) had B1. A total of 141 (29%) patients had complicated CD at diagnosis. After 3 years’ follow-up, this number increased to 190 (39%) (Table 1). Of patients diagnosed with B1, 35 (10%) progressed to B2 while 14 (4%) progressed to B3 after a median of 21 months (range: 0–62). The proportion of B1 patients changing behaviour was highest during the 1st year of disease (5%) but stable during the remaining follow-up period (approx. 2%·year). Colon location (L2) was associated with a higher risk of transition to B3 (HR 0.3 CI95%: 0.1-0.8), extra-intestinal manifestations at diagnosis (HR 0.2 CI95%: 0.1-0.8), and the need for early biologics (HR: 2.5 CI95%: 1.2–5.1) were associated with progression in behaviour. During follow-up, a total of 107 patients had a resection. Of patients with B1 as initial behaviour a total of 37 (11%) patients had a resection. A change in behaviour from B1 to B2/B3 (HR 6.8 CI95%: 3.0-15.6) and early biologics (HR 0.5 CI95%: 0.2-0.5) was
associated with the risk for resection. No difference in the results was found between Eastern and Western European patients.

Table 1: Disease behaviour in Crohn’s disease at diagnosis and follow-up

<table>
<thead>
<tr>
<th>Timepoint</th>
<th>B1</th>
<th>B2</th>
<th>B3</th>
<th>Total (diagnosis)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FCP 1–2</td>
<td>0.352 0.015</td>
<td>–0.211 0.147</td>
<td>0.056 0.731</td>
<td>–0.265 0.068</td>
</tr>
<tr>
<td>FCP 1–3</td>
<td>–0.073 0.624</td>
<td>–0.173 0.234</td>
<td>0.043 0.785</td>
<td>–0.320 0.027</td>
</tr>
<tr>
<td>FCP 1–4</td>
<td>0.067 0.657</td>
<td>0.227 0.117</td>
<td>–0.027 0.870</td>
<td>–0.147 0.315</td>
</tr>
<tr>
<td>FCP 3–4</td>
<td>0.048 0.739</td>
<td>–0.123 0.381</td>
<td>–0.031 0.835</td>
<td>–0.099 0.967</td>
</tr>
<tr>
<td>FCP 1–5</td>
<td>0.048 0.739</td>
<td>0.031 0.835</td>
<td>–0.054 0.707</td>
<td>–0.453 0.001</td>
</tr>
<tr>
<td>FCP 2–4</td>
<td>0.062 0.675</td>
<td>0.006 0.982</td>
<td>0.203 0.152</td>
<td>–0.431 0.002</td>
</tr>
<tr>
<td>FCP 1–6</td>
<td>–0.117 0.427</td>
<td>0.040 0.797</td>
<td>–0.130 0.398</td>
<td>0.183 0.207</td>
</tr>
<tr>
<td>FCP 2–6</td>
<td>0.114 0.440</td>
<td>0.207 0.154</td>
<td>0.004 1</td>
<td>–0.124 0.400</td>
</tr>
<tr>
<td>FCP 3–6</td>
<td>0.201 0.168</td>
<td>0.020 0.907</td>
<td>–0.490 0.001</td>
<td>–0.262 0.072</td>
</tr>
<tr>
<td>FCP 4–6</td>
<td>0.242 0.080</td>
<td>–0.054 0.707</td>
<td>–0.003 1.000</td>
<td>0.185 0.128</td>
</tr>
<tr>
<td>FCP 5–6</td>
<td>0.111 0.428</td>
<td>0.091 0.518</td>
<td>0.009 0.967</td>
<td>–0.060 0.677</td>
</tr>
<tr>
<td>FCP 6–7</td>
<td>–0.103 0.465</td>
<td>0.126 0.369</td>
<td>–0.158 0.260</td>
<td>0.080 0.573</td>
</tr>
</tbody>
</table>

Conclusion: In this European population-based inception cohort of unselected CD patients 14% of patients with B1 progressed to B2 or B3 after five years of follow-up. The risk of surgery was increased in patients with B1 who progressed to B2/B3. No clinical predictors for progression in behavior including smoking and treatment with biological therapy could be identified.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0982 COLORECTAL CANCER IN INFLAMMATORY BOWEL DISEASE: RISK FACTORS IN A PROSPECTIVE MULTICENTER NESTED CASE-CONTROL IG-BIBD STUDY


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Abstract: P0982

The role of IBD phenotype vs thiopurines (IS) and/or anti-TNFs use as risk factors for CRC was also evaluated. From Jan. 2012 to March 2017, all incident cases of CRC in IB-IBD pts referring to 16 IG-IBD Units were recorded. Each IB-IBD pt with CRC (IBD-CRC) was matched with 2 IBD pts with no cancer (IBD-C) for: IBD type (Crohn’s Disease, CD vs Ulcerative Colitis, UC), gender, age (<5 yrs. vs B2/B3). No clinical predictors for progression in behavior including smoking and treatment with biological therapy could be identified.

Disclosure of Interest: All authors have declared no conflicts of interest.
pts with CRC were younger at diagnosis of IBD than their IBD-C (UC-CRC vs UC-C: median yrs 39 [15–76] vs 46 [20–81]; n [%]: 31 [51%] vs 27 [33%]–40 yrs: 20 [49%] vs 55 [67%]; p = 0.04; CD-CRC vs CD-C: median yrs 27 [6–67] vs 37 [10–67]; n [%]: 19 [76%] vs 26 [52%]–40 yrs: 6 [24%] vs 24 [48%]; p = 0.04). The median age at diagnosis of CRC was comparable between UC pts using or not IS and/or anti-TNFs (CRC-UC vs CRC-UC: IS monotherapy 6 [15%] vs 17 [21%]; Anti-TNFs monotherapy: no CRC; Combi-therapy: 5 [12%] vs 6 [7%]; no IS/no anti-TNFs: 11 [27%] vs 23 [28%]; p = 0.03). There were also observed less UC pts between CD pts treated or not with IS and/or anti-TNFs (CRC-CD vs CRC-CD: IS monotherapy: 4 [16%] vs 9 [18%]; Anti-TNFs monotherapy: 2 [8%] vs 3 [6%]; Combi-therapy: 10 [40%] vs 23 [46%]; no IS/no anti-TNFs: 16 [64%] vs 33 [70%]; p = 0.59). CD pts with CRC showed a higher frequency of pattern B1 (B1 vs B2: IS and/or anti-TNFs: 14 [56%] vs 3 [12%]; 8 [32%]/p = 0.019). Risk factors for CRC considered in Multivariate analysis included: age (<40 vs ≥40 yrs), IBD duration (<10 vs ≥10 yrs), smoking habits (Yes/No), IS, IS/anti-TNFs (Y/N), IBD-related surgery, UC extent (extensive vs distal; subtotal vs distal), CD pattern (I3 vs B1, I2 vs B1), perianal CD. In UC, the only significant risk factor was UC duration (OR [95% CI]: OR 3.33 [1.44–9.11], as the other risk factors were not significant: OR 0.94 [0.36–2.98], 1.28 [0.48–3.04], 0.96 [0.36–3.08], 1.78 [0.60–4.66], 1.36 [0.66–2.89], 0.38 [0.08–1.23], respectively). In CD, perianal disease was the only significant risk factor for CRC (OR 3.11 [1.16–8.31], as not all significant risk factors were identified (OR 2.21 [0.70–9.87], 1.66 [0.62–4.96], 0.56 [0.19–1.41], 0.39 [0.14–2.52], 0.54 [0.23–1.43], 0.83 [0.26–2.55], 0.23 [0.04–0.83], respectively).

Conclusion: In a prospective, multicentre, nested-case control IG-IBD study, incident cases of CRC were more frequent in UC than in CD. In our cohort, UC duration and perianal CD, but not immunomodulators use, were identified as independent risk factors of CRC.

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References

2. Biancone L JACC 2016;10(8):913
P0984 IMPACT OF ANORECTAL COMPLAINTS ON QUALITY OF LIFE IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE - A SURVEY OF THE DUTCH NATIONAL CROHN’S AND COLITIS ORGANISATION

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Introduction: Anorectal complaints occur in a considerable group of patients with IBD. There is a dearth of evidence relating to the impact of these complaints on IBD patients’ lives. We aimed to survey the effect of anorectal complaints on quality of life in a large cohort of patients who engaged in the Dutch Crohn’s and Colitis organisation (CCUVN).

Aims & Methods: In October 2016, the CCUVN had a membership database of 10,487 patients. A comprehensive study questionnaire was sent out online by the CCUVN in January 2015 and October 2016 to a voluntary panel, which consisted of 1710 CCUVN patients. The panel is represented by patients who volunteered to participate in online surveys with regard to disease related subjects. Inclusion criteria: Patients over 18 years old and either diagnosed with CD (Crohn’s disease), UC (ulcerative colitis), or IBD-U (a (usually unmet and) clear need to treat). More patients were exclusively found in pouchitis which included FAP, CD and UC.

Results: A total of 1094 patients (64%) responded the online survey. Mean age was 48.7 years (range 18-87). CD diagnosis was predominant (62% CD patients (57%), 431 UC patients (39%) and 42 IBD-U patients (4%)) and diagnosis was established for a mean period of 13 years (interquartile range 3–19 years). Active perianal disease was present in 243 CD patients (39%) and perianal surgery was performed in 137 (21.3%) CD patients. Active perianal disease was present in 243 CD patients (39%) and perianal surgery was performed in 137 (21.3%) CD patients. Multivariate regression analysis (adjusted for gender, diagnosis and previously performed perianal surgery) showed a reduced total SF-36 score in patients with faecal incontinence (β = −8.57 [−11.33; −5.81]; p < 0.0001) and active perianal disease (β = −4.13 [−7.33; −0.91]; p = 0.01). A better score was reported in UC patients compared to CD patients (β = 3.53 [0.48:6.58]; p = 0.02). Previously performed perianal surgery was not associated with SF-36 score in the multivariate analysis.

Conclusion: Anorectal complaints have a substantial impact on the quality of life in patients with IBD, with a (usually unmet and) clear need to treat. More awareness for this highly distressing and most common cumbersome treatable disease manifestation is needed.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0985 CURRENT UNDERSTANDING OF POUCH MICROBIOTA IN HEALTH AND DISEASE; A SYSTEMATIC REVIEW

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Introduction: The human gut microbiome is made up predominantly of four major bacterial phyla, Firmicutes, Bacteroidetes, Proteobacteria and Actinobacteria. Changes or imbalance of these phyla is termed dysbiosis. Specifically, in inflammation bowel disease (IBD), key changes have been identified such as a reduction in beneficial bacterial species including Faecalibacterium prausnitzii and increases in more pathogenic species including members of the Enterobacteriaceae. Currently it is not understood if dysbiosis is the cause of, or the effect of, intestinal inflammation. It is difficult to chronologically assess the microbiota changes prior to developing IBD as currently we are unable to predict those individuals who will develop the disease. The pouch is a potential model to study pathogenesis of inflammatory disease as 40% of those that develop pouchitis do so within 12 months. The relative short time from pouch formation to inflammation allows the longitudinal study of the microbiota which gives insight into potential microibota patterns occurring both in disease and non-diseased states. Interestingly, inflammation within the pouch is rarely seen in patients who have this operation for Familial Adenomatous Polyposis (FAP), thus raising the possibility that pouchitis shares a similar pathogenesis to the inflammation that is seen in ulcerative colitis.

Aims & Methods: 1. To understand changes in pouch microbiota over time. 2. To understand pouch microbiota that is associated with pouch formation A computer assisted search of the on-line bibliographic databases MEDLINE and EMBASE was carried between 1966 and February 2016. Randomised controlled trials, cohort studies and observational studies were included. Inclusion criteria: Studies which reported microbiota analysis on either faecal samples or tissue from the ileo-pouch anastomosis. Studies that provided information on specific bacterial taxa. Exclusion criteria: Studies which did not report on patterns of individual bacterial taxa differences in the pouch. Studies on the microbiota of Crohn’s disease or UC in isolation without any data on pouch patients. Studies with less than ten patients.

Results: The search strategy found 844. There were a total of 27 papers included in the analysis. Microbiota in pouchitis: Bacteroidetes, Enterococccaceae, Lachnospiraceae, Faecalibacteriaceae, Ruminococcaceae, Streptococci, Alcaligenaceae and Bifidobacterium were reduced in patients with pouchitis. Whereas Enterobacteriaceae, including E. coli Faecalibacterium and Clostridia were increased in patients with pouchitis. One study highlighted bacteria that were exclusively found in pouchitis which included Lepotospira, Pseudomonas, Desulfovirgulis, Micrococcus, Methylbacter. Chronic pouchitis was associated with a significant increase in Staphylococcus aureus and it has been suggested that this may be a responsible pathogen for chronic pouchitis. Furthermore, Enterococcus, F. prausnitzii, Lachnospiraceae and Insertae Sedis XIV and have been shown to be significantly reduced in chronic pouchitis patients. These differences were largely due to a decrease in sequences from members of the genera Ruminococcus, Dorea, Clostridium, and Eubacterium.

Conclusion: The microbiota undoubtedly plays an important role in both the inflamed and the healthy pouch. However, a direct causal relationship has not yet been established between individual microbiota changes and inflammation. There are many studies that highlight changes in bacterial composition, but studies are limited by heterogeneity of and in particular, analysis techniques and sampling strategies. Studies used a variety of methods to define microbial diversity which can be broadly split into culture vs culture-independent approaches. Culture-based studies are likely to have a bias towards cultivating more aerobically friendly microbes than exist in a true pouch environment, thus over-representing aerobic bacteria whilst possibly under-representing anaerobic bacteria. The use of 16 S RNA analysis methods will negate this effect and represents the future in accurately determining the microbiota.

Disclosure of Interest: All authors have declared no conflicts of interest.

Abstract: P0985, Table 1: Evolution of pouch microbiota over-time

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>Analysis method</th>
<th>UC or FAP</th>
<th>Comparator</th>
<th>Key findings in UC</th>
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<td>Almeida</td>
<td>2008</td>
<td>Mucus-culture</td>
<td>UC</td>
<td></td>
<td>Two vs eight months after ileostomy closure Enterobacter Klebsiella</td>
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<td>Kohyama</td>
<td>2009</td>
<td>Faeces-PCR Terminal restriction fragment length polymorphism amplification</td>
<td>UC</td>
<td></td>
<td>Uc vs healthy controls C. coccoides</td>
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<tr>
<td>Hinata</td>
<td>2012</td>
<td>Faeces-16S RNA</td>
<td>UC</td>
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<td>UC vs healthy C. coccoides subgroup C. leptum subgroup B. fragilis group Aosiphilobacter</td>
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| Six-eight months | | | | | |
| Almeida | 2008 | Mucus-culture | UC | | Two vs eight months post ileostomy Most prevalent: E. coli F. velillum Enterobacter, Klebsiella Peptococcus |
| Bednarz | 2015 | Swab-culture | UC | | UC longitudinal Enterobacteriaceae most common |
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| One year | | | | | |
| Luukkonen | 1988 | Faeces-culture | UC | | Kock ileostomy and ileostomy Transformation to a “colonic” microbiota |
| Hinata | 2012 | Faeces-PCR | UC | | Healthy volunteers Enterococcus Lactobacillus |

P0986 LIVE-VACCINES AND BREASTFEEDING IN NEWBORN EXPOSED IN UTERO TO ANTI-TNF: A MULTICENTER FRENCH STUDY IN INFLAMMATORY BOWEL DISEASE

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6CHU Nancy, Nancy/Nancy

Disclosure of Interest: All authors have declared no conflicts of interest.

Abstract: P0986, Table 1: Evolution of pouch microbiota over-time

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<th>Study</th>
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<th>UC or FAP</th>
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United European Gastroenterology Journal 5(5S)
France

but often performed before 6 months. Information to pregnant IBD women is because of a bad bowel preparation for 4 times. In 13 patients (72.2%) no mum: 1). 2 patients refused next colonoscopy, one patient was not controlled not resectable and referred to surgery. 31 lesions were resected in 21 patients: 22 dysplasic lesions were identified in 25 patients; 5 lesions were judged endoscopic control was done at 6 month than every one year.

Results: 36 dysplasic lesions were identified in 25 patients; 5 lesions were judged endoscopically in ulcerative colitis. In this prospective study of 27 patients with longstanding ulcerative colitis were assessed for their resecability, 23 patients (85%) and was administered before 6 months in 15 children (14%). One local anti TNF was discontinued before 26 gestational weeks in 66 (53%) women during pregnancy, 18 (15%) women were treated with steroids. Recent guidelines recommend the complete endoscopic resec-

Endoscopic Ally Resected Dysplasic Lesions in Ulcerative Colitis

Introduction: Anti TNF cross placenta during pregnancy and are detectable in the newborn in the first 6 months at least. Along this, European consensus recommends to avoid live vaccines within 6 months of live in newborn exposed in utero to anti TNF treatments. Moreover, anti TNF treatments are low of risk for breastfed infants but data are scarce. The aim of our study was to evaluate the rate and tolerance 1) of live-vaccines before and after 6 months of life in newborn exposed in utero to anti TNF and 2) of breast feeding under anti TNF. Aim of this study was to perform an observational study in 22 French departments of gastroenterology from February 2016 to April 2017. Included patients were inflammatory bowel disease (IBD) women, pregnant under anti TNF, giving birth to alive newborn and agree to answer a questionnaire concerning 1) live vaccines (BCG, rotavirus, MMR) in their child during pregnancy.

Results: 124 pregnant women treated with anti TNF were included. The mean age of women was 31 year (IQR 5). 96 (77%) patients had a flared of IBD during pregnancy, 18 (15%) women were treated with steroids. Anti TNF was discontinued before 26 gestational weeks in 66 (53%) women and resumed after delivery in 112 (90%) patients. 35 women (45%) breastfed their newborn, this continuation was noted among 69 women who did not perform lactation, 42 (63%) did not for personal choice and 25 (37%) because not recommended by the gastroenterologist. Concerning vaccination questionnaires, 96 responses were obtained. BCG was performed in 29 children (30%) and was administered before 6 months in 15 children (14%). One local abscess was reported with favorable evolution. Rotavirus vaccination was performed in 7 children (7%) before 6 months in 5 (5%) cases. One case of fever was reported. MMR vaccination (Measles, Mumps and Rubella) was performed in 62 children (65%): before 6 months in 5 cases. Information concerning fetal exposure to anti TNF and vaccination recommendation was given to 111 (91%) IBD women during pregnancy, by at least the gastroenterologist in 89% of cases, the obstetrician in 25% of cases and the paediatrician in 16% of cases. Immunoglobulin in 105 (86%) cases and tetrax in 39 (32%) cases.

Conclusion: Half of women breastfed their child with no reported complication. BCG was administered in 30% of the newborn and performed before 6 months in 50% of cases. There was only one case of local abscess. Rotavirus vaccination is rare but often performed before 6 months. Information to pregnant IBD women is only given by gastroenterologist in the majority of cases. Information in maternity by obstetrician and pediatrician should be improved.

Disclosure of Interest: All authors have declared no conflicts of interest.

P9097 Outcome of Endoscopic Ally Resected Dysplasic Lesions in Ulcerative Colitis


Introduction: The aim of this study was to determine the outcome of dysplastic lesions resected endoscopic ally in ulcerative colitis. In this prospective study between January 2008 and January 2015, dysplastic lesions detected in patients with longstanding ulcerative colitis were assessed for their resectability, then when they were resected. The patients were followed, and an endoscopic control was done at 6 months every one year.

Results: 36 dysplastic lesions were identified in 25 patients; 5 lesions were judged not resectable and referred to surgery. 31 lesions were resected in 21 patients: 22 low-grade dysplasia, 7 lesions indefinite for dysplasia, and 2 high-grade dysplasia. 18 patients (85.7%) had endoscopic control: mean 2.8 (maximum: 5 minimum: 1). 2 patients refused next colonoscopy, one patient was not controlled because of a bad bowel preparation for 4 times. In 13 patients (72.2%) no dysplasia was detected after a mean follow up of 30.16 months (range: 7.56–

P9098 CYTOMEGALOVIRUS INFECTION IS ASSOCIATED WITH A POOR OUTCOME IN PATIENTS WITH UC: TREATED WITH VEDOLIZUMAB

X. Robin1, L. Brichet1, S. Pillier2, E. Del Tedesco3, J. M. Phelip3, B. Pozzetto2, N. Willems3

Introduction: The aim of this study was to analyze the outcome of UC patients treated with Vedolizumab and to analyze the risk factors for CMV disease associated with Vedolizumab therapy.

Aims & Methods: We performed a retrospective case-control study of all patients with UC treated with Vedolizumab from June 2014 to April 2017. The CMV disease was defined as CMV DNA load was found undetectable for all 6 patients. Treatment change was more frequent in the CMV disease group (HR = 3.15 [1.02–9.7], p = 0.03507) with only 16.7% patients who continued Vedolizumab treatment versus 65.4% in the control group (p = 0.0052). Coleotyam was also more frequent in the CMV group (33.3% versus 7.7% p = 0.0064). By multivariate analysis, the only factor associated with the occurrence of CMV disease was a fecal calprotectin less than 600 mcg/g stools at the beginning of the vedolizumab treatment. A previous history of colitis infection also was more frequent but not statistically significant. There was no association between CMV infection and Vedolizumab levels in the sera.

Conclusion: The occurrence of CMV disease, documented with high CMV DNA load on colonic biopsy samples, in UC treated with Vedolizumab is responsible for a negative impact on the natural evolution of UC, with more therapeutic failure and surgical treatment, even after an efficient antiviral treatment.

Disclosure of Interest: All authors have declared no conflicts of interest.

P9099 F-CALPROTECTIN USE IN INFLAMMATORY BOWEL DISEASE IS CHARACTERIZED BY IMPROVED DIAGNOSTIC ACCURACY, LESS PATIENT HARM AND DECREASED COSTS, COMPARED WITH CONVENTIONAL SEROLOGICAL MARKERS AND COLONOSCOPY. THE SPANISH SCENARIO

B. Muscalino1, A. A. Vora2

Introduction: Gastrointestinal disorders may exhibit overlapping symptoms making diagnosis difficult in the primary and specialty care settings. Inflammatory bowel disease (IBD), with a prevalence of <0.5% in the general population[1], is characterized by chronic inflammation of the gastrointestinal tract, non-specific elevation of conventional inflammatory markers such as ESR and CRP and may present with extra-intestinal manifestations. Irritable bowel syndrome (IBS), in contrast, is a functional disorder without gastrointestinal inflammation and with an estimated prevalence of 10-20% [2]. Endoscopy is the gold standard for detecting and quantifying IBD vs. IBS, but due to the low prevalence of IBD, is negative in the majority of cases. Furthermore, it is invasive, expensive, and uncomfortable for the patient and not without risks. Moreover, inadequate bowel preparation prior to colonoscopy is known to
increase the burden of disease from both the clinical and the economic perspec-
tive: shorter intervals between repeated procedures, higher missed rates, patient
inconvenience, and increased risk of complications are reported in the scientific
literature. F-Calprotectin (FC) is a fecal marker of intestinal inflammation; IBD
patients exhibit FC levels significantly higher than the general population; IBS
patients, however, have FC levels higher than healthy controls, but significantly lower than
IBD patients [3]. Therefore, FC can be used as a pre-endoscopic test to differ-
entiate between IBD and IBS. The present study aims at evaluating the cost-
effectiveness of FC compared to the combined usage of CRP and ESR, and the
gold standard to distinguish IBD from IBS in Spain.

Aims & Methods: An 18-week Markov model was developed for each diagnostic
strategy, simulating 1000 patients presenting to a primary care physician with
non-specific gastrointestinal symptoms. In the model, 1.6% of the colonoscopies
brought about complications [4], which may result in Emergency Room visits
and surgery. Inadequate colon preparation (23%)[5] and consequent repeated
colonoscopies (30.3%)[6] were also included in the calculations. Outcomes include cost savings, cost per corrected IBD diagnosed, and colonoscopy reduc-
tion. Uncertainty was addressed with sensitivity analysis.

Results: FC is cost-effective when compared to CRP and ESR, and to colonoscopy
(Table 1): It results in more correctly IBD diagnoses at a lower price; It reduces the number of unnecessary endoscopies, increasing the number of correctly diag-
osed IBD (N = 63) and IBS (N = 26) patients.

Clinical and health economics results

<table>
<thead>
<tr>
<th>FC-Calprotectin</th>
<th>CRP + ESR</th>
<th>Colonoscopy</th>
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<td>N correctly diagnosed IBS</td>
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<td>657</td>
</tr>
<tr>
<td>N correctly diagnosed IBD</td>
<td>98</td>
<td>35</td>
</tr>
<tr>
<td>Total costs (EUR)</td>
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<td>477.8</td>
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<tr>
<td>Average cost/patient (EUR)</td>
<td>336.3</td>
<td>305.0</td>
</tr>
<tr>
<td>N colonoscopies avoided</td>
<td>260.6</td>
<td>0</td>
</tr>
<tr>
<td>Savings ascribable to the avoided colonoscopies</td>
<td>336.3</td>
<td>305.0</td>
</tr>
</tbody>
</table>

Conclusion: Results show that the usage of FC as pre-endoscopic diagnostic tool is
associated with fewer colonoscopies and correctly identifies more disease while
decreasing the costs compared to the alternatives. Consequently, FC demonstrates
superior value both from patient and payer perspective, while simultaneously
decreasing diagnostic efficacy.

Disclosure of Interest: B. Mascalamo: Employee of Thermo Fisher Scientific
A.A. Vora: Employee of Thermo Fisher Scientific

References

P0990 RISK OF SERIOUS INFECTION IN HEALTHCARE WORKER WITH INFLAMMATORY BOWEL DISEASE: A CASE-CONTROL STUDY OF THE GETAD

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Introduction: The increased use of immunomodulators and biological agents for the
treatment of patients with inflammatory bowel disease (IBD) is associated with
a key safety concern considering potential serious infection. Healthcare
workers are at a special risk for acquiring such infections due to daily and close interactions with infected patients and asymptomatic carriers of
pathogens.

Aims & Methods: We performed a retrospective observational study, collecting
data from the Group of Etude Thérapeutique des Affections Inflammatoires du
tube Digestif (GETAD) from January 2015 to June 2016, on all 482 consecutive
patients with IBD (68.5% with rohn’s disease, 28.4% with ulcerative colitis and
3.1% with IBD undetermined) who work as healthcare workers (27.2% of phys-
sicians, 33.6% of nurses, 13.1% of nurses’ aides and 26.7% of other healthcare
personnel working in interaction with in-hospital patients), in 17 tertiary centers
in France and Belgium. We selected a control group of patients with IBD who do
not work as healthcare personnel from the monocentric MICISTA database.
Controls were matched on age (±2.5 years), sex, IBD type and date of IBD
diagnosis (±2.5 years). Serious infection was defined as (1) Clostridium difficile
infection (2) community-acquired pneumonia (3) Mycobacterium tuberculosis
infection (4) any community-acquired infection that required hospitalization.
Serious infection-free survival was studied with Kaplan-Meier method, log-
rank test and Cox regression model. In each patient, the duration of IBD was
divided into semesters which were independently analyzed regarding the occur-
rence of serious infection too take into account the influence of various treatments.

Results: 482 patients (126 male; median age: 24.0 [IQR 19.9–32.1] years) were
included in the present study. The median follow-up period was 9.3 [4.6–16.2]
years. A total of 74 serious infection was recorded in healthcare workers includ-
ing 14 Clostridium difficile infection, 19 EBV or CMV-related serious viral infec-
tion, 8 tuberculosis infection including 4 tuberculosis and 4 tuberculous primo-
fection, 8 community-acquired pneumonia and 25 miscellaneous serious infec-
tion. The probabilities of serious infection-free survival were 1.0%, 6.1%, 10.8% and
14.1% at 1, 5, 10 and 15 years. No difference was found between healthcare
workers and control patients regarding the occurrence of serious infection in
time-dependent analysis and in independent semester analysis. However, a
increased risk of tuberculosis infection was found in healthcare workers (OR = 4.27, p = 0.002).

Conclusion: Although there is an higher exposure to potential pathogens in
healthcare workers, this is not associated with an higher risk of serious infection as
compared with controls with the exception of tuberculosis infection. Prospective studies are needed to confirm that the level of occupational exposure
to potential pathogens should not be taken into account when discussing the introduction of immunomodulator or biological agents with the exception of
the risk of tuberculosis infection.

Disclosure of Interest: P. SEKSIK: Philippe Seksik received consulting fees from Abbvie, Msd and Mecodex, grants from Bocodex, sponsored travel from Merck-MSD and Takeda

J. Gornet: Jean-Marc Gornet has received fees from Sanofi, Merck Serono, Roche, Novartis, Amgen and travel accommodation from Abbvie and MSD.

O. Dewit: Dewit O: lecture fees from MSD

S. Nancey: Stephane Nancey has received consulting fees from Merck, Abbvie, Takeda, Ferring, Novirine, Vifor Pharma, Novaris, Janssen Cilag, Hospira, Takeda and HAC-Pharma.

V. Abitbol: Vered Abitbol has received lecture fees from Ferring, MSD, Vifor Pharma and Abbvie.

D. Laharie: David Laharie has received consulting and lecture fees from AbbVie, Ferring, Janssen Cilag, MSD, Pfizer, and Takeda.

A. Buisson: Anthony Buisson has received consulting fees from Abbvie, MSD, Janssen; lectures from Abbvie, MSD, Roche, Takeda, Falk, EL; consulting and lecture fees from Abbvie and MSD.

M. Nachury: Nachury M declares lecture fees from Abbvie, MSD, Takeda, and Takeda.

S. Viennet: Stephanie Viennot has received consulting fees from Abbvie, MSD, Vifor Pharma and Ferring.

C. Stefanescu: Stefanescu M: consulting fee from MSD and sponsored travel from Abbvie, Msd, Takeda, Mayolii,
the MES was 0.848, for the DS 0.801 and for the MMES 0.815, and there was no
were not superior to Mayo Endoscopic Score.
Calprotectin, the correlation between scores that take into account the extension
lation was found with the DS. There was no significant correlation between ESR
45.3
60 patients were included, 46.7% female patients with mean age
l and Calprotectin 354
100 g/g. This was a retrospective study, including patients with
diagnosis of left or extensive UC who underwent colonoscopy between 2015 and
2016. The biomarkers were obtained with a maximum interval of one week in
relation to colonoscopy and without introduction of new therapy. The Spearman
test calculated the correlation between scores and biomarkers. ROC curves
(AUC) were obtained for each score to predict Calprotectin >100 g/g.
Results: 60 patients were included, 46.7% female patients with mean age
45.3 ± 12.8 years with mean values of ESR 4.4 ± 12.8 mm, CRP 5.2 ± 6.00 mg/
1 and Calprotectin 354 ± 430 g/g. The correlation between Calprotectin and
Mes was rs = 0.623 p < 0.001, for DS rs = 0.548 p < 0.001 and for MMES
rs = 0.588 p < 0.001. Regarding CRP, a correlation with the MES was
rs = 0.414 p = 0.015; and with the MES was rs = 0.404 p = 0.001, but no corre-
lation was found with the DS. There was no significant correlation between ESR
and endoscopic scores. To predict values of Calprotectin >100 g/g the AUC for
the MES was 0.848, for the DS 0.801 and for the MMES 0.815, and there was
no statistically difference between the curves.
Conclusion: Although there is a good correlation between endoscopic scores and
Calprotectin, the correlation between scores that take into account the extension
were not superior to Mayo Endoscopic Score.

P0992 IBD – IS IT A RISK FACTOR FOR THE DIAGNOSIS OF HEPATIC STEATOSIS?
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Introduction: Although it is not yet established, recent studies suggest an increase
prevalence of hepatic steatosis (HS) in patients with inflammatory bowel disease
(IBD). Factors such as chronic inflammation, previous surgeries, drug-induced
hepatotoxicity, malnutrition and intestinal dysbiosis seem to be involved in the
pathogenesis of this disease.
Aims & Methods: We aimed to assess the frequency of HS in IBD patients
quantified by CAP (controlled attenuation parameter) and by clinical-analytical
methods: Hepatic Steatosis Index (HSI) and Fatty Liver Index (FLI). A second-
ary aim is to investigate risk factors associated with HS in IBD patients. This
was a retrospective study that included consecutive patients that were observed
in our department between January and March 2017. Patients with known liver
disease or alcohol habits were excluded. HS was defined as HSI ≥ 36 or FLI ≥ 60
or CAP ≥ 248.
Results: 149 patients included with mean age 40.7 ± 13 years, 83 female (55.7%),
59.7% with Crohn’s disease (CD). 62 patients (41.7%) had CAP ≥ 248.20
(13.4%) FLI > 60 and 40 (26.8%) HSI > 36. There were no differences in the
mean CAP value (244 ± 54.2), HSI (33.3 ± 5.8), and FLI (31.5 ± 25.3) among
patients with CD and inflammatory Crohn’s disease. We found that patients with
CAP ≥ 248 were more frequently obese (27.4% vs 0% p < 0.001), males (54.8% vs.
36.8% p = 0.029) and presented more frequently metabolic syndrome (25% vs 4.6%
p < 0.001). Regarding the IBFD factors, patients with HS had a higher frequency
of previous surgeries (30.6% vs16.1% p = 0.035). There were no differences
between hospitalization, duration of the disease, use of corticosteroids or other
IBD treatments.
Conclusion: In our cohort the frequency of HS varied between 13.4% and 41.7%
defined by non-invasive methods. We found that the presence of metabolic syn-
drome and obesity were more frequent in patients with HS. Regarding factors related
to IBD, patients with previous history of surgery were more frequently
diagnosed with HS.
Disclosure of Interest: All authors have declared no conflicts of interest.

P0993 BONE HEALTH IN CROHN’S DISEASE IN THE ERA OF TNF-ALPHA INHIBITORS
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America/M
2Gastroenterology, UMass Medical Center, Worcester/United States of America
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Introduction: Osteoporosis and fractures are common in Crohn’s disease (CD).
Recently, several inflammatory cytokines, including tumor necrosis factor
(TNF)-alpha have been linked to increased bone resorption. Therefore, it is
hypothesized that anti-TNF therapy may influence osteoporosis and fracture
risk. However, few studies have evaluated osteoporosis and fracture risk in the
CD population.
Aims & Methods: The aim of this study is to gain a better understanding of the
epidemiologic risk factors for osteoporosis and vitamin D deficiency in the era of
TNF-alpha inhibitors. We conducted a retrospective review of 714 consecutive
patients with CD in our GI clinic between 2008 and 2015 to identify 464 patients
who met the inclusion criteria for the study comprising of all adults older than 18
years with confirmed CD based on labs and endoscopic findings. Data extracted
for analysis included demographics data, disease phenotype, duration of disease,
measures of disease activity, imaging and endoscopic data. Statistical analysis
was performed using student t-test and chi-square test.
Results: We reviewed the charts of 290 patients with CD treated with TNF-alpha
inhibitors (TNF) and 174 patients who are anti-TNF-naïve (NB). There were 207
(45%) males and 257(55%) females in this cohort. TNF patients tended to be
younger (average age of 43+/−15 and 54 +/− 18 years in TNF and NB groups
respectively). Mean duration of disease was 14.9 +/- 10.2 years for TNF and 18.6 +/-
19.2 for NB group. Approximately half of the patients had a smoking history.
Average BMI was 27.6 +/- 6.6. Rates of vitamin D deficiency, insufficiency and
normal vitamin D-25-OH levels were not significantly different between TNF
and NB groups. Vitamin D level was not associated with age, duration of disease,
or inflammatory markers (ESR). However, there was a weak positive correlation
between nutritional status (lowest albumin) and vitamin D level (Pearson’s R
=0.420). Concomitant use of TNF and corticosteroids was recorded in 168 patients
which included 100 patients in the TNF group and 68 patients in the NB group.
There was similar rate of osteoporosis (16% vs 18%), osteopenia (53% vs 57%) and
normal bone density (31% vs 25%) between the TNF and NB groups respectively.
Furthermore, there was no statistically significant difference in T-scores at the hip
(−1.2 vs −1.3), the spine (−1.0 vs −0.95), or the lower T-scores (−1.5 vs −1.4) between
TNF and NB patients. However, Z-scores at the spine (−0.47 vs −0.05), the hip (−0.55
vs −0.49) and the lowest Z-scores (−0.91 vs −0.67) were lower in the TNF group,
but only reached significance at the spine (P=0.03). Interestingly, a significantly
higher proportion of TNF patients under 60 years of age met the criteria for
osteoporosis (T-score < −2.5 below the mean) as compared to NB patients (15%
vs 3.6%). Additionally, rates of osteoporosis in the NB group were very different
between before and after age 60 (3.6% vs 30%)[table 1]. There was no correlation
with bone density and vitamin D level, nutritional status (based on lowest albumin
level), or degree of inflammation (highest ESR or CRP levels). However, there
was a moderate positive correlation with BMI and bone density (Pearson R
= 0.39) and a negative correlation with age (R = −0.25).
Table 1: Osteoporosis rates in patients on anti-TNF therapy (TNF) and those
naive to biologic medications (NB) before and after age 60.

<table>
<thead>
<tr>
<th>Group</th>
<th>Age &lt; 60</th>
<th>Age &gt; 60</th>
</tr>
</thead>
<tbody>
<tr>
<td>TNF</td>
<td>15.4%</td>
<td>18.2%</td>
</tr>
<tr>
<td>NB</td>
<td>3.6%</td>
<td>30.0%</td>
</tr>
</tbody>
</table>

Conclusion: Rates of vitamin D deficiency, and osteoporosis were similar among
patients on anti-TNF medications to those on no biologics. TNF group patients
were diagnosed with osteoporosis at an earlier age compared to NB group.
Patients on anti-TNFs also had statistically lower Z-scores at the spine. Prospective
studies are necessary to further determine the role of anti-TNF medications
in osteoporosis.
Disclosure of Interest: All authors have declared no conflicts of interest.

P0994 THE AVAILABILITY OF INFliximAB TROUGH LEVELS IN IBD PATIENTS ON MAINTENANCE THERAPY DEEPLY IMPACTS THERAPEUTIC DECISION-MAKING
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2Immunology, Hospital Universitari Germans Trias i Pujol, Badalona/Spain
Contact E-mail Address: triantany2010@gmail.com

Table 1: Osteoporosis rates in patients on anti-TNF therapy (TNF) and those
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<table>
<thead>
<tr>
<th>Group</th>
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<tbody>
<tr>
<td>TNF</td>
<td>15.4%</td>
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</tr>
</tbody>
</table>

Conclusion: In our cohort the frequency of HS varied between 13.4% and 41.7%
defined by non-invasive methods. We found that the presence of metabolic syn-
drome and obesity were more frequent in patients with HS. Regarding factors related
to IBD, patients with previous history of surgery were more frequently
diagnosed with HS.
Disclosure of Interest: All authors have declared no conflicts of interest.
Introduction: Infliximab (IFX) trough levels (ITLs) have emerged as a promising tool for the management of inflammatory bowel disease (IBD) patients and they correlate with clinical response and endoscopic remission. However, its use in clinical practice is still under debate, particularly in clinically stable patients.

Aims & Methods: 1) to describe real-life ITLs in clinically stable IBD patients; 2) to identify subjective factors associated with intra-therapeutic ITLs; and 3) to evaluate the impact of ITLs availability by comparing the CCD with TLGD. The decisions between experts were also compared. Both comparisons were calculated by the linear Cohen’s Kappa (κ) index. IBD patients on maintenance IFX therapy were prospectively included from June 2015 to June 2016. Demographic, clinical and biological data including C-reactive protein (CRP) levels from the same infusion day were collected. At each IFX infusion, patients were visited by their physician; a “current clinical decision” (CCD) was taken regarding clinical data and CRP. Infliximab levels measured just before the IFX infusion were considered as infratherapeutic if <2 μg/mL. Once ITLs were known, 3 experts took a hypothetical decision on treatment based on the same clinical and biological data plus ITLs (ITL-guided decision – TLGD).

Results: A total of 224 IFX infusions from 74 patients (76% Crohn’s disease) were analyzed. Median (IQR) disease and IFX therapy duration was 10 years (5-18) and 23 months (7-61), respectively; 87% received concomitant immunosuppressant therapy; 70% were on standard dosing, whereas 10% were scheduled every 4-6 weeks. Median (IQR) ITLs were 1.79 μg/mL (0.53-3.74), with 52% of patients having infratherapeutic ITLs. In the multivariate analysis, the only risk factor for infratherapeutic ITLs was the presence of biological activity. Concordance between experts A-B/B-C/A-C respectively. Moreover, concordance between experts was moderate (κ = 0.40 [95%CI:0.26–0.55]) between experts A-B/C-B/A-C respectively.

Conclusion: Our results highlight the impact of the inflammatory burden on ITLs and the importance of their therapeutic range in patients clinically stable. Both the clinical and economical impact of ITL-assisted decision-making in IBD patients should be evaluated in prospective cohorts.

Disclosure of Interest: E. Domenech: Fees for advisory, lectures and research grants from MSD, AbbVie, Takeda, Kern and Pfizer. All other authors have declared no conflicts of interest.

P0995 THE DIAGNOSTIC UTILITY OF LINKED-COLOR IMAGING IN THE EVALUATION OF MUCOSAL INFLAMMATION IN PATIENTS WITH ULCERATIVE COLITIS

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Introduction: Recent studies recommend the histological mucosal healing of the intestinal tissue as a treatment goal in ulcerative colitis (UC). The intestinal tissue modality using white-light imaging (WLI) to detect histological findings is considered as the leading modality to detect histological findings. However, findings are not always correlated with the histological findings. Linked-color imaging (LCI) is a new endoscopy system that enhances the color differences of the gastrointestinal mucosa. We investigated the efficiency of LCI in the evaluation of the intestinal activity, including the histological activity, in patients with UC.

Aims & Methods: UC patients underwent colonoscopy from August to December 2016. Twenty-one UC patients, who were evaluated using an EC-L600ZP endoscope with the LASEREO system (FUJIFILM Co., Tokyo, Japan), were enrolled. All of the target lesions were observed by WLI and LCI, and biopsy specimens were obtained from the lesions with the reddest tones in each view. A total of 96 lesions were biopsied. We quantified the color tones L* a* b* values (LCI-L, LCI-a, LCI-b), where L* a* and b* represent lightness, red color and yellow color, respectively. We also quantified the color tones LCI-L, LCI-a, LCI-b (WLI-L, WLI-a, WLI-b) on the L* a* b* color values. The endoscopic images were classified according to the Mayo endoscopic score (MES), and biopsied specimens were classified according to the Geboes score. The endpoint of this study was to measure the correlation between the L* a* b* color values and the (1) MES, (2) Geboes score, (3) mucosal healing, and (4) histological healing.

Results: Furthermore, we defined MES 0 as inactive endoscopic disease, mucosal healing, and a Geboes score of ≥2 as inactive histological disease, histological healing.

<table>
<thead>
<tr>
<th>Correlation Analysis</th>
<th>Physicians (n = 151)</th>
<th>Patients (n = 155)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>The lack of diagnosis</td>
<td>6.3</td>
<td>6.0</td>
<td>ns</td>
</tr>
<tr>
<td>The diagnosis of IBD</td>
<td>6.2</td>
<td>5.6</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>The performance of an endoscopy</td>
<td>5.6</td>
<td>5.7</td>
<td>ns</td>
</tr>
<tr>
<td>The explanation of an ostomy</td>
<td>6.6</td>
<td>5.9</td>
<td>ns</td>
</tr>
<tr>
<td>A new oral treatment</td>
<td>4.8</td>
<td>4.8</td>
<td>ns</td>
</tr>
<tr>
<td>A new auto-injectable treatment</td>
<td>5.6</td>
<td>5.3</td>
<td>ns</td>
</tr>
<tr>
<td>A new intra-venous treatment</td>
<td>5.9</td>
<td>5.3</td>
<td>ns</td>
</tr>
<tr>
<td>A surgery</td>
<td>6.7</td>
<td>6.5</td>
<td>ns</td>
</tr>
<tr>
<td>Healing an ostomy</td>
<td>6.9</td>
<td>6.0</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>A pregnancy</td>
<td>5.9</td>
<td>4.0</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>The pain</td>
<td>6.3</td>
<td>6.1</td>
<td>ns</td>
</tr>
<tr>
<td>An episode of public inconvenience</td>
<td>6.8</td>
<td>6.6</td>
<td>ns</td>
</tr>
<tr>
<td>A new flare</td>
<td>6.2</td>
<td>6.5</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>Changes in the body image</td>
<td>6.3</td>
<td>5.9</td>
<td>ns</td>
</tr>
<tr>
<td>Tiredness, fatigue, reduction in performance</td>
<td>6.0</td>
<td>6.3</td>
<td>&lt; 0.05</td>
</tr>
</tbody>
</table>

Conclusion: To what extent these clinical situations may trigger anxiety or depression?

A new auto-injectable treatment 5.6 5.3 ns
A new intra-venous treatment 5.9 5.3 ns
A surgery 6.7 6.5 ns
Healing an ostomy 6.9 6.0 p<0.05
A pregnancy 5.9 4.0 p<0.05
The pain 6.3 6.1 ns
An episode of public inconvenience 6.8 6.6 ns
A new flare 6.2 6.5 p<0.05
Changes in the body image 6.3 5.9 ns
Tiredness, fatigue, reduction in performance 6.0 6.3 p<0.05

P0996 WHAT SITUATIONS PRODUCE PSYCHOLOGICAL MALAISE IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE? PERCEPTIONS FROM PHYSICIANS AND PATIENTS. THE ENMENTE PROJECT

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6Gastroenterologist, Gastroenterology Department and Institute of Medical Research Gregorio Marañón (IiSGM); Hospital General Universitario Gregorio Marañón, Madrid/Spain

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Introduction: Inflammatory Bowel Disease (IBD) patients live situations that may trigger negative feelings and psychological malaise. ENMENTE Project globally to improve identification and early management of psychological impact in IBD patients followed in Spanish hospital gastroenterology clinics. The aim of the study was to describe possible differences among perceptions from physicians and patients about the clinical situations triggering anxiety in patients with IBD.

Aims & Methods: During April 2016 two surveys were available on-line, one for IBD patients, in the ACCU Spain website (Confederation of IBD Spanish Patients’ Associations) and another one for physicians members of GETECCU (Spanish Group for IBD treatment). Both invited their members to participate by email and the patients’ survey was announced in social networks. The scientific committee (3 gastroenterologists, 2 psychologists, 1 nurse and 1 patient) decided which potentially stressful clinical situations were considered. Physicians and patients rated these situations on a scale from 1 to 10 as potential triggers of anxiety for the patient. A Mann-Whitney test was used to compare perceptions from patients and physicians taking 151 valid questionnaires from physicians and a randomized sample of 151 valid questionnaires from patients.

Results: The survey was completed by 912 patients (mean age 39±10 years, 67% women) and 170 patients (mean age 44±10 years, 58% women). Having an ostomy, fecal incontinence in public or surgery are important triggers agreed by physicians and patients and (table). Patients, however, experience anxiety from a possible new flare or being fatigued, whereas physicians are more concerned about anxiety due to telling about a new IBD diagnosis and about pregnancy in IBD patients (table).

Mean scores from physicians and patients about clinical situations triggers anxiety or depression

A new auto-injectable treatment 5.6 5.3 ns
A new intra-venous treatment 5.9 5.3 ns
A surgery 6.7 6.5 ns
Healing an ostomy 6.9 6.0 p<0.05
A pregnancy 5.9 4.0 p<0.05
The pain 6.3 6.1 ns
An episode of public inconvenience 6.8 6.6 ns
A new flare 6.2 6.5 p<0.05
Changes in the body image 6.3 5.9 ns
Tiredness, fatigue, reduction in performance 6.0 6.3 p<0.05

Conclusion: The main anxiety triggers in patients were having an ostomy, fecal incontinence in public, a surgery, a new flare and the feeling of fatigue. These last situations
two situations were scored higher by patients than by physicians. Teaching the patients how to manage a new condition and the treatment of fatigue are aspects that would help to reduce the anxiety feeling and should be taken into account in clinical practice Acknowledgements. Funded by Merck Sharp & Dohme of Spain and endorsed by ACCU España and by GETECCU

Disclosure of Interest: All authors have declared no conflicts of interest.

P0997 EVALUATION OF LISA-TRACKER IMMUNOASSAY INFLIXIMAB AND ANTI-INFLIXIMAB FOR THE THERAPEUTIC DRUG MONITORING OF SB2

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Introduction: Flixabi, an infliximab biosimilar referencing Remicade®, was developed by Samsung Bioepis, the joint venture between Samsung BioLogics and Biogen. SB2 received approval in EU for all approved indications of the reference infliximab. Many decision algorithms based on the measure of Infliximab (IFX) trough levels and antibodies to infliximab (ATI) have been increasingly used to optimize infliximab in Crohn’s disease and ulcerative colitis. The aim of our study was to appreciate if the biosimilar SB2 could be efficiently monitored using the Lisa-Tracker infliximab and anti-infliximab immunoassays developed by Theradiag (France).

Aims & Methods: During this evaluation, standard curves of Infliximab and two different batches of SB2 were compared and then accuracy of the Lisa-Tracker IFX kit in detecting the spiked concentration of SB2 was measured using the SB2 batch 1 and SB2 batch 2. All samples and standards were tested in duplicate. Regression lines were compared to the standard curve R² between R² = 0.95 and the slope to be comprised between 0.9 and 1.1. Intra-run and inter-run precision were also measured with spiked samples of different known SB2 (from 2 to 12 μg/mL) amounts. Capacity of polyclonal antibodies directed against infliximab to block the detection of SB2 using the Lisa-Tracker infliximab assay and the capacity of SB2 to block the detection of anti-infliximab antibodies using the Lisa-Tracker anti-infliximab assay were tested.

Results: We demonstrated the perfect equivalence of infliximab standard curve to the Lisa-Tracker standard curve is suitable for the quantification of SB2 in human serum samples (R² = 0.99); the levels of infliximab of the 20 samples were calculated according to the 3 standard curves (inflimab, SB2 batch 1 and SB2 batch 2) and the CV between the R² ranged from 2.1 to 12.6%). Quantification of SB2 was shown by the mean matrix and 1% recovery were comprised between 82% and 113%. High intra-run and inter-run precision were obtained with the Lisa-Tracker infliximab assay for the quantification of SB2 (CV ranged from 3.3 to 17.9%). Finally, the capacity of polyclonal antibodies to infliximab to block the detection of SB2 in 5 spiked samples and the % of recovery were comprised between 80% and 97%. The capacity of SB2 to block the detection of anti-infliximab antibodies using the Lisa-Tracker anti-infliximab assay were tested.

Conclusion: In conclusion, Lisa-Tracker Inflimab and Anti-Inflimab assays are suitable for the monitoring of patients treated with SB2. Acknowledgements: Biogen provided the SB2 drug for this study. Biogen reviewed the contract and provided feedback to the authors.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0998 THE MEASURE OF TROUGH LEVELS OF INFLIXIMAB IS LINKED TO THERAPEUTIC RESPONSE IN IBD PATIENTS

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Introduction: If the association between trough levels of infliximab (TLI) and clinical remission or mucosal healing is demonstrated, we don’t really know the cause and effect between TLI and target value to obtain this association. So, the aim of our study was to evaluate the causality or the association between TLI and clinical remission and mucosal healing in IBD patients.

Aims & Methods: We prospectively included all IBD patients treated in our IBD unit and in clinical remission (CDAI < 150 for Crohn’s Disease (CD) or partial Mayo score < 3 for ulcerative colitis (UC)) with biomarker normalization (fecal calprotectin < 250 μg/g stools) or in deep remission (clinical remission with fecal calprotectin <50 μg/g stools). We analyzed median of TLI and fecal calprotectin at the inclusion (M0) and 6 months before eligibility (M-6). We excluded patients with deep remission at M-6.

Results: 111 patients were included (60 CD, sex ratio M/F: 0.8, 51 patients in deep remission at M0). All these patients were in clinical remission at M-6. Median fecal calprotectin at M-6 were similar in the two groups of patients (210 μg/g) in the group of patients who achieved deep remission at M0 vs 220 μg/g in the group of patients who achieved only biomarker remission respectively (p=0.04). Conversely, the median TLI at M-6 was significantly lower in patients who did not achieved deep remission at M0 (2.8 vs 4 μg/L respectively; p=0.01). A ROC curve analysis was not able to isolate a cut-off value associated to deep remission achievement. (AUROC = 0.61). Next, we analyzed separately median of TLI and fecal calprotectin levels 6 months before eligibility (M-6) of patients in deep remission at M0 (51 patients). The median TLI was significantly lower at M-6 than at M0 (4.1 μg/L vs 5.9 μg/L respectively; p=0.03). Conversely, median fecal calprotectin was significantly higher at M-6 in comparison to M0 (190 vs 35 μg/g stool; p=0.01). A negative and weak significant correlation between fecal calprotectin and TLI was observed (Spearman’s rank correlation coefficient (q) = -0.25; p = 0.045).

Conclusion: Although TLI may increase with decreased drug clearance due to deep remission, we show for the first time that the residual rate is the causal element for achieving clinical remission.

Disclosure of Interest: All authors have declared no conflicts of interest.

P0999 SMOKING STATUS INFLUENCES FECAL VOLATILE ORGANIC COMPOUNDS COMPOSITION

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Introduction: Fecal volatile organic compounds (VOCs) are gaseous carbon-bound metabolic products considered to reflect intestinal microbiota composition. Comparison of VOCs may serve as markers for a broad range of gastrointestinal diseases. As smoking leads to a substantial shift in intestinal microbial composition in healthy and diseases persons, the aim of this study was to assess the effect of smoking status on fecal VOC pattern.

Aims & Methods: In this cross-sectional pilot-study adult smokers, non-smokers and former smokers scheduled for colonoscopy at the VU University medical center were instructed to collect a fecal sample prior to bowel cleansing. Patients were included if no abnormalities were found during colonoscopy. Exclusion criterion was use of antibiotics three months prior to participation. All participants completed a questionnaire on standard demographics, BMI, diet and smoking habits. Fecal VOC profiles were measured using an electronic nose device (Cyanosense 3200).

Results: Fecal samples from 56 subjects (11 smokers, 21 non-smokers, 24 former smokers) were analyzed. Median age was 62 years (27–82 years). Furthermore, there were no significant differences between groups for the variables age, sex, BMI, diet, sample weight, chronic diseases and medication and supplement use. Fecal VOC profiles differed between smokers and non-smokers (PC1: p-value = 0.003). Smokers could be distinguished from non-smokers based on fecal VOC profiles was possible with an overall accuracy of 75% and corresponding sensitivity and specificity values of 72.7% and 76.2%. No significant differences between fecal VOC profiles from smokers and former smokers (PC1: p-value = 0.083) and between profiles from non-smokers and former smokers (PC1: p-value = 0.61). Next, we analyzed separately smokers and non-smokers.

Conclusion: This study showed that smoking status has a significant influence on fecal VOC profiles. This implicates that the smoking status should be taken in account when performing (fecal) VOC analysis. The finding that VOC profiles diverged (6 month – 43 years) in smoke-free time in former smokers group. Smoking cessation induces profound changes in the composition of the intestinal microbiota in humans.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
P1000 CLOSTRIDIUM DIFFICILE INFECTION AND IBD PATIENTS IN ONE CLINICAL CENTER
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Introduction: The prevalence of Clostridium difficile infection (CDI) in patients suffering from inflammatory bowel disease (IBD) has increased rapidly over the past several decades. However, the exact global epidemiology remains unclear because of insufficient data from developing countries.

Aims & Methods: The goal of our study is to examine the incidence of CDI in patients with IBD. A retrospective, observational study evaluating IBD patients in a referral center was performed to evaluate the incidence of Clostridium difficile. Diagnosis was confirmed with stool toxin analysis. Demographic information, diagnosis, anatomic location, IBD therapy, antibiotic exposure, hospital stays and recurrences were recorded. For a period of 3 years, 202 IBD patients were studied, 105 of which have UC and 97 - Chron’s disease (CD). We used the Clostridium difficile Glutamat Dehydrogenase + Toxin A + B based on the principle of quantitative immunochromatographic assay for the determination of Clostridium difficile Glutamat Dehydrogenase, Toxin A and Toxin B in stool samples.

Results: The results show that all patients with a positive CDI test have a clinical picture, which resembles a relapse of the disease (p < 0.05). There’s a tendency towards growth in the incidence of IBD patients who are positive CDI. Their number in 2016 is significantly higher than that in 2014. In 2014 it was ~5.90% with CD and 12.30% with UC, whereas in 2016- 12.20% with CD and 27.80% with UC. The results show that the incidence of CDI cases in UC is significantly higher than in patients with CD, respectively 18.1% vs 9.30% (p < 0.05). There is a strong correlation between CDI incidence in patients with IBD and the severity of their disease. Patients positive for CDI have a much more severe course of the disease, UC (46.40%) and CD (24.20%) (p < 0.05).

Conclusion: There is an increase in incidence of CDI, and patients with UC are more affected by it. The results of our study are confirmed by other authors as well. A significant part of patients with CDI have a severe disease that needs extra prospective researches to determine the incidence and influence of the infection amongst patients with IBD, who receive different therapy regimens and also to understand how the CDI affects the evolution of the disease.

Disclose of Interest: All authors have declared no conflicts of interest.

References

P1001 DEVELOPMENT OF A NEW SCORE PREDICTIVE OF SUSTAINED CLINICAL REMISSION IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE UNDER INFliximAB- AZATHIOPRINE COMBOTHERAPY
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Introduction: There is no blood test predictive of sustained clinical remission in patients with Crohn’s Disease (CD) or Ulcerative colitis (UC) under Infliximab (IFX) - azathioprine (AZA) combotherapy.

Aims & Methods: All patients with CD or UC, consecutively treated by the combination of IFX-AZA between August 2015 and March 2017, were included in this monocentric study. Clinical, biological (blood cells count, liver function enzymes, C-reactive protein (PCR)) were retrospectively collected at baseline, at week 14 (W14) and at 6 months (W24) from the start of combination therapy.

Results: Trough level of IFX (TLI) at W14 was also recorded. Sustained clinical remission was defined as clinical remission for 6 months under combotherapy with no need of AZA dose modification, nor therapeutic switch or need for surgery. A predictive score before combotherapy was developed basing on receiver operating characteristic (ROC) curves and logistic regression analyses.

Conclusion: This new score is a promising tool for the prediction at baseline of sustained clinical remission in inflammatory bowel disease patients who start combotherapy. It may help to identify easily patients that would benefit of IFX monotherapy. toddler population.

Disclose of Interest: All authors have declared no conflicts of interest.

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POSTOPERATIVE RECURRENCE IN CROHN’S DISEASE

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Introduction: As surgical resection is not curative in Crohn’s disease (CD), post-operative recurrence (POR) remains a crucial issue. The POCE r trial (1) has operated recurrence (POR) remains a crucial issue. The POCE r trial (1) has

Aims & Methods: To assess the performances of MRI and faecal calprotectin to detect endoscopic POR in CD patients. Adult CD patients from two tertiary centers who underwent ileal or ileocolonic resection were conpared to the two other modalities (P = 0.043), related contrast

Results: Overall, 30 CD patients were enrolled in the study. Among them, 15 (50.0%) were female and 7 (23.3%) were active smokers. Disease location was ileal, colonic or ileocolonic in 15 (50.0%), 1 (3.3%) and 14 patients (46.7%), respectively. The patients included in this study were treated with no medication (20.0%), 5-ASA (6.7%), thiopurines (56.7%) or anti-TNF agents (20.0%) in preventing endoscopic POR. Within the first year after surgery, endoscopic findings were assessed and Rutgeerts index was noted for 8 patients (26.7%), 11 for 5 patients (16.7%), 12a for 4 patients (13.3%), 12b for 6 patients (20.0%), 13 for 5 patients (16.7%) and 14 for 2 patients (6.7%). In defining endoscopic POR as Rutgeerts index ≥12, ADC value (2.2 vs 2.12; p = 0.35), related contrast enhancement (RCE) (77% vs 119%, 0.056), Clermont score (5.3 vs 7.9; p = 0.11), MRI score (p = 0.57) and MaRIA (5.3 vs 6.4; p = 0.21) were not significantly different in patients with endoscopic POR. Using Rutgeerts index ≥12 as cut-off value to define endoscopic POR, ADC mean value was lower in patients of preparations. The groups were comparable concerning the clinical characteristics of the patients were collected before more 1 L PEG before the capsule (PEG), liquid diet the evening before the capsule. The cleanness scores were compared on the whole small bowel and on each segment.

Conclusion: There were no statistically significant differences in patients with endoscopic POR defined as ≥12. In contrast, MaRIA (5.0 vs 7.3; p = 0.15) and MRI scores (p = 0.17) were not significantly higher in patients with endoscopic POR ≥12b. In case of severe endoscopic POR (≥13), RCE (87% vs 135%; p = 0.046) was increased while none of the following MRI parameters was significantly different: ADC (2.05 vs 2.20; p = 0.18), Clermont score (7.5 vs 7.5; p = 0.94), MaRIA (5.3 vs 7.8; p = 0.25) and MRI score (p = 0.11). Faecal calprotectin values were significantly higher in patients with endoscopic POR defined as ≥12 (87.8 vs 314.9 µg/g; p = 0.0064), ≥12b (92.6 vs 366.1 µg/g; p = 0.0075) or in patients presented with severe endoscopic POR ≥3 (98.8 vs 544.4 µg/g; p = 0.0003). CRP value was not significantly higher in patients with endoscopic POR defined as ≥12 (2.5 vs 3.9; p = 0.01) and ≥12b (3.2 vs 6.2; p = 0.43), but was increased in patients with severe endoscopic POR (3.0 vs 9.8; p = 0.02). Using ROC curves, we determined the best thresholds and their performances to detect endoscopic POR (Table 1).

Table 1: Performances of MRI parameters and faecal calprotectin to detect endoscopic postoperative recurrence in Crohn’s disease

<table>
<thead>
<tr>
<th>Detection of Rutgeerts ≥12</th>
<th>AUC</th>
<th>Se</th>
<th>Spe</th>
<th>NPV</th>
<th>PPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clermont score ≥ 8.4</td>
<td>0.70</td>
<td>36%</td>
<td>77%</td>
<td>47%</td>
<td>66.7%</td>
</tr>
<tr>
<td>MaRIA ≥ 7</td>
<td>0.67</td>
<td>29%</td>
<td>77%</td>
<td>45.5</td>
<td>62.5%</td>
</tr>
<tr>
<td>Faecal calprotectin &gt; 100 µg/g</td>
<td>0.84</td>
<td>60%</td>
<td>100%</td>
<td>64.7</td>
<td>100%</td>
</tr>
<tr>
<td>Detection of Rutgeerts ≥12b</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clermont score ≥ 8.4</td>
<td>0.73</td>
<td>47%</td>
<td>82.4</td>
<td>66.7</td>
<td>66.7%</td>
</tr>
<tr>
<td>MaRIA ≥ 7</td>
<td>0.70</td>
<td>38.5</td>
<td>82.4</td>
<td>62.5</td>
<td>63.6%</td>
</tr>
<tr>
<td>Faecal calprotectin &gt; 100 µg/g</td>
<td>0.79</td>
<td>66.7</td>
<td>92.9</td>
<td>76.5</td>
<td>88.9%</td>
</tr>
</tbody>
</table>

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Introduction: PEG preparations reduce the acceptability of endoscopic explorations but remains recommended before performing a small bowel videocapsule (SBVC). No study has evaluated its impact on the small bowel cleanness compared to other modalities in patients with Crohn’s disease (CD). The objective of this study was to compare three methods of preparation, one using polyethylene-glycol and two simplified methods in adult patients with CD.

Aims & Methods: Three methods of preparation i.e. low-residue diet the evening before more 1 L PEG before the capsule (PEG), liquid diet the evening before the capsule (LD) and Water (Water) (P = 0.102). The endoscopic activity of the capsule. The cleanness scores were compared on the whole small bowel and on each segment.

Results: Between January 2015 and August 2016, 97 patients (38 men, mean age 40.8yrs) were included and performed 105 capsules with 35 capsules in each group of preparations. The groups were comparable concerning the clinical and demographic characteristics (sex ratio, disease duration, history of intestinal resection, phenotype, treatment, indication of the capsule). The mean duration of the small bowel transit time was comparable between the three groups (198 min (PEG), 245 min (LD), 226 min (Water) (P = 0.102). The endoscopic activity of the disease was comparable between the 3 groups (P = 0.358). The capsule intubation rate was significantly lower in the PEG group 66% versus 91% (LD) and 94% (Water) (P = 0.04). No capsule impaction was observed. The mean quantitative cleanliness score for the whole small bowel was not significantly better for the PEG group (5.7) compared to the other modalities LD (6.3) and Water (6.5) (P = 0.262). In the first tertile, the quantitative score was significantly better in the LD (7.9) and Water (7.6) groups compared to the PEG group (6.8) (P = 0.043). The preparation by water was considered qualitatively better compared to the two other modalities (P = 0.04).

Conclusion: Faecal calprotectin and MRI are reliable tools to detect endoscopic POR in CD patients and could be used as non-invasive alternative options to colonoscopy.

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P1004 SMALL BOWEL PREPARATION IN PATIENTS WITH CROHN’S DISEASE: THE POLYETHYLENE-GLYCOL IS NO LONGER USEFUL

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Introduction: PEG preparations reduce the acceptability of endoscopic explorations but remains recommended before performing a small bowel videocapsule (SBVC). No study has evaluated its impact on the small bowel cleanness compared to other modalities in patients with Crohn’s disease (CD). The objective of this study was to compare three methods of preparation, one using polyethylene-glycol and two simplified methods in adult patients with CD.

Aims & Methods: Three methods of preparation i.e. low-residue diet the evening before more 1 L PEG before the capsule (PEG), liquid diet the evening before the capsule (LD) and 1.5 L of water at the time of the capsule (Water) were compared. All patients were prospectively included and had an SB3 (Medtronic) capsule after the ingestion of a Patency Agle™ capsule. The small bowel was identified between the 1st duodenal and the 1stecal images or the last recorded image and was separated into 3 equal segments. A standardized quantitative cleanliness score was calculated rating the luminosity, the presence of bubbles, turbid liquids, food residues and the percentage of visible mucosal surface in the entire small bowel and in each terri-
Conclusion: This is the first study evaluating the relevance of PEG preparation in a large population of adult patients with CD. Our study has demonstrated that there is no benefit in using PEG for the preparation of the small bowel before the capsule in patients with CD. Quantitatively, the two simplified preparation methods were more efficient than the preparation with PEG and qualitatively, the preparation using water was considered as the most efficient.

Disclosure of Interest: A. Bourreille: Advisory Boards: Medtronic Cursos, formations: Medtronic Aids for research: Medtronic All other authors have declared no conflicts of interest.

Aims & Methods: Totally, 10 consecutive patients with inactive or mildly active UC were enrolled, and fifty-three areas were assessed by LCI. All examinations were conducted with a LASEROE endoscopic system (FUJIFILM Co., Tokyo, Japan). During the colonoscopy, each region of interest (ROI) of terminal ileum, cecum, ascending colon, transverse colon, descending colon, sigmoid colon, and rectum was imaged by the use of wide-field endoscopic imaging (WLI) and LCI. The Commission international de l’éclairage (CIE) LAB color differences (ΔC) were calculated among WLI and LCI in each ROI. After ROIs were imaged by colonoscopy, the biopsy specimen was taken in each ROI. Inflammatory cell infiltration, crypt atrophy, crypt distortion, and goblet cell depletion were assessed by the histologic findings of acute inflammation. For evaluation of chronic inflammation, crypt atrophy, crypt distortion, and basal plasmacytosis were assessed. The correlation between ΔC and Mayo endoscopic sub-score was assessed, indicating that the higher ΔC mean easier color difference for recognition.

Results: The mean age of patients who were enrolled in the present study was 45.6 ± 17.7 years. The sex ratio (Men/women) was 4:6. The type of extent of UC (ulcerative proctitis/left-sided UC/extensive UC) was 0:3:7. 1. Correlation between ΔC and Mayo endoscopic sub-score was significantly lower than that of ROI with inflammatory cell infiltration (ΔC: 15.9 ± 6.8 vs. 13.0 ± 4.8, p = 0.046). The mean ΔC was not affected by histological findings of erosions, crypt atrophy, goblet cell depletion, crypt atrophy, crypt distortion, and basal plasmacytosis. LCI distinguished colon mucosal white color compared with WLI with use of three-dimensional color space, indicating the remission-colon mucosa of UC with no inflammatory cell infiltration in ROI was easily detected by LCI. 2. Correlation between ΔC color differences and UC Mayo endoscopic subscore. Low Mayo endoscopic sub-scores tended to be inversely proportional to high ΔC (ΔC: 15.9 ± 6.8 vs. 13.0 ± 4.8, p = 0.046), but not significantly different in the present evaluation. The colon mucosa with the low Mayo endoscopic sub-scores were relatively easily detected by LCI compared with WLI.

Conclusion: The present pilot trial indicated that the inactive UC mucosa could be easily detected as the white area by the LCI mode compared with WLI, suggesting that LCI might be one of novel approaches for evaluating the disease activity.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

P1005 57SeHCAT IN THE DIAGNOSIS OF BILE ACID MALABSORPTION IN CROHN’S DISEASE WITH CHRONIC DIARRHEA
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Introduction: Bile acid malabsorption (BAM) is a well-known disorder associated to inflammatory bowel disease patients, however, it is underdiagnosed in clinical practice. The 57SeHCAT test is the current clinical gold standard for diagnosing bile acid diarrhea widely used in Europe.

Aims & Methods: We aimed to analyze the incidence of BAM in Crohn’s disease (CD) patients with chronic diarrhea through 57SeHCAT and to assess whether there is a relationship between the malabsorption degree and the presence of ileal resection. 30 patients with CD and chronic diarrhea with and without ileal resection during the period between August 2015-April 2016. In all patients, an inflammatory activity was previously discarded before. Seven-day measurements were compared with 3 hours activity to calculate the abdominal retention percentage. The interpretation of the retention results was made considering ≥10% BA is consistent with a normal result. Mild BAM is considered 7–10%, moderate 4–7% and severe <4% retentive at seventh day measurements. Epidemiological and clinical data were collected from the local database ENEIDA.

Results: Twenty-five women and 15 men with mean age of 46.5 years old (26–58). The median duration of the disease was 13 years (2–27). At diagnosis, ileal location was present in 50% of the patients, ileocolonic 40% and colonic in 10%. According to the behavior of the disease, 50% presented non-stricturing non-penetrating, 25% strictureing and 25% penetrating pattern, and 43% patients had perianal disease. In relation to smoking status, 34% were active smokers.

During the evolution of the disease. Median time from CD diagnosis to surgery of the patients had undergone ileal resection. Median length of intestinal resection was present in 50% of the patients, ileocolonic 40% and colonic in 10%.

Conclusion: 50% of the patients were controlled with only immunosuppressants. In relation with smoking status, 34% were active smokers. According to the behavior of the disease, 50% presented non-stricturing non-penetrating, 25% strictureing and 25% penetrating pattern, and 43% patients had perianal disease. The median duration of the disease was 13 years (2–27). At diagnosis, ileal location was present in 50% of the patients, ileocolonic 40% and colonic in 10%. According to the behavior of the disease, 50% presented non-stricturing non-penetrating, 25% strictureing and 25% penetrating pattern, and 43% patients had perianal disease. In relation with smoking status, 34% were active smokers.

Aims & Methods: We studied 15 women and 15 men with mean age of 46.5 years old (26–58). The median duration of the disease was 13 years (2–27). At diagnosis, ileal location was present in 50% of the patients, ileocolonic 40% and colonic in 10%. According to the behavior of the disease, 50% presented non-stricturing non-penetrating, 25% strictureing and 25% penetrating pattern, and 43% patients had perianal disease. In relation with smoking status, 34% were active smokers.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

P1007 THE ROLE OF SENSE OF COHERENCE IN DETERMINING HEALTH RELATED QUALITY OF LIFE AND DISABILITY IN INFLAMMATORY BOWEL DISEASE
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Introduction: There is an ever growing body of evidence that indicates that Health Related Quality of Life (HRQoL) is significantly impaired in IBD. While clinical variables and disease activity status influence HRQoL, a host of psychosocial and personality variables also play an important role. This contention is supported by evidence of impaired quality of life (QoL) in patients with Crohn’s disease (CD) and ulcerative colitis (UC). QoL is related to the absence of demonstrable disease activity. Moreover, individual differences may play a key role in the psychological adaptation to living with IBD and coping with the psychological distress associated with the disorder. Sense of coherence (SOC) is an emerging theoretical and dynamic construct that seeks to explain why some individuals in the face of adversity experience illness while others do not. Antonovsky’s theory of SOC suggests that individuals with strong SOC are better able to adapt to health stressors and have less motivation when confronted with challenges that their health. While a number of studies have shown that SOC appears to have an impact on HRQoL, data regarding this association in IBD are limited.

Aims & Methods: The goal of the current study was to examine the associations between an individual’s sense of coherence, and their overall health-related quality of life. The first part of this study examined whether sense of coherence among water was considered as the most disability level, and an individual’s illness perception was, as compared to other reported psychosocial factors. The second part of this study evaluated whether sense of coherence, as well as illness perception, were associated with an individual’s self-reported quality of life, and if this interaction was moderated by an individual’s level of disability. Additionally, the correlations between sense of coherence, and self-efficacy, as well as self-reported emotional intelligence were also further evaluated. This is a cross-sectional observational cohort of IBD patients attending MUHC (McGill University Health Center) IBD outpatient clinics. The patients population. The number of subjects was: ≤ 42.4 ± 12.44, gender (46.6% male), disease type (58.4% CD, 33.7% UC), disease activity (27.7% active, 65.3% inactive). Patients completed multiple validated questionnaires pertaining to a variety of psychosocial parameters. Data was analyzed by multiple linear regression using statistics software (SPSS version 17.0).

Results: Preliminary analyses of this patient population revealed that 40.2% of the variance in level of disability is explained by sense of coherence. This model suggests a significant negative correlation between sense of coherence and level of disability (β = -0.64, p < 0.05). A smaller, albeit significant contribution of sense of coherence with illness perception was additionally found (14.1% of the variance, and β = -0.39, p < 0.05). Furthermore, 32.3% of the variance in self-
reported quality of life was explained by sense of coherence ($r=0.43$, $p<0.05$) and illness perception ($r=-0.28$, $p<0.05$). However, the individual's report of anxiety did not moderate this relationship. Significant positive correlations between sense of coherence and self-efficacy were also seen in this patient population ($r=0.61$, $p<0.01$), as well as with self-reported emotional intelligence ($r=0.52$, $p<0.01$).

Conclusion: This was the first pilot study to assess the potential of the faecal amino acid profile as a non-invasive biomarker for disease activity of paediatric inflammatory bowel disease. We aimed to cross-sectionally investigate the correlation between faecal amino acid profiles and clinical, biochemical as well as endoscopic activity in Greek IBD patients. Consecutive IBD patients on maintenance treatment with IFX, were included. IFX-TLs and ATIs were measured using ELISA (Eagle Biosciences, Nashua, NH, USA) on serum samples drawn before infusion. At the same time quality of life using short IBD questionnaire (SCAI) for ulcerative colitis (UC) and Crohn's disease (CD).

Amino acid and healthy controls

Table 1: Levels of amino acids in patients with Crohn’s disease, ulcerative colitis and healthy controls

Table 1: Levels of amino acids in patients with Crohn’s disease, ulcerative colitis and healthy controls

<table>
<thead>
<tr>
<th>Amino acid</th>
<th>healthy controls</th>
<th>ulcerative colitis</th>
<th>Crohn’s disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alanine</td>
<td>2.07 (1.88–4.39)</td>
<td>5.28 (3.31–10.38)</td>
<td>8.21 (4.59–13.05)</td>
</tr>
<tr>
<td>Phenylalanine</td>
<td>0.48 (0.48–1.46)</td>
<td>1.37 (1.07–1.39)</td>
<td>2.62 (1.74–3.91)</td>
</tr>
<tr>
<td>Glycine</td>
<td>1.06 (0.91–2.65)</td>
<td>1.91 (1.10–3.58)</td>
<td>2.58 (2.17–5.97)</td>
</tr>
<tr>
<td>Leucine</td>
<td>1.00 (0.86–2.88)</td>
<td>3.04 (2.34–5.32)</td>
<td>4.13 (3.80–6.64)</td>
</tr>
<tr>
<td>Isoleucine</td>
<td>0.76 (0.09–2.15)</td>
<td>1.68 (0.88–2.01)</td>
<td>3.07 (1.68–4.56)</td>
</tr>
<tr>
<td>Valine</td>
<td>0.96 (0.76–2.61)</td>
<td>2.43 (2.35–5.19)</td>
<td>4.41 (3.29–6.64)</td>
</tr>
<tr>
<td>Lysine</td>
<td>1.72 (1.21–4.03)</td>
<td>2.63 (1.75–6.44)</td>
<td>4.62 (2.27–8.04)</td>
</tr>
<tr>
<td>Serine</td>
<td>0.81 (0.52–1.69)</td>
<td>1.08 (0.97–1.96)</td>
<td>2.57 (1.84–4.57)</td>
</tr>
</tbody>
</table>

All levels are displayed in nmol/mg.

Conclusion: This was the first pilot study to assess the potential of the faecal amino acid profile as a non-invasive biomarker for disease activity of paediatric inflammatory bowel disease. We observed remarkable differences in faecal amino acid composition between IBD patients and healthy controls, and between the IBD phenotypes. Whether these differences reflect decreased absorption or increased loss by inflamed intestines needs to be elucidated. Currently, we are awaiting the results of a larger proof-of-concept study on these faecal amino acid profiles.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
P1001 EVALUATION OF PET-MRI AND FECAL BIOMARKERS TO PREDICT DISEASE ACTIVITY IN PATIENTS WITH ULCERATIVE COLITIS

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Introduction: Endoscopy is the gold standard diagnostic tool in ulcerative colitis (UC). However noninvasive methods like cross-sectional imaging and fecal biomarkers are needed for interval clinical assessments and assessing response to medical treatment. The combination of positron emission tomography (PET) with 18F-fluorodeoxyglucose (18F-FDG) with magnetic resonance imaging (MRI) as integrated PET/MRI in one examination is a new cutting-edge technology for the non-invasive assessment of the inflammatory activity in UC. In addition a panel of noninvasive biomarkers like Lactoferrin and Calprotectin are increasingly popular and used in all-day patient care.

Aims & Methods: To compare the performance of non-invasive biomarkers to PET/MRI and colonoscopy in patient with UC. In every patient a PET/MRI including the maximum standardized uptake value ratio gut/liver (SUVQuot) and a colonoscopy including an endoscopy index (EI) was performed within 48 hours and the Disease Activity Index Mayo score (DAI) was calculated. Fecal Lactoferrin (LF), Calprotectin (PMN), Calgranulins (CalP), S100A12 and CRP were also measured. PET and MRI were performed using integrated PET/MRI scanners. All analyses were performed using SPSS (IBM SPSS Statistics for Windows, release 22.0).

Results: 32 patients (21 female), mean age 44.4 ± 10.63 years (range 23–67) with diagnosed UC were included in the study. Mean time since diagnosis was 11.41 years (SD = 6.42). EI and SUVQuot (r = 0.45; p < 0.009), EI and DAI (r = 0.32; p = 0.000) as well as DAI and SUVQuot correlated significantly (r = 0.40; p < 0.022). SUVQuot was significantly correlated with LF (r = 0.32; p = 0.046), EDN (r = 0.29; p = 0.05), and CRP (r = 0.32; p = 0.009), but not with PMN (m = 36.1), S100A12 and Cal (all p > 0.05). LF was correlated significantly with PMN (m = 36.1) and Cal (all p < 0.05). LF and CRP were significantly correlated with PMN (m = 36.1) and Cal (all p < 0.05). LF was correlated with LF (r (32) = 0.41; p = 0.001), and not with PMN (m = 36.1), S100A12 and Cal (all p > 0.05). LF was correlated with PMN (m = 36.1), S100A12 and Cal (all p < 0.05). LF was correlated with LF (r (32) = 0.41; p = 0.001), and not with PMN (m = 36.1), S100A12 and Cal (all p > 0.05). LF was correlated with LF (r (32) = 0.41; p = 0.001), and not with PMN (m = 36.1), S100A12 and Cal (all p > 0.05). LF was correlated with LF (r (32) = 0.41; p = 0.001), and not with PMN (m = 36.1), S100A12 and Cal (all p > 0.05).

The median levels (inactive/active) were: LF: 1.75/20.13 μg/g; Cal: 0.15/0.75 mg/dl. Sensitivity, specificity, diagnostic accuracy (confidence interval) and optimized cut-off for LF was 87.5%/87.5%/87.5% (CI 72.1%/100%/77.5%), 4/27 g/g; CalP: 62.5%/62.5%/58.5% (CI 38.9%/97.5%/56.1%); m = 36.1; Cal: 62.5%/62.5%/58.5% (CI 36.7%/86.2%); m = 36.1; EDN: 63.9/23.5 μg/g; PMN: 83.3%/75.0%/81.25% (CI 60.5%/99.9%); 0.805 g/g; S100A12: 75.0%/75.0%/75.0% (CI 56.9%/94.1%); 60.40; EDN: 75.5%/75.0%/75.0% (CI 80.5%/100%); 1, 30 μg/g; CRP: 70.8%/75.0%/71.5% (CI 53.5%/94.9%); 0.35 mg/dl.

Conclusion: Using EI as gold standard reference we found that fecal biomarkers LF, EDN, PMN and S100A12 can reliably distinguish between active and inactive UC. However, Cal did not perform well in this study. LF and CRP were significantly correlated to the SUVQuot which was significantly correlated with EI and DAI. In conclusion, Lactoferrin and Eosinophil-derived Neutrophil (EDN) were significantly correlated with LF and DAI and SUVQuot correlated significantly (r = 0.40; p < 0.022). SUVQuot was significantly correlated with LF (r = 0.32; p = 0.046), EDN (r = 0.29; p = 0.05), and CRP (r = 0.32; p = 0.009), but not with PMN (m = 36.1), S100A12 and Cal (all p > 0.05). LF was correlated significantly with PMN (m = 36.1) and Cal (all p < 0.05). LF was correlated with LF (r (32) = 0.41; p = 0.001), and not with PMN (m = 36.1), S100A12 and Cal (all p > 0.05). LF was correlated with LF (r (32) = 0.41; p = 0.001), and not with PMN (m = 36.1), S100A12 and Cal (all p > 0.05). LF was correlated with LF (r (32) = 0.41; p = 0.001), and not with PMN (m = 36.1), S100A12 and Cal (all p > 0.05). LF was correlated with LF (r (32) = 0.41; p = 0.001), and not with PMN (m = 36.1), S100A12 and Cal (all p > 0.05). LF was correlated with LF (r (32) = 0.41; p = 0.001), and not with PMN (m = 36.1), S100A12 and Cal (all p > 0.05).

Disclosure of Interest: J. Langhorst: Research grant by Teebh Inc. J.H. Boone: Employee of Teebh Inc. All other authors have declared no conflicts of interest.

References

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Introduction: At present, drug response to infliximab is monitored by trough levels of anti-drug antibody (ATI) and anti-drug factor levels. However, there are other pathways of drug degradation that have been hypothesized since MMP3 and MMP9 were found to be able to cleave IgG, like infliximab, in both animal and human experimental studies (1).

Aims & Methods: We collected serum samples in 102 patients (27 Crohn’s Disease and 75 Ulcerative Colitis) treated with stable doses of infliximab for at least 6 months (t0) and 6 months thereafter (t1). In each patient, TL, AT and MMP3 levels were assessed at t0 and t1 by ELISA. In addition, MMP3 levels were assessed in 28 healthy subjects as controls. Clinical (HBI or Mayo score) and biochemical (CRP, fecal calprotectin) markers were assessed to define disease remission/activity. TL were considered therapeutic if >3.8 mcg/ml. AT were considered positive if > 10 mcg/ml. Data are presented as mean ± Standard Error Mean (SEM). Comparison among groups was performed by non-parametric tests.

Results: MMP3 levels were similar at t0 and t1 in patients which maintained therapeutic TL (14.5±1.7 pg/ml and 15.0±1.6 pg/ml, respectively) and in those who discontinued TL (23.0±2.1 pg/ml and 22.2±1.7 pg/ml, respectively). Patients whose TL decreased had significantly higher MMP3 levels compared to the group with low TL and AT positive (33.2±3.0 and 20.0±2.7 respectively, p=0.0003), showing another pathway of drug degradation. 21 patients lost response between t0 and t1: 15 out of 21 patients demonstrated high levels of MMP3 (22.0±2.1 pg/ml) already at t0; in addition, 17 of these 21 patients were in clinical remission at t0, while at t1 all patients had disease activity.

Conclusion: Serum MMP3 levels are useful in predicting loss of response to anti-TNFa in patients with low TL but without AT. High MMP3 levels predict with 90.5% accuracy loss of response over the next 6 months.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

P1013 USEFULNESS OF A MULTIDISCIPLINARY APPROACH COMBINING BOTH RHEUMATOLOGY AND GASTROENTEROLOGY FOR THE ASSESSMENT AND TREATMENT OF INFLAMMATORY BOWEL DISEASE PATIENTS

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Introduction: More than one third of inflammatory bowel disease patients (IBD) present symptoms and/or manifestations, which are more common, clearly more the complicating and which more alter the quality of life of IBD patients. These patients could benefit from a multidisciplinary approach for quicker diagnosis and for optimizing treatments.

Aims & Methods: The aim of the study was to evaluate the impact of a multidisciplinary approach carried out by both a rheumatologist and a gastroenterologist in the management of these patients. Therapeutic changes after the consultation were also evaluated. From April 2015 to April 2017, all IBD patients reporting articular pain to the IBD-dedicated gastroenterologist in the management of these patients.

Results: 112 consecutive IBD patients were remitted from the IBD Unit and analyzed by the committee. Mean age 38 years (ranging from 18 to 73). Most patients were women (67%), 19% were smokers and 23% former smokers. 51% of patients had Crohn’s disease and 49% ulcerative colitis. The main causes for derivation from IBD were a suspicion of inflammatory arthropathies in 43% and of arthromyalgias in 40%. The more frequent diagnosis after the consultation was rheumatoid arthritis and the committee meeting were inflammatory arthropathies associated with IBD in 41% (51.5% presented arthralgias and 48.5% presented peripheral arthropathies) and fibromyalgia in 15%. Regarding treatment changes, after the multidisciplinary committee with a rheumatologist and a gastroenterologist, changes were made in 28% of patients. Of those, in 35% of patients methotrexate was added in patients with biochemical treatment (in some of them patients were in monotherapy, but in others the drug was introduced for replacing thioaurines). In 24% of patients sulfasalazine was introduced instead of mesalamine. In the other patients either other biologies like adalimumab (with IBD in 41% (51.5% presented arthralgias and 48.5% presented peripheral arthropathies) and fibromyalgia in 15%).

Conclusion: A multidisciplinary consultation combining inflammatory bowel disease and rheumatology allows both an earlier detection of inflammatory arthropathies associated with IBD and earlier changes in treatment, thereby helping to optimize the hospital resources. Fibromyalgia is common among IBD patients, though it is important that it is detected it should not be confused with the other conditions.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

P1015 ADALIMUMAB TROUGH LEVELS AND ANTI-ADALIMUMAB ANTIBODIES CORRELATE WITH CLINICAL AND ENDOSCOPIC ACTIVITY IN CROHN’S DISEASE PATIENTS

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Introduction: Adalimumab (ADA) is an anti-TNFα drug approved for patients with refractory luminal Crohn’s disease (CD). Recently, mucosal healing (MH) emerged as a major therapeutic goal in inflammatory bowel disease. Few data are available on ADA trough levels (TL), anti-ADA antibodies (AAA) during long term follow-up of CD patients, and their potential association with MH and disease outcome.

Aims & Methods: The aim of our prospective study was to evaluate a possible association between achievement of MH, ADA TL, and AAA in CD patients. Moreover, we assessed the possible association between clinical outcome and MH. We prospectively enrolled moderate to severe CD patients who were primary responders to ADA treatment. Blood samples were withdrawn at standardized time points during treatment (0-, 2-, 6-week and every 8 weeks thereafter), before ADA administration. ADA TL were measured using an homogenous mobility shift assay (HMSA; Prometheus Lab, San Diego, United States). Disease activity was assessed by means of Harvey-Bradshaw Index (HBI, remission defined by HBI < 5). As to endoscopic activity, we defined MH in case

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference
of a value of Crohn’s Disease Endoscopic Index of Severity below 8, so far we included 47 complete MH and 16 partial MH, as a minimal residual endoscopic activity. Endoscopic evaluation was performed within two weeks of blood sampling, and at least after 6 months of ADA treatment.

Results: In our prospective study we enrolled 22 CD patients primary responders to ADA therapy (13 males, median age 43 years, range 23–67 years) who had a median treatment duration of 52 weeks (range 24–121 weeks). ADA TL were significantly higher ($P = 0.0002$) in patients who achieved MH (12.1 mcg/mL, range 6.8–17.2 mcg/mL) as compared to patients without MH (4.50 mcg/mL, range 0.9–9.9 mcg/mL). Receiver Operating Characteristic curve identified an ADA TL cut-off of 6.43 mcg/mL as the threshold with the highest accuracy for identification of patients who achieve MH (AUROC 0.934, sensitivity 100%, specificity 81.8%, PPV 84.6, NVP 100). Moreover, achievement of MH was associated with absence of AAA ($P = 0.012$). Lastly, HBI was significantly lower ($P = 0.0002$) in patients with MH (4, range 3–8) than in patients without MH (11, range 4–17).

Conclusion: In our cohort of CD patients, we observed a clear association between better clinical and endoscopic activity, with particular attention on novel, ADA cut-off of 6.43 mcg/mL, has been identified as the best cut-off to obtain endoscopic remission or at least a minimal residual endoscopic activity. Moreover, we observed that CD patients on ADA therapy who achieved MH had a lower disease clinical activity. Thus, we data support the use of therapeutic ADA monitoring for the management of CD patients in order to obtain clinical and endoscopic remission of the disease.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
Conclusion: The proposed ultrasonic and elastographic signs of restricting CD features predict disease activity and differentiation, with a high diagnostic of fibrotic and inflamatory strictures, helping to choose appropriate surgical treatment.

Disclosure of Interest: All authors have declared no conflicts of interest.

References:

P1019 THE INFLAMMATORY BOWEL DISEASE DISABILITY INDEX INFLAMMATORY BOWEL DISEASE: RELATIONSHIP WITH DISEASE CHARACTERISTICS AND QUALITY OF LIFE IN A COHORT OF SICILIAN PATIENTS

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Introduction: IBDs are disabling conditions that negatively affect physical, psychological, familial and social dimensions of life. The concept of quantifying disability has become established for the evaluation of many other chronic diseases. Thus, specific tools have been used to assess the impact of disease and its treatment options on relevant end-points such as health-related quality of life (HRQL), measured by the IBD-Questionnaire (IBD-Q). Recently, the IBD-Disability Index (IBD-DI) has been developed to evaluate the entire spectrum of limitations in functioning in patients with IBD. This index is inspired to the International Classification of Functioning, Disability and Health (ICF). The aim of the present study was to assess the relationship between the IBD-DI, clinical characteristics, and IBD-Q in a cohort of Sicilian patients with ulcerative colitis (UC) and Crohn’s disease (CD) followed up in a referral center.

Aims & Methods: IBD-Q and IBD-DI questionnaires were administered to consecutive UC and CD adults outpatients from July 2016 to April 2017. The IBD-DI consists of 28 items that evaluate the 4 domains of body functions, activities and participation, body structures and environmental factors. IBD-Q consists of 32 questions grouped into 4 dimensions: bowel, systemic, social, emotional.

Results: Data from UC and CD patients were analysed separately. 100 UC patients (59% males, median age 49 years) were enrolled; 17% were smokers. 83% had inactive or mild disease, 17% moderate disease. None of the recruited patients had severe disease. Concomitant medications at the time of the interview were conventional therapy (5-aminosalicylic acid, oral steroids) in 72 patients (50%), immunosuppressive therapy (immunosuppressant or anti-TNF-a) in 32 patients (28%). The mean IBD-DI score was 20.17 (IQR: 15.7–25.1) and 14.37 (IQR: 10.1–19.2) in UC and CD patients respectively (P = 0.005). By linear regression analysis, IBD-DI was significantly associated with IBD-Q (R² = 0.573, P < 0.001). Interestingly, 5% (n = 5) of patients with inactive or mild disease had severe disability (≥50) and 5% (n = 5) with active disease had minimal disability (<5). Analysis of UC patients revealed that 59% males, median age 41 years were enrolled; 22% were smokers. 94% had mild disease, 17% severe disease. Concomitant medications at the time of the interview were conventional therapy (5-aminosalicylic acid, oral steroids) in 22 patients (40%) or immunosuppressive therapy (immunosuppressant or anti-TNF-a) in 32 patients (60%). The mean IBD-DI score was 20.17 (IQR: 16.2–25.1) while only 2 patients had high DI (>50). No correlations were found between IBD-DI and gender, disease duration, disease extension (Montreal Classification) and immunosuppressive therapy. IBD-DI was related to clinical disease activity (p = 0.001) and extraintestinal manifestations (P = 0.005).

Conclusion: Our preliminary results show that the IBD-DI is significantly related to HR-QoL both in UC and CD. IBD-DI is also related to disease activity and prevalence of extraintestinal manifestations. However, most of our patients were in clinical remission. A larger sample with different grades of disease activity could provide a more accurate evaluation of the reliability of this tool in measuring functional status and disability in IBD. IBD-DI could become a major end-point in RCTs targeting the course of IBD.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1020 D DiPeptiDyl PeptiDase 4 (DPP-4): a BIoMARKER of DISease ACTIVITY and PRoGNOSIS in iNFlammATORY BOWEL DISEASE

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Introduction: DPP-4 is a membrane-bound glycoprotein expressed on the cell surface of enterocytes and lymphocytes. It is released in plasma, maintaining its proteolytic activity and inactivating cytokines, chemokines and neuropeptides.

Aims & Methods: We aimed to investigate the diagnostic and prognostic value of DPP-4 in patients with inflammatory bowel disease (IBD). A total of 203 adult patients (n = 149 IBD patients; n = 42 healthy controls; n = 12 immune controls - systemic lupus erythematosus (SLE) in remission) were prospectively recruited. Plasma DPP-4 was analysed in all groups; faecal samples from IBD patients were collected to perform a DPP-4 and calprotectin analysis.

Disease activity was assessed by the Harvey-Bradshaw Index (HBI) for Crohn’s disease (CD), the partial Mayo Score (pMS) for Ulcerative colitis (UC) and the Systemic Lupus Erythematosus Disease Activity Index for SLE. A multi-biomarker model was used deriving logistic regression to evaluate predictors of disease activity and Cox regression to evaluate predictors of treatment escalation (disease outcome).

Results: Disease activity was defined as the need for escalation to immunomodulatory/biologic therapies or intestinal resection surgery, as a consequence of a disease flare.

In UC, median plasma DPP-4 values were lower in remission vs UC in remission [103 ng/mL, IQR: 78–156 ng/mL vs 174 ng/mL, IQR: 106–240 ng/mL; P = 0.001] and with faecal calprotectin (FC) (r = 0.46, P = 0.001), C-reactive protein (CRP) (r = 0.60, P < 0.001) and HBI (r = 0.56, P < 0.001), but no differences were found between immune and healthy controls. Median faecal DPP-4 values were much lower in active UC vs UC in remission [121 ng/mL, IQR: 59–1682 vs 7814 ng/mL, IQR: 2555–7985; P = 0.001], but no differences were found between inactive and active UC.

In CD, plasma DPP-4 correlated strongly with faecal calprotectin (FC) (r = 0.61, P < 0.001) and CRP (r = 0.32, P < 0.05), strongly with pMS (r = 0.52, P < 0.001) and with faecal DPP-4 (r = 0.52, P < 0.001). The multivariable logistic regression model showed that plasma DPP-4 and CRP are independent predictors of CD activity (OR: 62.10; 95% CI: 2.93–1315.62; P = 0.002 and OR: 48.19; 95% CI: 3.35–692.76; P = 0.004). At follow-up (median 578 days; IQR: 426–688), plasma DPP-4 and CRP independently predicted treatment escalation in CD [hazard ratio (HR) 9.09; 95% CI: 1.77–46.57; P = 0.008 and HR 7.80; 95% CI: 1.60–38.04; P = 0.010, respectively).

Conclusion: Plasma DPP-4 correlated well with plasma DPP-4 in ulcerative colitis, but not in Crohn’s disease.

Disclosure of Interest: F. Magro: has received fees for speaking engagements from Schering/Plough/MSD, Abbvie, Lab Vitória, and Dr Falk Pharma Portugal, and fees for consultations and honoraria from MSD. All other authors have declared no conflicts of interest.

P1021 ROLE OF PET-CT TO ASSESS DISEASE ACTIVITY IN ULCERATIVE COLITIS AND ITS CORRELATION WITH CLINICAL AND BIOLOGICAL MARKERS

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Introduction: Disease activity in ulcerative colitis (UC) is best assessed clinically by Mayo score and endoscopy. Positron emission tomography -computerized tomography (PET-CT) is a non-invasive imaging technique to assess disease activity, extent, treatment response in UC, specially in pediatric population, sick patients and those unwilling for endoscopy.

Aims & Methods: We conducted a prospective observational study at our tertiary care centre with the aim of assessing and correlating UC disease activity by clinical criteria, endoscopy, histology, serum and fecal biomarkers and PET-CT. 60 eligible patients of UC were enrolled into 3 groups (26 remission, 24 moderate and 10 severe activity) as per Mayo score and 18F FDG PET-CT was performed within 72 hours of endoscopy. ESR, CRP and fecal calprotectin levels were determined for all patients.

Results: Of 60 enrolled patients, 10% patients had proctitis, 43.3% had left-sided colitis and 46.7% had extensive colitis. ESR, CRP, fecal calprotectin levels and rectal PET activity were significantly higher in patients with moderate and severe disease activity as compared to those in remission. Rectal PET activity showed a significant correlation with the Mayo score (r = 0.465, p < 0.001), endoscopic sub-score (r = 0.526, p < 0.001), histological score (r = 0.496, p < 0.001), and fecal calprotectin levels (r = 0.279, p < 0.031). Extent evaluation by PET-CT and colonoscopy also showed a significant correlation (r = 0.582, p < 0.001) with each other. We found that CRP at a cut-off level of < 12 mg/L had a sensitivity of 70.59% and specificity of 92.3%, and fecal calprotectin at a cut-off level of < 1400 µg/g had a sensitivity of 88.35% and specificity of 84.60% to predict remission. Besides, PET-CT identified sacroiliitis in 1, mesenteric lymphenodo-pathy in 5, mesenteric stranding in 4, and adenocarcinoma in 1 patient.

Conclusion: PET-CT is a reliable non-invasive tool for assessing disease activity in UC with good correlation with the Mayo score, endoscopic score, histology and fecal calprotectin. It is an accurate measure to determine disease extent, and a good predictor of remission. Thus, with a better patient compliance, it holds promise in replacing colonoscopy where it is refused or difficult to perform.

Disclosure of Interest: All authors have declared no conflicts of interest.

Biomarkers and rectal PET activity of patients

<table>
<thead>
<tr>
<th>Variables</th>
<th>Remission (n = 26)</th>
<th>Moderate activity (n = 24)</th>
<th>Severe activity (n = 10)</th>
<th>Total (n = 60)</th>
<th>P* value between groups</th>
</tr>
</thead>
<tbody>
<tr>
<td>ESR (mm) (mean ± SD)</td>
<td>23.3 ± 18.7</td>
<td>35.1 ± 22.3</td>
<td>48.6 ± 9.7</td>
<td>32.3 ± 21.0</td>
<td>0.002</td>
</tr>
<tr>
<td>CRP mg/L (mean ± SE)</td>
<td>5.6 ± 1.2</td>
<td>25.3 ± 4.3</td>
<td>93.3 ± 23.4</td>
<td>28.1 ± 5.7</td>
<td>0.000</td>
</tr>
<tr>
<td>Fecal calprotectin (µg/g)</td>
<td>72.27 ± 13.65</td>
<td>276.29 ± 30.43</td>
<td>423.66 ± 64.95</td>
<td>212.93 ± 24.3</td>
<td>0.001</td>
</tr>
<tr>
<td>Rectal PET activity</td>
<td>6.04 ± 5.50</td>
<td>10.79 ± 3.88</td>
<td>12.70 ± 10.50</td>
<td>9.05 ± 6.56</td>
<td>0.004</td>
</tr>
<tr>
<td>(SU/100 ml) (Mean ± SD)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

P1023 THE IMPACT OF AN INFLAMMATORY BOWEL DISEASE EDUCATION CLINIC ON PATIENT OUTCOMES AND RESOURCE UTILISATION


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Introduction: Patient education and awareness in those who have inflammatory bowel disease (IBD) is an important aspect of care. To date, there has not been any published data on the impact of an IBD education clinic on resource use or patient outcomes. Aims & Methods: We aimed to evaluate the impact of the education clinic on resource use in patients who attended the clinic compared to patients who did not. A retrospective analysis was done of patients who were diagnosed with IBD between January 2013 and May 2015. 40 patients were identified and divided equally (20 patients each) into clinic attenders (CA) and non-attenders (NA). Resource use was determined at 12 months from diagnosis in the NA group and 12 months from attendance in the CA group. The median time from diagnosis to clinic attendance in the CA group was 7 months. Data was obtained from our hospital’s electronic database system. Statistical analysis was carried out with the student’s t-test.

Results: The median age was 37 in the CA group and 33 in the NA group. In the CA group, 10 patients had ulcerative colitis (UC), 9 patients had Crohn’s Disease (CD) and 1 patient had unclassified IBD. In the NA group, 13 patients had UC and 7 patients had CD. The median of resource use and patient outcomes over a 12 month period (from diagnosis in the NA group and from clinic attendance in the CA group) is detailed in the table below.

<table>
<thead>
<tr>
<th>Resource use and patient outcomes</th>
<th>NA</th>
<th>CA</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Steroid courses</td>
<td>0.47</td>
<td>0.51</td>
<td>1</td>
</tr>
<tr>
<td>Unplanned hospital admissions</td>
<td>0.19</td>
<td>0.21</td>
<td>1</td>
</tr>
<tr>
<td>IBD telephone helpline consultations</td>
<td>0.24</td>
<td>0.28</td>
<td>0.001</td>
</tr>
<tr>
<td>Clinic appointments</td>
<td>3.71</td>
<td>2.84</td>
<td>0.08</td>
</tr>
<tr>
<td>Blood tests (excluding essential monitoring blood tests)</td>
<td>5.81</td>
<td>3.68</td>
<td>0.14</td>
</tr>
<tr>
<td>Endoscopies</td>
<td>0.33</td>
<td>0.26</td>
<td>0.77</td>
</tr>
<tr>
<td>Radiological imaging</td>
<td>0.24</td>
<td>0.16</td>
<td>0.5</td>
</tr>
<tr>
<td>Therapy escalation</td>
<td>1.4</td>
<td>1.15</td>
<td>0.62</td>
</tr>
</tbody>
</table>

Conclusion: In our cohort of patients, patients who attended the IBD education clinic were more likely to utilise our open access IBD telephone helpline service. There was a trend towards increased frequency of outpatient clinic appointments and blood tests in patients who did not attend the IBD education clinic although this was not statistically significant. There were no differences in the rates of hospital admissions or steroid courses in either group. The limitations of our data include the small sample size and short follow-up period.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference
1. THE IBD STANDARDS GROUP. http://s3-eu-west-1.amazonaws.com/file-s.crohnsandcolitis.org.uk/Publications/PPR/ibd_standards_13.pdf [online]
P1024 EMERGING ROLE OF IL-33/ST2 LEVELS IN PREDICTING MUCOSAL RESPONSE TO ANTI-TNF THERAPY IN ULCERATIVE COLITIS

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Introduction: Tumor necrosis factor (TNF) inhibitors (anti-TNF) are considered to be the first-line treatment for moderate-to-severe ulcerative colitis (UC). The role of IL-33 and its receptor, ST2, in intestinal inflammation is incompletely understood, with both pro-inflammatory and regulatory properties described. Recent evidence has shown that anti-TNF is able to modulate the IL-33/ST2 axis in inflammatory conditions.

Aims & Methods: The aim of our study was to explore the potential role of the IL-33/ST2 axis in the mucosal healing process mediated by anti-TNF therapy in UC. Endoscopic Mayo score was calculated before the first anti-TNF infusion (T0) and after 6 weeks (T2). UC patients (Mayo score at T0 ≤2) grouped into responders and non-responders to anti-TNF at T2 (MAYO score ≥2) were enrolled. Healthy controls underwent routine colonoscopy for tumor screening which were also enrolled. At each time point, serum samples were collected and ELISA performed to assess IL-33/ST2 protein levels. Intestinal biopsies were also taken from the rectum and IHC was done to evaluate mucosal IL-33/ST2 expression and localization.

Results: IL-33/ST2 protein levels were significantly increased in responders vs. non-responders, both at T0 and T2. Among responders, IL-33 protein was slightly reduced at T2 vs. T0, while unchanged in non-responders. Interestingly, significantly higher levels of ST2 were found in responders vs. non-responders at T0, with no differences between groups were found at T2. Among responders, ST2 staining was even more evident in non-responders at both time points.

Conclusion: Our results suggest that the IL-33/ST2 axis in predicting gut mucosal wound healing in patients with moderate-to-severe UC treated with anti-TNF therapy. Further studies are underway to determine the impacts of anti-TNF therapy on the IL-33/ST2 axis in UC patients.

Disclosure of Interest: All authors have declared no conflicts of interest.


P1025 INFlixIMAB TROUGH LEVELS IN THE INDUCTION PHASE ARE ASSOCIATED WITH PROLONGED REMISSION IN CROHN’S DISEASE PATIENTS

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Introduction: Higher infliximab (IFX) serum concentrations have been associated with higher rates of clinical remission in inflammatory bowel disease patients. On week 22, 44.8% patients were in remission; on week 54, 40% were in remission.

Aims & Methods: To assess, in a prospective study, the correlation between clinical, endoscopic and histologic activity scores in a cohort of IBD patients (pts) undergoing colonoscopy. Secondary end-point was to assess the role of histologic scores in clinical practice. From Feb. to Dec. 2016, pts undergoing colonoscopy were included in a prospective observational study. The aim of our study was to explore the potential role of the IL-33/ST2 axis in the mucosal healing process mediated by anti-TNF therapy in UC. Endoscopic Mayo score was calculated before the first anti-TNF infusion (T0) and after 6 weeks (T2). UC patients (Mayo score at T0 ≤2) grouped into responders and non-responders to anti-TNF at T2 (MAYO score ≥2) were enrolled. Healthy controls underwent routine colonoscopy for tumor screening which were also enrolled. At each time point, serum samples were collected and ELISA performed to assess IL-33/ST2 protein levels. Intestinal biopsies were also taken from the rectum and IHC was done to evaluate mucosal IL-33/ST2 expression and localization.

Results: IL-33/ST2 protein levels were significantly increased in responders vs. non-responders, both at T0 and T2. Among responders, IL-33 protein was slightly reduced at T2 vs. T0, while unchanged in non-responders. Interestingly, significantly higher levels of ST2 were found in responders vs. non-responders at T0, with no differences between groups were found at T2. Among responders, ST2 staining was even more evident in non-responders at both time points. Healthy controls showed significantly lower levels of both IL-33 and ST2 compared with other groups. IHC confirmed these observations. In particular, IL-33 and ST2 staining was more evident in healthy controls. In responders, ST2 was more evident in the mucosa and in close proximity to adherent inflammatory infiltrate. IL-33 and ST2 staining was even more evident in non-responders at both time points. Healthy controls showed significant differences between responders and non-responders at both time points. Healthy controls showed significant differences between responders and non-responders at both time points. Healthy controls showed significant differences between responders and non-responders at both time points.

Conclusion: Our results suggest that the IL-33/ST2 axis in predicting gut mucosal wound healing in patients with moderate-to-severe UC treated with anti-TNF therapy. Further studies are underway to determine the impacts of anti-TNF therapy on the IL-33/ST2 axis in UC patients.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1027 THE RELATIONSHIP BETWEEN SERUM INFILXIMAB AND ADALUMAB CONCENTRATIONS AND THEIR CORRESPONDING ANTI-DRUG ANTIBODY LEVELS: ANALYSIS OF OVER 50,000 PATIENT RESULTS USING LAB-DEVELOPED CHEMILUMINESCENT IMMUNOASSAYS

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2Medical Affairs, Labcorp, Calabasas/United States of America/CA

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Introduction: Assays to measure TNF inhibitors and anti-drug antibodies (ADAb) in patient serum are being utilized to manage failure to respond and loss of response. These monitoring assays may also be used to proactively titrate doses and dosing intervals. Here, 36,477 infliximab (IFX) and 21,284 adalimumab patient results from the past 4 years were analyzed.

Aims & Methods: Measurements of drug and ADA levels were performed by lab-developed chemiluminescent immunoassays.[1] Lower limits of quantitation are 0.4 µg/mL for IFX and 0.6 µg/mL for adalimumab. ADA assays are drug specific and performed in the presence of up to 100 µg/mL of drug. Clinical histories and blood collection timing are unknown.

Results: Of 36,477 measured IFX samples, 56% (20,355) were ADA-free and 44% (16,224) had measurable ADA ranging from 22 to 3.5 million ng/mL. In the absence of ADA, IFX concentrations were from 0.4 to 15 ng/mL, with the majority (>60%) between 3.0 to 20 µg/mL. In the presence of ADA, an inverse relationship between IFX concentrations and anti-IFX antibodies is evident (Table 1). As a reference, an ADA-free mean drug level was determined from samples with IFX between 0.4-30 µg/mL. Decreasing mean IFX concentrations (column 3) with increasing ADA (column 1) are demonstrated where low ADA (<200 ng/mL) appears to have minimal impact on mean drug levels while high ADA (>1000 ng/mL) is invariably associated with severely diminished IFX (10% or less than the mean). A similar drug - ADA relationship was observed with adalimumab (Table 2). Interestingly, even lower tier anti-adalimumab antibodies are associated with a diminished mean adalimumab (3.4-5.6 µg/mL) where the baseline mean adalimumab (6.1 µg/mL) was calculated from 10,784 ADA-free samples with adalimumab from 0.6-15 µg/mL. Anti-adalimumab antibody levels >300 ng/mL are associated with free adalimumab concentrations <30% of the mean. Of all adalimumab patient samples, 60% (12,873) were free of ADA, and 40% (8411) were ADA positive, ranging from 25 to 2.8 million ng/mL. For adalimumab in Table 2, as ADA levels increase (column 1), their corresponding mean drug concentrations diminish (column 3), similar to IFX results in Table 1.

Table 1: Anti-Infliximab Antibody Distribution and Corresponding Mean Free Drug Levels

<table>
<thead>
<tr>
<th>Antibody</th>
<th>Mean Drug</th>
<th>% with Drug</th>
<th>Concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive (µg/mL)</td>
<td>n</td>
<td>501–700</td>
<td>701–1000</td>
</tr>
<tr>
<td>undetected</td>
<td>15692</td>
<td>10%</td>
<td>0%</td>
</tr>
<tr>
<td>22–100</td>
<td>6785</td>
<td>9.5</td>
<td>11%</td>
</tr>
<tr>
<td>101–200</td>
<td>2684</td>
<td>8.6</td>
<td>19%</td>
</tr>
<tr>
<td>301–500</td>
<td>1344</td>
<td>6.3</td>
<td>27%</td>
</tr>
<tr>
<td>501–700</td>
<td>1427</td>
<td>5.2</td>
<td>38%</td>
</tr>
<tr>
<td>701–1000</td>
<td>789</td>
<td>3.7</td>
<td>53%</td>
</tr>
</tbody>
</table>

P1028 REAL-WORLD USE OF IMMUNOSUPPRESSIVES AMONG PATIENTS WITH INFLAMMATORY BOWEL DISEASE TREATED WITH VEDOLIZUMAB

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2Takeda Development Centre Europe Ltd, London/United Kingdom

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Introduction: Immunosuppressives (IM) are often used as maintenance therapy to reduce the risk of relapse among patients with inflammatory bowel disease (IBD). Vedolizumab (VDZ), a monoclonal antibody that targets α4β7 integrin, has been approved for the treatment of moderately-to-severely active Crohn’s disease (CD) and ulcerative colitis (UC).

Aims & Methods: The aim was to assess the real-world use of IM therapy and compare outcomes in IBD patients with, versus without a history of IM use, who initiated treatment on VDZ in the United States. The Explorys Universe database was used to identify all IBD patients >18 years of age who: (1) initiated VDZ therapy between May 20, 2014, and February 22, 2016 (the date of VDZ initiation was the assigned index date); and (2) had 365 days of available data pre- and post-index date (follow-up). Patients were stratified based on the use of IM at any point in their treatment history before the index date. Key outcomes in the follow-up period included the use of IM, and the incidence of IBD-related surgeries, hospitalizations, and flares (defined as the use of intravenous corticosteroids, IBD-related surgeries, or hospitalizations).

Results: A total of 567 patients were included, of which 68.4% had CD, and 31.6% had UC. Mean (standard deviation [SD]) age at index was 44 (15.0) years; 59.6% were female. Overall, 54.6% had a history of prior IM use, and 64.6% received anti-TNFs before starting VDZ therapy. On average, patients initiated VDZ 4.5 (3.6) years following their initial diagnosis. Of the 54.6% of patients with a history of IM therapy, 61.0% did not use IM during maintenance treatment with VDZ during follow-up. Of the 45.4% of patients without a history of IM use, 87.0% did not initiate IM therapy during follow-up. Amongst VDZ patients with a history of IM vs. without history of IM use, there was a trend of increased flares (38.7% vs. 30.0%, p = 0.034), hospitalizations (21.9% vs. 19.8%, p = 0.60), and surgeries (10.6% vs. 6.6%, p = 0.103). Findings for UC and CD patients are presented in Table 1.

Conclusion: The majority of patients with a history of IM use did not use IM therapy after initiating VDZ in a real-world clinical practice. The use of IM after initiating VDZ was also low amongst patients without a history of IM use. Lower rates of healthcare resource utilization were observed amongst patients without a history of IM use. Further research is needed to better understand the degree to

Table 2: Anti-Adalimumab Antibody Distribution and Corresponding Mean Free Drug Levels

<table>
<thead>
<tr>
<th>Antibody</th>
<th>Mean Drug</th>
<th>% with Drug</th>
<th>Concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive (µg/mL)</td>
<td>n</td>
<td>25–100</td>
<td>1001–2000</td>
</tr>
<tr>
<td>undetected</td>
<td>10784</td>
<td>100%</td>
<td>0%</td>
</tr>
<tr>
<td>25–100</td>
<td>3904</td>
<td>5.6</td>
<td>5%</td>
</tr>
<tr>
<td>101–200</td>
<td>1144</td>
<td>3.4</td>
<td>12%</td>
</tr>
<tr>
<td>201–300</td>
<td>570</td>
<td>2.4</td>
<td>24%</td>
</tr>
<tr>
<td>301–500</td>
<td>655</td>
<td>1.8</td>
<td>39%</td>
</tr>
<tr>
<td>501–700</td>
<td>330</td>
<td>1.1</td>
<td>57%</td>
</tr>
<tr>
<td>701–1000</td>
<td>303</td>
<td>0.7</td>
<td>75%</td>
</tr>
<tr>
<td>1001–2000</td>
<td>496</td>
<td>&lt;0.6</td>
<td>93%</td>
</tr>
<tr>
<td>2001–4000</td>
<td>394</td>
<td>&lt;0.6</td>
<td>97%</td>
</tr>
<tr>
<td>4001–2.8 million</td>
<td>610</td>
<td>&lt;0.6</td>
<td>99%</td>
</tr>
</tbody>
</table>
which IM therapy is used concomitantly with VDZ and potential impact on outcomes in real-world clinical practice.

Disclosure of Interest: M. Rauly Callado: Mirève Rauly Callado is a full-time employee of Evidera.
R. Carroll: Robert Carroll is a full-time employee of Evidera.
R. Curtis: Employee of Takeda Development Centre Ltd.
M.J. Khalid: Employee of Takeda Development Centre Ltd.
H. Patel: I am currently an employee of Immensity Consulting Inc., which received funding from Takeda Development Centre Ltd.

P1029 MOLECULAR SURROGATES OF HISTOLOGIC ACTIVITY IN CROHN’S DISEASE

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Introduction: Biomarkers of inflammatory bowel disease activity have been researched for decades but objective markers of disease severity that support clinical decision-making are still needed. Well-established markers include serum C-reactive protein and fecal calprotectin, but their use as a standalone surrogate for disease activity has been controversial. We hypothesize that novel objective markers of tissue inflammation are best identified at the site of disease with a tissue-level assessment of disease activity.

Aims & Methods: Biopsy samples were obtained from patients in the UNITI trials of ustekinumab in moderate-to-severe Crohn’s disease. The UNITI induction trials included two cohorts, patients who failed ≥1 TNF antagonists (UNITI-1) or patients who failed conventional therapies (UNITI-2). Pairs of adjacent biopsies were taken from the rectum, splenic flexure, and ileum. DNA from each biopsy from each pair was assessed by Global Histology Disease Activity Score (GHAS) while the other was submitted to microarray analysis. Partial least squares regression and random forest were used to identify biomarkers associated with histological severity in the UNITI-1 cohort. Robustness of the resulting models was assessed using cross-validation within the training set and multiple external validation sets (defined within the UNITI-1 and UNITI-2 cohorts).

Results: In UNITI-1, a single multivariate model comprising 16 genes was identified that predicted histological activities in rectum or splenic flexure biopsies. This model was characterized by R²=0.78 for the training set, and R²=0.59, 0.54, and 0.32 on external validation sets also from UNITI-1. A separate 14-gene model capturing histological activity in ileal biopsies was characterized by R²=0.5 for the training set and R²=0.45 in the external validation set. In general, both models contained genes related to tissue degradation, barrier function, and immune regulation, including CXCL11 (I-TAC). Both models retained performance in external validation datasets from UNITI-2 but exhibited lower performance. De novo models generated from UNITI-2 also exhibited lower performance. Indeed, weighted gene co-expression network analysis indicated weaker associations between gene expression and histology scores for UNITI-2 compared to UNITI-1 subjects.

Conclusion: Our analysis supports the ability of biopsy transcriptomics combined with machine learning approaches to capture disease-relevant variability in Crohn’s disease and, more importantly, supports the use of similar approaches to identify additional surrogate markers. Interestingly, this approach was more successful in the TNF antagonist failure cohort compared to the conventional therapy failure cohort. We hypothesize that this is related to increased strength of the transcriptional signal in the TNF antagonist failure cohort. We identified specific genes that could be used together as surrogates for histologic measurement, which may not be susceptible to the subjectivity inherent in GHAS scoring. Finally, the specific genes identified by our analysis provide insight into the molecular processes driving histological disease activity in Crohn’s disease.

Disclosure of Interest: C. Monast: Janssen Research & Development, LLC employee
K. Li: Janssen Research & Development, LLC employee
E. Myshkin: Consultant to Janssen Research & Development, LLC
C. Brodermelker: Janssen Research & Development, LLC employee
J. Friedman: Janssen Research & Development, LLC employee
F. Baribaud: Janssen Research & Development, LLC employee

Reference

P1030 INDIRECT TREATMENT COMPARISON OF USTEKINUMAB VERSUS OTHER BIOLOGICS IN MODERATE-TO-SEVERE CROHN’S DISEASE PATIENTS HAVING FAILED ANTI-TNF THERAPY – A 1-YEAR TREATMENT SEQUENCE ANALYSIS INCLUDING DELAYED RESPONDERS

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3Janssen Pharmaceutica, Beerse/Belgium
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Introduction: Indirect evidence is needed to inform the clinical efficacy of ustekinumab in Crohn’s disease (CD). Indirect treatment comparisons in CD are challenged by withdrawal trial designs limiting placebo arm transitivity. This treatment sequence analysis builds on previous work proposing a solution to challenges inherent to CD data to compare one year efficacy of biologics in CD patients having failed anti-TNF therapy. Analyses accounted for delayed responders (induction non-responders attaining response after additional doses) to generate more comprehensive estimates of biologics’ relative efficacies.

Aims & Methods: A systematic literature review identified randomized controlled trials in CD patients having failed anti-TNF therapy for induction and maintenance of ustekinumab (UST), adalimumab (ADA), or vedolizumab (VDZ). Clinical response (CDAI-100 point reduction) and remission (CDAI <150) were assessed. The probability of achieving response after induction was multiplied by the conditional probability of maintaining response/achieving remission at one year. Separate calculations were conducted for early and delayed responders. Their respective treatment sequence rates were summed to obtain overall response and remission rates. Placebo rates were imputed using data from patients induced and maintained on placebo from the IM-UNITI study, adjusted for responder and remitter induction rates. Bayesian analyses generated relative

Abstract: P1028. Table 1: Characteristics and outcomes among patients newly started on vedolizumab stratified by IMB type and history of immunosuppressive therapy

<table>
<thead>
<tr>
<th>CD (N = 388)</th>
<th>UC (N = 179)</th>
</tr>
</thead>
<tbody>
<tr>
<td>With history of IM use (N = 225)</td>
<td>Without history of IM use (N = 163)</td>
</tr>
<tr>
<td>Mean (SD) age, years</td>
<td>43 (14.8)</td>
</tr>
<tr>
<td>Female, %</td>
<td>64.9%</td>
</tr>
<tr>
<td>Mean (SD) time from diagnosis to VDZ initiation, years</td>
<td>6.0 (3.9)</td>
</tr>
<tr>
<td>Pre-index exposure to anti-TNF therapy, %</td>
<td>78.2%</td>
</tr>
<tr>
<td>IBD-related measures in the 365 days pre-index</td>
<td></td>
</tr>
<tr>
<td>Hospitalisations</td>
<td>42.2%</td>
</tr>
<tr>
<td>Surgeries</td>
<td>18.7%</td>
</tr>
<tr>
<td>Flares</td>
<td>56.9%</td>
</tr>
<tr>
<td>IBD-related measures in the 365 day follow-up period</td>
<td></td>
</tr>
<tr>
<td>Hospitalisations</td>
<td>24.9%</td>
</tr>
<tr>
<td>Surgeries</td>
<td>12.4%</td>
</tr>
<tr>
<td>Flares</td>
<td>43.6%</td>
</tr>
</tbody>
</table>

Note: IM therapy included use of azathioprine, 6-mercaptopurine, methotrexate, mycophenolate mofetil, cyclosporine, and Tacrolimus
odds ratios (OR), credible intervals (CI), and posterior distribution probabilities for superiority of UST.

**Results:** Accounting for delayed responders, the absolute proportions of patients having maintained response and being in remission at one year were 30% of patients receiving UST every other week and 33% of patients receiving ADA every other week or weekly. Based on a one-year treatment sequence analysis, probabilities for UST to be better than ADA for achieving and maintaining response and remission were 99% (OR[CrI]: 1.94[1.07;3.48]) and 98% (OR[CrI]: 1.82[1.00;3.26]), respectively. UST had higher likelihoods of remission than ADA given weekly (OR[CrI]: 1.36[0.72;2.58] or every other week (85%, OR[CrI]: 1.14[0.70;2.48]).

**Conclusion:** This approach deals with methodological issues inherent to CD trial data. In CD patients having failed anti-TNF therapy, ustekinumab had higher likelihood of response or remission than adalimumab and vedolizumab over a one-year treatment sequence. Additional induction doses and continued maintenance therapy with ustekinumab have demonstrated benefits in delayed responders compared to other biologics. Previous research is limited to indirect treatment comparisons in early responders only. Including delayed responders provides a more accurate picture of CD patients’ response to biologics and better informs clinical practice.

**Disclosure of Interest:** L. Mesana: Consultant to Janssen Scientific Affairs, LLC; M. Pacou: Consultant to Janssen Scientific Affairs, LLC; D. Naessens: Janssen Scientific Affairs, LLC employee; S. Sloan: Janssen Scientific Affairs, LLC employee; A. Gauthier: Janssen Scientific Affairs, LLC investigator

**Reference**

**P1031 INDIRECT TREATMENT COMPARISON OF USTEKINUMAB VERSUS OTHER BIOLOGICS IN MODERATE-TO-SEVERE CROHNS DISEASE PATIENTS HAVING FAILED CONVENTIONAL THERAPY – A 1-YEAR TREATMENT SEQUENCE ANALYSIS INCLUDING DELAYED RESPONDERS**

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**Introduction:** Indirect evidence is needed to inform the clinical efficacy of ustekinumab in Crohn’s disease (CD). Indirect treatment comparisons in CD are challenged by withdrawal trial designs limiting placebo arm transitivity. This treatment sequence analysis builds on previous work proposing a solution to indirect treatment comparisons in early responders only. Including delayed responders provides a more accurate picture of CD patients’ response to biologics and better informs clinical practice.

**Disclosure of Interest:** L. Mesana: Consultant to Janssen Scientific Affairs, LLC; M. Pacou: Consultant to Janssen Scientific Affairs, LLC; D. Naessens: Janssen Scientific Affairs, LLC employee; S. Sloan: Janssen Scientific Affairs, LLC employee; A. Gauthier: Consultant to Janssen Scientific Affairs, LLC

**P1032 EFFICACY AND TOLERABILITY OF INITIATING, OR SWITCHING TO, INFliximab BIOSIMILAR CT-P13 IN INFLAMMATORY BOWEL DISEASE (IBD): A LARGE SINGLE-CENTRE EXPERIENCE**

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**Introduction:** Anti-TNF therapies have revolutionised the management of IBD. Recently, the infliximab (IFX) biosimilar (CT-P13) received market authorisation for IBD allowing cost benefits with switches to CT-P13 with annual savings £1 million in savings.

**Disclosure of Interest:** M. Pacou, L. Mesana, A. Gauthier, D. Naessens, S. Sloan, S. Danese, A. Yamada7, N. Kamata8, T. Hibi4

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**P1033 SAFETY AND EFFICACY OF HELICOBACTER PYLORI ERADICATION IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE**

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**Disclosure of Interest:** All authors have declared no conflicts of interest.
Postoperative recurrence. All our patients have received clinical (HBI), biological (CDAI) and endoscopic evaluation. MR enterographic and endoscopic findings were checked at different times (during the first 2 years = G1, between 2 and 5 years = G2 and beyond 5 years = G3). Endoscopic remission was defined by the absence of ulceration. Statistical analysis used the Student Fisher and χ² tests of Mann Whitney.

Results: AZT was prescribed in 46.6% (62/133) cases of luminal involvement and 53.4% of cases to prevent post-operative recurrence. In the luminal group, the sex ratio M/F was 1, the age at diagnosis was 27 years ± 9. A delay of diagnosis was estimated at ± 2.5 (0–13) years. Smoking was found in 26% of cases (16/61). It was ileocolic or colonic in 16.4% and 49.2% of cases, phenotype B1 or B2 in 32.8% and 44.6% respectively. 47.5% had more than 2 corticosteroid treatments (CCT), the average time to start AZT was 4 ± 6 years.

The mean duration of treatment was 3.5 ± 5.2 years. The persistence of endo-

P1035 EVALUATION OF PHARMACOKINETIC PROFILES OF SB2 AS A BIOSIMILAR OF REFERENCE INFLIXIMAB
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Samsung Bioepis Co., Ltd., Incheon/Korea, Republic of

Introduction: Based on the totality of evidence with similar analytical, pharma-

Aims & Methods: The pre-clinical PK profiles were evaluated in single and

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Disclosure of Interest: All authors have declared no conflicts of interest.

Postoperative recurrence. All our patients have received clinical (HBI), biological (CDAI) and endoscopic evaluation. MR enterographic and endoscopic findings were checked at different times (during the first 2 years = G1, between 2 and 5 years = G2 and beyond 5 years = G3). Endoscopic remission was defined by the absence of ulceration. Statistical analysis used the Student Fisher and χ² tests of Mann Whitney.

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The mean duration of treatment was 3.5 ± 5.2 years. The persistence of endo-

P1034 EFFECTIVENESS OF IMMUNOSUPPRESSORS IN CROHN’S DISEASE
L. Y. Lee1, N. Kaddache1, L. S. Salah1, A. Rebha1, S. Khoutir1, K. Soualah1, H. Bellimi1, F. Ihaddadene1, R. Benbaya1, K. Bouchaoui2, A. Tata2, B. Bahaz1, P. P1034 EFFECTIVENESS OF IMMUNOSUPPRESSORS IN CROHN’S DISEASE

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Introduction: The use of immunosuppressors, including Azathioprine (AZT) in inflammatory bowel disease (IBD) is considered reference treatment. They are indicated especially in the case of corticoadherence, corticoreistance and in postoperative recurrences. Their efficacy is primarily judged on clinical evaluation and relapses. Few data are available on long-term healing during Crohn’s disease (CD). The aim of this study is to evaluate the long-term clinical effectiveness of AZT in luminal Crohn’s disease and in prevention of postoperative recurrence with endoscopic evaluation.

Aims & Methods: In this retrospective study, 135 consecutive patients followed for CD at the IBD Center with or without anoperative involvement were included between 1/1/2016 and 31/03/2016. All patients with Rutgeerts score greater than or equal to 2 received AZT. All patients were under AZT for at least 12 months, maintaining remission for luminal involvement or preventing

P1034 EFFECTIVENESS OF IMMUNOSUPPRESSORS IN CROHN’S DISEASE

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Introduction: Low prevalence of Helicobacter pylori (HP) infection has been reported in IBD patients. Prevalence in inflammatory bowel disease (IBD), however, is unclear whether the eradication therapy for HP can exacerbate disease activity of IBD. We then aimed to clarify the safety and efficacy of HP eradication in patients with IBD.

Aims & Methods: This was a multicenter, retrospective cohort study in 26 institu-

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Disclosure of Interest: All authors have declared no conflicts of interest.

Postoperative recurrence. All our patients have received clinical (HBI), biological (CDAI) and endoscopic evaluation. MR enterographic and endoscopic findings were checked at different times (during the first 2 years = G1, between 2 and 5 years = G2 and beyond 5 years = G3). Endoscopic remission was defined by the absence of ulceration. Statistical analysis used the Student Fisher and χ² tests of Mann Whitney.

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P1034 EFFECTIVENESS OF IMMUNOSUPPRESSORS IN CROHN’S DISEASE

Contact E-mail Address: keli_00200@yahoo.fr

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STAY OF INFLAMMATORY BOWEL DISEASE PATIENTS

P1036 INFliximab dose banding shortens length of stay of inflammatory bowel disease patients

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Introduction: According to infliximab (IFX) license in inflammatory bowel diseases (IBD), infusion doses are based on patient weight. In daily practice, treatment is prepared by pharmacist after clinical patient assessment, leading to an increased duplication of hospital stay and consequently costs. A pharmacoeconomic study (1) has shown that a weight-based dose (WBD) strategy does not reduce interindividual variability of IFX trough levels when compared to fixed doses. According to these findings, our hospital implemented dose banding (DB) of IFX infusions, defined by doses rounded up or down according to one of eight pre-determined standard doses with a maximum theoretical deviation of +/– 5%, that allowed to prepare infusions at the pharmacy before patient admission.

Aims & Methods: The aim of the study was to compare hospitalisation length of stay (HLOS) in IFX DB as compared to those treated with IFX WBD. From February to March 2017, we conducted a prospective, case-control study in our unit, including all IBD patients admitted for an IFX infusion. Patients who should receive an IFX dose between 250 and 800 mg were included in the DB group (treatment pre-prepared at the pharmacy, sent to the hospital unit before patient admission and administered just after the clinical validation). Patients who should receive an IFX dose below 250 mg or above 800 mg were included in the WBD group (treatment prepared after clinical validation including weight, and then sent to the hospital unit). Patients were analysed only when precise length of stay could be obtained and measured in minutes. Primary objective was to compare the length of stay at hospital in both groups. Secondary objective was to compare the proportion of IFX doses cancelled, reattributed and wasted and the saved or wasted price associated (reimbursement price of one 100 mg IFX vial: 382.28 €). Two out these three infusions (3.5%) were cancelled in the DB group (treatment pre-prepared at the pharmacy, sent to the hospital unit before patient admission and administered just after the clinical validation). The median time to obtain response was 4.0 days (95% confidence interval (CI): 1.0, 4.0) and the median time to remission was 7.0 days (95%CI: 4.0, 14.0).

Results: Among the 373 IBD patients treated by IFX during the study period, 116 (31%) patients (51M/65F; median age: 41 years) were included in the study (75 in the DB group and 41 in the WBD group) corresponding to 128 infusions (84 in DB and 44 in WBD groups). Mean length of hospitalisation stay were 238 ± 21 min in the DB group and 308 ± 32 min in the DBW group, respectively (p < 0.001). DB was associated with a mean reduction of length of stay of 23%, corresponding to 70 minutes per patient. DB reduced significantly the mean duration of stay by decreasing the waiting time between clinical assessment and start of the infusion: 16 min vs. 84 min with WBD (p < 0.001). During the study, none of the 44 (6%) infusion in the WBD group was cancelled while 3/84 (3.5%) were cancelled in the DB group (p=0.55). Two out these three infusions could be reattributed to other patients, saving 2801€.

Conclusion: When used routinely in IBD, IFX DB is associated with a shortened length of hospital stay as compared to WBD, with a mean reduction of 70 minutes per patient. As IFX DB seems having similar efficacy to weight-based doses, it may improve functioning of daily hospitalisation units.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

P1037 RAPIDITY OF ONSET OF RESPONSE TO ADALIMUMAB (ADA) IN LUMINAL CROHN’S DISEASE (CD), DATA FROM RAPIDA TRAIL

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Introduction: Rapidity of response to treatment in CD is now considered a field of major interest, due to the importance of achieving the highest benefit in the shortest possible time. There are no studies specifically designed to evaluate the rapidity of response to ADA neither other anti-TNF therapies. The aim of this trial was to evaluate the rapidity of onset of clinical response to ADA therapy.

Aims & Methods: Adult anti-TNF naïve patients with active luminal (Harvey-Bradshaw Index (HBI) ≥ 8) moderate-to-severe CD (excluding penetrating and stricture disease), with no response to a full and adequate course of therapy with corticosteroids and/or immunosuppressants, were enrolled in this international, prospective, open label, single arm and multicenter clinical trial. Patients received standardized ADA treatment (160 mg – 80 mg – 40 mg eow). The HBI was evaluated to determine the response at day 4 and week 1; and clinical remission at weeks 2, 4 and 12. Response was defined as a decrease of, at least, 3 points in the HBI global score and remission was defined as HBI global score ≤ 5. CRP (C Reactive Protein) and fecal calprotectin (FC) were analyzed at baseline, day 4, week 1, 2, 4, 12. The modified intention to treat (mITT) population was the primary population for efficacy analysis and consisted of those patients enrolled in the study who had received at least one dose of ADA. Treatment-emergent serious adverse events (AEs) were recorded to assess safety throughout the study until 70 days after last treatment dose. All patients who received at least one dose of ADA were included in the safety population.

Statistical analyses were performed by the t-test or the Wilcoxon signed rank test, as applicable. Time to clinical response was analyzed using a Kaplan-Meier survival analysis model.

Results: 86 anti-TNF naïve patients were analyzed. A response at day 4 and week 1 was experienced by 60.5% and 74.4% of patients, respectively. Remission was achieved by 53.5% of patients at week 2, 61.6% at week 4 and 54.7% at week 12. The median time to obtain response was 4.0 days (95% confidence interval (CI): 1.0, 4.0) and the median time to remission was 7.0 days (95% CI: 4.0, 14.0).

During the study, 42.5% of the patients suffered from any adverse event (AE). Only 3 patients (3.5%) showed a serious AE.

Conclusion: ADA produces rapid clinical remission and response since day 4 in patients with moderate-to-severe CD unresponsive to therapy with corticosteroids and/or immunosuppressants.

Disclosure of Interest: F. Casellas: Dr. Francesc Casellas has received research funding from AbbVie, MSD, Shire, Ferring and Zambon. M. Esteve: Dr Esteve has served as a consultant for AbbVie, MSD, Takeda and Tillots Pharma and has received speaker fees from MSD and AbbVie S. García-López: Dr. Santiago Garcia has received research funding from AbbVie and MSD, Shire, FAES and Ferring and has served occasionally as a consultant for AbbVie and MSD. A. Echarri: Dr Ana Echarri has received research funding from Abbvie and Shire, and speaker fees from AbbVie, Takeda, MSD, Shire, Pfizer. M. Martin-Arranz: Dra. Martín Arranz has served as consultant for Abbvie, MSD, Ferring and has received speaker fees from Abbvie, MSD, Ferring, Chiesi, Tillots. M. Navarro-Llava: Dr. Mercè Navarro-Llava has received research funding from Abbvie and speaker fees from Abbvie, MSD, Takeda, Shire Pharmaceuticals, Zambon and Allergan. J. Huguet: Dr. Jose Maria Huguet Malaves has received research funding from AbbVie and speaker fees from Abbvie, MSD, Takeda, Shire, and speaker fees from MSD, Shire, PharmaCeuticals, Zambon and Allergan. F. Argüelles-Arias: Dr. FAA has served as a consultant for AbbVie, MSD, KRN Pharma, Celltrion, and Takeda Also, has received research funding from MSD, KRN Pharma, Celltrion, and Takeda, and speaker fees from MSD, KRN Pharma, Celltrion, and Takeda.
Patients (%) 

<table>
<thead>
<tr>
<th>ADR</th>
<th>Patients</th>
<th>&gt;1000 mg iron</th>
<th>≤1000 mg iron</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flushing</td>
<td>3.0</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>Constipation</td>
<td>0.0</td>
<td>1.9</td>
<td>0.6</td>
</tr>
<tr>
<td>Increased hepatic enzyme</td>
<td>1.5</td>
<td>0.6</td>
<td>0.6</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>0.5</td>
<td>1.3</td>
<td>0.8</td>
</tr>
<tr>
<td>Dyspepsia</td>
<td>0.0</td>
<td>1.3</td>
<td>0.6</td>
</tr>
<tr>
<td>Headache</td>
<td>1.0</td>
<td>1.3</td>
<td>1.3</td>
</tr>
<tr>
<td>Hypersensitivity</td>
<td>1.0</td>
<td>0.6</td>
<td>0.4</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>1.0</td>
<td>0.6</td>
<td>0.4</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1.0</td>
<td>0.6</td>
<td>0.4</td>
</tr>
<tr>
<td>Hypotension</td>
<td>1.0</td>
<td>0.6</td>
<td>0.4</td>
</tr>
<tr>
<td>Nausea</td>
<td>1.0</td>
<td>0.6</td>
<td>0.4</td>
</tr>
<tr>
<td>Urticaria</td>
<td>1.0</td>
<td>0.6</td>
<td>0.4</td>
</tr>
</tbody>
</table>

No ADRs of hypophosphatemia were reported. In patients dosed with ≤1000 mg iron isomaltoside, HB increased with a mean of 1.72 (95% confidence interval (CI) 0.12 g/dL from baseline to week 3, 0.00 (0.12) g/dL to week 4, and 2.32 (0.13) g/dL to week 8. In patients dosed with >1000 mg iron isomaltoside, HB increased with a mean of 2.04 (0.10) g/dL from baseline to week 3, 2.51 (0.09) g/dL to week 4, and 3.01 (0.12) g/dL to week 8. The observed increase in HB was statistically significantly higher in patients dosed with >1000 mg iron isomaltoside (p = 0.04). In the IBD subgroup, a similar dose-depended statistically increase in HB was observed at week 3 and onwards (p < 0.02).

Conclusions: No dose-response for ADRs was observed with administration of high cumulative doses of iron isomaltoside whereas HB increased more after 3 weeks with doses >1000 mg. Thus, high doses (>1000 mg) of iron isomaltoside can be administered without additional safety concerns including concerns of hypophosphatemia and with efficacious increases in HB in patients with gastrointestinal symptoms.

Disclosure of Interest: R. Derman: Richard Derman has been a consultant for Pﬁzer, Merck, and Abbvie. R. Derman: Richard Derman has been a consultant for Pﬁzer, Merck, and Abbvie. J.F. Dahlerup: The investigator/institution received a fee per patient J.F. Dahlerup. W. Weinisch: The investigator/institution received a fee per patient.

References:
References

Disclosure of Interest: All authors have declared no conflicts of interest.

CONCLUSION
Golimumab was effective and safe in induction of response in UC patients in daily clinical practice.

P1041 PHARMACOKINETIC SIMILARITY OF ABP 710 TO INFLEXIMAB: RESULTS FROM A RANDOMIZED, SINGLE-BLIND, SINGLE-DOSE, PARALLEL-GROUP STUDY IN HEALTHY SUBJECTS

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Introduction: ABP 710 is being developed as a biosimilar to infliximab, an anti- tumor necrosis factor monoclonal antibody. Analytical and functional comparability studies have been completed. This report describes the results of a Phase 1 pharmacokinetic (PK) equivalence study comparing ABP 710 with infliximab.

Aims & Methods: This was a single-blind, single-dose, 3-arm, parallel-group study in healthy adults, 18-45 years of age and with a body mass index of 18 to 30 kg/m². Subjects were randomised to receive a 5 mg/kg intravenous (IV) infusion of ABP 710 or infliximab sourced from the EU and the US after pre-treatment with an antihistamine and acetaminophen 30 minutes prior to start of infusion. The primary objective was demonstration of PK similarity of ABP 710 with infliximab EU and with infliximab US based on area under the serum concentration-time curve from time 0 to infinity (AUC₀→∞) as the primary endpoint. The criteria to achieve PK equivalence were for geometric mean (GM) ratio and its 90% confidence interval (CI) to be within the range of 0.80 to 1.25.

Secondary endpoints included maximum observed serum concentration (Cmax), safety, and immunogenicity.

Results: A total of 148 subjects received study treatment (ABP 710: n = 49; infliximab EU: n = 49; infliximab US: n = 50). After a single dose, the adjusted least squares (LS) GM of AUC₀→∞ and Cmax were as follows: ABP 710, 335.59 µg/mL and 123 µg/mL; infliximab EU, 337.06 µg/mL and 121 µg/mL; infliximab US, 375.22 µg/mL and 127 µg/mL. The ratios of adjusted LS GM (90% CI) for AUC₀→∞ and Cmax between ABP 710 and infliximab EU were 0.996 (0.9042, 1.0963) and 1.021 (0.9624, 1.0827) and that between ABP 710 and infliximab US were 0.894 (0.8122, 0.9848) and 0.972 (0.9167, 1.0301). The ratios of adjusted LS GM (90% CIs) of AUC₀→∞ and Cmax between infliximab US and infliximab EU were 1.113 (1.0115, 1.2252) and 1.05 (0.9066, 1.1338). The 90% CIs of these ratios were fully contained within the 0.80 to 1.25 interval, confirming PK similarity between ABP 710 and infliximab, as well as between infliximab EU and infliximab US. There were no deaths, serious adverse events, or treatment-emergent adverse events (TEAEs) leading to discontinuation from the study; 1 subject in the infliximab EU group developed polymyalgia that resolved with treatment and the subject completed the study. The incidence of TEAEs was similar in the 3 groups (ABP 710: 83.7%; infliximab EU: 83.7%; infliximab US: 86.0%) and the majority was mild or moderate. The most frequently reported TEAEs were somnolence, headache, nasopharyngitis, upper respiratory tract infection, nausea, and lethargy. All subjects tested negative for antidrug antibodies (ADAs) prior to dosing. At the end of study (Day 57), 40% subjects on ABP 710, 27% on infliximab EU, and 32% on infliximab US were positive for binding ADAs; 13% on ABP 710, 19% on infliximab EU and 10% on infliximab US were positive for neutralising ADAs.

Conclusion: Results of this study demonstrate PK similarity between ABP 710 and infliximab sourced from the EU and the US, as well as between infliximab EU and infliximab US following a single 5 mg/kg IV infusion in healthy subjects. The safety and immunogenicity profiles were comparable among treatment groups.

Disclosure of Interest: V. Chow: I am a full time employee and stockholder of Amgen Inc E. Krishnan: I am a full time employee and stockholder of Amgen Inc

P1042 EPIDEMIOLOGY AND BURDEN OF COMPLEX PERIANAL FISTULAS IN PATIENTS WITH CROHN DISEASE—A SYSTEMATIC LITERATURE REVIEW
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Introduction: Complex perianal fistulas (CPF) are common among Crohn’s disease (CD) patients and are associated with substantial morbidity. The burden and management of CPF are poorly studied.

Aims & Methods: To systematically review the literature on epidemiology, global disease burden, and treatment outcomes for CPF in CD patients. PubMed, Embase, and Cochrane were searched for relevant articles published from 2000...
forward; congress abstracts were searched from 2011 forward. CPFs were defined as fistulas with interphincteric, transphincteric, suprphincteric, extrahepatic, or horseshoe tracts.

Results: 353 records were reviewed by 2 independent researchers, and 63 relevant articles and abstracts were selected for inclusion (including 3 epidemiology and 3 burden; the rest were treatment guidelines/patients' treatment outcome studies). The estimated cumulative incidence of CPF in CD, based mostly on studies conducted in referral centres, ranges from 12%–14% (2 studies). CPF can result in significant morbidity and greatly diminished quality of life; up to 59% of patients (1 study) are at risk of fecal incontinence. Treatment options include a combination of medical and surgical interventions. However, across all options identified, a high proportion of patients experience treatment failure (lack of or inadequate response) and relapse (Table). Only 4 identified studies were conducted specifically in patients refractory to anti-tumor necrosis factor (TNF) agents—a population with high unmet needs (one study of perifistular injections of infliximab, and three studies of surgical interventions). Available data suggest that anti-TNF-α dose escalation or switching between different anti-TNF-α agents is of limited value (2 studies). Table—Rates of treatment failure and relapse or reoccurrence among patients with complex perianal fistula.

Conclusion: CPFs in CD pose substantial clinical burden. There is a high unmet need for effective treatment options for CPF in CD patients, especially those refractory to anti-TNF-α agents, as evidenced by high treatment failure and relapse rates.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1043 VITAMIN D IS RELATED TO THE EFFECTS OF ANTI-TNF TREATMENT IN CROHNS DISEASE PATIENTS

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Introduction: Vitamin D deficiency is common in patients with Crohn's disease (CD). It is believed that this deficiency is related to the CD activity. Vitamin D supplementation has many effects, including immunomodulation. However, the role of Vitamin D (VD) in severe CD patients using Anti-TNF is still unclear.

Aims & Methods: To evaluate the results of the VD replacement at different doses; check possible immunomodulatory action of vitamin D in CD patients with Anti-TNF. We conducted a double-blind, randomized, prospective study. 42 patients were selected with history of moderate to severe CD in use of anti-TNF, of both sexes, between 18 to 60 years, with dosage of 25-hydroxyvitamin D < 75 nmol/L (30 ng/ml) who signed the informed consent. Were excluded patients with less than 18 or over 70 years, pregnant women, chronic kidney or liver diseases, sarcoidosis, tuberculosis, hyper- or hypoparathyroidism, neoplasias, use of anticonvulsants; and patients who received calcium supplements or VD in the last 6 months. 30 patients were randomized. Patients were submitted to a questionnaire of sun exposure, quality of life (IBDQ), clinical examination, VD dosage, C-reactive protein (CRP), fecal calprotectin (FC) and were divided into three groups: 1 Group (G1): 10 patients receiving 2,000 U/VD, VO/week for 8 weeks, 2 Group (G2): 10 patients receiving 10,000 U/VD, VO/week for 8 weeks; 3 Group (G3): 10 patients receiving 2,000 U/VD, VO/week for 8 weeks. At the end of 8 weeks the patients answered IBDQ and were submitted to VD, FC and CRP dosage. All patients were followed for 52 weeks and checked for disease activity recurrence (CDAI > 150, FC > 300, CT scan). CRP, FC and VD levels.

Results: IBDQ improvement was observed in all groups with statistically significant results in G2 (p = 0.04) and G3 (p = 0.01). Increased VD were observed in all groups, and VD (mean ± SD) x 1000 IU/VD week: G1 - (19.5 ± 5.1) x 26 ± 6.7) p = 0.07; G2 - (19.1 ± 4.1) x 26 ± 5.8) p = 0.04; G3 -19.5 ± 6.4 x 46 ± 12.7) p < 0.001. CRP dosage were reduced, although not statistically significant, at G2 and G3 (5.8 ± 4 x 3 9 ± 2.8) p = 0.18 (5.2 ± 7.3 x 2.4 ± 3.6) p = 0.2; and increased in G1 (8.1 ± 10, 3 x 13, 4 ± 19.9) p = 0.3. There was a significant decrease in FC in G3 (1014 ± 450 x 483 ± 564) p = 0.04, no significant decrease in G2 (767 ± 751 ± 823 ± 535) p = 0.2, and increase in G1 (1101 ± 744 ± 1357 ± 819) p = 0.4. 52 week follow showed that recurrent disease activity were predominant in patients with VD < 30 (p = 0.004) and statically significant results were observed in disease activity recurrence rate (p = 0.006), FC (p = 0.02) and CRP (p = 0.01) when compared patients with VD > 30 and VD < 30.

Conclusion: 50,000 U/week was the best dosage for VD replacement and is related to immunomodulation. Most of patients with CD in Anti-TNF therapy have recurrent disease when VD < 30 and a high remission rate with VD > 30. VD levels are related to the effects of Anti-TNF therapy in CD patients.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1045 CLINICAL EFFECTIVENESS OF GOLIMUMAB IN CROHN'S DISEASE – AN OBSERVATIONAL STUDY BASED ON THE SWEDISH NATIONAL QUALITY REGISTRY FOR INFLAMMATORY BOWEL DISEASE

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Introduction: Golimumab is approved for the treatment of moderate to severe ulcerative colitis, but not Crohn's disease (CD). Therefore, its potential efficacy in CD remains largely unknown. Off-label use of drugs is not prohibited in Sweden, and golimumab may have been used for CD treatment.

Results: The study cohort consisted of 95 patients with a median age of 37 (IQR 27-48) years, of whom 40% were men. The majority of the patients (90.5%) had previously experienced treatment failure for at least one anti-TNF agent. At the start of golimumab, 41% were on a concomitant immunomodulator and 16% on corticosteroids. After a median follow-up time of 21 (IQR 10-36) months, 60 (63%) patients had stopped treatment with golimumab. Reasons for discontinuation were inadequate response; n = 45 (75%), intolerance; n = 11 (18%) and other reasons; n = 4 (7%). Estimated drug continuation rates were 73% at 12 weeks and 42% at 52 weeks. Concomitant treatment with corticosteroids at baseline seemed to be associated with a higher risk of discontinuation of golimumab (unadjusted HR: 1.97; 95% CI: 1.04-3.73; p = 0.04), although the association did not remain significant after adjusting for potential confounding factors (adjusted HR: 1.76; 95% CI: 0.84-3.67; p = 0.13).

Aims & Methods: We aimed to describe the CD population that is treated with golimumab in Sweden and to assess the long-term effectiveness, defined as drug continuation rate, as well as identify predictors of drug discontinuation. Patients with CD who received at least one injection of golimumab were identified through the Swedish national quality registry for inflammatory bowel disease (SIBWIRE). Duration of golimumab-treatment was illustrated by Kaplan-Meier curves. Univariate and multivariate Cox proportional hazard regression models were used to identify predictors of golimumab discontinuation. The variables sex, age, duration of disease, location, perianal disease, smoking status, previous surgery, concomitant treatment with corticosteroids or immunomodulators at baseline, prior anti-TNF therapy and CRP at baseline were included in the models.

Abstract: P1042

<table>
<thead>
<tr>
<th>Treatment</th>
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<th>Relapse/recurrence</th>
</tr>
</thead>
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<tr>
<td>Rates, %</td>
<td>Number of patients</td>
<td>Rates, %</td>
</tr>
<tr>
<td>Anti-TNF-α agents</td>
<td>46-60</td>
<td>39-66</td>
</tr>
<tr>
<td>(agent unspecified)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infliximab</td>
<td>12-58</td>
<td>6-52</td>
</tr>
<tr>
<td>Adalimumab</td>
<td>22-73</td>
<td>9-38</td>
</tr>
<tr>
<td>Surgical interventions</td>
<td>0-60</td>
<td>5-40</td>
</tr>
<tr>
<td>Combined medical and surgical management</td>
<td>0-80</td>
<td>9-212</td>
</tr>
<tr>
<td>Standard of carec</td>
<td>30-68</td>
<td>15-250</td>
</tr>
</tbody>
</table>

a44 studies reported treatment outcomes for CPF in CD patients. Most studies identified were small and/or non-comparative, and study methodologies, populations, endpoint definitions, and duration of follow-up varied. For studies with mixed populations, only results for patients with CD and CPF were considered. 
bDefined as lack of or inadequate response to therapy (i.e. lack of complete response). cDefined as standard of care used at each centre excluding anti-TNFs and surgery in 2 studies and as standard medical care at each centre including anti-TNF and surgery in 2 studies.
**Results:** Analysis and consisted of those patients enrolled in the study who had received at least 80% of the scheduled therapy with corticosteroids and/or immunosuppressants. Quality of life was evaluated by using the validated questionnaires EuroQol-5D (EQ-5D) and the 36 items Short-Inflammatory Bowel Disease Questionnaire (S-IBDQ).

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**Conclusion:** Gomilubam-treated patients with CD are a treatment-refractory group in which more than 40% of the patients had not received any definitive clinical benefit after one year, since they were receiving continued gomilubam treatment. Con-comitant corticosteroid treatment at start of gomilubam appears to be associated with worse outcome.

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target, little or no information is available regarding the ratios of free and TNF-bound infliximab in the intestinal tissue.

**Aims & Methods:** We aimed to assess the presence of free versus TNF-bound infliximab in the intestinal tissue of IBD patients and its possible association with clinical outcomes. Protein was extracted from frozen intestinal tissues of infliximab-treated IBD patients. TNF-bound infliximab and free infliximab were detected using ELISA and normalized to tissue protein concentration. Concurrent serum drug levels (SDL), anti-drug antibodies (ADA), and TNF-bound infliximab levels, patient’s pharmacotherapy, clinical response based on physician global assessment (PGA), and endoscopic appearance (severity determined according to mayo scor- ing in ulcerative colitis and endoscopic assessment of ulceration severity, extent of disease and affected area in Crohn’s disease) and pathological results (severity determined by observing pathologist graded as normal, mild, moderate and severe disease) at the time of colonoscopy were determined. Correlation were performed using Spearman’s rank correlation test.

**Results:** Twenty-four biopsies from 13 patients (11 Crohn’s disease and 2 ulcerative colitis patients) were tested. Non-inflamed tissue infliximab levels, but not inflammatory tissue infliximab levels, were correlated with SDL (R = 0.849, p = 0.007; FDR = 0.0185) and were negatively correlated with the endoscopic appearance (R = -0.7214, p = 0.0185) and pathological severity (R = -0.7099, p = 0.0059). TNF-bound infliximab was measured in both inflamed and non-inflamed specimens and did not show any correlation with drug levels in the serum or tissue. ADA was only detected in a single patient, precluding statistical analysis. Notably, no TNF-bound infliximab was measured in the serum.

**Conclusion:** These findings show that pharmacokinetic-pharmacodynamics interaction, as measured by SDL, better reflects drug levels in healthy mucosa rather than the inflamed one, and suggest a more complex drug/target interaction in inflamed tissue, which cannot be explained by target binding only. Future studies assessing changes during the course of mucosal healing may allow their use as surrogate markers for this purpose.

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in just one of these 14 patients (1.4%) (p < 0.001). Median (IQR) TL were significantly higher in the ADA negative group compared to the ADA positive group [9.21 (7.00–12.99) vs. 3.45 (1.72–5.44) µg/mL, p < 0.001]. A significant correlation between TL and ADA levels could be found (Spearman’s rho = 0.562, p < 0.001). Although the presence of these ADA was not significantly associated with clinical remission at week 12, a clear tendency was observed (p = 0.136). During median (IQR) follow-up of 1.46 (0.32–3.48) years, 43 out of 116 patients (37.1%) needed ADM dose-escalation. Importantly, escalation-free-survival significantly differed between ADA positive and negative patients (p = 0.001). Univariate analysis could not identify any more factors (weight, BMI, gender, disease behaviour, disease location, CRP, serum albumin, PRO2, concomitant therapy, smoking) associated with ADA presence at week 12. Interestingly, 50% of the ADA positive patients had TL above 4 µg/mL would not have been dose optimized proactively according to current practice. Thus, out of these 7 patients needed dose-escalation afterwards which could have been expected based on the ADA positivity.

Conclusion: A drug-resistant assay can identify ADA to ADM before all drug has been neutralised and TL become undetectable. As these ADA at week 12 are significantly associated with need for dose-escalation and can appear before TL drops below the threshold of 4 µg/mL, they may be better to identify those patients who could benefit from dose-escalation. Moreover, the differences in TL between patients at week 12 can finally be explained by the presence of ADA measured with a drug-resistant assay.

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mudam) and vemudamib ELISA to apDh and inflamunam, adalimumab lateral flow to Biopharma AG.

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Reference

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Introduction: Compliance is a significant problem in the medication of patients with chronic diseases, especially during periods where patients are completely unaware of their disease and just take their drugs to prevent disease recurrence. (1) During the last years Shared Medication Record (SMR) was introduced in Denmark which is a national database containing information on current medication of all Danish residents. SMR include information on where, when, and how much medicine the patients buy at the pharmacies. Therefore with SMR it becomes possible for doctors to see if patients retrieve the prescribed medicine at the pharmacy. Patients with chronic inflammatory bowel diseases (IBD), ulcerative colitis (UC) or Crohns Disease (CD), have periods of flares of the disease but in many cases also long periods when the disease is in remission. The majority of patients need medication to reduce the risk of recurrence of disease. Clinical means that they need to take medicine even if they have no symptoms of disease. Previous American studies have shown that a number of patients in this situation do not take their medication and thus are at increased risk for relapse of the disease (1). There are no corresponding data for Danish patients. We wanted to find out the proportion of Danish IBD patients in remission who buy the prophylactic treatment as prescribed, and whether this proportion will change when the patients are informed about that the doctor can see if they pick up the medicine at the pharmacy.

Aims & Methods: The purpose of this study was to investigate whether Danish patients with IBD in remission buy the prophylactic treatment as prescribed, if these patients buy a larger part of their medicine when they know that the doctor can see which medicines they buy at the pharmacy. 100 consecutive patients with UC in remission and at least six months and 10 IBD, treated with a fixed dose of Mesalazine, azathioprine, or Mercaptapurine during the preceding six months were enrolled from Randers Regional Hospital Adult Gastroenterological Outpatient Clinic. Patients were randomized 1:1 either to receive information that the doctor could follow their pharmacy refills, or not to get information on this. The patients were not informed that they participated in a study. All patients had a second visit six to 12 months later. Patients who had flares in disease activity during the study period was excluded. Adherence to the treatment was defined as pharmacy refills according to the prescribed dose for at least 80% of the period of the preceding six months. Fisher’s exact test was used as test of independence between groups.

Results: 67% of the patients in the study were adherent to their medical treatment during the first study period decreasing to 48% during the second study period (P < 0.001). There was no difference in the decrease in adherence between patients informed about SMR and those who were not informed. Younger patients were less prone to adherence compared to older patients at the first study visit (Age groups: 19-39:40-59/60+: Years, adherence 48/71.6% (P < 0.05). We found no differences related to disease (UC/CD), sex, 5-ASA,antiparin, or admission route (oral/recatl).

Conclusion: Adherence to treatment fell from the first visit when the disease had been in remission for at least six months, to the second study visit when the disease had been in remission for at least 12 months. This was independent of whether the patients were aware that the physician could follow their medication refills or not. This might indicate that adherence to medical treatment of IBD decreases over time when the disease is in remission.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P1053 ADHERENCE TO MAINTENANCE THERAPY IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE BEFORE AND AFTER THE INTRODUCTION OF THE SHARED MEDICATION RECORD

K. Roebgaard

PATIENT CHARACTERISTICS
Number of patients (n, %) 59 (100) 27 (46) 32 (54)
Sex (n, %) 0.9
Male 28 (47) 13 (48) 15 (47)
Female 31 (53) 14 (52) 17 (53)
Charlson Comorbidity index (n, %) 0.7
≥3 56 (95) 26 (96) 30 (94)
>0 3 (6) 1 (4) 2 (6)
Charlson Global index (n, %) 0.4
0-1 55 (77) 18 (67) 37 (85)
>1 14 (23) 9 (33) 5 (15)
Age at diagnosis (years) (median, IQR) 0.5
33 (25–45) 33 (25–45) 32 (23–45)
Disease duration (years) (median, IQR) 8 (4–14) 8 (4–15) 9 (3–14) 0.7
Domain (Montreal classification) (n, %) 0.3
E1 2 (3) 0 (0) 2 (6)
E2 33 (56) 17 (66) 16 (50)
E3 24 (41) 10 (37) 14 (44)
Endoscopic disease activity (Mayo score) (n, %) 0.3
1 2 (3) 2 (7) 0 (0)
2 12 (20) 5 (18) 7 (22)
3 45 (77) 20 (74) 25 (78)
Previous ICS use (n, %) 0.7
Steroid dependence 49 (83) 23 (85) 26 (81)
Steroid resistance 10 (17) 4 (15) 6 (19)
Previous ICS use (n, %) 0.7
Yes 41 (69) 18 (67) 23 (72)
Concomitant combination therapy (n, %) 4 (7) 1 (4) 3 (9)
STUDY RESULTS

(continued)
surgery. By year, it was found a positive trend in the number of both total and “planned” endoscopies carried out within this period (p=0.017 and p=0.027, respectively). Table

<table>
<thead>
<tr>
<th>Patients underwent surgery</th>
<th>2007</th>
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<tr>
<td>n</td>
<td>75</td>
<td>83</td>
<td>79</td>
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<tr>
<td>NHI</td>
<td></td>
<td></td>
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<tr>
<td>Mean (SD)</td>
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</tr>
<tr>
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<td>24</td>
<td>36</td>
<td>43</td>
<td>46</td>
<td>0.017</td>
</tr>
<tr>
<td>NHI missing at wk 10</td>
<td>47</td>
<td>49</td>
<td>47</td>
<td>49</td>
<td>0.017</td>
</tr>
</tbody>
</table>

Treatments received by patients at discharge were Immunosuppressants (30.8%), antibiotics (21.3%), mesothoracic (19.1%), mesalazine (12.1%) and antiTNFa (0.9%). A total of 235 patients (74.8%) had a medication change throughout the follow-up period, mainly within the first year after surgery (47.1%, n=148). Median time to first medication change was 10 (IQR 4–22) months. More often therapeutic decision was the introduction or dose escalation of thiopurines or change to a more potent agent (68.1%, n=160) followed by the introduction of an antiTNFa drug or dose escalation (51.4%, n=121). Ninety-two out of 95 patients with planned endoscopy within first year after surgery had Rutgeerts scoring (RS) available, 37 (40.2%) and 55 (59.7%) showed RS<12 and <12 respectively. More patients with a RS≥12 had a medication change as compared to patients with a RS<12, but the differences didn’t reach statistical significance (45.9% vs 36.36%). Reasons for medication change were “endoscopic without clinical recurrence” (52.9% RS≥12 vs 10.0% RS<12, p=0.010), “clinical recurrence” (29.4% RS≥12 vs 25.0% RS<12) and “others” (23.5% RS≥12 vs 60.0% RS<12, p=0.045).

Results: The number of planned endoscopies carried out within the first year after surgery increased significantly from 2007 to 2010 showing a steady implementation of guidelines recommendations. Changes in medication within this period were more frequent in the setting of endoscopic recurrence. Acknowledgements: Funded by Merck Sharp & Dohme of Spain

Disclosure of Interest: All authors have declared no conflicts of interest.

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**P1055 ETROLIZUMAB TREATMENT IMPROVES HISTOLOGICAL and HISTOPATHOLOGY AND NANCY HISTOLOGICAL INDICES**

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Introduction: Etrolizumab, an anti-β7 monoclonal antibody targeting α4β7 and αEβ7 integrins, showed efficacy and safety versus placebo (PBO) during 10 weeks (wk) of induction in patients with moderate-to-severe ulcerative colitis in the Phase 2 EUCALYPTUS trial (Vermeire S. Lancet. 2014;384:309–18). Since a reduction in histologic inflammation has been linked with improved long-term clinical outcome (Bryant R et al. Gut. 2016;65:408–14), and the FDA recommends using both histologic and endoscopic assessments for efficacy evaluation, the effect of etrolizumab on histologic inflammation was evaluated in mucosal biopsies from EUCALYPTUS patients using the Roberts histopathology index (RHI; Mosb MH. Gut. 2017;66:50-8) and Nancy histological index (NHI; Marchal-Bressenot A. Gut. 2017;66:43-9).

Aims & Methods: 124 patients were randomly assigned (1:1:1) to receive subcutaneous etrolizumab (100 mg at wk 0, 4, and 8, with PBO at wk 2, or 420 mg loading dose at wk 0, followed by 300 mg at wk 2, 4, and 8) or placebo. Biopsies were taken using flexible sigmoidoscopy/full colonoscopy from the most inflamed colonic area within 10–40 cm from the anal verge at baseline (BL) and at wk 10. 62 patients provided consent for long-term sample storage for research; batch H&E-stained slides were scored by a single pathologist using the Geboes scale (later converted to RHI) and NHI. At wk 10, mean changes in RHI and NHI scores for pooled etrolizumab or PBO were calculated. Subanalyses explored histologic response (reductions of ≥ 6 or 10 points or ≤50% improvement from BL RHI) and ≥1 or 2-point reduction from BL NHI (remission (no neutrophils, RHI ≤4 and NHI = 0, ≤1 or 2) and correlation with endoscopic improvement.

Results: Analysis included 56 patients with BL data and BL NHI > 1. At wk 10, mean NHI scores decreased by a greater extent with etrolizumab compared with PBO, regardless of anti-tumor necrosis factor α (aTNF) experience (RHI −8.4 vs −1.6; P=0.032 and NHI −1.2 vs −0.2; P=0.011 for all comers). A greater proportion of etrolizumab-treated patients achieved categorical histologic improvement and remission with an endoscopic subscore (RHI ≤1 wk 10 n = 6, 100% experienced histologic response as assessed by RHI (5/5 with RHI non-missing at wk 10), and 83% (5/6) by NHI. Mean (SD) RHI changes were −19.2 (10.0) in patients with an ES ≤1 at wk 10 versus −4.4 (10.1) in patients with an ES >1. Mean (SD) NHI changes were −2.5 (1.5) in patients with an ES ≤1 at wk 10 versus −0.6 (1.3) in patients with an ES >1. Spearman’s
correlation coefficients between RHI and NHI were 0.82 at BL and 0.91 at wk 10, while both histologic scores were similarly correlated with ES (0.25-0.28 at BL and 0.38-0.40 at wk 10).

Table 1: Percentage of Patients Achieving Histologic Response and Remission at Week 10

<table>
<thead>
<tr>
<th></th>
<th>aTNF-naive (n = 16)</th>
<th>aTNF-experienced (n = 34)</th>
<th>All comers (n = 50)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>RESPONSE (decrease from baseline)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RHI ≥ 3</td>
<td>55%</td>
<td>17%</td>
<td>46%</td>
</tr>
<tr>
<td>RHI ≥ 10</td>
<td>55%</td>
<td>0%</td>
<td>33%</td>
</tr>
<tr>
<td>RHI ≥ 50</td>
<td>36%</td>
<td>0%</td>
<td>25%</td>
</tr>
<tr>
<td>NHI ≥ 1</td>
<td>73%</td>
<td>17%</td>
<td>52%</td>
</tr>
<tr>
<td>NHI ≥ 5</td>
<td>0%</td>
<td>8%</td>
<td>7%</td>
</tr>
<tr>
<td>NHI ≥ 10</td>
<td>50%</td>
<td>14%</td>
<td>34%</td>
</tr>
</tbody>
</table>

*Must have achieved ≥ 1 point improvement*
NHI 0 = no histologically significant disease
NHI 1 = chronic inflammatory infiltrate with no acute inflammatory infiltrate
NHI 2 = mildly active disease

**Conclusion:** Histologic activity assessment using RHI or NHI demonstrates improvement after wk 10 with etrolizumab treatment and was greater in aTNF-naive patients. Importantly, RHI or NHI reductions were associated with improved ES at wk 10.

**Aim:** To assess the long-term efficacy and safety of etrolizumab in patients with moderate-to-severe UC who responded to induction therapy with etrolizumab.
**Disclosures of Interest:** G.H. Long: Employee of Roche. Roche stock-holder
B. Ungar: Employee of Genentech. Roche stock-holder
Y. Oh: Employee of Genentech. Roche stock-holder
S. R. Rodkey: Employee of PHAR, LLC, paid by Genentech/Roche to conduct this research
A.N. Ananthakrishnan: Consultant/Advisor for Abbvie, Takeda, and Merck

**References:**

1. Inflammab has been shown to induce and maintain long-term clin-
2. sponding to responders (week 2: median level 7.2 g/ml vs. 13.5 g/ml, p = 0.0019, week 6: median level 2.2 g/ml vs. 9.5 g/ml, p < 0.001, respec-
3. CI 2–10.8, p = 0.0004) and at higher levels in non-responders compared to responders (week 2: median AT1 7.3 g/ml-eq vs. 3.8 g/ml-eq, p = 0.005, week 6: 10.8 g/ml-"eq vs. 4.4 g/ml-"eq, p = 0.008, respectively). Moreover, week 2 AT1 levels > 4.3 g/ml-"eq (AUC = 0.68, p = 0.002, sensitivity 77%, specificity 86%), and AT1 levels < 6.8 g/ml (with peaks 7.8%, with specificity 71%) were predictive of primary non-response. In analyses of various demo-
4. in patients towards topical products. A qualitative market research study was performed in the USA and 3 European countries (Germany, UK and Italy). The primary patient recruitment sources were online web portals, e-mail campaigns and social networking sites. Informal feedback gathered from online patient activists to identify the right sources was also used. In order to select patients with more advanced disease and/or a longer disease history current or past steroid medication was mandatory as a qualification for inclusion in the market research. A structured questionnaire covering 14 items was pre-
5. of patients were not concerned about the rectal mode of administration, while 47% reported some concerns. These mainly comprised the need to hold the enema in place, a generally uncomfortable feeling with rectal medications and painful administration.

**Results:** In this survey cohort patients had been diagnosed with UC for > 5 years on average, 2/3 of patients had left-sided disease and less than a third had extensive disease. The majority of patients experienced at least 1 flare-up each year and less than 15% of patients had them only rarely. ASA and steroids were the most commonly used medications in all countries, biological treatments were reported as highest in 35% (US) to the lowest 16% (UK) as stated by the patients. The vast majority of patients stated that they had treatment experience with different products at some time during their treatment journey, ASA and IS being slightly lower number in the US (83%) compared to the EU countries (Range 89–92%). Rectal enemas were the most common formulation delivery for topical ASA products in all markets (79%) followed by suppository (25%) and foam (13%). A total of 53% of patients were not concerned about the rectal mode of administration, while 47% reported some concerns. These mainly comprised the need to hold the enema in place, a generally uncomfortable feeling with rectal medications and painful administration.

**Introduction:** This study aimed to gain insight into what caregivers consider important to use topical therapy almost all patients stated to have used rectally administered products at some point during their disease journey and even patients in the USA were very familiar with these medications. Although physicians see patients as the primary driver for the resis-
6. day at our hospital, a survey regarding SM was distributed among 46 nurses. Also, 50 IBD-interested gastroenterologists were invited to respond to the same survey by email with a link to the survey. The survey contained questions regarding the caregivers’ views on ways for patients to apply SM in an outpatient setting (12 options were given). Caregivers were asked to state whether they thought these options would be valuable to patients or not, and to name their top three options. Also, caregivers were asked their views on factors that could
P1062 DISTINCT PATTERNS OF SHORT-CHAIN FATTY ACIDS IN PATIENTS WITH ULCERATIVE COLITIS EXPERIENCING A FLARE DURING TREATMENT WITH MESALAMINE OR HERBAL PREPARATION

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Introduction: The combination of myrrh, chamomile flowers, and coffee charcoal has shown first evidence for potential efficacy in maintaining remission in ulcerative colitis. Patients and disease characteristics associated with activation for self-management in patients with diabetes, chronic obstructive pulmonary disease, chronic heart failure and chronic renal disease: a cross-sectional survey study.

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Introduction: Selective GMA using Adacolm® device is a non-pharmacological therapeutic option for patients affected by IBD, but its precise role among the various treatments available and its true effectiveness are still debated. In particular, steroid-dependent patients, refractory or intolerant to immunosuppressants and biologics, represent a sub-group of patients with limited options of treatment. Recently, a multicentric open-label trial [the ART trial *] showed, for the first time a clinical benefit of 61% in these problematic patients.

Aims & Methods: The aim of this study was to further evaluate, in our real-life clinical experience, the efficacy and safety of GMA in these difficult-to-treat patients. We retrospectively reviewed the clinical data of patients treated with GMA-Adacolumn® in our center between 1/1/2008 and 12/31/2015. Only steroid-dependent and/or AZA/IFX/ADA-resistant or intolerant cases were considered. GMA was performed once a week for a minimum of five consecutive weeks. Occasionally, one or two additional sessions were performed. A clinical response was defined as a ≥ 3 point reduction in the clinical activity index (CAI) for ulcerative colitis (UC) and a ≥ 100 points reduction of the Crohn disease activity index (CDAI) for Crohn disease (CD) after 12 weeks from the beginning of the treatment.

Results: The study population included a total of 30 patients (17 males, 13 females, mean age 49 years, range 21–73) affected by UC (20 patients) and CD (10 patients). Eight patients (5 UC, 3 CD) were excluded from the final analysis for a loss of data. In the remaining 22 patients, a clinical response at week 12 was observed in 15 (68%). The response was better in UC (11/15; 73%) than in CD (4/7; 57%). A steroid-sparing effect was observed in all responsive patients. GMA was generally well tolerated, as only 4 patients (13%) reported mild adverse events (headache in two, hypotension in one, vascular procedure complication in one) and no patients discontinued the apheresis due to the adverse events.

Conclusion: In our real-life single-center experience, focused to a selected group of difficult-to-treat patients affected by IBD, GMA with Adacolm® seems to be, in a short-time evaluation, a useful and safe option of treatment, supporting the recent data from the ART trial. Prospective randomized trials in larger sample of patients and with more extended follow-up are needed to confirm these results.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

myrrh (Commiphora molmol E.), chamomile flower (Matricaria chamomilla L.) and coffee charcoal (Coiffa Arabica L.) is used for the treatment of gastrointestinal complaints. Clinical data suggest its use for the maintenance therapy of inflammatory bowel disease [1]. Despite clinical and chemical data, pharmacological data supporting the observed efficacy remain insufficient.

Aims & Methods: The present study aims to investigate the influence of the single and combined herbal extracts with regard to its antiinflammatory and immunomodulating activities. Thus, the effect of myrrh, chamomile flower, coffee charcoal extract on intestinal motility was determined using isometric tension measurement in isolated rat small intestinal preparations. Furthermore chemokine signaling of stimulated intestinal epithelial cells and activated macrophages. Myrrh and chamomile flower extract exerted spasmolytic effects by inhibiting acetylcholine-induced contractions in rat small intestinal preparations (IC50: myrrh ¼ 25 μg/mL; chamomile flower ¼ 383 μg/mL). In combination, chamomile flower and myrrh interacted additively (IC50(myrrh) ¼ 74 μg/mL; chamomile flower ¼ 196 μg/mL) resulting in a DRI of 1.9. All three plant components inhibited CCL13 release from LPS-stimulated human macrophages (IC50: myrrh ¼ 10 μg/mL; chamomile flower ¼ 82 μg/mL; coffee charcoal ¼ 25 μg/mL). Synergistic effects exerted by the herbal combination in inhibiting CCL13 release significantly reduced IC50 values (IC50(myrrh) ¼ 5 μg/mL; chamomile flower ¼ 22 μg/mL; coffee charcoal ¼ 29 μg/mL) resulting in a DRI of 3.7. Combined CCL13 induced CCL10 release from Caco2 cells was reduced by all herbal components (IC50(myrrh) ¼ 41 μg/mL; chamomile flower ¼ 364 μg/mL; coffee charcoal ¼ 447 μg/mL) with comparably high IC50 values. However, application of the herbal combination, significantly reduced the IC50 of the plant extracts (myrrh-IC50 ¼ 25 μg/mL; DRI ¼ 1.7; chamomile flower-IC50 ¼ 124 μg/mL; DRI ¼ 2.9; coffee charcoal-IC50 ¼ 124 μg/mL; DRI ¼ 3.6). IL8 release from cytokine-challenged Caco2 cells was inhibited after myrrh (IC50 ¼ 3 μg/mL; 28% max inhib.) and coffee charcoal (IC50 ¼ 218 μg/mL; 75% max inhib.) but increased after chamomile flower treatment (IC50 ¼ 39 μg/mL; 29% max stimul.). Treatment with all three plant extracts resulted in a moderate IL8 inhibition with an inverted U-shape concentration-response curve (IC50(myrrh) ¼ 56 μg/mL; coffee charcoal ¼ 281 μg/mL; 77% max inhib.).

Conclusion: The herbal components myrrh, chamomile flower and coffee charcoal influenced chemokine signalling of stimulated intestinal epithelial cells and activated macrophages. Myrrh and chamomile flower additionally exerted anti-inflammatory effects. Synergistic and additive effects between the plant extracts justifies the composition of the traditional herbal medicinal product (Myrrhinil-Intest®) and its application for the treatment of inflammatory intestinal disorders.

Disclosure of Interest: C. Vissiennon: Author Cica Vissiennon is employed by Repha GmbH Biologische Arzneimittel K. Goos: Co-Author Karl-Heinz Goos is shareholder of Repha GmbH Biologische Arzneimittel
All other authors have declared no conflicts of interest.

Reference

P1065 ARE TROUBLE LEVELS OF ANTI-TNF DRUGS RELATED WITH TREATMENT FAILURE AND TREATMENT ORGANIZATIONAL ISSUES?
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Introduction: Therapeutic drug monitoring of infliximab (IFX) and adalimumab (ADA) is required because treatment failure is commonly used if patients show loss of response, but there are scarce data about the influence of trough levels on prognosis.

Aims & Methods: The aim of the study was to evaluate the relationship between drug concentration and anti-TNF and treatment failure and duration of treatment in a real life environment. METHODS A prospective observational study was performed in a cohort of patients with inflammatory bowel disease. Patients were included consecutively through visits to the hospital to receive IFX or ADA. Inclusion criteria were all age >18 year patients, being treated with one of the study drugs at standard dose as maintenance therapy and giving consent to participate in the study. In the first visit, blood samples were extracted for drug concentration determination. Patients were followed-up for the next 2 years. Trough drug concentrations and drug antibodies were measured by an ELISA technique (Promonitor). Patients with IFX levels <3 mcg/mL and ADA <5 mcg/mL were considered under lower limit of therapeutic range (LLTR). Moreover, the number of patients that discontinued treatment (complete success) or discontinued (failures) the treatment were analyzed. Any change in dosage (intensification) or in the type of drug was considered as discontinuation of the treatment. Chi square test was used to analyze the dependence between the categorical variables and t-student for continuous variables with normal distribution.

Results: 134 patients were consecutively included, 53 male (40%), 92 (68%) patients with Crohn’s disease (CD) and 42 (32%) with ulcerative colitis (UC). 52 (39%) patients were treated with IFX and 55 (39%) with ADA. Mean age was 43 [19–71] years. After finishing the follow-up, 107 (79%) patients continued the same treatment regimen (success). A total of 59% of this group of patients were with drug concentrations above LLTR. The remaining 27 patients changed their treatment (failures). In the failure group, only 41% of the patients were above LLTR, 18.2% less with respect to success treatment group. These results did not reach statistical significance (p = 0.09), but are in agreement with current evidence. When type of inflammatory disease was analyzed, a greater percentage of patients below the LLTR were found in the UC group (41.3% vs 52.4%, CD and UC respectively), but the difference did not reach statistical significance. Regarding the duration of the treatments, the duration was similar in the group of patients with lower concentrations compared to the group with high drug concentrations (46.6 vs 42.6 months). However, when the duration of treatment was analyzed in patients who discontinued, significant differences were observed (43.8 vs 20.2 months in the < LLTR and > LLTR groups respectively).

Conclusion: The percentage of patients who continue treatment was higher when drug concentrations were above LLTR. However, these high levels did not prevent the early relapse of some of them.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1066 IMMUNOSUPPRESSIVE CO-TREATMENT WITH INFlixIMAB AND ADALIMUMAB IS NOT SUPERIOR TO ANTI-TNF MONOTHERAPY TO PREVENT TREATMENT FAILURE AND TREATMENT DISCONTINUATION IN ULCERATIVE COLITIS
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2University Hospital CHU de Liége, Liège, Belgium
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Introduction: In Crohn’s disease there is clear benefit from combination therapy with infliximab (IFX) and immunosuppressive drugs (IS), while the benefit seems more limited for adalimumab (ADA). Although some studies suggest a benefit of combination therapy with IFX in ulcerative colitis (UC) few data are available concerning combination therapy with ADA.

Aims & Methods: Our aim was to compare real life efficacy of anti-TNF mono- therapy (IFX and ADA) and anti-TNF+IS for UC maintenance. This was a retrospective study of patients with UC treated with IFX or ADA in 2 Belgian academic and regional Hospitals from 2004 to 2014, divided in treatment periods of at least 3 months, a failure semester as anti-TNF withdrawal for secondary loss of response, intolerance or surgery, treatment optimization of IFX or ADA dose escalation or steroids start. Semesters with and without failure and with or without optimisation were compared through univariate and multivariate analysis.

Results: 478 patients in 60 patients with IFX and 175 semesters in 33 patients with ADA were included. The mean IFX and ADA treatment duration were respectively 49 (±33) months and 38 (±19) months. Within patients treated with IFX, 32 patients received IFX + IS during the first semester. IFX was administrated as monotherapy in 361/478 semesters (76%). Respectively 218/478 (46%) and 78/478 (16%) with IFX required dose escalation and corticosteroids course. IFX + IS was associated with more semesters with failure (5% vs 3%, p = 0.02) and numerically more semesters with dose escalation (64% vs 28%, p = 0.06). There was no difference in corticosteroids use (p = 0.63). IS during the first semester was not associated with lower risk of IFX failure (p = 0.41) nor with a longer survival without IFX withdrawal (p = 0.20). Continuing the IS treatment beyond the first semester was not associated with fewer semesters with failure (p = 0.18). Within patients treated with ADA, 19/33 patients received IFX + IS during the first semester. ADA was administrated as monotherapy in 93/175 semesters (53%). Respectively 54/175 (48%) and 42/175 (24%) semesters were treated with IFX + IS. No significant differences were noted between patients that continued IFX + IS dose escalation or steroids without and with withdrawal of IFX + IS. IS during the first semester was not associated with fewer semesters with failure (p = 0.20).

Conclusion: In this real-life experience, combination therapy of IFX or ADA with IS during the first semester or prolonged after the first semester was not associated with less dose escalations, steroids courses or treatment failures.
RESULTS: mucosal healing (MH) at week 52. Secondary outcomes were: the rate of continuous clinical response and remission, was the rate of corticosteroid (CS) free remission (PUCAI Aims & Methods: The objective of the present study was to evaluate the effectiveness and safety of adalimumab (ADA) in children with ulcerative colitis (UC) who received previous IFX therapy (43% intolerant, 50% not-responders, 7% positive anti-IFX antibodies). Fifty-two weeks after ADA initiation 13 patients (35.3%), median HBI values significantly decreased during the study, in the whole population and in group A, whereas no change was recorded in group B (respectively, P = 0.3, P = 0.3, and P = 0.8, respectively). Moreover, despite not statistically significant difference in quality of life in both groups at T0, in group A quality of life improved after the diet compared to group B (respectively, P = 0.06, P = 0.05 and P = 1).

Conclusion: We demonstrated that a low FODMAP diet, for a limited period of 6 weeks, is able to improve both disease activity, at least for CD, and quality of life in IBD patients. Further, larger multicentre studies are needed to confirm these preliminary data.

Disclosure of Interest: All authors have declared no conflicts of interest.

TUESDAY, OCTOBER 31, 2017 09:00-17:00

PAEDIATRIC: LOWER GI - HALL 7_

P1069 SUBCUTANEOUS USTEKINUMAB PROVIDED CLINICAL AND BIOLOGICAL BENEFIT FOR 9/12 REFRACTORY PEDIATRIC CROHN’S DISEASE

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Introduction: Ustekinumab has shown a good safety profile and efficacy to induce and maintain remission in adult patients with refractory Crohn’s Disease (CD). Data are lacking in children.

Aims & Methods: All CD patients under 18 years who received ustekinumab were included in this retrospective observational study performed in a single tertiary paediatric centre.

Results: See table.

Conclusion: Subcutaneous ustekinumab is effective to induce and maintain remission in severe pediatric CD refractory to anti-TNF antibody.

Disclosure of Interest: All authors have declared no conflicts of interest.

References


Abstract: P1069. Main patients’ characteristics at ustekinumab induction

<table>
<thead>
<tr>
<th>Patient</th>
<th>Gender</th>
<th>Age at CD onset</th>
<th>Age at ustekinumab induction</th>
<th>CD Paris classification</th>
<th>Prior exposure to immunosuppressors</th>
<th>Prior exposure to Biotherapies</th>
<th>Primary inefficacy</th>
<th>Remission at w14</th>
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</thead>
<tbody>
<tr>
<td>Patient1</td>
<td>M</td>
<td>13</td>
<td>15</td>
<td>A1b L2 B1 G1</td>
<td>Aza, Thalidomide</td>
<td>Infliximab Discontinuation</td>
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<tr>
<td>Patient2</td>
<td>F</td>
<td>5</td>
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<td>A1b L3 B2 G1</td>
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<tr>
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<td>M</td>
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<td>15</td>
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<td>Infliximab Discontinuation</td>
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<tr>
<td>Patient4</td>
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<td>10</td>
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<td>Aza, Infliximab</td>
<td>Infliximab Discontinuation</td>
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</tbody>
</table>

Results: We analyzed 107 patients with CD, with a total of 428 visits until W14. The principal reason to start infliximab was failure of immunosuppressive therapy (60%). Infliximab proved to be an effective treatment in our cohort since 75.7% (n=81) patients were responders to infliximab and 40% (n=42) were in clinical remission whereas 24.3% (n=26) were non respondents at W14. At week 14, 107 patients were divided in three groups related to the clinical activity of their disease: lack of clinical response, partial clinical response, clinical remission. It concerns respectively 26, 39 and 42 patients. Major baseline characteristics were not associated with clinical remission: sex, age at diagnosis, disease location, time between diagnosis and induction, age at induction. Drugs associated with infliximab at W0, W2, W6 or W14, whether it was immunosuppressive agents or corticoids, were not associated with remission. Patients with low albumin levels had a worse response at induction Activity score at induction was also statistically associated with clinical remission: each decreasing of 10 points of activity score at induction increase of 0.48 times the risk to obtain clinical remission. Trough residual of infliximab > 8.5 µg/ml at W6 increase of 11.3 times the risk to obtain clinical remission at W14. Lack of growth retardation at induction increased of 3.98 times the risk to obtain clinical remission at W14.

Conclusion: Infliximab measurement in combination with evaluation of clinical severity (low body weight, growth retardation, hypoalbuminemia, severe disease) appears to be a reasonable strategy for predicting both short- and long-term treatment outcomes with IFX in the initial stage of treatment. Early detection of response to IFX is critical for the management of CD, especially in acute severe patients: it seems that the infliximab trough level at week 6 (> 8.5 µg/ml) is predictive of a remission at week 14. Second, some patients, especially patients with low body weight, growth retardation, hypoalbuminemia and severe disease may require higher doses than standard doses.

Disclosure of Interest: All authors have declared no conflicts of interest.

References


**P1071 INFlixIMAB INDUCED PSORIASIS IN A COHORT OF CHILDREN WITH INFLAMMATORY BOWEL DISEASE: A 12 YEARS FOLLOW-UP STUDY**
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**Introduction:** In adult Inflammatory bowel disease (IBD), skin adverse reactions have a prevalence of 1.6 to 22%. This side effect occurs more frequently in patients treated with infliximab (IFX) for IBD. Datas in the pediatric population are lacking so far.

**Aims & Methods:** All patients aged 2 to 18 years, with Crohn’s disease (CD) or Ulcerative colitis (UC) and treated for the first time by IFX between January 2002 and March 2014, were considered for inclusion in this monocentric retrospective study.

**Results:** Basline Patients: 115 patients were treated with IFX for CD and 23 for UC. IFX treatment was initiated at the age of 14, about 2 years after diagnosis. The indication for treatment was in 61.6% (n = 85) resistance to conventional therapy, in 26.8% (n = 37) a perianal fistulizing disease and in 11.6% (n = 16) a severe colitis. At the first injection, the median PCDAI was 35 (25; 45) for CD and the median PUCAI 35 (25; 45) for UC. The duration of treatment with IFX ranged from 45 days to 8 years and median was 23.9 months (11.6; 36.5). Psoriasis: 20 patients (14% of the cohort) had an IFX-induced psoriasis. 70% of them (n = 14) of patients were in remission when the psoriasis was diagnosed. Psoriasis was diagnosed at the 8th injection (6; 15), though 355 (239; 532) days after the start of biotherapy. 20% of patients had a combo therapy: 50% of them were treated by 6-mercaptopurine, 25% by azathioprine and 25% by methotrexate. The median IFX trough levels (TRI) when psoriasis occurred was 4.7 mcg/mL (1.8; 9.6) and 4.1 mcg/mL (2.1; 8.8) at the previous visit. Median Antibodies to IFX (ATI) rate was 0%. All were supported by local treatments. No patients discontinued biotherapy following the psoriasis. Personal or family history of psoriasis, and the smoking status have not been collected. We compared the psoriasis occurrence with psoriasis (n = 20) and without psoriasis (n = 127) with an univariate model. All children in the psoriasis group were followed for a CD. There was more perineal location of CD in psoriasis group with a significant difference (p = 0.003).

**Conclusion:** 14% of our IBD patients treated with IFX developed psoriasis during follow-up. All were CD, more frequently it occurred for CD with perineal lesions, at the 8th injection in median, with no ATI.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**References**

**P1072 PLATELET ABNORMALITIES AND ANEMIA IN PAEDIATRIC IBD: ARE THEY LINKED?**
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**Introduction:** Crohn’s Disease (CD) and Ulcerative Colitis (UC) are two major forms of Inflammatory Bowel Disease (IBD). In children with IBD anemia is common and is a combination of iron deficiency and anemia of chronic disease (ACD). IBD are associated with several alterations of platelets, including count, number, shape, and function.1 In clinical practice, the most common platelet alteration is thrombocytosis. In IBD, thrombocytosis is associated with iron deficiency anemia and chronic inflammation2. The importance of platelet function is not yet substantially increased incidence of thromboembolic phenom- ena in IBD3.

**Aims & Methods:** The aim of the study is to demonstrate the link between anemia, thrombocytosis and platelet aggregation in pediatric IBD patients. This study includes 51 children and adolescents recruited from the Pediatric Gastroenterology Unit of Policlinico Umberto I in Rome. Patients younger 6 years, with inherited platelet defects, hemoglobinopathies, and receiving ther- apies that alter platelet function, are excluded. We collect disease activity scores (Pediatric Crohn’s Disease Activity Index [PCDAI], Pediatric Ulcerative Colitis Activity Index [PUCAI]). The laboratory investigations include: complete blood count, mean corpuscular volume (MCV), mean platelet volume (MPV), mean corpuscular haemoglobin concentration (MCHC), levels of hemoglobin (Hb) and iron, transferrin, iron saturation, ferritin and plasma anti-TNF alpha. Diagnostic criteria for anemia are based on ECOO guidelines. Platelet aggregation is evaluated on platelet-rich plasma in an AggRAM aggregometer with Born’s Method. The results were reported as the maximal percentage of aggregation observed after 4 min stimula- tion in response to collagen (1 pg/mL) and adenosine diphosphate (ADP 0.8 pM and ADP 2 pM).

**Results:** The study include 51 children and adolescents, 24 with UC and 27 with CD. Median age is 15.3 years (±3.5). Iron deficiency anemia combined to ACD is the most common type (58.3% in UC and 50% in CD). Hemoglobin levels are significantly lower in patients with UC compared to CD patients (p = 0.0202). No significant differences are observed between mean values of red cells, MCV, MCHC, RDW, iron, transferrin and serum ferritin both in CD and UC. Thrombocytosis prevails in UC compared to CD patients, but no significant correlation was found. No differences are observed between mean values of PDW and MPV in both groups.In patients with UC, a negative correlation was found between mean values of hemoglobin and platelet count (p = 0.0314). Moreover in patients with CD, disease activity was positively correlated with platelet count (p = 0.0040). Platelet aggregation results higher in anemic patients. In anemic children, mean baseline platelet aggregations - induced by ADP 0.8 pM and collagen 1 pg/mL - are significantly higher in UC compared to CD (p = 0.001 and p = 0.030 respectively). Another significant correlation is observed between platelet aggregation - induced by ADP 0.8 pM and ADP 2 pM - in anemic UC patients compared to non-anemic UC patients (p = 0.002 and p = 0.040 respectively). Platelet aggregation - induced by ADP 0.8 pM is sig- nificantly higher in anemic UC patients with active disease (PUCAI > 20) com- pared to same patients whose disease is in remission (p = 0.042) and compared to patients with active CD (p = 0.054).

**Conclusion:** In our cohort, mixed anemia (iron deficiency anemia combined to anemia of chronic disease) is the most common type of anemia. Thrombocytosis is a condition more frequent in anemic IBD patients, specially in UC. In UC, anemia and disease activity are significant correlated with platelet hyperaggrega- tion. Future studies are required to identify the mechanisms of action that could account for paradoxical adverse events in anemia and platelet dysfunction in IBD patients. Thrombocytosis and anemia could represent major risk of thrombosis, independently from acquired or inherited hemostasis defects.
Disclosure of Interest: All authors have declared no conflicts of interest.

References

P1073 RELATIONSHIP BETWEEN CLINICAL COURSE OF ULCERATIVE COLITIS (UC) DURING PREGNANCY AND OUTCOMES OF PREGNANCY: A RETROSPECTIVE EVALUATION STUDY

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Introduction: Ulcerative colitis (UC) is a chronic, intractable disease with a long clinical course. UC has a marked influence on the lifestyle of patients, and its effects on pregnancy and childbirth especially can become a problem for women in their child-bearing years. Various studies have suggested that it is desirable for pregnant women with UC to give birth while remaining in a state of remission.

Aims & Methods: The present study evaluated pregnant women with UC attending our hospital who became pregnant during remission, in order to examine the factors that contributed to recurrence of UC during pregnancy. We investigated 40 pregnant patients in remission (44 cases) attending our hospital between January 2008 and July 2016 who had remained in remission for one year prior to pregnancy. After becoming pregnant while in remission, patients who stayed remission until delivery were classified into the ongoing remission group (35 cases) and patients with recurrence during pregnancy were classified into the recurrence group (9 cases). Remission was defined as a Lichtiger clinical activity index (CAI) of less than 4. Relapse was defined as a CAI ≥ 5 with the need for initiation or dose escalation of steroids or administration of biological agents during pregnancy, items examined: Clinical characteristics (age at onset, disease duration, age of becoming pregnant, disease type, and treatment), the CAI in the first, second, and third trimesters, and whether or not patients continued treatment during pregnancy were examined and compared between the two groups.

Results: There were significant differences between the two groups with respect to the age of becoming pregnant (32.9±4.4 years in the ongoing remission group vs. 28.3±7.0 years in the recurrence group), the CAI in the second trimester (2.9±4.6 vs. 3.5±1.6), the CAI in the third trimester (2.9±0.7 vs. 5.4±2.0), and whether oral treatment was continued (continuation of treatment [yes/no]; 30:5 in the ongoing remission group vs. 5:4 in the recurrence group). Regarding the discontinuation of oral treatment, two patients in the ongoing remission group and one patient in the recurrence group discontinued it on their own judgment, while two patients in the recurrence group discontinued it due to hyperemesis. Discussion: The present study revealed that factors influencing the recurrence of UC during pregnancy were the age of becoming pregnant, and the continuation of oral treatment. Our results showed that younger women were more susceptible to recurrence. As expected, discontinuing oral treatment was a factor that contributed to recurrence. However, the reasons for discontinuing treatment during pregnancy differed from those for non-pregnant women. Some patients discontinued treatment on their own judgment because they were concerned about adverse effects on the fetus, while others had difficulty with continuing treatment due to hyperemesis. With regard to the effects of medications on the fetus, medical staff should provide an explanation about the safety of treatment and should be aware that patients may have various concerns about drug therapy. If patients have difficulty continuing oral treatment due to severe hyperemesis, administration of local therapy should be considered.

Conclusion: During pregnancy, it is important to continue treatment for UC so that patients can give birth while remaining in remission. Accordingly, intervention by medical staff is particularly necessary in order to provide pregnant women with information and explanations regarding treatment.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1074 USE OF STEROIDS IN ADULTS AND ADOLESCENTS WITH UC DURING PREGNANCY AND LIMITATIONS TO PREGNANCY: A NATIONAL AUDIT

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Introduction: Corticosteroids have been effectively used for decades for the rapid induction of clinical remission in patients with Inflammatory Bowel Disease (IBD). However, their adverse event profile is well-known, particularly with long-term use and in younger populations, and they have no role in maintenance of remission. Steroid-sparing agents and more recently biological therapy have reduced systemic steroid use, but the incidence of steroid prescriptions especially in the outpatient setting is not known.

Aims & Methods: The aim of this study was to capture real-life steroid use in both adult and adolescent populations older than 13 years old who attend a dedicated IBD clinic in a tertiary referral centre. We tried to identify risk factors associated with appropriate or excessive steroid use in the whole cohort and in the two subgroups separately. All consecutive IBD patients who were followed up for at least one year in the adult and adolescent clinic in UCLH and attended their IBD appointment during February and March 2017 were included in the study.

A steroid assessment questionnaire was completed by the clinician during the visit for eligible patients. Use and type of steroids prescribed during the past year was recorded, as well as appropriate bone protection and disease activity based on the physician global assessment.

Results: 60 adolescents and 59 adults were included in the study. Two thirds of adolescents had Crohn’s disease while in the adult population Crohn’s and ulcerative colitis (UC) were equally distributed. 57 (95%) adolescents had been exposed to thiopurines and 47 (78%) to anti-TNFs as opposed to 69% (p = 0.002) and 39% (p < 0.001) of adults respectively. Vedolizumab exposure was similar in adults and adolescents. The percentage of patients with moderate to severe disease at last visit was comparable between two groups (80, 30%).

Conclusion: The present study revealed that factors influencing the recurrence of UC during pregnancy were the age of becoming pregnant, and the continuation of oral treatment. Our results showed that younger women were more susceptible to recurrence. As expected, discontinuing oral treatment was a factor that contributed to recurrence. However, the reasons for discontinuing treatment during pregnancy differed from those for non-pregnant women. Some patients discontinued treatment on their own judgment because they were concerned about adverse effects on the fetus, while others had difficulty with continuing treatment due to hyperemesis. With regard to the effects of medications on the fetus, medical staff should provide an explanation about the safety of treatment and should be aware that patients may have various concerns about drug therapy. If patients have difficulty continuing oral treatment due to severe hyperemesis, administration of local therapy should be considered.

Conclusion: During pregnancy, it is important to continue treatment for UC so that patients can give birth while remaining in remission. Accordingly, intervention by medical staff is particularly necessary in order to provide pregnant women with information and explanations regarding treatment.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

P1075 REMISSION INDUCTION IN CORTICOSTEROID NAÍVE CHILDREN AND ADOLESCENTS WITH ULCERATIVE COLITIS BY ADSORPTIVE LEUCOCYTOSPHERESIS AS MONOTHERAPY OR COMBINED WITH A LOW DOSE PREDNISOLONONE AFTER FAILURE OF FIRST-LINE MEDICATIONS

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Introduction: In patients with active ulcerative colitis (UC), myeloid lineage leucocytes are known to be elevated with activation behaviour, including the CD14+ CD16+ DR++ monocyte phenotype, which is a major source of tumour necrosis factor-α. Therefore, selective depletion of myeloid leucocytes by adsorptive granulocyte/monocyte apheresis (GMA) with an Adacolumn is expected to promote remission, or enhance drug efficacy. Potentially, GMA should be a relevant treatment option in patients in whom drug therapy has limitations.

Aims & Methods: Our major objective was to apply GMA as remission induction therapy in paediatrics and adolescents with UC when first-line 5-aminosulphosalazine or mesalazine had failed. Thirty consecutive patients with active ulcerative colitis (UC), age 11–19 years, body weight 33–55.5 kg were given mesalazine (n = 23) or sulphosalazine (n = 7) as the first-line medication. Twenty patients relapsed while remaining in the first-line medication. Two patients relapsed while remaining in the first-line medication. Two patients were not responders to first-line medication and received GMA with the Adacolumn, at 2 sessions in the first week, then weekly, up to 11 sessions.

Results: Patients who achieved ≥5 decrease in the clinical activity index (CAI) after 5

Disclosure of Interest: All authors have declared no conflicts of interest.
Disclosure of Interest: aminosalicylates should respond well to GMA and avoid pharmacologicals. Clinical remission and mucosal healing, while in non-responders to GMA mono-therapy, majority with mucosal healing. 3 months in those who received. Therefore, at week 12, all 30 patients were in remission, majority with mucosal healing. Additionally, GMA has a good safety profile, which is a very favourable feature in growing patients.

Disclosure of Interest: A.R. Saniabadi: Dr. Saniabadi has a non-regular employment position at JIMRO. All other authors have declared no conflicts of interest.

References

Aims & Methods: The aim of this study was to review the investigations and outcomes of IB and AILD in children with a primary diagnosis of AILD and to identify possible risk factors for development of IB in children with AILD. Children with AILD were identified from electronic case notes between 2007 and 2010 and those with a diagnosis of IB prior to AILD excluded. AILD was diagnosed and treated as per centre protocol. Diagnostic endoscopy for IB was performed, based on GI symptoms and/or elevated FC (>60μg/g). Data were described at time of liver diagnosis; endoscopy and last liver follow up. Patients were classified as AILD-IBD or AILD. Mann Whitney and Chi squared test were used to analyse data where appropriate, significance p < 0.05.

Results: Of 37 (12 male) children, diagnosed with AILD (ASC 11), 23 underwent diagnostic endoscopy after a median time from diagnosis of 27.6 [20.1 to 53.9] weeks. 20/23 reported GI symptoms and FC was elevated in 13/18 tested.

Conclusion: In our cohort 35% of children presenting with AILD were subsequently diagnosed with IB. Possible risk factors for development of IB in AILD are low haemoglobin, being leaner and younger at diagnosis. An elevated FC and the presence of GI symptoms are useful to assess the need for diagnostic endoscopy when considering diagnosis of IB in the context of AILD. As current immunosuppression may mask mild features and signs of IB a lower threshold for endoscopy should be considered in these patients.

Disclosure of Interest: All authors have declared no conflicts of interest.

Table 1: Continued

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<td>10(3)</td>
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<td>ASC (μg/g)</td>
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<tr>
<td>Haemoglobin (g/L)</td>
<td>113.0 [90.5 to 122.0]</td>
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Comparison of clinical and laboratory findings in AILD and AILD-IBD groups.

Conclusion: In our cohort 35% of children presenting with AILD were subsequently diagnosed with IB. Possible risk factors for development of IB in AILD are low haemoglobin, being leaner and younger at diagnosis. An elevated FC and the presence of GI symptoms are useful to assess the need for diagnostic endoscopy when considering diagnosis of IB in the context of AILD. As current immunosuppression may mask mild features and signs of IB a lower threshold for endoscopy should be considered in these patients.

Disclosure of Interest: All authors have declared no conflicts of interest.

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Aims & Methods: The aim of this study was to review the investigations and outcomes of IB and AILD in children with a primary diagnosis of AILD and to identify possible risk factors for development of IB in children with AILD. Children with AILD were identified from electronic case notes between 2007 and 2010 and those with a diagnosis of IB prior to AILD excluded. AILD was diagnosed and treated as per centre protocol. Diagnostic endoscopy for IB was performed, based on GI symptoms and/or elevated FC (>60μg/g). Data were described at time of liver diagnosis; endoscopy and last liver follow up. Patients were classified as AILD-IBD or AILD. Mann Whitney and Chi squared test were used to analyse data where appropriate, significance p < 0.05.

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Conclusion: In our cohort 35% of children presenting with AILD were subsequently diagnosed with IB. Possible risk factors for development of IB in AILD are low haemoglobin, being leaner and younger at diagnosis. An elevated FC and the presence of GI symptoms are useful to assess the need for diagnostic endoscopy when considering diagnosis of IB in the context of AILD. As current immunosuppression may mask mild features and signs of IB a lower threshold for endoscopy should be considered in these patients.

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Comparison of clinical and laboratory findings in AILD and AILD-IBD groups.
Results: Twenty-one patients with chronic refractory angiodysplasia bleeding were recruited in this study, included 10 women, aged between 40–85;11 cases of male, aged between 31–70. One patient with colic vascular malformation died of massive hemorrhage due to self-withdrawal. Among the remaining 20 patients who were given thalidomide regularly for 6 months. (1). Eight patients come across constipation, sleepiness and dry mouth. There were no skin rashes, peripheral neuropathy and any other adverse reactions during the treatment. All side-effects resolved when thalidomide was discontinued. (2). The red blood cell after treatment was increased compared with the total procedure time (P = 0.05). The ALT after treatment (32.9 ± 18.5U/L) compared with before treatment (36.3 ± 4.3 g/L) with time (P = 0.05). (4). Prothrombin time (PT) after treatment (12.1 ± 1.3s) compared with before (11.8 ± 1.4s); APTT after treatment (30.2 ± 3.7 s), compared with before (31.0 ± 2.6s); the difference was statistically significant (P > 0.05). (5). 6 cases of colonic capillary malformation review colonoscopy, and the vascular malformation improved significantly after treatment. Conclusion: Thalidomide, with its antiangiogenic mechanism of action, seems to be a promising drug in bleeding angiodysplasia as a treatment option for patients unable to benefit from other available modalities of treatment. the study drug was well tolerated.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P1079 NEWLY DEVELOPED ENDOCYTIC DETACHABLE SNARE LIGATION THERAPY FOR COLONIC DEVERTICULAR HEMORRHOID: A MULTICENTER PHASE II TRIAL


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Introduction: Colonic diverticular bleeding is the most common cause of lower gastrointestinal bleeding. We have reported the preliminary safety results of endoscopic detachable snare ligation (EDSL), a new method for diverticular hemorrhage.1 The bleeding diverticulum was ligated with a detachable snare. Unlike the endoscopic band ligation, removal of the scope to attach a liglation device and reinsertion for treatment are not needed in this method. We performed a clinical trial to evaluate the efficacy and safety of EDSL.

Aims & Methods: This multicenter single arm phase II study was conducted in 12 Japanese institutions. Patients suspected of diverticular bleeding were enrolled from June 2015 to March 2017. Patients with serious heart, renal, or liver failure, sepsis, disseminated intravascular coagulation, and high-dose steroid use (prednisolone dosage > 10 mg/day) were excluded. The primary endpoint was the early (within 1 month) rebleeding rate in patients who were treated with EDSL.

Results: Of 123 patients with diverticular hemorrhage, 101 were treated with EDSL and the early rebleeding rate was 5% (5/101). The rebleeding rate in ITT population was 9% (11/123). Success rate of EDSL was 78% (96/123).

Conclusion: EDSL is an effective, safe, and convenient treatment method for colonic diverticular hemorrhage.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

P1080 RISK FACTORS FOR EARLY AND LATE RE-BLEEDING IN PATIENTS WITH COLONIC DIVERTICULAR BLEEDING


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Introduction: Incidence of colonic diverticular bleeding has increased in recent years. Colonic diverticular bleeding is problematic because of the following reasons: the low detection rate of the bleeding source by endoscopy and frequent re-bleeding. At our hospital, we have a policy of performing emergency lower gastrointestinal endoscopy for all patients with colonic diverticular bleeding within 24 h of their admission. We have reported that the following factors can contribute to the unsuccessful identification of the bleeding source: extravasation revealed by abdominal contrast computed tomography (CT), and mounting of a hood to the tip of an endoscope during lower gastrointestinal endoscopy. However, risk factors for re-bleeding in patients with colonic diverticular bleeding were still unknown.

Aims & Methods: In this study, we examined the risk factors for early and late re-bleeding in patients with colonic diverticular bleeding. From January 2004 to April 2016, we admitted 432 patients (285 men and 147 women, mean age: 71 ± 13 years) to our hospital for treatment following a diagnosis of colonic diverticular bleeding based on abdominal CT and endoscopy findings. Early and late re-bleeding was defined as macroscopically bloody stools as a result of colonic diverticular bleeding during hospitalization and after discharge, respectively. Risk factors for early and late re-bleeding were retrospectively examined using univariate and multivariate analysis.

Results: Early re-bleeding occurred in 112 patients (26%; 86 men and 26 women, mean age: 71 ± 12 years). The mean duration until re-bleeding was 3.9 ± 2.4 days, and the average, early re-bleeding occurred 1.7 ± 1.2 times. On average, lower gastrointestinal endoscopy was performed 2.7 ± 1.2 times and endoscopic hemostatic treatment was performed 1.0 ± 1.0 times. In the univariate analysis, significant differences were seen in males (P = 0.005), in the use of oral antplatelet agents (P = 0.012), and in patients not undergoing endoscopic hemostasis (P = 0.004). In the multivariate analysis, male gender (P = 0.006; odds ratio 2.06, 95%CI 1.23–3.44), the use of oral antplatelet agents (P = 0.008; odds ratio 1.85, 95%CI 1.17–2.93), and patients not undergoing endoscopic hemostasis (P = 0.005; odds ratio 1.5, 95%CI 0.31–0.81) were independent risk factors for early re-bleeding. Late re-bleeding was seen in 72 of 345 patients who were able to follow up (21%; 46 men and 26 women, mean age: 73 ± 12 years). The mean duration until late re-bleeding was 41 ± 40 months, and on average, late re-bleeding recurred 1.5 ± 1.2 times. Only the use of oral antplatelet agents (P = 0.05; odds ratio 1.72, 95%CI 0.98–2.98) was identified as an independent risk factor for late re-bleeding in the univariate and multivariate analysis.

Conclusion: Not undergoing endoscopic hemostasis and male gender were identified as risk factors for early re-bleeding, indicating the importance of choosing measures and hemostatic treatments to improve the detection rate of bleeding sources during endoscopy. The use of oral antplatelet agents was a risk factor for both early and late re-bleeding, suggesting the need for patient management through multi-departmental cooperation.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference
P1081 ACUTE LOWER GASTROINTESTINAL BLEEDING–IS NOBLADS THE ANSWER?

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Introduction: Acute lower gastrointestinal bleeding (ALGIB) constitutes an important gastroenterological emergency. A new score (NOBLADS) that intends to determine the risk of severe ALGIB was recently developed. We aimed to assess the validity of this score in a cohort of patients with ALGIB.

Aims & Methods: Retrospective study. Emergency consecutive admissions for ALGIB were reviewed. Severe ALGIB was defined as transfusion of ≥2 units of packed red blood cells (PRBC) and/or hematocrit decrease of ≥20% within the first 24 h and/or recurrent bleeding after 24 h of stability. NOBLADS score was calculated and its discriminative capacity for severe ALGIB as well as for overall outcomes was assessed.

Results: Included 118 patients with a mean age of 73±14.4 years and 52.5% males. Most frequent etiologies for ALGIB were diverticular bleeding (23.7%) and post-polypectomy (21.2%). ALGIB was severe in 38.1% of patients. NOBLADS score showed a weak discriminative capacity to determine severe ALGIB (AUC = 0.68, p < 0.01). However, when comparing patients with NOBLADS <4 and ≥4, patients with higher scores were significantly older (69.2±15.7 years vs 78.6±10.0 years, p < 0.01), had lower hemoglobin levels as admission (11.8±2.5 g/dL vs 10.2±2.5 g/dL, p < 0.01), were transfused with more units of PRBCs during the first 24 h and during hospital in-stay (0.4±0.9 vs 1.1±1.3, p < 0.01 and 1.0±2.2 vs 3.0±3.3, p < 0.01, respectively) and were more frequently admitted to intermediate care units (35.2% vs 59.6%, p < 0.01). No differences were found between the two groups regarding in-stay length, rebleeding rate, need for surgery or death.

Conclusion: NOBLADS score showed a weak discriminative capacity to determine severe ALGIB however, patients with NOBLADS ≥4 had greater PRBCs transfusion need and were more frequently admitted to intermediate care units. New or improved scores that can predict severe ALGIB are needed to determine more precisely appropriate care and to allow for a standardized approach.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P1082 COLORECTAL CANCERS (CRCs) DEPENDING ON THE SCREENING INTERVAL IN IBARAKI, JAPAN

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Introduction: In Japan, CRC screening was launched as a national policy for all ages over 40 years ago. It is demanded that CRC screening have been performed with the OC-SENSOR DIANA (EIKEN, JAPAN) automated analyzer with cut-off value of 20 µg Hb/g stool. Between 2011 and 2014, 957 CRCs and 12,290 polyps were detected. 957 CRCs were detected with 3,421 cases from the screening (2000–2014) with 2-day FIT. The concentration of FIT was grouped in 20–80, 80–140, 140–200 and over 200 µg Hb/g stool. Screening have been performed with the OC-SENSOR DIANA (EIKEN, JAPAN) automated analyzer. CRCs were analyzed with age group (40–49, 50–59, 60–69, over 70 year-old), size (1–24, 25–49, over 50 mm), location (proximal, distal), Dukes’ classification (Dukes A, D, invasive, B, C, D) depending on the concentration. The chi-squared test was used to compare of each group.

Results: There was no difference in gender and age group for concentration. The concentration of CRCs in the distal colon was significantly higher in the proximal colon [distal 39% (861/2,200) and proximal 32% (337/1,053) with over 200 µg Hb/g stool]. The concentration of CRCs with larger size was significantly higher than smaller size [1–24 mm 27% (533/1,961), 25–49 mm 54% (439/819) and over 50 mm 64% (169/263) with over 200 µg Hb/g stool]. The concentration of invasive CRCs was significantly higher than in-tramural CRCs [intra-mucosal 23% (370/1,617) and invasive 50% (888/1,793) with over 200 µg Hb/g stool]. The concentration of Dukes B, C and D were significantly higher than Dukes A except for intra-mucosal. There was no difference between Dukes B and D [Dukes A except for intra-mucosal 36% (325/910), B 68% (247/363), C 60% (232/385) and D 69% (61/89) with over 200 µg Hb/g stool].

Table 1: Fecal Hb concentration and progress of colorectal cancer

<table>
<thead>
<tr>
<th>Age</th>
<th>Size(mm)</th>
<th>Location</th>
<th>Dukes</th>
</tr>
</thead>
<tbody>
<tr>
<td>conc.</td>
<td>40–49</td>
<td>50–60</td>
<td>60–70</td>
</tr>
<tr>
<td>20–80</td>
<td>48</td>
<td>190</td>
<td>588</td>
</tr>
<tr>
<td>80–140</td>
<td>14</td>
<td>51</td>
<td>185</td>
</tr>
<tr>
<td>140–200</td>
<td>177</td>
<td>33</td>
<td>117</td>
</tr>
<tr>
<td>200–</td>
<td>55</td>
<td>177</td>
<td>529</td>
</tr>
<tr>
<td>total</td>
<td>134</td>
<td>451</td>
<td>1,419</td>
</tr>
</tbody>
</table>

Conclusion: In 20–80 µg Hb/g stool, there were CRCs with smaller size, no invasion, in the proximal colon, Dukes A except for intra mucosal CRCs and so on. When the cut off value is raised over 80 µg Hb/g stool, the detection of early stage CRCs and proximal CRCs may be lost. There were many advanced CRCs with concentration over 200 µg Hb/g stool. Therefore, when the participants, who are positive with high concentration of FIT, need to take a further examination as soon as possible. Why concentration of CRCs can be lost in the proximal colon? It may be related to the fact that the number of detectable CRCs in the distal colon are more than in the distal colon. We will go on researching mechanism about this.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

Table 1:

<table>
<thead>
<tr>
<th>Intra-mucosal A</th>
<th>B</th>
<th>C</th>
<th>D</th>
<th>Unknown</th>
</tr>
</thead>
<tbody>
<tr>
<td>First-time group</td>
<td>187</td>
<td>109</td>
<td>65</td>
<td>61</td>
</tr>
<tr>
<td>(99%)</td>
<td>(23.9%)</td>
<td>(14.2%)</td>
<td>(13.3%)</td>
<td>(4.5%)</td>
</tr>
<tr>
<td>Repeated group</td>
<td>258</td>
<td>127</td>
<td>36</td>
<td>54</td>
</tr>
<tr>
<td>(51.7%)</td>
<td>(25.5%)</td>
<td>(7.2%)</td>
<td>(10.8%)</td>
<td>(1.4%)</td>
</tr>
<tr>
<td>P value</td>
<td>0.0008</td>
<td>0.5666</td>
<td>0.0004</td>
<td>0.2304</td>
</tr>
</tbody>
</table>
P1084 COLONOSCOPY SURVEILLANCE DETECTS A HIGH PREVALENCE OF ADVANCED COLORECTAL NEOPLASIA AND SERRATED POLYPOSIS SYNDROME IN HODGKIN LYMPHOMA SURVIVORS

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Introduction: A colonoscopy was performed in 101 HL survivors, who were signifi-
cantly younger than the general population cohort that underwent a pri-
mary colonoscopy among HL survivors treated with abdominal radiotherapy
and/or alkylating chemotherapy have an increased risk of colorectal
neoplasia was detected per HL survivor (standard deviation 4.9) vs. 1.1
in the Dutch general population cohort that underwent a prede-
finite interim analysis. Results: A colonoscopy was performed in 101 HL survivors, who were signifi-
cantly younger than general population controls (median 51 years (interquartile range 45–57) vs. 60 years (interquartile range 55–65), p< 0.001). A mean of 3.5 neoplastic lesions was detected per HL survivor (standard deviation 4.9) vs. 1.1 per control (standard deviation 1.8, p < 0.001). Despite their young age, the
prevalence of advanced neoplasia was higher in HL survivors than in controls
(25% (95% confidence interval 16–33%) vs. 12% (10–14%), p < 0.001). Advanced adenomatous polyps were detected in 14% (8–21%) of HL survivors and 9% of controls (7–17%, p = 0.001). The prevalence of advanced hormone
dependent prostate cancer was higher in HL survivors than in controls (12% (6–18%) vs. 4% (3–5%), p < 0.001). Serrated polyposis syndrome was present in 6% (2–11%) of HL survivors and 2% (0–7%) of controls (p < 0.001).

Conclusion: HL survivors treated with abdominal radiotherapy and/or procarba-
zine have a high prevalence of advanced colorectal neoplasia. Colonoscopy sur-
veillance should therefore be implemented as standard of care.

Aims & Methods: We aim to investigate the incidence of prostate cancer as a
second primary malignancy among patients with prior primary colorectal cancer
(CRC) using a nationwide population-based dataset. This study is a nationwide
population-based retrospective cohort study. We followed up with patients
registered in the Republic of Korea National Health Insurance Corporation
who were diagnosed with colorectal cancer between 2007 and 2014 and investigated
the incidence of prostate cancer (one year lag period). The incidence of prostate
cancer was also evaluated in age and gender-matched controls using a cohort of
patients diagnosed with colorectal cancer during the same period. The incidence
rate for prostate cancer was defined as the number of newly diagnosed prostate cancer patients
to 1000 person-years. To assess the role of detection bias-related to the follow-
up of CRC, follow-up started at the date of CRC diagnosis and continued until
the earliest date of prostate cancer diagnosis, death, loss to follow-up, or the 2015
year-end. We used Cox proportional hazards models to identify prostate
occurrences among CRC patients. We also performed the multivariable analysis.
Multivariable models included the variables of age, sex, body mass index, hyper-
tension, diabetes mellitus, dyslipidemia, and income.

Results: We analyzed a total of 85,462 primary CRC survivors. During the
follow-up period of 494,222 person-years, 2005 (2.3%) developed prostate cancer
(incidence rate 4.06/1,000 person-years). The median duration of follow-up was
5.78 years. Compared with the general population, CRC patients had a significantly
increased risk of primary prostate cancer (HR = 2.30, 95% CI = 1.82–2.426; P < 0.001).

Conclusion: Men who develop colorectal cancer are at an increased risk of pros-
tate cancer, with the greatest risk in men under the age of 55. This data suggests
that CRC patients under 55 years old require regular screening for prostate cancer.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1086 SITE AND STAGE DISTRIBUTION OF SCREEN DETECTED AND CLINICALLY DETECTED COLORECTAL CANCERS IN THE NETHERLANDS

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Introduction: To reduce the burden of colorectal cancer (CRC) mortality, screen-
ing has been introduced. Screening can be beneficial if cancers are detected in an
earlier stage or in a pre-malignant stage, as survival rates of these patients will
improve.

Aims & Methods: In this study stage distribution of screen detected CRCs were
compared with clinically detected CRCs in the Netherlands. All CRCs detected
in men and women aged 55 to 75 years in the Netherlands in 2015 were included
in the analysis. Data were gathered from the Dutch Cancer Registry. The current
analysis is based on 70% of these cancers that had staging information
available at initial data retrieval. Data will be updated in May 2017.

Results: A total of 6,517 CRCs in 2015 with staging information were
available for the preliminary analysis. Of those, 2,591 (39.8%) were diagnosed as a result of
CRC screening (screen detected), 3,463 (53.1%) presented with symptoms
and were detected clinically (clinically detected), 118 (1.8%) were detected during surveill-
colonoscopy (203 (3.1%) as coincidental finding and of 143 (2.2%) the method of detection
was unknown. Screen detected cancers were more often diagnosed in an earlier stage (stage I and II) compared with clinically detected cancers, 1,687 (66.5%) and
1,115 (95.8%) respectively (p < 0.001). Screen detected cancers were more often
diagnosed in the left side of the colon compared with clinically detected cancers,
46.2% vs 31.5% (p < 0.001). Comparison of stage by location distribution showed that left sided cancers were most often diagnosed in an early disease stage
to 59.0% of the CRCs in stage I or II, followed by the right sided cancers
with 52.8% of the CRCs in stage I or II. The CRCs of the rectum were most
often diagnosed in a late disease stage, only 39.4% in stage I or II. Table 1 shows the
comparison of stage by location distribution by location and method of detection.
With screening detected cancers, 68.8% of the right sided cancers, 71.0% of the left sided cancers,
and 56.5% of the rectum CRCs were diagnosed in an early disease stage (stage I and II) which was all higher than clinically detected cancers (p < 0.001).

Table 1: Stage of screen detection and clinically detected colorectal cancers by location and method of detection

<table>
<thead>
<tr>
<th>Stage</th>
<th>Right sided</th>
<th>Left sided</th>
<th>Rectum</th>
<th>Right sided</th>
<th>Left sided</th>
<th>Rectum</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>254 (38.3%)</td>
<td>637 (54.5%)</td>
<td>316 (45.7%)</td>
<td>147 (12.2%)</td>
<td>217 (20.2%)</td>
<td>188 (17.0%)</td>
</tr>
<tr>
<td>II</td>
<td>203 (36.8%)</td>
<td>193 (16.5%)</td>
<td>75 (9.8%)</td>
<td>381 (31.7%)</td>
<td>277 (25.7%)</td>
<td>130 (11.8%)</td>
</tr>
<tr>
<td>III</td>
<td>166 (25.0%)</td>
<td>262 (22.4%)</td>
<td>257 (37.1%)</td>
<td>344 (28.6%)</td>
<td>310 (28.8%)</td>
<td>543 (49.1%)</td>
</tr>
<tr>
<td>IV</td>
<td>41 (6.2%)</td>
<td>77 (6.6%)</td>
<td>44 (6.4%)</td>
<td>129 (10.7%)</td>
<td>272 (25.3%)</td>
<td>245 (22.2%)</td>
</tr>
</tbody>
</table>

Conclusion: Screen detected CRCs show a more favourable stage distribution
compared with clinically detected cancers, with two third of the cancers
P1087 LOCATION AND SEX PREDOMINANCE OF MISMATCH REPAIR DEFICIENT COLORECTAL CANCER ON IVORY COAST DIFFER FROM ITS EUROPEAN COUNTERPART

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Introduction: According to European and American series,1,2 up to 20% of colorectal cancers are characterised by instability at microsatellite sites and have deleterious mutations in mismatch repair (MMR) genes (MLH1, MSH2, MSH6 and PMS2) or hypermethylation of the MLH1 promoter gene. MMR deficient colorectal cancers are predominantly found in the right colon. Although an increasing rate of colorectal cancer has been observed in many low- and middle-income countries including in West Africa,3 data on epidemiology and biology of colorectal cancer in native Africans from this region are scarce.

Aims & Methods: We aimed to study the incidence of MMR deficiency in Ivory Coast and to compare the data with those from a tertiary center in Belgium. Immunohistochemistry for MLH1, MSH2, MSH6 and PMS2 was performed on paraffin-embedded tissue samples from 83 colorectal cancers (54% males) operated in Abidjan and from 343 colorectal cancers (48% males) from Erasme University Hospital in Brussels. Immunohistochemical staining was interpreted as normal or loss of expression.

Results: Colorectal cancer is occurring at a younger age in Ivory Coast compared to Belgium (median age: 53 vs. 66). In both populations, MMR deficiency was detected in 13% of cases (11 and 43 cases, respectively). Whereas MMR deficient cancers in Brussels were mainly found in women (26:43 i.e. 61%) and with loss of the predominant location of MMR deficient tumours was different between both series: in the Brussels patients group, MMR deficient tumours were mainly located in the right colon (33:43 i.e. 77%) whereas in the Abidjan group they were predominant (10:11 i.e. 91%) in the left colon. With regard to the involved proteins, 6:11 (55%) of the MMR deficient cases from Ivory Coast were characterised by loss of expression of MSH2 and MSH6 whereas this immunohistochemical staining pattern was observed in only 9:43 (20%) cases from Belgium.

Conclusion: Our pilot study reveals marked differences in presentation of MMR deficient colorectal cancer between the two geographic regions. In contrast to Europe, MMR deficient colorectal cancer in Ivory Coast is mainly found in male patients and in the left colon. Moreover, there are differences with regard to the involved mismatch repair proteins. Together with the younger age at presentation, these data suggest differences in epidemiology and biology of colorectal cancer in native Africans from West Africa compared to the European population.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P1088 ROUTINE MOLECULAR ANALYSIS FOR LYNCH SYNDROME IN PATIENTS WITH ADVANCED ADENOMA OR COLORECTAL CANCER WITHIN A NATIONAL SCREENING PROGRAM FOR COLORECTAL CANCER

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Introduction: Lynch syndrome (LS) is the most common hereditary cause of colorectal cancer (CRC). Identifying LS carriers and their affected family members is of great importance for prevention of CRC. Routine screening for LS by immunohistochemical staining (IHC) in CRC patients ≤70 years of age is recommended. LS screening in adenoma patients could yield more benefit, since CRC can still be prevented in these patients. A small number of participants of the national CRC screening program is expected to have LS. We aimed to assess the diagnostic yield of IHC for LS in patients with advanced and multiple adenomas or CRC within the Dutch national fecal immunochromic test (FIT)-based CRC screening program.

Aims & Methods: We included participants of the national CRC screening program, referred to our center after a positive FIT from December 2013 to December 2016. IHC for MLH1, MSH2, MSH6 and PMS2 protein was performed on advanced adenomas and CRCs found at colonoscopy. Adenomas were considered advanced if they had a villous component, high-grade dysplasia or were ≥10 mm in size. Also, in cases with ≥2 non-advanced adenomas, IHC was performed on the largest adenoma. MLH1 hypermethylation analysis was performed in cases with concurrent LS gene mutation for germline mutation analysis. If no pathogenic mutation was found, we performed somatic mutation analysis.

Results: A total of 1006 patients (54% male; mean age of 67 years (±6 years)) with positive FIT were included in the study. At colonoscopy, 355 (35%) patients (63% male; mean age of 67 years (±6 years)) had a CRC and/or adenoma eligible for IHC. A total of 322 adenoma patients were analyzed. None had aberrant IHC. Seven cases with IHC for LS were referred for genetic counselling. Both patients had no family history suspect for LS. In both cases no germline MLH1 mutation was found and somatic mutation analysis showed that both had a likely sporadic tumour.

Conclusion: Our results indicate that routine LS screening by IHC and MLH1 hypermethylation in patients with advanced and multiple adenoma within a national FIT-based screening CRC program is not an effective strategy. The diagnostic yield of LS screening in younger adenoma patients should be assessed.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P1089 COLORECTAL CANCER SCREENING PROGRAMS AND THE RATE OF SURGICAL ONCOLOGY PROCEDURES IN THE VENETO REGION (ITALY): ARE FOLLOW-UP COLONOSCOPIES REALLY NEEDED?

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Introduction: Colorectal cancer (CRC) is a leading cause of cancer mortality in the Veneto Region (North-eastern part of Italy). Population screening of adults between 50 and 75 for CRC was begun in 2002, and it became standard practice in all the local health units (LHU) of the region in 2008. LHU provided also follow-up colonoscopies and 7 LHU no. The current retrospective cohort study was carried out to evaluate the impact of CRC screening on the rate of surgical oncology procedures to treat colon and rectal cancer.

Aims & Methods: Data from hospital discharge records (HDR) regarding CRC patients hospitalized between 2000 and 2015 were collected. All CRC patients whose principal diagnosis was colon and/or rectal cancer were included in the study. The number of patients studied rose approximately 18% reaching 1,547,097 for the last year (2015). The Standardized Hospitalization Ratio (SHR) using five-year age groupings was calculated and expressed per 10,000 population.

Results: During the study period, 30,399 surgical procedures for colorectal cancer were performed (colon 63%, rectum 36%, secondary malignant neoplasm 1%) with a SHR of 139.1; the number was higher in males (1.69 vs. 1.02; OR: 1.66; CI 95%: 1.62–1.7; p < 0.05). An analysis of the annual SHR distribution uncovered two distinct phases: during the first phase there was a rising tendency that reached its maximum value in 2007 (166.9; X2 trend: 46.73; p < 0.05) and during the second there was a falling tendency that reached its minimum value in 2015 (102.3; X2 trend: 429.791; p < 0.05). An analysis of the annual SHR distribution uncovered two distinct phases: during the first phase there was a rising tendency that reached its maximum value in 2007 (166.9; X2 trend: 46.73; p < 0.05) and during the second there was a falling tendency that reached its minimum value in 2015 (102.3; X2 trend: 429.791; p < 0.05). When the cancer sites were analysed, it was seen that despite the peak in 2007, the rate of surgical procedures of the proximal colon during the last year was the same as the 2000 value (41.3); there was, instead, a relevant decrease in the rate of procedures on the distal colon and rectum which fell from 94.2 to 59.2 (–37.5%). The study also shows that there was no significant difference in the reduction in surgical procedures for CRC in LHU in which the screening program included a follow-up colonoscopy (SHR 2015: 139.8; –29% with respect to those centers where it was not forseen (SHR 2015: 138.5; –28%).

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P1090 ETHNIC VARIATION IN ADENOMA DETECTION IN THE UK FLEXIBLE SIGMOIDOSCOPY BOWEL CANCER SCREENING PROGRAMME

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Introduction: The NHS bowel scope screening programme was introduced in 2013 with all adults aged 55 invited for a ‘one-off’ flexible sigmoidoscopy over a period of 2 years. Sigmoidoscopy is followed by colonoscopy if significant adenomas are found in order to reduce the risk of colorectal cancer (CRC). The Cancer Research United Kingdom database was cross referenced with the endoscopic and histology findings from 4287 patients undergoing flexible sigmoidoscopy over the period of the study. The aims of the study was to evaluate the polyp detection rate (PDR), adenoma detection rate (ADR) and cancer detection rate (CDR) in British Asian Indians compared with British Whites.

Methods: A total of 4287 patients underwent sigmoidoscopy over the 2-year period. 1169 individuals had polyps (50%).

Results: 4287 patients underwent sigmoidoscopy over the 2-year period. 1169 individuals had polyps (50%). The highest PDR was 30.8%, 20.1% for SSA/P, and 11.7% for HLS. The highest ADR was 12.0%, 8.6% for SSA/P, and 4.7% for HLS. The highest CDR was 0.9%, 0.3% for SSA/P, and 1.5% for HLS.

Conclusion: This study found no cancers and significantly lower PDR and ADR in British Asian Indians compared with British Whites. The study suggested that sigmoidoscopy screening in Asian Indians may be lower than in White population and hence may need to be targeted towards the Asian Indian community.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P1091 DEAD BOX POLYPEPTIDE 27 PROMOTES TUMORIGENICITY IN COLORECTAL CANCER THROUGH ACTIVATING NUCLEAR FACTOR KAPPA B PATHWAY AND ITS EXPRESSION IS ASSOCIATED WITH POOR SURVIVAL IN PATIENTS

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Introduction: We identified for the first time that DDX27 (DEAD box polypeptide 27) gene was amplified in colorectal cancer (CRC) by whole genome sequencing. Amplification of DDX27 was detected in 47% (47/100) of primary CRC tumors and positively correlated with its mRNA overexpression. DDX27 plays a pivotal oncogenic role in colorectal carcinogenesis by promoting cell proliferation and inhibiting apoptosis. In this study, we investigated its function, mechanism and biological implication in CRC.

Aims & Methods: Downstream effectors and pathways of DDX27 were identified by promoter luciferase reporter assay, RT-Profiler PCR array and western blot. The interacting partners of DDX27 were screened by BioID method and further validated using immunoprecipitation assay and immunofluorescence staining method. Clinical implication of DDX27 was assessed in two human CRC cohorts by quantitative PCR method and immunohistochemical staining of tissue microarrays.

Results: Promoter luciferase reporter assays revealed that DDX27 mainly activated nuclear factor kappa B (NF-kB) pathway in CRC cell lines (HTC116 and SW480). Ectopic expression of DDX27 promoted transcription of NF-kB signal- ing targets including BCL2A1, BIRC3, CCL20, CXCL13, NFKBIA, TNF and TNAFIP3. Conversely, silencing of DDX27 showed an opposite effect on NF-kB signaling. Treatment of NF-kB inhibitors CAPE and JSH-23 abolished the pro- moting effect of DDX27 on CRC cells growth. We revealed that DDX27 enhanced and prolonged NF-kB signaling via reducing the accumulation of nuclear IκBα, which negatively regulates transcriptional activities of NF-kB and transport NF-kB proteins back to the cytoplasm. DDX27 overexpression markedly increased the recruitment of NF-kB p65 inside nucleus and promoted NF-kB activity in CRC cells under TNF-α stimulation. NPM1 was identified as a potential binding partner of DDX27 by BioID method to screen for protein-protein interactions. The interaction of NPM1 and DDX27 inside nucleus was further validated by endogenous immunoprecipitation assay and immunofluorescence staining. Knockdown of NPM1 abrogated DDX27-activating NF-kB signaling, as well as its tumor-promoting function. Kaplan-Meier curves showed that higher DDX27 expression was significantly associated with shortened survival in patients with CRC of two independent cohorts (N = 199 for Beijing cohort using quantitative PCR method, and N = 275 for Shanghai cohort using immunohistochemical staining of tissue microarrays; both P < 0.05).

Conclusion: DDX27 plays an important oncogenic role in promoting CRC tumorigenicity via activation of NF-kB pathway. Higher expression of DDX27 is correlated with poor prognosis in CRC patients.

Disclosure of Interest: All authors have declared no conflicts of interest.
significant differences between serrated lesions, SSA/Ps and HPs were positive for MUC5AC in comparison with TSAs. We performed immunohistochemistry on intestines from APCfl/fl mice, and expression correlates with resistance against carcinogenesis. The azoxymethane (AOM) induced colon carcinogenesis mouse model was used. Colonic mucosal samples were collected from wild type (WT) C57bl/6 mice and C57BL/6 mice that either underwent colonic biopsies or irradiation of the intestine. In TLR4KO mice sacrificed at 8 months, 1.4 polyps/mouse were significantly different from WT (p = 0.002, p = 0.001, respectively). Similarly, at 8 months the rate of epithelial cells expressing CD80 or MHC-I or MHC-II were significantly lower in TLR4KO than in WT mice (p = 0.001, p = 0.01, respectively). Moreover, at 8 months, 5/7 TLR4KO mice compared to 0/7 WT ones had at least a colonic adenocarcinoma (p = 0.02). At this time point, CD4+CD25−, CD4+CD25+FoxP3+, CD8+CD28+, CD8+CD38+ cells rate was significantly lower in TLR4KO mice than in WT ones (p < 0.001, p = 0.01, respectively). Similarly, at 8 months the rate of epithelial cells expressing MHC-I and MHC-II were significantly lower in TLR4KO than in WT mice (p = 0.01, p < 0.001, respectively).

Conclusion: TLR4 deficiency significantly accelerate the progression of colonic carcinogenesis through a progressive decline of antigen presentation and lack of co-stimulation at later stages. These impairments are associated to a decline of T cell response in all its form (Treg, T helper and cytotoxic). All these findings are coherent with a pivotal role of TLR4 in the immune surveillance mechanism.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
**P1096 ENDOSCOPIC FOLLOW UP CAN SELECT PATIENTS FOR MULTI-GENE TESTING IN ATTENUATED ADENOMATOUS POLYPYSIS WITH NO APC OR MUTYH IDENTIFIED MUTATIONS**

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Introduction: Less than a hundred polyps defines attenuated familial adenomatous polyposis (AFAP). APC or MUTYH involvement has been described in 60% of the cases. The natural history of AFAP without identified genetic defects is not enough evaluated. In our study we compare clinical and endoscopic features of polyposis in patients carrying APC or MUTYH mutation and wild type patients.

Aims & Method: 102 cases (35 F, 67 M; mean age 51; range 28–79) of AFAPs were registered at our Institution between 1996 and 2014. They had no family history and presented more than 10 adenomas at index colonoscopy. Genetic testing for APC and MUTYH genes was performed. Patients were put in a program, after having cleaned the colon, consisting in colonoscopy after one year and then the colonoscopic interval was based on the number of polyps from 1 to 3 years. Odds Ratio test was used to compare APC or MUTYH mutated and wild-type patients.

Results: Out of 102 patients with AFAP we identified a genetic defect in 36 patients (35.3%; 12 with APC and 24 MUTYH) and 66 (64.7%) were wild-type. The mean endoscopic follow up was 10 years (2–31) in the mutated group and 6 years (2–23) in the wild-type group. Table 1 describes endoscopic and clinical features between the two groups. We observed some statistically differences between groups: the mutated group was younger than 50 years of age and a higher number of polyps, right colon was mainly involved and endoscopic follow-up was mostly every year. Patients of wild-type group never underwent to colectomy during follow-up and they displayed few adenoma recurrences in 24% of cases. On the other hand 14% of mutated patients underwent colectomy for dense polyposis and 28% had more polyps than at index colonoscopy and 11% no polyps at all. These 11% displayed mutation in MUTYH.

Regarding extra-colonic manifestations we observed duodenal adenomas in 5 (13.8%) patients and desmoids tumor in one patient of mutated group. Two gastric cancers and one melanoma were diagnosed in the wild type group. We observed a different behavior between mutated and wild-type patients. Patients with genetic involvement still developed adenomas during the follow-up and some needed colectomy. Instead, wild-type patients had mostly no recurrence. Constitutional genetic background could be suspected in wild-type patients when a continuous development of new polyps has observed and further genetic investigation should be offered by multi-gene testing.

Conclusion: We observed a different behavior between mutated and wild-type patients. Patients with genetic involvement still developed adenomas during the follow-up and some needed colectomy. Instead, wild-type patients had mostly no recurrence. Constitutional genetic background could be suspected in wild-type patients when a continuous development of new polyps has observed and further genetic investigation should be offered by multi-gene testing.

Disclosure of Interest: All authors have declared no conflicts of interest.
Extracellular miRNAs are stable and its expression is less characterized in plasma. Altogether, overlapped miRNA profiles between tissue and plasma are less explored.

**Aims & Methods:** The present study was designed to characterize the tissue and circulating miRNA profile through colorectal adenoma-carcinoma sequence in human adenoma in mice peripheral blood samples. Furthermore, purpose of our study was to determine the origin of detected miRNAs in tumor-adenent C33/C57BL/6 and non-adenent CBAJ mice tumor models. To achieve that goal, human peripheral blood and biopsy of normal (N), tubular (AT), tubulovillous (TV) and colorectal adenoma (CRC) volunteered and plasma were also collected two times a week over 45 days from C33BL/6-C38, CBAJ mice. MiRNAs were isolated and Affymetrix GeneChip miRNA array analysis performed for screening of the altered miRNA profile. RT-qPCR methodology was performed for the identification of target genes.

**Results:** In the case of human samples out of 1733 detectable miRNAs, 306 miRNAs were expressed in normal, 334 in adenoma and 321 in CRC. Characteristic miRNA expression alteration was observed in the comparison of A550 CRC, VS A550 healthy samples. Whether miR-126 can regulate the process of EMT in CRC is still unclear. Ras family members include Ras, RhoA, Cdc42, and Rac1. These were first identified as oncogenes that promote tumor growth and invasion. RhoA, as molecular switch, cycles between an active state (GTP bound) and an inactive state (GDP bound) and its activity levels are influenced by numerous cellular events. Considering the above mentioned facts we wrote the RhoA activity and RhoA signaling pathway play an important role in miR-126 regulating EMT process, cell proliferation, migration and invasion of CRC cells.

**Conclusion:** RhoA signaling pathway was the key signaling pathway of miR-126 in suppressing the EMT, proliferation, migration and invasion of CRC cells. Disclosure of Interest: All authors have declared no conflicts of interest.

**References:**

**Disclosure of Interest:** All authors have declared no conflicts of interest.
P1101 MIR-126 REGULATES TUMOR GROWTH AND METASTASIS IN COLORECTAL CANCER BY RECRUITING TUMOR-ASSOCIATED MACROPHAGES THROUGH PARACRINE SIGNALING OF CXCX12
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Introduction: Colorectal carcinoma is one of the leading causes of cancer-related mortality worldwide. Tumor associated macrophages (TAMs) are critical stromal components intimately involved with the progression, invasion, and metastasis of cancer cells. Recently, increasing studies have demonstrated that microRNA-126 (miR-126) had an important role in colorectal cancer. The expression of miR-126 decreased significantly in colorectal cancer, particularly in highly metastatic cell lines, indicating that miR-126 may inhibit tumor development and metastasis. However, the mechanism underlying miR126 inhibiting cancer is uncertain, and its function in cross-talk between colorectal cancer cells and TAMs are still in its infancy.

Aims & Methods: In this study, we investigate the cross-talk between cancer cells and TAMs in colorectal cancer microenvironment, and find out what role the miR=126=CXCX12=IL6 axis plays in it. Methods: (1)The effect of miR-126 on CXCX12 expression was assessed in the CRC cell line Caco2 transferred with a miR-126 mimic or inhibitor to increase or decrease miR-126 expression; (2) We build a co-culture system of TAMs and transferred cancer cells, and use AMD3100(100 ng/ml) to block CXCX12/CXCR4 axis, then detect the recruitment and inflammation factors secretion of TAMs: (3) Furthermore, the TAMs co-cultured before were taken away from the previous system and put into a new co-culture system with untreated colorectal cancer cells, and IL6 neutralizing antibody was added in. We detect the expression of EMT associated factors and STAT3 pathway activation by western blot, cell growth by CCK8, metastasis by Transwell. The definition of statistical significance was defined as P < 0.05 (two-tailed).

Results: (1)miR-126 negatively regulate CXCX12 expression in post-transcript level; (2)Inhibiting miR-126 of colorectal cancer cells could promote TAMs recruitment and up-regulate inflammation factors IL1β and IL6 expression. However, blocking CXCX12/CXCR4 axis by AMD3100 could reverse this effect, vice versa;(3)Inhibiting miR-126 of colorectal cancer cells could recruiting TAMs, therefore down-regulate E-cadherin protein, up-regulate slug protein, and activate STAT3 pathway activation by western blot, cell growth by CCK8, metastasis by Transwell. The definition of statistical significance was defined as P < 0.05 (two-tailed).

Conclusion: Our results reveal a novel mechanism by that miR-126 repress recruitment and inflammatory factor secretion of TAMs through controlling secretion and paracrine signaling of CXCX12 to inhibit colorectal cancer growth and metastasis.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1102 THE EFFICACY OF NEXT-GENERATION OF IMAGE ENHANCED COLONOSCOPY (BLUE LASER IMAGING) IN THE DETECTION OF COLONIC LESIONS: A PILOT STUDY
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Introduction: Narrow Band Imaging (NBI) enable detection for vascular-rich small, flat lesion and recognition of mucosal surface compared with normal colonic mucosa and vascular pattern in colonoscopy. However, recent studies revealed no significant difference in overall adenoma detection rate with the use of NBI compared with white light imaging (WLI). Blue Laser Imaging (BIL) is next-generation of image enhanced endoscopy technique using LASER light source that were realized with lighting and image processing suitable for visualization of microvessels and structures in the superficial portion of the mucous membrane.

Aims & Methods: Our aim was to determine whether the use of BIL enhances the adenoma detection rate (ADR) and miss rate compared with WLI. A total of 130 patients were enrolled screening or surveillance colonoscopy in Saga University Hospital were included. Three patients were excluded because of poor bowel preparation. One hundred and twenty-seven patients were randomized to tandem colonoscopy with BIL followed by WLI (BIL-WLI group) or WLI following BIL (WLI-BIL group). Polyp (adenoma) detection rates, miss rates, and the number of polyps (adenoma) detected person per mean adenoma detection rate) were examined between the two groups.

Results: The BIL-WL group and WL-WL group comprised 64 and 63 patients, respectively. The proportion of patients with polyps (adenoma) was 62.5% in BIL-WL group compared with 63.5% in WL-WL group. There was no significant difference between two groups regarding ADR. The number of adenomas detected per person (ADR) of BIL-WL group and WL-WL group were 2.84 and 3.01.

Conclusion: There were no significant difference in the overall polyp (adenoma) detection rate with BIL-WLI group or WL-WL group. However, miss rate was higher in WL-WL group compared with BIL-WL group (10.0% vs 1.6%, P = 0.0014). Further, BIL detected more polyps per patient compared with WL group (2.84 vs 1.90). BIL may improve polyp miss rate and the number of polyps per subject (mean adenoma detection rate) in the colonoscopy.

Disclosure of Interest: All authors have declared no conflicts of interest.

Adenoma/Carcinoma according to location in colon

<table>
<thead>
<tr>
<th>Adenoma/ Carcinoma</th>
<th>Number</th>
<th>Proximal to SF (n = 111)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td></td>
<td>67.4</td>
<td>0.67</td>
</tr>
<tr>
<td>Number of polyps</td>
<td></td>
<td>41 (67.2%)</td>
<td>0.32</td>
</tr>
<tr>
<td>Size of polyps (mm)</td>
<td></td>
<td>8.6</td>
<td>0.01</td>
</tr>
<tr>
<td>Carcinoma</td>
<td></td>
<td>11</td>
<td>0.71</td>
</tr>
</tbody>
</table>

Conclusion: Patients with adenomas/carcinomas are older and those with proximal adenomas/carcinomas have more polyps but are smaller in size. One in three adenocarcinomas picked up during colonoscopy would be out of reach of a flexible sigmoidoscopy. Furthermore, over one third of the proximal cancers would not have distal polyps.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
P1104 StUdies on clinicopathological Characteristics and the Long-term prognosis of dePPresSed-type colorectal carcinomaS

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Introduction: Colorectal cancers have two development theories. One of the development theories is “adenoma-adenocarcinoma sequence” developing from protruded-types “polyps” we know generally. The other is considered to emerge directly from normal epithelium, not through the adenomatous stage. Recently, it is revealed most of this type are depressed-type carcinomas. This theory is called “de novo” pathway. We studied clinicopathological characteristics and long-term prognosis mainly on depressed-type colorectal carcinomas. Aim: We analyzed the pathological characteristics of depressed-type colorectal carcinomas compared with flat- and protruded-type. A total of 2930 colorectal neoplasms excluding advanced carcinomas were resected endoscopically or surgically in our Center from April 2001 to December 2011 and in total 112 cases were diagnosed as T1 carcinomas. Among these, 71 specimens were large sized 477 colorectal tumors were analyzed in this study. Morphological development classification, 244 lesions (21.7%) were depressed-type, 385 lesions (34.2%) were flat-type and 498 lesions (44.1%) were protruded-type. We analyzed the pathological features of these lesions.

Results: The rate of distant metastasis or recurrence was 0.9% (10/1127). Among these 10 cases, 5 cases were developed from depressed-type lesions and one showed a para-aortic lymph node metastasis and four showed a lung metastasis. The rate of submucosal invasion in all the lesions was 72.4% in depressed-type, 3.2% in flat-type and 2.9% in protruded-type. Within less than 5 mm in diameter, that was 10.6%, 0% and 0% respectively. Among T1 carcinomas, the rate of vessel invasion was 64.3% in depressed-type, 34.3% in flat-type and 38.4% in protruded-type. Most of poorly differentiated or mucinous adenocarcinoma was 17.2%, 10.4% and 13.5%, that of massively submucosal invasion was 94.7%, 71.7% and 67.9%, and that of tumor budding was 36.5%, 16.1% and 17.3%, respectively. The rates of these pathological factors were significantly higher in depressed-type lesions. On the other hand, the rate of adenomatous component was 4.9%, 52.2% and 50.8%, respectively. It was significantly lower in depressed-type lesions, suggesting that they emerge directly from normal epithelium, not through the adenomatous stage.

Conclusion: Depressed-type colorectal carcinomas invade massively even when they are small. They had higher risks of vascular invasion, poorly differentiated or mucinous adenocarcinomas, massive invasion and tumor budding than flat- or protruded-type. For their rapid growth and malignant potential, whether the lesion is depressed-type or not is very important in the diagnosis of colorectal carcinomas.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1104 the diagnostic value of hypoxia induced extracellular vesicles in colorectal cancer patient PlasMa

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Introduction: Hypoxia signaling has been found to enhance cancer cell survival, chemoresistance, motility, tumour angiogenesis as well as self-renewal capacity and proliferation of putative cancer stem cells. One of the key player in hypoxia is carbonic anhydrase IX (CAIX) which is a hypoxia-inducible enzyme. CAIX is overexpressed in a variety of cancers including colon cancer and plays a crucial role in maintaining favourable intracellular pH in hypoxia. There is also evidence that extracellular vesicle (EV) production is increased in response to hypoxia and promotes adaptive response of cancer cells and we have previously demonstrated, that CAIX positive EVs secretion is increased in response to hypoxia in colorectal cancer cells.

Aims & Methods: Within this study, we explored a possibility to use CAIX for the isolation of hypoxic EVs from colorectal cancer (CRC) patients’ plasma. EVs were isolated from plasma samples of 27 CRC patients and 25 healthy donors (HD) by using sequential centrifugation, filtration and size-exclusion chromatography steps. EVs where quantified by Nanoparticle tracking analysis (NTA) and CAIX positive EVs where determined by ApoeeaA50.

Results: Statistically significant increase in the amount and size of EVs was observed between CRC and HD cohorts based on NTA data. ApoeeaA50 data revealed that there is a tendency for the percentage of CAIX-positive EVs to increase with the stage of CRC and is higher in stage III-IV CRC patients than in HD. In addition, it is higher in patients with metastases than without distant metastases.

Conclusion: There is an increased total EV number, EV size and CAIX positive EV amount in CRC patient plasma compared to HD plasma, that might have diagnostic and prognostic value. (Financed by Latvian Council of Science and University of Helsinki.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1105 EnDOScopic OBSerVations of microsurFacE struCTures May reflect Molecular subClones in colorectal tuMorS

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Introduction: Recent cancer genome analyses identified extensive genetic intratumoral heterogeneity (ITH), suggesting a Big Bang model in which tumors grow in a Darwinian fashion. ITH may be a key mechanism to maintain tumorigenicity in the presence of genetic/epigenetic stress. ITH of KRAS mutations was frequently observed in colorectal cancers (CRCs), suggesting that these were founder mutations.

Aims and Methods: We aimed to clarify the association between ITH of driver mutations and clinicopathological characteristic in colorectal tumors. A total of 711 specimens from 477 colorectal tumors were analyzed in this study. The specimens were obtained from respective portions. BRAF, KRAS and TP53 mutations were analyzed by pyrosequencing and direct sequencing. Hot spot mutations of 50 cancer related genes were analyzed using the Ion PGM sequencer.

Results: ITH of KRAS and TP53 mutations was frequently observed in colorectal tumors with multiple subclones. Heterogeneity of KRAS or TP53 mutations between early and advanced subcomponents (e.g., KRAS G12D in early portion and KRAS G13D in advanced portion) progressively increased during the progression of colorectal cancer. Genetic analysis with endoscopic, clinical and histopathological data was carried out for 207 patients and 148 CRCs. 52 CRCs (35%) were considered ITH of KRAS or TP53. Up to 6 representative polyp biopsy specimens were collected and stored in a formalin-free medium and finally embedded in paraffin-blocks, followed by histopathological assessment. Targeted Next Generation Sequencing (TNGS) was performed with the extracted DNA from the paraffin-embedded tissue blocks. Up to 10000 reads were generated for each sample. Our studies revealed the existence of subclones in CRCs, and the potential of detecting them using less invasive endoscopy.

Conclusion: Our results demonstrate that the detection of ITH of KRAS/TP53 mutations is critical for the prognosis of colorectal carcinomas. Intratumoral heterogeneity in the microstructure of CRCs may represent molecular subclones in early colorectal lesions and may be predictive of the malignant progression.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1107 The genesis study: Genetic biopsy for prediction of surveillance intervals after endoscopic resection of colonic Polyps

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Introduction: Colorectal cancer (CRC) is an important contributor to cancer mortality and morbidity worldwide. 80% of CRCs arise via the adenoma-carcinoma sequence, 10-20% CRCs by sessile serrated adenomas (SAs). Hyperplastic polyps are regarded harmless. Current surveillance strategies for CRC following polypectomy are determined by endoscopic and histopathological factors. Such a distinction has also been challenged.

Aims & Methods: The study was aimed for molecular characterization of colonic polyps in patients who underwent screening colonoscopy. Correlation of the genetic analysis with endoscopic, clinical and histopathological data was attempted to potentially better define relevant risk marker or sub-groups at risk for prediction of surveillance intervals. 100 Patients were enrolled in this study. Usually no risk patient (TNCT2552) were classified as high grade adenomas (78%; 80% of clusters). Up to 6 representative polyp biopsy specimens were collected and stored in a formalin-free medium and finally embedded in paraffin-blocks, followed by histopathological assessment. Targeted Next Generation Sequencing (TNGS) was performed with the extracted DNA from the paraffin-embedded tissue blocks. Up to 10000 reads were generated for each sample. Our studies revealed the existence of subclones in CRCs, and the potential of detecting them using less invasive endoscopy.

Results: In 100 patients, 234 polyps were removed. 121 polyps (54.0%) were sized <10 mm, 71 (31.7%) were ≥10 mm. For 32 polyps (14.3%) no size was available. 90 polyps (40.2%) were located in the left, 126 polyps (56.3%) in the right colon, for 8 polyps (3.6%) no location was noted. 112 polyps (50.6%) were adenomas and 110 polyps (49.1%) non-adenomatous lesions. No data were available
P1108 QUANTITY, FRAGMENT LENGTH AND GLOBAL DNA METHYLATION LEVEL ALTERATIONS OF CIRCULATING CELL-FREE DNA IN COLORECTAL ADENOMA, CANCER AND INFLAMMATORY BOWEL DISEASES

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Introduction: Cell-free DNA (cfDNA) is circulating in human plasma and its amount is different in certain physical conditions. It is well known, that in healthy people the quantity of cfDNA is very low, but it rises in chronic disorders such as cancer. At the same time, very high cfDNA level can be measured in cancer patients during physical exercise.

Aims & Methods: We aimed to analyze cfDNA changes (quantity, fragment length, global DNA methylation level) in physiological conditions (during physical exercise) and in neoplastic and inflammatory colorectal diseases. Plasma was separated from 64 patients (16 colorectal carcinomas (CRC), 13 colorectal adenomas (AD), 19 inflammatory bowel disease (IBD), and 16 normal (N) donors without evidence of disease). Plasma samples were also collected from 6 healthy athletes before, during and after physical training. cfDNA amount was quantified with Qubit fluorometry (Invitrogen). CfDNA fragment length distribution was assessed by Bioanalyzer 2100 using High Sensitivity DNA assay (Agilent). Global DNA methylation was analysed by bisulfite pyrosequencing of long interspersed nuclear element-1 (LINE-1) (Qiagen).

Results: High cfDNA amounts were observed in plasma samples of patients with colorectal adenoma (20.61 ± 10.70 ng/ml), colorectal cancer (24.13 ± 20.02 ng/ml) and IBD (22.27 ± 14.60 ng/ml) compared to healthy subjects (10.33 ± 3.22 ng/ml). Highly elevated cfDNA amounts were found in plasma samples of patients during physical exercise (66.17 ± 29.00 ng/ml), while the cfDNA amount decreased after physical activity (51.87 ± 39.80 ng/ml).

Conclusion: cfDNA amount is different in certain physical conditions. It is well known, that in healthy people the quantity of cfDNA is very low, but it rises in chronic disorders such as cancer. At the same time, very high cfDNA level can be measured in cancer patients during physical exercise.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

P1110 URINE-NMR METABOLOMICS FOR SCREENING OF ADVANCED COLORECTAL ADENOMA AND EARLY STAGE COLORECTAL CANCER


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Introduction: A dynamic portrait of the metabolic status of living systems, has demonstrated its great potential for use in the diagnosis of various cancers by applying advanced analytic techniques and bioinformatics tools. Recently, very few metabolic markers in CRC have been consistently discovered, but metabolic profiling of patients with CRC including precancerous lesion in colorectum remains poorly understood and warrants investigation due to its non-invasive sampling method.

In this study, we investigate the differences in urine metabolic profiles between patients with colorectal neoplasia (CRN) including CRC and precancerous lesion, and healthy volunteers using a NMR-based urine metabolic study. Moreover, we evaluate applicability as diagnostic tool of urine metabolomics for early detection of precancerous colorectal lesion with high sensitivity and specificity. Urine metabolic profiles of patients with colorectal neoplasia were analyzed by NMR spectroscopy, which has several advantages including reliable degree of reproducibility, easy-to-identify metabolites, high throughput output, and non-destructive sample treatment, has not been applied to urine samples.

Aims & Methods: In this study, we investigate the differences in urine metabolic profiles between patients with colorectal neoplasia (CRN) including CRC and precancerous lesion, and healthy volunteers using a NMR-based urine metabolic study. In addition, we evaluate applicability as diagnostic tool of urine metabolomics for early detection of precancerous colorectal lesion with high sensitivity and specificity. Urine metabolic profiles of patients with colorectal neoplasia were analyzed by NMR spectroscopy, which has several advantages including reliable degree of reproducibility, easy-to-identify metabolites, high throughput output, and non-destructive sample treatment, has not been applied to urine samples.

Results: After patients underwent endoscopic resection or surgical resection for CRC, advanced adenoma has been diagnosed in 36 patients, stage O CRC in 24 patients, stage I CRC in 8 patients, stage II CRC in 7 patients, stage III CRC in 13 patients and stage IV CRC in 4 patients. CEÁ and CA 19-9 levels for patient with stage I to IV CRC and healthy control were also assessed. Among patients with CRC stage I to IV CRC, CA 19-9 were increased in 19/24 (80%) patients and healthy individuals with 9/10 (90%) respectively. The sensitivity and specificity of CA and CA 19-9 were 6.2% and 99.3%.

Conclusion: The OPLS-DA model was validated by cross-validation and the predictions model indicated statistically significant difference between pre-invasive CRC as well as advanced CRC and normal with a Q2 value of 0.71. Furthermore, the prediction validation study, the sensitivity and specificity for diagnosing pre-invasive CRC was 96.2% and 95%, respectively. The grades predicted by the PLS-DA model showed that area under the curve was 0.823 for taurine, 0.783 for alanine and 0.842 for 3-aminoisobutyrate. In multiple receiver operating characteristics curves analyses, taurine, alanine, and 3-aminoisobutyrate were good discriminator for CRC patients.

Disclosure of Interest: NMR-based urine metabolic profiles significantly and accurately discriminate between patients with pre-invasive CRC as well as CRC.
advanced CRC, and healthy control with high accuracy. It demonstrates an applicability of urinary SMRT metabolomics as screening tool for accurate diagnosis of pre-invasive CRC.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P1111 VALIDATION OF THE USE OF A FAEAL IMMUNOCHEMICAL TEST FOR HEMOGLOBIN (FIT) IN PATIENTS PRESENTING TO PRIMARY CARE WITH NEW BOWEL SYMPTOMS

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Introduction: Symptoms alone are poor predictors of underlying colorectal pathology. Only 14% of patients referred for colonoscopy from primary care have significant bowel disease (SBD), colorectal cancer (CRC), high risk adenoma (HRA, defined as ≥3 or any ≥1 cm) and inflammatory bowel disease (IBD). We have reported that undetectable faecal haemoglobin (f-Hb), measured by a faecal immunochromatographic test (FIT) is a good rule-out test for SBD.1,2 Since December 2015, GPs in Tayside have been encouraged to use FIT test as an adjunct to history, examination and mandatory blood tests in patients referred with bowel symptoms. Referrals are vetted by a Consultant and triaged to test or clinic. We have examined the impact of the introduction of the FIT test on referral rates and colonoscopy yield.

Aims & Methods: Patients in primary care with new bowel symptoms were encouraged to complete a FIT in addition to blood count and renal function check. We prospectively recorded FIT tests received, referrals to secondary care and colonoscopy findings over 1 year from December 2015 to December 2016. FIT tests were analysed by HMJACKarc (Kyowa Medex Co. Ltd., Japan) with an analytic range of <10 to >400µg Hb/g faeces. Referral rates with FIT were examined along with clinical findings at colonoscopy.

Results: 5,655 FIT tests were received. 76.2% had undetectable f-Hb, and 152 (2.7%) were untestable. 4,108 patients were referred of whom 2,338 (57%) returned a FIT. In 1,378 patients with a FIT result vetted to colonoscopy, 284 had SBD (20.6%); 86 CRC, 124 HRA and 74 IBD. 44% of patients examined along with clinical findings at colonoscopy. We prospectively recorded FIT tests received, referrals to secondary care and colonoscopy findings over 1 year from December 2015 to December 2016. FIT tests were analysed by HMJACKarc (Kyowa Medex Co. Ltd., Japan) with an analytic range of <10 to >400µg Hb/g faeces. Referral rates with FIT were examined along with clinical findings at colonoscopy.

Conclusion: A FIT test is an essential adjunct to the history, examination and blood tests in the assessment of bowel symptoms. Undetectable f-Hb is reassuring Primary Care that SBD is unlikely and referrals to secondary care have reduced. At colonoscopy, yield of SBD has increased and is high in those with detectable f-Hb. Excluding patients with co-existing anaemia or diarrhoea, an undetectable f-Hb is a good rule-out test and will miss only 5% of all SBD. Furthermore, f-Hb concentration could aid triage irrespective of symptoms.

Disclosure of Interest: C.G. Fraser: Prof. Callum Fraser has undertaken consultancy with Immunometrics, Ocean, New Jersey, USA; Mode Diagnostics, Glasgow, Scotland; and Kyowa-Medex Co., Tokyo, Japan: and has received travel support from Alpha Labs, Eastleigh, UK. All other authors have declared no conflicts of interest.

References

P1113 ARTIFICIAL INTELLIGENCE CAN PREDICT THE PRESENCE OF LYMPH NODE METASTASIS IN T1 COLORECTAL CANCER

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Introduction: Most T1 colorectal cancers (CRCs) undergo surgical colectomy in western countries with established clinical guidelines despite the low incidence (approximately 10%) of lymph node metastasis (LNM). Therefore, many patients without LNM undergo unnecessary surgeries.

Aims & Methods: To reduce unnecessary surgeries, we aimed to predict the risk of LNM in T1 CRCs by using artificial intelligence (AI). Data on 690 consecutive patients with T1 CRCs who had undergone colectomy between April 2001 and March 2016 were retrospectively analyzed. Data of a randomly selected 590 patients were used for machine learning for the AI model, which analyzed five clinicopathological factors: tumor location, lymphatic invasion, vascular invasion, tumor budding and histological invasion. The remaining 100 patients served as a test set for validating the AI model and output the predicted LNM as positive or negative. To validate the AI model, sensitivity, specificity and
accuracy and calculated and compared with American, European and Japanese guidelines (1–5).

**Results:** Sensitivity was 100% (95% CI, 56%–100%) in all models. Specificity and accuracy of the AI model, American, European and Japanese guidelines were 68% (58%–78%) vs. 45% (35%–56%) vs. 12% (6%–21%) vs. 8% (3%–13%) and 71% (61%–80%) vs. 50% (40%–60%) vs. 20% (13%–29%) vs. 16% (9%–25%), respectively. The rate of unnecessary surgeries of the AI model was calculated as 29% in comparison with American 50% (P = 0.004, odds ratio [OR] 2), European 80% (P = 0.001, OR 10), and Japanese 84% (P = 0.001, OR 13).

Conclusively removing unnecessary surgeries compared with current guidelines while providing high sensitivity. AI will help in making decisions as to whether additional surgery is indicated after endoscopic resection of T1 CRCs. Grant support: Grants-in-Aid for Scientific Research (Number 17K1972) from the Japan Society for the Promotion of Science.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**References**


3.65% were superficial submucosal carcinomas (<1000μm). During UEMR, two cases (both using AUTOCUT mode) of spurting bleeding were observed (4.45%). Hemostasis was easily achieved in both cases by dipping. No patient required blood transfusion. One patient had abdominal pain on the day after resection without signs of pneumatoperitoneum on CT scan. There was no perforation or delayed bleeding.

Conclusion: This study supports the existing data indicating acceptable rates of technical success and low incidence of adverse events with UEMR. The results of this study without cup were similar with the previous ones using cup. Further comparative studies with and without cup, using different settings and especially between UEMR and traditional EMR are needed.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P1117 ADENOMA DETECTION RATE INFLUENCES RISK PREDICTION OF METACHRONOUS ADVANCED COLORECTAL NEOPLASIA IN LOW-RISK PATIENTS

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Introduction: Current guidelines recommend surveillance colonoscopy after 10 years or surveillance in 5-10 years in individuals with no or 1-2 non-advanced adenomas.

Aims & Methods: We hypothesized that risk of metachronous advanced colorectal neoplasia varies based on clinical characteristics and colonoscopy quality. We identified 7,171 participants with no or non-advanced adenomas at first-time screening colonoscopy. The risk of metachronous AN at surveillance colonoscopy 3-5 years later was investigated according to clinical characteristics and endoscopist adenoma detection rate (ADR).

Results: In multivariate analyses, strong associations between increasing age, male sex, current smoking, family history of colorectal cancer, follow-up interval, increasing number of adenoma, and low ADR and risk of any metachronous colorectal neoplasia were observed. For metachronous AN, increasing age, male sex, increasing number of adenoma, and low ADR were independent risk factors. Among patients with 1-2 small adenomas, women with age ≥60 years or men comprised a hidden-risk group, which had 5.3% risk of metachronous AN at surveillance. Women <60 years old with 1-2 low-risk adenomas had very low risk (1.2%) of metachronous AN as individuals with no adenoma. Furthermore, incidence of metachronous AN was significantly higher in individuals who were considered cured after endoscopic ADRE (<32%) than in those screened by endoscopists with a higher ADR (≥32%) (3.2% vs. 0.6%, respectively; P=0.001).

Conclusion: According to patient and adenoma characteristics, and ADR of the endoscopist, the risk of metachronous AN varies among low-risk patients. In recommending surveillance colonoscopy, these factors should be taken into consideration.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P1118 EXPERIENCE OF PER ANAL ENDOSCOPIC MYECTOMY (PAEM)

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Introduction: The technique of endoscopic submucosal dissection has recently been improved, and large and complexed lesions such as those invading ileocecal valve and appendix orifice can be resected en bloc. However, lesions accompanying severe fibrosis in the submucosal layer and exhibiting the muscle retraction (MR) sign are often difficult to be resected completely. We devised a new method called ‘Per Anal Endoscopic Myectomy’ for such lesions involving severe fibrosis, in which dissection is done between the inner circular and outer longitudinal muscles instead of between submucosal layer and muscle layer.

Aims & Methods: The aim of this study is to examine the usefulness and safety of PAEM. PAEM cases performed in our hospital and an affiliated hospital were retrospectively reviewed. When fibrosis in the submucosal layer was suspected, pocket creation method was applied and if severe fibrosis with MR sign was found, PAEM was selected. In PAEM procedure, after dissecting circumferentially around the fibrotic area with a double tunneling method, the inner circular muscle is cut in a circular manner, which makes the outer longitudinal muscle clearly visible. The space between the inner circular and outer longitudinal muscles is sparse and suitable traction with the tunneling method makes it easier to dissect this space. PAEM was performed only for rectal lesions, and no clip closure was carried out after the procedure in most cases.

Results: Ten rectal lesions were treated with PAEM between July 2015 and March 2017. Among them, 7 cases including 2 cases with mucosal cancer, 4 cases with submucosal invasion, and 1 case with deep submucosal invasion were resected en bloc with negative margin. The other 3 cases showed tumor invasion to the muscle layer and the vertical margin was positive. The clinical course after PAEM was preferable in all cases. Three cases which achieved resection with negative margin but found lymphovascular invasion of the tumor underwent additional surgery or adjuvant chemoradiation. In surgical cases, they could permit anus-preservation.

Conclusion: PAEM for lesions exhibiting MR sign with severe fibrosis will enable complete ganglion en bloc resection and make accurate pathological diagnosis. No complications were recorded in our experiences. Further investigation into the significance of PAEM would be needed.

Disclosure of Interest: T. Toyonaga: Dr. Toyonaga invented the Flush knife-BT in conjunction with Fujifilm, and received royalties from its sale. All other authors have declared no conflicts of interest.

References

P1119 LOCAL RECURRENCE AFTER ENDOSCOPIC MUCOSAL RESECTION FOR HIGH-RISK LESIONS: MAY WE BETTER PLAN THE ENDOSCOPIC FOLLOW-UP ACCORDING TO PROCEDURAL, TECHNICAL AND HISTOPATHOLOGICAL CHARACTERISTICS?
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Introduction: Endoscopic mucosal resection (EMR) is an increasingly used technique for the removal of large sessile and flat-laterally-spreading colorectal lesions. At present, surveillance colonoscopies are ever performed to ensure detection and adequate treatment of residual or recurrent adenoma (RA), which, occurring in 10–40% of non-pedunculated lesions, currently represents the main limitation of this technique. Fortunately, endoscopic detection of RAs in the post EMR scar is currently highly accurate using HD-WL (high definition-white light) and NBI (narrow band imaging). Anyway, indications for follow-up
colonicoscopy and optimal time intervals are currently unclear. An adequate United European Gastroenterology Journal 5(5S) A557

P1020 TREATMENT STRATEGY FOR LOCAL RECURRENCES AFTER ENDOSCOPIC RESSECTION OF COLORECTAL NEOPLASMS

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Introduction: Local recurrences after endoscopic resection (ER) frequently occur, and recently, the efficacy of EMR appears lower than that of ESD, especially for lesions of low or high grade dysplasia. We conducted a series of five retrospective studies encompassing 400 patients treated with EMR or ESD. In this study, we present the findings from a single center, prospective, randomized, un-blinded, non-comparative study to determine the optimal treatment strategy for local colorectal neoplasms.

Aims & Methods: The study was designed to compare the efficacy of EMR and ESD for local recurrences of colorectal neoplasms. The primary endpoints were complete response rate (CRR) and local recurrence-free survival (LRFS) at 1 year.

Results: 60 patients were enrolled (30 EMR, 30 ESD). The median age was 69 years (range: 33-85) and the median tumor size was 22 mm (range: 5-70). The median follow-up time was 13 months (range: 1-36). The local recurrence rate was 7% in the EMR group and 13% in the ESD group. The CRR at 1 year was 93% in the EMR group and 87% in the ESD group. The LRFS at 1 year was 100% in the EMR group and 94% in the ESD group.

Conclusion: EMR is an effective and safe treatment for local recurrences of colorectal neoplasms. However, ESD may be necessary for lesions with higher risk of recurrence.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

PI121 A COMPARATIVE STUDY OF EFFICACY OF CHEMOTHERAPY AFTER ENDOSCOPIC COLONIC STENTING VS. THAT AFTER COLORECTAL SURGERY IN THE MANAGEMENT OF OBSTRUCTIVE COLORECTAL CANCER
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Introduction: Endoscopic stent placement in acute large-bowel obstruction due to colorectal cancer has been established as a palliative therapy or bridge to surgery with good outcomes in Japan. While, efficacy of chemotherapy after endoscopic colon stenting has not been evaluated. This study is a prospective, multicenter study evaluating the efficacy of chemotherapy after endoscopic colon stenting for local recurrences.

Aims & Methods: The aim of this study was to evaluate efficacy of chemotherapy after endoscopic colon stenting by comparing with that after surgery. Sixty five patients with colorectal cancer of stage IV presenting obstructive symptom visit our hospital from January 2012 to December 2016 were classified into SC group who have underwent chemotherapy after endoscopic colon stenting (32 patients) and OC group who have undergone chemotheraphy after surgery (25 patients). The patients’ background, adverse effects of chemotherapy and 3 months survival were compared between groups.

Results: There have not been any significant differences in patient age (65.5 ± 9.3 in SC vs. 61.5 ± 14.1 in OC, p = 0.21), male to female ratio (25:7 in SC vs. 14:9 in OC, p = 0.16) and performance status (0.6 ± 0.7 in SC vs. 0.7 ± 0.8 in OC, p = 0.66). The average colorectal obstruction scoring system (0, requiring continuous decompressive procedure; 1, No oral intake; 2, Liquid or enteral nutrition; 3, Soft solids, low-residue, and full diet with symptoms of strictures; 4, Soft solids, low-residue, and full diet without symptoms of strictures) score was significantly severe in OC (1.7 ± 1.1) than in SC (0.7 ± 0.9, p = 0.01). Adverse effects included perforation (1), stent slippage (6), re-obstruction by tumor progression (3) in SC, and ileus (1), abdominal abscess (1), renal insufficiency (1) in OC. The frequency of combined use of molecular target drugs (Beverazumab/Pantitumab/ Cetuximab) at first chemotherapy has significantly differed (p < 0.01) between SC (0.11/9) and OC (12/40). The median survival day was not significantly different between SC (595) and OC (459, p = 0.93). In SC, survival was found significantly longer with additional surgery (913, n = 13) than without (325, n = 19, p < 0.01). In OC, survival did not significantly differ between with resection of the primary tumor (666, n = 16) and without (595, n = 7, p = 0.93).

Conclusion: This study has demonstrated that the survival of SC was identical to that of OC, and additional surgery was found to significantly improve the prognosis in SC. Chemotherapy after endoscopic colon stenting was considered tolerable as a palliative therapy or bridge to surgery for obstructive colorectal cancer.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference
Cetuximab) at first chemotherapy has significantly differed (p < 0.01) between SC (0.11/9) and OC (12/40). The median survival day was not significantly different between SC (595) and OC (459, p = 0.93). In SC, survival was found significantly longer with additional surgery (913, n = 13) than without (325, n = 19, p < 0.01). In OC, survival did not significantly differ between with resection of the primary tumor (666, n = 16) and without (595, n = 7, p = 0.93).

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Conclusion: This study has demonstrated that the survival of SC was identical to that of OC, and additional surgery was found to significantly improve the prognosis in SC. Chemotherapy after endoscopic colon stenting was considered tolerable as a palliative therapy or bridge to surgery for obstructive colorectal cancer.

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Disclosure of Interest: All authors have declared no conflicts of interest.

Reference
delivery system passage (e.g. Niti-S Colon Stent, Taewoong-Medical, Seoul, South Korea) or when a guidewire was unable to be passed through the stricture because of limited maneuverability of the endoscope, procedures below were followed. (1) A thinner scope, PCF-PQ260L, with a 2.9 mm tip and a 2.8 mm channel (Olympus Medical Systems, Tokyo, Japan) is inserted and advanced to the stricture, facilitated by its “passive bending” feature. An ultrathin endoscope (for transnasal use) or a gastroscope are alternatives. (2) A guidewire (GW, 0.035 inch Jagwire) is traversed through the stricture by coordinating manipulation of an ERCP-catheter (Article-No.0130211; MTW Endoskopie, Wesel, Germany). (3) Fluoroscent examination through the catheter to delineate the lesion. (4) For colonoscopy replacement, withdraw the scope and the catheter, leaving only GW. (5) Before reinserstion of the SCC, insert the catheter from the channel until it sticks out of the scope tip. (6) Pass GW backward into the catheter tip. Then move the catheter over GW and advance it further to connect with another catheter tip. (7) Gently move the SCC ("over the catheter") into the rectum and advance it in the more straightened (less winding) intestine. (8) After the colonoscope is advanced only as proximally as possible, shift to a standard TTS maneuver (withdraw only the catheter, leaving GW and insert the SEMS delivery along GW past the stricture where it is deployed). Results: See table. Conclusion: AOver-the-catheter9 colonoscope replacement (OTC-CR) technique can be a Salvage maneuver which facilitates a successful SEMS placement in MRO cases with peritoneal disseminations that preclude a conventional TTS procedure. Readiness of thin endoscopes and appropriate rigidity and force transmissibility of an ERCP-catheter that enable advancement of an SCC with maximum safety are thought to be linked to reduced chances of technical failures. Disclosure of Interest: All authors have declared no conflicts of interest. References 1. Japanese Colon Stent Safe Procedure Research Group (http://colon-stent.- com/001_mainpage_en.html) 266, F Sigmoid colon Sigmoid colon Intrinsic PCF-PQ260L Close Success/Success 2 66, F Sigmoid colon Sigmoid colon Intrinsinc PCF-PQ260L Close Success/Success 3 76, M Pancrease Sigmoid colon Extrinsic PCF-PQ260L Away SCJ Close Success/Success 4 41, F Transverse colon (resected) Sigmoid colon Sigmoid colon Extrinsic GIF-Q260J Close Success/Success 5 55, F Ovary Sigmoid colon Extrinsic EG-580NW Away Success/Success 6 49, F Stomach Transvers colon Extrinsic PCF-PQ260L Close Success/Success 0 – 3 3 CROSS, ColorOlo Obstruction Scoring System (Reference 1) Among 63 pulliative MCO cases, initial attempt to place a 22 mm SEMS by TTS procedure was unsuccessful in 6 cases (Table), all of whom had peritoneal dissemination. The reasons for technical failures were; impossible insertion of an SCC to the stricture due to carcinomatous adhesions or narrowing in 5 cases and failure in passing GW through the stenosis due to a limited viewing angle to the stricture in one case. With OTC-CR, approach to the main stenosis with a thinner (alternative) scope, GW traverse, "over-the-catheter" replacement to the SCC, and a 22 mm SEMS placement were successful in all of the 6 cases with adequate clinical improvements (CROSS score change). Notably, ultimate TTS procedures were possible from reinserted SCC distant from the stricture in 3 cases. No adverse events occurred during the procedures.

P1123 RESULT OF THE FIRST ROUND OF THE COLORECTAL CANCER SCREENING PROGRAMME IN THE BALEARIC ISLANDS (SPAIN) M. Florido1, M. Novellsa2, M. Heredía2, E. Miro3, C. Sanchez-Contador4, J. Gelabert1, S.P. Ortega1, J. Reyes1, P. Garcia-Cortes3, J.A. Lucero2, Z. Salman2, C. Rodrigueza2, A. Rua2, M.J. Garcia2 1Gastroenterology, Hospital Comarcal de Inca, Inca/Spain 2Gastroenterology, Hospital Can Misses, Ibiza/Spain 3Gastroenterology, Hospital Mateu Orfila, Mahon/Spain 4Dirección General De Salud Publica I Participación, Conselleria de Sanitat, Palma/Spain Contact Email Address: monica.florido@hcm.es Introduction: Colorectal cancer (CRC) is the most common cause of cancer in western countries. In Balearic Islands 700 new cases per year are diagnosed. The cost-effectiveness of CRC screening programmes are clearly demonstrated in the studies and the important public health problem of CRC justifies the development of control strategies. The aim of this study is to present the results and impact during the first round of the program in Balearic Islands. Aims & Methods: The first round includes the period from January 2015 through December 2016. The program has been developed in the areas of Menorca, Ibiza, Formentera and Tramuntana (Majorca), including 50% of the Balearic Islands population. The target population (people who reside in these areas aged between 50 and 69 years old) was 75,757 individuals. Exclusion criteria. Colonscopy performed in the previous 5 years, previous diagnosis of CRC, follow-up colorectal cancers because colon disease and severe illness-contraindication for the participation. People received the invitation by letter. Quantitative immunochromatographic occult fecal blood testing (i-FOBT/OC-Sensor) was the screening method. The kit was delivered at pharmacies joined the program. The samples were deposited in urns placed in health centres. Participants who tested positive (≥100 ng/ml) were referred to pre-endoscopy evaluation and follow-up colonscopy. The colonoscopies were performed according to the quality criteria of guidelines. Results: Overall participation rate (number of people who provide their i-FOBT sample) was 36.5% (n = 21,555). Positive rate of i-FOBT was 7% (1438) and 94.3% of those positive tests underwent a colonoscopy (5.7% of exclusions in pre-endoscopy evaluation). 996 colonoscopies were performed. 47 adenomas with high grade dysplasia, 24 carcinomas in situ and 6 adenocarcinomas were found. Only 19% of these adenocarcinomas were T3 or T4 lesions while the rest presented earlier stages. 26% of colonoscopies were classified as high risk (≥5 adenomas or at least one ≥20mm). They have been reported 2 cases of colon perforations, both resolved by endoscopic treatment. Conclusion: We observed an acceptable participation rate in the first round of the colorectal cancer screening programme of the Balearic Islands. The index of positivity rate of i-FOBT and the results of the endoscopic explorations are according with the observed in other colorectal cancer screening programmes. We can conclude a successful development of the first round of the programme in our area. Disclosure of Interest: All authors have declared no conflicts of interest. References Segnan N, Patnick J, von Karsa L, et al., editors. European guidelines for quality assurance in colorectal cancer screening and diagnosis. First edition. Luxembourg: European Commission, Publications Office of the European Union; 2010. Kaminski MF, Wieszyc P, Rupinski M, Wojciechowska U, Didkowska J, Kraszewsk a E, Kobielu J, Franzczyk R, Rupinska M, Kocot B, Chaber-Ciopinska A, Puchlewski J, Polkowski M, Regula J. Gastroenterology. 2017 Apr 17. pii: S0016–5085(17)35441–0. doi: 10.1053/j.gastro.2017.04.006.
Aims & Methods: Thirty Thai IBS patients, and age and sex matched 20 Thai controls were included. Four biopsy samples were taken from each of the sigmoid colon and the rectum during a standard colonoscopy. Sections from these biopsy samples were immunostained for serotonin, peptide YY, oxyntomodulin (enteroglucagon), pancreatic polypeptide, somatostatin, Msi 1, and neurogh 3. The densities of immunoreactive cells were determined with computerized image analysis (1).

Results: In both the colon and rectum, the density of serotonin cells was lower in IBS patients than controls. Whereas the density of PYY cells was increased in both the colon and rectum of IBS-D, it was reduced in IBS-M and IBS-C. The density of oxyntomodulin cells was reduced in both the colon and rectum of all IBS subtypes. While the density of PP cells was unaffected in the colon, it was reduced in the rectum. Somatostatin cell density was unaffected in both the colon and rectum. The densities of Msi 1 and neurogh 3 were unchanged in both the colon and rectum.

Conclusion: The present findings of abnormal densities of the large-intestine enteroendocrine cells in Thai patients combined with previously reported changes in Western IBS patients (2) support the notion that intestinal enteroendocrine cells are involved in the pathophysiology of IBS. However, the changes in the enteroendocrine cells differed from those in Western patients. The present observations highlight that IBS differs in Asian and Western countries, and show that the changes in large-intestine enteroendocrine cells in Asian and Western IBS patients might be caused by different mechanisms.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P1126 SUBJECT GLOBAL SATISFACTION SCORE TO ASSESS OVERALL EFFECT OF NALDEMEDINE COMPARED WITH PLACEBO ON CONSTIPATION AND ABDOMINAL SYMPTOMS IN SUBJECTS WITH CHRONIC NON-CANCER PAIN AND OPIOID-INDUCED CONSTIPATION

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Introduction: Opioid-induced constipation (OIC) is a common side effect of opioid therapy that significantly affects multiple aspects of a patient’s life. Naldeemedine (NAL) is a peripherally-acting mu-opioid receptor antagonist developed for the treatment of OIC. In Phase 3 studies, NAL improved the frequency of spontaneous bowel movements, straining, consistency of stools, and patient assessment of constipation symptoms (PAC-QOL) and quality of life (PAC-QOL), measures of patient’s quality of life, compared with placebo (PBO). The aim of this analysis is to assess the impact of NAL on overall satisfaction and to show if a simple score can assess the impact of treatment of OIC with NAL 0.2 mg once daily on patient’s satisfaction with constipation and abdominal symptoms at the last study visit. The number and proportion of subjects in each grade were calculated and the overall difference between groups was assessed by Wilcoxon rank sum test. The mean subject global satisfaction score (SGSS) was also compared between groups. For SGSS scores, from 1 to 7 were replaced with scores from 1 to 7.

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<th>Score</th>
<th>Global satisfaction category, n (%)</th>
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<td>1</td>
<td>Markedly improved (7)</td>
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<tr>
<td>2</td>
<td>Markedly improved (6)</td>
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<td>7</td>
<td>Markedly worsened (1)</td>
</tr>
</tbody>
</table>

P-value between groups* 0.0005 < 0.0001 < 0.0001

*Wilcoxon rank sum test

Conclusion: Treatment of OIC with NAL 0.2 mg once daily for 12 or 52 weeks led to greater satisfaction with constipation and abdominal symptoms compared with PBO, consistent with previously-reported improvements of PAC-SYM and PAC-QOL with NAL compared with PBO. The proposed SGSS appears to be a simple way to assess the impact on quality of life of OIC treatment.


P1127 IBEROGAST PREVENTS CHANGES IN INTESTINAL PERMEABILITY INDUCED BY PSYCHOLOGICAL STRESS IN MICE

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Introduction: The herbal preparation STW 5 has been reported to increase intestinal chloride secretion. However, the ability of STW 5 to modulate paracellular and transcellular permeability remains currently unknown. Therefore, we aimed to...
to study the ability of STW 5 to modulate intestinal permeability under basal and regional stress conditions.

Aims & Methods: C57 bl6 mice were gavaged for 14 days with STW 5 (3 mL/kg). After 10 days of treatment, mice were subjected to water avoidance stress (WAS) for 4 consecutive days. In vivo permeability to FITC–Sulfonic Acid (FSA, 400 Da) and Horse Radish Peroxydase (HRP, 44KDa), total transit time and colonic transit (fecal pellet output - FPO) were assessed at Day 0 (D0), D10 and D14 of IB treatment. Ex vivo permeability to FSA and HRP was assessed on jejunum, ileum, proximal colon and distal colon at D14 using Ussing chambers. Corticosterone blood level was measured at D10 and D14.

Results: In vivo permeability to FSA and HRP as well as total transit time were not modified by STW 5 in basal and WAS conditions. However, STW 5 prevented the increase in permeability to HRP induced by WAS in the jejunal and proximal colon. Furthermore, while STW 5 tended to increase colonic transit as compared to control in basal conditions, it prevented the increase in transit induced by WAS. Finally, STW 5 did not modify the corticosterone induced by WAS.

Conclusion: Our study suggest that STW 5 can prevent WAS induced changes in paracellular and transcellular permeability in specific regions of the gastrointestinal tract. Such effects could contribute to the therapeutic effects of STW 5 in irritable bowel syndrome and support novel therapeutic indications for pathologies in which barrier functions are altered.

Disclosure of Interest: O. Kelber: Olaf Kelber is employed by Bayer H. Abdel-Aziz: Heba Abdel aziz is employed by Bayer M. Neunlist: This work was supported by a research grant to MN by Bayer All other authors have declared no conflicts of interest.

P1129 ALTERING SPHINGOSINE-1-PHOSPHATE WITH AGING INDUCES MOTILITY DYSFUNCTION OF COLON SMOOTH MUSCLE BY BKCA UPRREGULATION IN RATS

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Introduction: Large conductance Ca2+-activated K+ channel (BKCa channel) was shown to play critical roles in regulating smooth muscle contractility by modulating membrane potential, at the same time, age-associated changes in BKCa expression may contribute to the development of motility disorders of the gastrointestinal tract. Sphingosine-1-Phosphate (SIP), component of Sphingolipids in the cell membranes, may affect BKCa expression. Thus, in this study, we investigated whether altered SIP due to aging may affect the motility of colon smooth muscle (CSM) in rats.

Aims & Methods: Thus, in this study, we investigated whether altered SIP due to aging may affect the motility of colon smooth muscle (CSM)in rats. Forty Sprague-Dawley rats at the same age were randomly divided into five groups. After different times of administration, finally they were divided into different-age group: 10-week group, 20-week group, 40-week group, 60-week group and 80-week group. Colon motility function and contractility of circular muscle strips were measured. The expression of BKCa and phosphorylated myosin light chain (P-MLC) level were tested in colon tissues of rats with varying ages by immunohistochemical, RT-PCR and western blot. SIP levels in colon tissues were tested by LC-MS/MS analysis. Primary cultured colon smooth muscle cells (SMCs) from normal adult rats were used in complementary in vitro studies. In the absence and presence of SIP with different concentrations, the expression of BKCa, P-MLC level, single-channel activity, intracellular Ca2+ mobilization were tested. At the same time, in the presence and absence of SIP, SMCs were transfected with anti-SIP antibody. BKCa siRNA transfection was used to investigate whether P-MLC expression and intracellular Ca2+ mobilization were affected by BKCa expression in SMCs. The expression and phosphorylation of Akt, JNK, ERK, NFKb, and PKC were examined by western blot analysis to investigate the effect between SIP and BKCa.

Results: Aged rats showed prolonged colonic transit time and weakness of circular muscle contraction compared with the young (10 weeks old) SD rats. LC-MS/MS analysis exhibited that the levels of SIP were significantly higher in the CSM from aged rats, demonstrating that SIP varies depending on age. BKCa (α-subunit and β-subunit) levels in CSM were shown to increase in an age-dependent manner from 10- to 80-week-old rats by mRNA, protein and immunohistochemical, but P-MLC expression decreased. In colon SMCs by BKCa siRNA transfection, we found P-MLC levels increased. Exogenously added SIP upregulated BKCa in colon SMCs in a concentration-dependent manner. Circular muscle Ca2+ mobilization through inhibiting SIP and induced the decline of P-MLC. Our results also proved that SIP upregulated BKCa through the Akt/ERK/JNK pathways. The expression of BKCa decreased by treatment with inhibitor of Akt/ERK/JNK pathways or siRNA.

Conclusion: The results of our study show that altered SIP due to aging upregulates BKCa via the Akt/ERK/JNK mediated pathway in CSM. BKCa upregulation inhibits Ca2+ influx and MLC phosphorylation and thereby reduces the contractile force characterized by the contractile force. These findings represent the first evidence for the mechanism of the contractile dysfunction of CSM observed in older individuals, which may be implicated in age-associated gastrointestinal motility disorders.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P1130 DIABETES-RELATED ALTERATIONS IN THE EXPRESSION OF THE INFLAMMATORY CYTOKINES, TUMOR NECROSIS FACTOR ALPHA AND INTERLEUKIN 6 IN THE MYENTERIC GANGLIA AND ITS MICROENVIRONMENT OF DIFFERENT INTESTINAL SEGMENTS

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Introduction: Growing amount of evidence has indicated that increase of the hyperglycaemia-induced oxidative stress and decreased effectiveness of the endogenous antioxidant protection play the major role in the initiation of diabetes-related neuronal damage. Using a streptozotocin-induced diabetic rat model we recently demonstrated that nitricergic neuronal, which are key regulators of peristalsis, display different susceptibilities to diabetic damage and also to treatments in the distal part of the gastrointestinal tract. On these results we suggested the importance of the molecular differences in the microenvironment in the pathogenesis of diabetic nitricergic neuropathy.

Aims & Methods: Aim to reveal the quantitative differences in the expression of the pro-inflammatory cytokines like tumor necrosis factor alpha (TNFα) and interleukin 6 (IL6) in the myenteric ganglia and its microenvironment of the different intestinal segments, quantitative immunogold electron microscopy was used. Ten weeks after the onset of diabetes, segments from the duodenum, ileum and colon of diabetic and control rats were processed for post-embedding immunohistochemistry.

Results: The density of TNFα- and IL6-labeling gold particles was strictly region-dependent, with increasing to the distal part of the gastrointestinal tract of diabetic rats, the number of TNFα gold particles was significantly increased in the duodenal, decreased in the colonic myenteric ganglia, while did not show any significant differences in the ileal ganglia. The number of IL6 gold particles was not affected by diabetes in the myenteric ganglia of different gut regions. The diabetes-related alterations of TNFα- and IL6 expression were not protected by the immediate insulin replacement in any of the investigated intestinal segments. The differences in TNFα- and IL6 density were not significant in the capillary endothelium under different experimental conditions.

Conclusion: Based on these findings we presume that regionally alterations in the TNFα and IL6 expression are correlated with the diabetes-related region-specific nitricergic myenteric neuropathy.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P1131 ROLE OF SEMAPHORIN 3A IN THE POSTNATAL DEVELOPMENT OF THE ENTERIC NERVOUS SYSTEM

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Introduction: Critical developmental stages of the enteric nervous system (ENS) occur during the postnatal period leading to the formation of a mature neuronal network characterized by the assembly of enteric neurons into ganglia and the formation of a highly organized pattern of neuronal connectivity. However, the mechanisms underlying these maturation processes are poorly understood. Semaphorin 3A (SEMA3A) is a secreted protein playing key roles in the neuronal microenvironment of the central nervous system. Here, we studied the expres sion, the cellular distribution and the role of SEMA3A and its receptor neuroglian 1 (NRPI) in the maturation of enteric neurons.
Aims & Methods: Gene and protein expression of SEMA3A and its receptor NRP1 were analyzed in distal colon tissue by immunohistochemistry on day 1 (PN1) and day 3 (PN3) using specific antibodies. The impact of SEMA3A on neuronal outgrowth was assessed in cultures of enteric nerve cells cocultured with SEMA3A-transfected COS-7 cells.

Results: A peak of mRNA expression for SEMA3A and NRP1 was observed in neurons cocultured with SEMA3A-transfected COS-7 cells. The impact of SEMA3A on neuronal outgrowth was assessed in cultures of enteric nerve cells cocultured with SEMA3A-transfected COS-7 cells.

Conclusion: This study shows the expression of SEMA3A and its receptor NRP1 in the ENS during early postnatal period. Immunohistochemistry of colon tissue indicated that SEMA3A immunoreactivity was not associated with any specific cellular profile, but was distributed in small clusters disseminated throughout the tissue, a pattern consistent for a secreted protein. NRP1 was found in neurons, mainly associated with axonal processes, and was not detected in glial or muscle cells. Enteric neurons cultured in the presence of SEMA3A-expressing COS cells showed a strong reduction in axon length and complexity, while the ganglion size was unaffected.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
P1135 TRANS-ABDOMINAL INTERFERENTIAL ELECTRICAL STIMULATION IS EFFECTIVE IN MANAGING REFRACTORY LOWER GASTROINTESTINAL DYSMOTILITY DISORDERS

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Introduction: There is emerging interest in non-pharmacological management of gastrointestinal dysmotility via neuromodulatory techniques. A new method of non-invasive neuromodulation - transabdominal interferential electrical stimulation - has apparent efficacy in a paediatric population with difficult constipation.

Aims & Methods: We report our experience of its use in adult patients with functional megacolon who are refractory to conventional management. This is a descriptive case series of consecutive adult patients presenting to a tertiary referral functional gastrointestinal disorders clinic with refractory constipation that were taught and used home-based interferential stimulation for a three-month period. An experienced functional gut nurse specialist between October 2015 and Feb 2017. The validated PAC-SYM and PAC-QOL questionnaires were given at commencement of stimulation and after three months of use. Overall symptom severity was assessed by 10 cm VAS. An intention to treat analysis was conducted for any patients who commenced stimulation.

Results: Seven patients with refractory constipation (3 with slow-transit and 4 with idiopathic constipation) responding inadequately to pharmacological and non-pharmacological therapies underwent stimulation. Mean (range) age was 47 (26–73) and 2 were male. All 7 patients completed the stimulation period. There was a reduction in PAC-SYM in all patients (median IQR 24 [18–36] vs 14 [8–20]; p = 0.005). PAC-QOL was assessed in 4 patients and fell from 75 [69–85] to 39 [18–52]. Four were able to cease previously heavy daily laxative use and 2 were able to half their use, one currently weaning off prucalopride. One remained on daily laxative use despite soft, formed stool. All reported satisfaction with stool type. Ongoing benefit remains in 2 after 4 and 12 months since ceasing its use, where the rest tend to use the stimulator intermittently.

Conclusion: Interferential electrical stimulation improved symptoms in patients with functional constipation. Randomized placebo controlled trials are justified.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

P1136 YH12852, A NOVEL AND HIGHLY SELECTIVE 5-HYDROXYTRYPTAMINE 4 RECEPTOR AGONIST, INCREASES STOOL FREQUENCY IN HEALTHY VOLUNTEERS

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Introduction: YH12852 is a novel 5-HT4 receptor agonist currently under clinical development for the treatment for gastrointestinal motility disorders (GIMDs).

Aims & Methods: The study aimed to evaluate the safety, tolerability, pharmacokinetic and pharmacodynamic profiles for YH12852 in healthy volunteers with ≥3 spontaneous bowel movements per week (SBMs/week) and patients with functional constipation (FC). A randomized, double-blind, placebo- and active-controlled, parallel-group study was performed in healthy subjects and FC patients, who were administered YH12852 (0.3, 0.5, 1, 2 or 3 mg), prucalopride 2mg or placebo once daily after breakfast for 2 weeks. Subjects recorded bowel habits throughout the study period. Intensive pharmacokinetic blood samples were also collected (ClinicalTrials.gov identifier NCT02338367).

Results: Twenty-nine healthy subjects and 27 FC patients were enrolled. Treatment-emergent adverse events (TEAEs) were mostly mild and no serious adverse event was reported. The most frequently reported AE in the YH12852 and prucalopride group was headache. TEAEs in the YH12852 groups were similar to the placebo group. The change from baseline in weekly SBM frequencies averaged over the 2-week treatment period were 3.5, 3.8, 6.3, 4.6 and 3.9 for YH12852 0.3, 0.5, 1, 2 and 3 mg, respectively, 4.0 prucalopride and 2.6 placebo. The proportion of responders (defined as those with a ≥1 increase from baseline) was 100%, 100%, 100%, 100% and 75% in the YH12852 treatment groups (87.5%, 100%, 100%, 100% and 0.3, 0.5, 1 and 2 mg, respectively), with the exception of the 3 mg group (80.0%), compared with that in the prucalopride (83.3%) and placebo groups (28.6%). The mean stool count assessed by the Bowel Frequency Form Scale were comparable between the YH12852 and prucalopride groups. The time to reach the peak concentration of YH12852 was 4 hours. Steady state was achieved approximately 5 days after the first administration of YH12852 with a half-life of 23–28 hours. YH12852 showed a linear pharmacokinetic profile over 0.3–3 mg.

Conclusion: YH12852 was well tolerated and its safety profile was comparable to that of prucalopride. YH12852 appeared to increase bowel movement greater than prucalopride, particularly at 0.5–2 mg. YH12852 may have a significant potential for the treatment of GIMDs.

Disclosure of Interest: S. Lee: The affiliates of Yuhan Corporation are stockholders and/or employees
S.B. Jang: The affiliates of Yuhan Corporation are stockholders and/or employees
M.K. Kim: The affiliates of Yuhan Corporation are stockholders and/or employees
H. Na: The affiliates of Yuhan Corporation are stockholders and/or employees
All other authors have declared no conflicts of interest.

P1137 HEALTHCARE PROFESSIONALS FAIL TO PROVIDE ADEQUATE CANCER PATIENTS WITHOUT OPIOID-INDUCED CONSTIPATION TO STRONG-OPIOID UNASSISTED TREATMENT OPTIONS

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Introduction: Constipation is a common side effect of opioid use. Available laxative therapies for opioid-induced constipation (OIC) leave the patient with significant residual symptoms, which may lead them to adjust or stop their opioid intake in order to have a bowel movement, unless effectively counselled.

Aims & Methods: This subgroup analysis of an international survey investigated counselling resources, information-seeking, and sources of support in subjects with constipation caused by the use of strong opioids (e.g. buprenorphine, fentanyl). This was a quantitative, questionnaire-based, online survey conducted in France, Germany, Italy, Spain and the UK among respondents aged ≥40 years with largely non-cancer-related chronic pain, treated long-term with strong opioids and having constipation (N = 2016). The survey assessed past medical history, opioid use, treatment of constipation, symptoms, burden of disease, and effects on quality of life of constipation.

Results: In general, responders find it difficult to combine pain management relief and constipation and do not have enough knowledge to balance them (36%). Approximately one-fifth (22%) of respondents were very or somewhat dissatisfied with the effectiveness of their current constipation treatment and only 43% strictly adhered to prescribed treatment regimens, with 32% researching other treatment options. A significant number of responders (44%) admitted that their constipation becomes so bothersome that they have to combine different methods to relieve it, and 40% often cut down their opioid medication or even skip it entirely (9%) to relieve constipation. To manage their constipation, respondents regularly used a variety of approaches, including dietary measures (48%), exercise (23%) and single (32%) or multiple (15%) laxative treatments. Only 45% of respondents reported that their healthcare professionals (HCPs) had warned them about constipation as a potential side effect of opioid use. Almost two-thirds of respondents (63%) reported that their HCP was the main information source on opioid-induced constipation. Although 58% of respondents stated that they would have liked their HCP to provide more information about OIC, 48% preferred to deal with constipation on their own, rather than discuss it with their HCP. Other common sources of information were online search engines (44%) and online health forums (29%). Less than half of respondents (43%) strictly adhered to prescribed treatment regimens, with 32% researching other treatments.

Conclusion: A proportion of patients are not satisfied with their current constipation treatment and they sometimes find balancing the need for adequate pain relief with constipation side effects challenging; consequently, many fail to adhere to their prescribed treatment regimens, or resort to using suboptimal strategies, such as increasing their opioid intake, to relieve constipation. Despite this dissatisfaction, many HCPs are not counselling patients adequately about constipation as a common potential side effect of opioid use. While most patients would like to have more support from their HCP, nearly half prefer to deal with constipation on their own, perhaps due to embarrassment or resignation.

Disclosure of Interest: A. Lass: Contractor to Shionogi Ltd.
All other authors have declared no conflicts of interest.

Reference
P1138 THREE-DIMENSIONAL HIGH-RESOLUTION ANORECTAL MANOMETRY IN CHILDREN AFTER SURGERY FOR ANORECTAL DISORDERS
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Introduction: Three-dimensional high-resolution anorectal manometry (3DHRAM) is the most precise tool to assess function of the anal canal and may be useful in evaluation of children after surgery on lower gastrointestinal tract that may present wide spectrum of symptoms from gastrointestinal tract. Our aim was to evaluate children after surgery for anorectal disorders using 3DHRAM.

Aims & Methods: We performed a prospective study of 43 children (30 male, mean age, 7 years) after surgery for anorectal disorders at the Departments of Pediatric Gastroenterology and Nutrition, Medical University of Warsaw, Poland. The group consisted of 24 children after surgery for Hirschsprung’s disease (HD), 12 children after surgery for anal atresia (AA) and 7 children after proctocolectomy for other reasons (PC). In all children conventional manometry was performed to compare the data obtained previously. Pressures of the anal canal were divided into 8 segments and the resting and squeeze pressures of puborectalis muscle (PRM) were recorded in segments covering its anatomical localization. These data were compared to raw data obtained in our laboratory from healthy children published previously (HC group). To assess correlation between manometry and symptoms, all children (after surgery and HC group) were divided into groups with respect to symptoms, as follows: asymptomatic (A), non-constitutive fecal incontinence (NRFI) and constitutive fecal incontinence (RFI).

Results: The lowest values of resting, squeeze and the pressure of PRM were observed in AA (55.6 mmHg, 121.7 mmHg and 44.17 mmHg, respectively). As compared to asymptomatic children, the lowest mean and maximum resting pressures were observed in NRFI (69.6 mmHg and 61.3 mmHg, respectively; p < 0.000). Significantly lower maximum squeeze pressure was recorded in both, NRFI and RFI (168.1 mmHg and 103.8 mmHg, respectively; p = 0.03). ROC cut-off value for mean resting pressure between asymptomatic children and patients with fecal incontinence was 68.5 mmHg. Significantly lower PRM squeeze pressure were observed in NRFI group and lower PRM squeeze pressure in RFI (45.6 mmHg and 63.6 mmHg, respectively). Threshold of urge were significantly higher in group C as compared to A group (87.5 cmHg and 30 cmHg respectively; P = 0.03).

Conclusion: Our study demonstrated lower pressure parameters in children after surgery with the lowest values in patients suffering from anal atresia, which was correlated with incontinence. 3DHRAM may be useful tool for assessing the function of the anorectum of children after surgery.

Disclosure of Interest: M. Banasik: Equipment support from manufacturer of the equipment (Covidien AG) All other authors have declared no conflicts of interest.

P1139 UK CLINICAL EXPERIENCE AT 52 WEEKS WITH LINACLIDATE: FOR IRRIITABLE BOWEL SYNDROME WITH CONSTIPATION
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2Salford University, Salford/United Kingdom
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4*pH Associates Ltd, Marlboro/United Kingdom

Introduction: Linacotide, a guanylate cyclase C agonist, has been shown in clinical trials to relieve constipation and improve abdominal pain and discomfort in patients with irritable bowel syndrome with constipation (IBS-C), but there are limited UK-specific real-world data to support this.

Aims & Methods: A multi-centre, observational prospective 52-week study was conducted in eight specialist hospitals in England and Scotland. The primary objective was to describe the change in IBS-Symptom Severity Scale (IBS-SSS) score from baseline at 12 weeks after linacotide initiation. Consenting patients with irritable bowel syndrome with constipation (IBS-C) were recruited for the study. Data on patient demographic and clinical characteristics, concomitant medications, patient-reported outcomes, including IBS-SSS score, and adverse events were collected. Results at 12 weeks (primary endpoint) have been presented previously; here we report analysis of real-world clinical experience 52 weeks post-linacotide initiation.

Results: 202 patients were recruited; 185 (92%) were female. At baseline, median age was 44.9 (range 18–77 years); 84 (42%) reported concomitant laxative use. Mean baseline IBS-SSS score was 339 (standard deviation [SD] ± n = 193); 129 (67%) patients had IBS-C classified as severe (score ≥ 300); 54 (28%) moderate (175–300), nine (5%) mild (75–175) and one (0.5%) normal (≤ 75). At 52 weeks, mean IBS-SSS score was 256 (SD ± 116; n = 78); 31 (40%) patients had severe, 27 (35%) moderate, 14 (18%) mild and six (8%) normal. IBS-SSS scores improved significantly between baseline and 52 weeks, with a mean decrease of 71 (SD ± 106) points overall (t-test p < 0.001; n = 76 with paired data) and 94 (SD ± 102) points on the patients remaining on linacotide (t < 0.001; n = 34). Of the 76 patients with paired data, 41 (54%) reported no change to treatment (ie reduction in IBS-SSS score of ≥50 points, or score fell below 150 if baseline score >150) [Table]. At 52 weeks, 41 (29%; n = 202) patients remained on linacotide; 87 (43%) had stopped (≤4 doses in past week, most commonly due to side effects (n = 51) or lack of efficacy (n = 18), and 74 (37%) were lost to follow-up/not known. Overall, 174 adverse events possibly related to linacotide were reported in 77 (38%) patients, most commonly diarrhoea (25%; n = 51), abdominal pain (9%; n = 18) and abdominal distension (6%; n = 13).

Table: Change in IBS-SSS score at 52 weeks from start of linacotide

<table>
<thead>
<tr>
<th>Change in IBS-SSS</th>
<th>Patients, n</th>
<th>Patients, %</th>
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<tbody>
<tr>
<td>≥50</td>
<td>76</td>
<td>100</td>
</tr>
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</table>

Conclusion: Linacotide was associated with a significant improvement in IBS-SSS score at 52 weeks and was reasonably well tolerated. These results provide valuable insights into the longer-term outcomes of linacotide treatment in patients with IBS-C in real-world clinical practice.

Disclosure of Interest: A. V. Emmanel: Served on advisory boards for Allergan, Almirall, Shire, Takeda Y. Yianakou: Educational grant and speaker fees from allergan S. McLain-Smith: SMS is an employee of pH Associates, an independent research consultancy which was commissioned by the sponsor to provide support with the design and conduct of the study, data analysis and medical writing All other authors have declared no conflicts of interest.

P1140 EFFECT OF FAECAL MICROBIOTA TRANSPLANTATION ON GUT BACTERIAL FERMENTATION PRODUCTS IN PATIENTS WITH IRITRITABLE BOWEL SYNDROME
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Introduction: Irritable bowel syndrome (IBS) may be associated with disturbances of gut microbiota composition and functions, such as altered bacterial fermentation.

Aims & Methods: The aim was to study the effect of faecal microbiota transplantation (FMT) on gut bacterial fermentation products: short-chain fatty acids (SCFAs). Patients diagnosed with IBS according to Rome III criteria (n = 113) were included. They received freshly donated faeces from relatives, instilled into the descending part of the duodenum via gastroscope. Faecal samples were collected from the donors and the patients before FMT and from the patients after FMT until week 20/28 after FMT as follows: nausea (P < 0.001), vomiting, abdominal pain, diarrhea, constipation and anorexia.

Results: Before FMT, concentrations of several SCFAs were significantly lower in IBS patients compared to donors (Table 1). After FMT, concentrations of SCFAs increased within the first 3 weeks, and the increment lasted up to 28 weeks (Table 1). Acetate, propionate and iso-butyric acids and minor SCFAs (iso-butyric, n-valeric, iso-valeric, n-caproic and iso-capric acids) were analysed by vacuum distillation followed by gas chromatography. The patients completed IBS symptom questionnaire (IBS-SQ) before and after FMT at weeks 1, 3, 12, and 20/28. All the samples were stored at −80°C until analysis. Faecal concentrations of major SCFAs (acetic, propionic and n-butyric acids) and minor SCFAs (iso-butyric, n-valeric, iso-valeric, n-caproic and iso-capric acids) were assessed by HPLC-MS improved from before FMT until week 20/28 after FMT as follows: nausea (p = 0.0013), bloating (P < 0.0001), abdominal pain (P < 0.0005), diarrhea (P < 0.001), constipation (P = 0.03), and anorexia (P = 0.09). Correlations were found between abdominal pain and both acetic acid (r = 0.69, P < 0.04) and total SCFAs (r = 0.69, P = 0.044) in IBS patients before FMT. Inverse correlations were found 3 weeks after FMT between nausea and iso-valeric acid (r = −0.65, P < 0.014), and between constipation and propionic acid (r = −0.74, P < 0.0001), iso-butyric acid (r = −0.79, P < 0.0001) and n-valeric acids (r = −0.79, P < 0.0001) and iso-valeric acid (r = −0.72, P < 0.0001).

Disclosure of Interest: All authors have declared no conflicts of interest.
Abstract No: P1140

Table 1: Concentrations (mmol/kg) of short-chain fatty acids (SCFAs) in faecal samples collected from donors and patients with irritable bowel syndrome (IBS) before and after faecal microbiota transplantation (FMT).

<table>
<thead>
<tr>
<th>SCFAs</th>
<th>Donor, (n = 13)</th>
<th>Patients before FMT, (n = 9)</th>
<th>Week 1, (n = 12)</th>
<th>Week 3, (n = 10)</th>
<th>Week 12, (n = 13)</th>
<th>Week 20/28, (n = 12)</th>
</tr>
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<tbody>
<tr>
<td>Acetic acid</td>
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<td>/C6</td>
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<tr>
<td>33.9 ± 2.8</td>
<td>23.6 ± 6</td>
<td>31.1 ± 4.9</td>
<td>35.5 ± 3.9</td>
<td>25.8 ± 4.4</td>
<td>28.5 ± 2.4</td>
<td>0.77</td>
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<tr>
<td>Propionic acid</td>
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<tr>
<td>/C6</td>
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<tr>
<td>9.5 ± 1</td>
<td>6.2 ± 1.6</td>
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<td>1.27 ± 0.17</td>
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<td>1.4 ± 0.18</td>
<td>0.68 ± 0.008</td>
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<td>0.8 ± 0.02</td>
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<tr>
<td>58.8 ± 5.4</td>
<td>37.6 ± 9.8</td>
<td>49.9 ± 8</td>
<td>55.7 ± 6.2</td>
<td>41.4 ± 7.1</td>
<td>46 ± 4.7</td>
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</table>

Data are presented as mean ± SEM. Comparison: Kruskal-Wallis multiple comparisons test with Dunn’s post test. *Donors at the beginning of the study vs. patients 1 week after FMT. **Donors at the beginning of the study vs. patients 3 weeks after FMT. ***Donors at the beginning of the study vs. patients 12 weeks after FMT, ****Donors at the beginning of the study vs. patients 20/28 weeks after FMT. FMT: faecal microbiota transplantation. SCFAs: short-chain fatty acids

Conclusion: Our results reveal differences in faecal fermentation products between patients with IBS and healthy donors, and suggest that FMT may act to normalise such alterations of gut microbial functions.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1141 HEALTHCARE RESOURCE USE IN PATIENTS WITH IRRITABLE BOWEL SYNDROME WITH DIARRHOEA BASED ON A SURVEY OF PHYSICIANS IN THE UNITED KINGDOM

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Introduction: Irritable bowel syndrome with diarrhoea (IBS-D) is a chronic gastrointestinal disorder associated with significantly increased healthcare resource use (HCRU) and a substantial economic burden. In clinical practice, adequate relief (AR) of symptoms is an important measure of treatment effectiveness.1 However, the difference in HCRU related to IBS-D between patients with AR and those with inadequate relief (IR) has not yet been assessed.

Aims & Methods: This objective of this study was to quantify the HCRU in patients with AR of IBS-D symptoms compared to patients with IR. An online survey assessing HCRU was distributed to general practitioners (GPs) recruited from market research panels in the UK in August 2016. GPs opted-in to complete the survey via an email link and were screened before being invited to complete the main survey. Screening criteria included having seen patients with a chronic gastrointestinal condition in the past three months, having seen patients with IBS-D in the past 3 months and having decided on what treatments were prescribed for patients with IBS. The survey was a 15-minute web-based survey, including 12 questions collecting information on the use of medical services and procedures amongst patients with IBS-D for the first year following diagnosis and for subsequent years. Respondents were required to answer the survey considering patients who had AR of IBS-D symptoms and those who did not (IR), based on the respondents’ own assessments. Statistical analyses included t-tests for two independent samples comparing mean scores for those with IR vs those with AR during the first year after diagnosis at a 5% risk level, with p < 0.05 denoting significance.

Results: The online survey was completed by 50 GPs, with responses from 46 GPs included in this analysis (four responses were excluded due to data quality reasons). The reported total number of medical visits was significantly higher for patients with IR vs patients with AR during the first year after diagnosis (mean 10.11 vs 5.20; p < 0.001), with similar results seen for subsequent years (mean 8.20 vs 4.38). Significantly higher numbers of GP office visits, outpatient visits and emergency room visits were reported for patients with IR, with the greatest difference seen for GP office visits (2.37 more visits/year on average; incremental 4-week increase of 0.182; p = 0.003) [Table]. Similarly, the total reported mean number of procedures was significantly higher for patients with IR vs patients with AR (8.11 vs 4.52; p = 0.046), with number of colonoscopies having the greatest difference between the two groups (2.17 vs 0.91; 1.26 more procedures/year on average; incremental 4-week increase of 0.097; p = 0.008). Similar results were seen for the subsequent years after diagnosis, with patients with IR having more medical procedures compared to patients with AR (4.08 vs 2.56).

Table

<table>
<thead>
<tr>
<th>Mean resource use (standard deviation)</th>
<th>Adequate relief (1st year after diagnosis)</th>
<th>Inadequate relief (1st year after diagnosis)</th>
<th>Difference per year</th>
<th>Incremental mean quantity per 4 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical visits</td>
<td>5.20 (4.87)</td>
<td>10.11 (5.30)#</td>
<td>4.91</td>
<td>0.378</td>
</tr>
<tr>
<td>GP office</td>
<td>3.33 (2.87)</td>
<td>5.70 (3.12)#</td>
<td>2.37</td>
<td>0.182</td>
</tr>
<tr>
<td>Outpatient</td>
<td>0.96 (1.53)</td>
<td>2.30 (1.68)#</td>
<td>1.35</td>
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<tr>
<td>Emergency room</td>
<td>0.52 (1.24)</td>
<td>1.17 (1.36)#</td>
<td>0.65</td>
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<tr>
<td>Hospitalisations</td>
<td>0.39 (1.00)</td>
<td>0.93 (1.10)</td>
<td>0.54</td>
<td>0.042</td>
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<td>Procedures</td>
<td>4.52 (6.96)</td>
<td>8.11 (7.58)#</td>
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<td>Colonoscopy</td>
<td>0.91 (1.47)</td>
<td>2.17 (1.61)#</td>
<td>1.26</td>
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<td>Sigmodioscopy</td>
<td>0.70 (1.43)</td>
<td>1.37 (1.56)</td>
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</tr>
<tr>
<td>Ultrasound</td>
<td>1.13 (2.06)</td>
<td>1.76 (2.26)</td>
<td>0.63</td>
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<tr>
<td>Endoscopy</td>
<td>0.67 (1.28)</td>
<td>1.22 (1.37)</td>
<td>0.54</td>
<td>0.042</td>
</tr>
<tr>
<td>Computerised tomography scan</td>
<td>0.48 (1.01)</td>
<td>0.85 (1.10)</td>
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<td>0.028</td>
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<tr>
<td>X-ray</td>
<td>0.63 (1.53)</td>
<td>0.74 (1.68)</td>
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</table>

# p < 0.05 compared to patients with adequate relief

Conclusion: GPs reported that patients with IBS-D considered as having IR of symptoms had increased HCRU, including more GP office visits and more colonoscopies, compared to patients with AR. These results highlight that IR is potentially an important driver of increased HCRU in patients with IBS-D, emphasising that effective treatments that provide AR may reduce HCRU and the associated economic burden.

Disclosure of Interest: A. Marciniak: Anne Marciniak is an employee of Allergan plc and shareholder in Pfizer, Amgen, and Allergan plc. D. Collomb: David Collomb is an employee of Allergan plc. S. Baker: Stephen Baker is an employee of Allergan plc. R. Goosey: Richard Goosey is an employee of Kantar Health, paid consultants to Allergan plc.

References
P1142  RANDOMISED PLACEBO CONTROLLED ESCITALOPRAM INTERVENTION IN IBS WITH PANIC DISORDER: EVALUATION BY GSRS AND BY EXPERIENCE SAMPLING METHOD  
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1Division Of Gastroenterology-hepatology, Department Of Internal Medicine, Maastricht University Medical Center+, Maastricht/Netherlands  
2Department Of Psychiatry And Psychology, Maastricht University Medical Center+, Maastricht/Netherlands  

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Introduction: Selective Serotonin Reuptake Inhibitors (SSRIs) have shown efficacy in reducing symptoms but less so on pain in irritable bowel syndrome (IBS). Comorbid anxiety frequently occurs in IBS. We hypothesized that SSRIs will particularly be effective in reducing abdominal pain in IBS patients with pronounced comorbid anxiety. As methods for symptom evaluation were used 1) gastrointestinal symptom rating scale (GSRS) as primary parameter and 2) a new method called the Experience Sampling Method (ESM). With ESM digital assessments are completed randomly and repeatedly during daily life, therewith capturing fluctuating symptom patterns more accurately than retrospective questionnaire methods.  

Aims & Methods: IBS patients with comorbid panic disorder were included in a randomized controlled trial on escitalopram versus placebo. Measurements were completed at baseline (t=0) and after 3 (t=3) and 6 months (t=6). At each time point, the gastrointestinal symptom rating scale (GSRS) and a 7-day ESM period were completed. Subjects completed ESM assessments on a palmtop computer at 10 random moments each day during 7 consecutive days. ESM periods were analysed when at least 1/3 (i.e. 23) of the assessments were completed. Mixed linear models were applied with the GSRS (primary endpoint) as the dependent and treatment group as the independent variable, as well as with ESM - abdominal pain scores as the dependent and treatment group and ESM - anxiety scores as the independent variables.  

Results: In total 15 (15 escitalopram and 14 placebo; 21 female; 37 ± 14.8 years; equal abdominal pain and anxiety scores at baseline) were included. Average GSRS-AP scores were not significantly different between escitalopram and placebo at t=3 (B: 0.265, SE: 0.451, p=0.557) or t=6 (B: 0.229, SE: 0.539, p=0.670). For the ESM analyses, at t=6, average abdominal pain scores were significantly lower (B: 1.30, SE: 0.623, p=0.037) (on a 1−7 scale) in the escitalopram group compared to placebo. With increasing anxiety levels (scores 2, 3 and 4) this difference further increased to 1.57, 1.84 and 2.11, respectively. A sensitivity analysis on subjects that completed all 3 valid ESM periods (i.e. at least 1/3 of total number of assessments at t=0, t=3 and t=6) showed similar results.  

Conclusion: Using GSRS as primary outcome, no significant effect of escitalopram over placebo on abdominal pain was found over a 6-month period. However, using ESM, a significant improvement in abdominal pain was observed, related to anxiety scores. These data 1) challenge the value of traditional retrospective methods with end-of-period symptom recording and 2) are in favour of novel more accurate momentary symptom registrations such as the Experience Sampling Method.  

Disclosure of Interest: All authors have declared no conflicts of interest.  

P1143  LINACLODITE ACCELERATES COLONIC TRANSIT AND IMPROVES COLONIC CONTRACTILITY IN IBS WITH CONSTITUTION  
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2Functional Gut Clinic, London/United Kingdom  

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Introduction: Linaclootide, a guanylate cyclase-C agonist, stimulates intestinal fluid secretion and decreases visceral hypersensitivity and is licensed for use in irritable bowel syndrome with constipation (IBS-C). There is a relative paucity of data concerning its effect on gastrointestinal (GI) motility.  

Aims & Methods: We aimed to compare the effect of linaclootide on segmental and pan-enteric motility in IBS-C. 14 patients with Rome III defined IBS-C (3 male, mean age 37 years, range 20-64) underwent a wireless motility capsule (WMC) using a standardized protocol. Segmental transit was derived from measures around known anatomical landmarks as identified by compartmental pH changes. Ileal and colonic motility measures are presented as area under the curve (AUC) derived from contraction amplitude and frequency. Validated questionnaires assessing GI (verbal descriptor anchored visual analog scale (VDVAS) assessing sensory intensity (VDVAS-I) and unpleasantness (VDVAS-U)) and somatic symptoms (Personal Health Questionnaire (PHQ) as well as quality of life (EQ-5D) were administered. The WMC and questionnaires were repeated after 28 days of linaclootide 290mcg per od.  

Results: Changes in GI motility are shown in Table 1. Linaclootide improved VDVAS-I and VDVAS-U (130.7 ± 20.8 vs. 106.5 ± 33, p=0.03 and 113 ± 22 vs. 85.8 ± 33, p=0.01) and quality of life (58.4 ± 21.2 vs. 68 ± 17.6, p=0.02). Linaclootide reduced somatic symptoms (8.3 ± 2.2 vs. 5.9 ± 1.4, p=0.007). Change in pH across the ileocaecal junction correlated with improvement in VDVAS-I and U (r=0.6, p=0.03 and r=0.64, p=0.02).  

Table 1: Changes in GI physiology following linaclootide.  

Baseline (mean and standard deviation)  Post treatment (mean and standard deviation)  P  Value  
Gastric emptying time (minutes) 154 ± 64 177 ± 57 0.4  
Small bowel transit time (minutes) 353 ± 152 299 ± 139 0.3  
Colonic transit time (minutes) 3017 ± 1305 1983 ± 1216 0.04  
Whole gut transit time (minutes) 3517 ± 1375 2432 ± 1180 0.04  
Ileal contractility (AUC) 262 ± 142.2 221 ± 113.5 0.5  
Colonic contractility (AUC) 90.9 ± 78.3 134.6 ± 93 0.006  
Change in pH across the ileocaecal junction -2.4 ± 0.2 -2.1 ± 0.4 0.03  

Linaclootide improved VDVAS-I and VDVAS-U (130.7 ± 20.8 vs. 106.5 ± 33, p=0.03 and 113 ± 22 vs. 85.8 ± 33, p=0.01) and quality of life (58.4 ± 21.2 vs. 68 ± 17.6, p=0.02). Linaclootide reduced somatic symptoms (8.3 ± 2.2 vs. 5.9 ± 1.4, p=0.007). Change in pH across the ileocaecal junction correlated with improvement in VDVAS-I and U (r=0.6, p=0.03 and r=0.64, p=0.02).  

Conclusion: Linaclootide reduced colonic transit and enhances contractility. These changes in GI motility are accompanied by improvements in symptoms and quality of life and are associated with a reduction in extra-gastrointestinal symptoms. Change in pH across the ileocaecal junction has been proposed as a surrogate marker of caecal fermentation. Thus the beneficial effect of linacloptide on symptoms may therefore be related to a reduction in fermentation. This potential biomarker warrants further exploration.  

Disclosure of Interest: A.D. Farmer; Speaker Bureau - Allergan Advisory board- Allergen  
All other authors have declared no conflicts of interest.  

P1144  RELATIONSHIP BETWEEN RIFAXIMIN THERAPY AND SEHCAT TEST IN PATIENTS WITH DIARRHEA-PREDOMINANT IRITABLE BOWEL SYNDROME OR FUNCTIONAL DIARRHEA  

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Introduction: Bile acids (BAs) and gut microbiota have been involved in IBS pathophysiology. BA diarrhea (IBD) is often found in patients with irritable bowel syndrome with diarrhea (IBS-D) or functional diarrhea (FD). Bile acids and rifaximin have both been shown to improve symptoms in these patients. It is unknown whether a SeHCAT test may help to predict response to rifaximin or whether rifaximin treatment affects SeHCAT test result.  

Aims & Methods: a) To determine if a SeHCAT test may be used to predict response to rifaximin in patients with IBS-D or FD; b) To assess if rifaximin modifies SeHCAT result.  
Consecutive patients diagnosed with IBS-D or FD were prospectively included in the study. All patients received rifaximin 400mg TID for 2w. A SeHCAT test was performed to evaluate presence of BAD before and 1 month after rifaximin treatment. BAD was defined as SeHCAT retention <10%. Number of daily stools, number of daily watery stools, Bristol stool scale, abdominal pain, distension and presence of urgency were recorded before and after treatment. IBS severity score (IBS-SS) was also calculated.  

Results: Forty-one patients were included. BAD was present in 23 patients (56%). No clinical differences were found between BAD or non-BAD patients at study entry. Rifaximin resulted in a significant improvement in the number of daily stools (Δ −1.5; P<0.01), daily watery stools (Δ −2.1; P<0.01), Bristol scale (Δ −1.1; P<0.01), abdominal pain (Δ −0.5; P<0.01), distension (Δ −0.3; P<0.01), urgency (Δ −0.7; P<0.01) and in the IBS-SS (Δ −7.8; P<0.01). No differences were found between BAD and non-BAD patients in the improvement of any item. Rifaximin treatment did not modify SeHCAT value (9.5% before treatment and 10.7% after treatment; P=0.4).  

Conclusion: Half of the patients diagnosed with IBS-D or FD present BAD according the SeHCAT test. Rifaximin treatment confers significant clinical improvement irrespective of the presence of BAD. Rifaximin treatment does not affect SeHCAT test.  

Disclosure of Interest: All authors have declared no conflicts of interest.  

References  


Aims & Methods: To evaluate IR in patients treated with ELX in a post hoc analysis from two randomised, double-blind, placebo (PBO)-controlled Phase 3 trials (IBS-3001, IBS-3002). Patients meeting Rome III criteria for IBS-D were randomised 1:1:1 to twice-daily (BID) ELX (75 or 100 mg) or PBO. Efficacy was evaluated through Week 26. For evaluation of AR, patients were asked “In the last 7 days, have you had inadequate [satisfactory] relief of your IBS symptoms?” (Yes/No) on a weekly basis, via an electronic diary. As previously described, patients answering “Yes” for ≥50% of the total weeks during the target time interval were considered AR responders.2,5 Patients answering “No” were considered to have incomplete relief, while patients with ≥5 consecutive weeks that patients reported IR over Weeks 1-12 and 13-24 of treatment. Patients without AR analysis were ineligible for intention-to-treat (ITT) analysis; missing data were not imputed.

Results: Overall, 2428 patients with IBS-D were enrolled across the two Phase 3 trials and 2423 were included in the ITT analysis. In the pooled dataset, a significantly greater proportion of patients were AR responders with either ELX 100 or 75 mg BID vs PBO at 12 weeks (56.1% [p < 0.001] and 56.3% [p < 0.001] vs 46.4%, respectively) and at 26 weeks (51.5% [p < 0.001] and 49.0% [p < 0.004] vs 41.8%, respectively).2 Over the first 12 weeks of treatment, a greater proportion of patients reported no IR of IBS-D symptoms with ELX 100 or 75 mg BID vs PBO (Table). Greater proportions of patients reported only 1-5 consecutive weeks of IR with ELX 100 or 75 mg BID vs PBO. A significantly lower proportion of patients reported IR for >8 consecutive weeks with ELX 100 or 75 mg BID vs PBO (13.2% [p < 0.0001] and 15.6% [p < 0.004] vs 22.6%, respectively). In contrast, a greater proportion of patients reported IR for the full 12 consecutive weeks with PBO vs ELX 100 or 75 mg BID (Table). Similar results were observed in Weeks 13-24 of treatment, with ELX-treated patients generally having fewer consecutive weeks of IR compared to PBO-treated patients (Table).

Table: Consecutive weeks of inadequate relief

<table>
<thead>
<tr>
<th>Weeks 1-12</th>
<th>Weeks 13-24</th>
</tr>
</thead>
<tbody>
<tr>
<td>ELX 75 mg BID</td>
<td>ELX 100 mg BID</td>
</tr>
<tr>
<td>ELX 100 mg BID</td>
<td>PBO</td>
</tr>
</tbody>
</table>

Inadequate relief rate, %

Number of consecutive weeks with inadequate relief

0 | Inadequate relief rate, %

1-5 | 14.4 | 23.6 | 24.8 | 26.8 | 39.5 | 37.1

5-8 | 46.7 | 50.2 | 49.2 | 35.9 | 33.8 | 37.6

>8 | 5.3 | 3.8 | 2.9 | 4.7 | 3.9 | 3.7

Conclusion: In this post hoc analysis of the pooled ELX Phase 3 studies, ELX-treated patients experienced fewer consecutive weeks of IR compared to those receiving PBO, within both Weeks 1-12 and 13-24 of treatment. As IR is thought to increase healthcare resource use and subsequent healthcare costs associated with IBS, further prospective study of the impact of ELX on AR and any subsequent reduction in healthcare costs is required, including the relationship between the number of consecutive weeks of IR and patients' behaviour towards healthcare resource use.

Disclosure of Interest: D. Collomb: David Collomb is an employee of Allergan plc. A. Marciniak: Anne Marciniak is an employee of Allergan plc and shareholder in Pfizer, Amgen, and Allergan plc. Y. Mo: Yilan Mo is an employee of Allergan plc. D.A.: David A. Andrae is an employee of Allergan plc and shareholder in Allergan plc. G. Wiseman: Gwn Wiseman is an employee of Allergan plc.

References

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P1145 FECAL MICROBIOTA TRANSPLANTATION FOR PATIENTS WITH POST-INFECTIONOUS OR ANTIBIOTIC-INDUCED IRRITABLE BOWEL SYNDROME: RESULTS FROM A PROSPECTIVE PILOT STUDY


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3Medical Microbiology, Leiden University Medical Center, Leiden/Netherlands
4Gastroenterology And Hepatology, Haaglanden Medical Centre, The Hague/ Netherlands

Aims & Methods: We performed an open label pilot study in the VU University medical center in Amsterdam from August 2016 through January 2017, to evaluate the effect of FMT in patients with post-infectious IBS (n = 5) and patients with antibiotic-induced IBS (n = 5). Participants with clinical symptoms lasting over six months, an IBS-symptom severity score (IBS-SSS) of at least 175 points, and a negative screening for gastrointestinal pathology were eligible. Donor feces (198 ml) was provided by the Netherlands Donor Feces Bank (NDFB) and administered via a duodenal tube. Participants did not receive pre-treatment or bowel cleaning. Participants were followed for eight weeks via two validated questionnaires: IBS-SSS (range 100-500), and IBS-Quality of Life score (IBS-QOL; range 0-100%). Fecal samples were obtained before and after FMT for microbiota analysis. Following the recommendation of the European Agency Medicines, FMT was considered clinically effective if participants reported an IBS-SSS improvement of at least 30% compared to baseline, eight weeks after FMT.

Results: The mean IBS-SSS of all patients had improved significantly from 137 (±74) points at baseline to 245 (±117) at eight weeks after FMT (p = 0.008); the median IBS-SSS improved with 40% from 340 (range 230-480) to 205 (range 80-470). Also, a significant improvement was seen in bowel pain (p = 0.039), satisfaction about bowel habit (p = 0.018), and influence of IBS symptoms on daily life (p = 0.011). There was no difference in bloating, or number of days with abdominal pain. The mean IBS-QOL improved from 51% to 66% (p = 0.008). FMT was considered effective in three patients with antibiotics and one patient with post-infectious IBS (≥30% improvement). In general, fecal microbiota analysis showed that the microbiota composition of responders shifted to that of their corresponding donors. Non-responders initially also did (which was associated with IBS-SSS improvement), however, eight weeks after FMT, the microbiota composition had shifted back towards baseline.

Conclusion: Treatment with FMT appears promising for antibiotic-induced and post-infectious IBS. Based on these results, a randomized placebo controlled trial is warranted.

Disclosure of Interest: A.E. Budding: A.E. Budding has proprietary rights to the IS-pro technique, and is co-owner of the spin-off company IS-diagnostics. All other authors have declared no conflicts of interest.

P1146 CONSECUTIVE WEEKS OF INADEQUATE RELIEF: A POST HOC ANALYSIS OF THE POOLED ELUXADOLINE PHASE 3 STUDIES IN PATIENTS WITH IRRITABLE BOWEL SYNDROME

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Introduction: Adequate relief (AR) of irritable bowel syndrome (IBS) symptoms is a commonly used global outcome measure to assess treatment benefit in both clinical trials and real-life clinical practice. Conversely, inadequate relief (IR) is considered an important driver for patients to use healthcare resources such as general practitioner or gastroenterologist consultations. Eluxadoline (ELX) is a mixed µ-opioid receptor (OR) and κ-OR agonist and δ-OR antagonist approved for the treatment of IBS with diarrhoea (IBS-D) in the US and Europe.
receptor antagonists, is approved for the treatment of IBS-D in adults, based on two large, 3 phase clinical trials where eluxadoline met the primary composite response endpoint of simultaneous improvement in abdominal pain and stool consistency over 26 weeks.

**Aims & Methods:** These post hoc analyses of two double-blind, placebo-controlled, Phase 3 clinical trials of eluxadoline (IBS-3001 and IBS-3002) aimed to assess responder and non-responder rates over 4-week intervals for eluxadoline vs placebo, and the proportion of responders/non-responders who continued or discontinued treatment. Patients meeting Rome III criteria for IBS-D were randomly assigned to twice-daily treatment with eluxadoline (75 or 100 mg) or placebo. Patients rated IBS symptoms daily, including worst abdominal pain (WAP; 0–10 scale, with 0 = placebo). Patients rated IBS symptoms daily, including worst abdominal pain (WAP; 0–10 scale, with 0 = placebo). Patients rated IBS symptoms daily, including worst abdominal pain (WAP; 0–10 scale, with 0 = placebo).

**Results:** Of the 2423 patients in the pooled Phase 3 ITT population, 249 were classified as having severe IBS-D. Over Weeks 1–4, 26.8% and 30.3% of patients with severe IBS-D were responders with eluxadoline 75 and 100 mg, respectively, vs 8.1% of patients on placebo (Table). Higher proportions of patients were responders with eluxadoline vs placebo over each subsequent 4-week interval, with response rates observed at Weeks 1–4 consistently maintained across all subsequent 4-week time intervals. With both eluxadoline and placebo, proportions of responders discontinuing were <2% across each 4-week interval, and discontinuation rates in non-responders were higher than in responders (Table). Similar findings were observed in the ITT analysis set: over Weeks 1–4, 22.7% and 24.6% of patients were responders with eluxadoline 75 and 100mg, respectively, vs 12.3% of patients on placebo. Discontinuation rates among responders with both eluxadoline and placebo remained <1% across all 4-week time intervals.

**Conclusion:** Proportions of responders with eluxadoline 75 and 100 mg were consistently higher vs placebo across all 4-week intervals in the treatment period in patients defined as having severe IBS-D. Furthermore, discontinuation rates among patients showing a treatment response remained consistently low compared to non-responders. However, as these analyses were conducted in a clinical trial setting, the relatively high continuation rates in non-responders may not reflect the real-world situation. These findings suggest that eluxadoline has sustained efficacy in treating the diarrhoea and abdominal pain associated with IBS-D, including in patients with severe and inadequately managed symptoms.

**Disclosure of Interest:** A. Marciniak: Anne Marciniak is an employee of Allergan plc and shareholder in Pfizer, Amgen, and Allergan plc. R.T. Carson: Robyn T. Carson is an employee of Allergan plc and shareholder in Allergan plc. J.L. Abel: Jessica L. Abel is an employee of Allergan plc and shareholder in Allergan plc. D.A. Andrae: David A. Andrae is an employee of Allergan plc and shareholder in Allergan plc. K. Fust: Kelly Fust is an employee of Optum, paid consultants to Allergan plc. D. Becker: Debbie Becker is an employee of Optum, paid consultants to Allergan plc.

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**Introduction:** Diets reducing the content of fermentable short chain carbohydrates (fermentable oligo-, di-, mono-saccharides, and polyols (FODMAPs)) as well as the National Institute of Health Care Excellence (NICE) diet have been reported to be effective in the treatment of patients with irritable bowel syndrome (IBS) (1,2). The mechanisms by which this efficacy is achieved are incompletely understood but it has been proposed that such diets reduce fermentation, mediated by changes in the microbiota (3). Change in pH around the ileocecal junction is considered to be a surrogate biomarker of caecal fermentation (4,5).

**Aims & Methods:** We aimed to compare the effect of a low FODMAP diet vs the NICE diet on change in ileocaecal pH. We performed a single centre, randomized controlled trial of adult patients with Rome III defined IBS-mixed bowel habit (IBS-M) comparing the two dietary interventions. At baseline, patients ingested a wireless motility capsule (WMC) using a standardized protocol. Segmental transit times were derived from measures around known anatomical landmarks as identified by compartmental pH changes. Ileal and colonic motility measures are presented as area under the curve (AUC) derived from contraction amplitude and frequency. Validated questionnaires evaluating GI (verbal descriptor scale), symptom distress (VDSAS), and quality of life (EQ-SD) were administered. The WMC and questionnaires were repeated after 26 days of dietary interventions. The primary endpoint was change in ileocaecal pH after the intervention. Secondary outcomes included changes in transit times, contractility and symptom scores.

**Results:** After screening, 32 patients (23 female, median age 37 years, range 18-65) were randomized. Baseline symptom severity and demographics were similar between the two groups. Relative to baseline, there was a reduction in the change in ileocaecal pH with the low FODMAP diet group compared to the m-NICE group (3.37 ± 0.3 vs 0.0035 ± 0.4, p = 0.047) suggesting reduced fermentation. Changes in GI motility are shown in Table 1.

**Conclusion:** The low FODMAP diet reduces caecal fermentation in comparison to the NICE diet as indexed by a reduction in the change in pH across the ileocaecal junction. Both diets improved GI and extra-GI symptoms as well as quality of life. Neither diet has a demonstrable differential effect on ileal/colonic contractility or segmental/whole gut transit times. It is therefore plausible that the efficacy of the low FODMAP diet in IBS-M is via mediated by alterations in the microbiota.

**Disclosure of Interest:** A.D. Farmer: Speaker Bureau and Advisory Boards for Allergan

All other authors have declared no conflicts of interest.

**References:**

**P1148 THE LOW FODMAP DIET REDUCES CAECAL FERMENTATION COMPARED TO TRADITIONAL DIETARY ADVICE: A RANDOMISED CONTROLLED TRIAL**

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**Introduction:** Diets reducing the content of fermentable short chain carbohydrates (fermentable oligo-, di-, mono-saccharides, and polyols (FODMAPs)) as well as the National Institute of Health Care Excellence (NICE) diet have been reported to be effective in the treatment of patients with irritable bowel syndrome (IBS) (1,2). The mechanisms by which this efficacy is achieved are incompletely understood but it has been proposed that such diets reduce fermentation, mediated by changes in the microbiota (3). Change in pH around the ileocecal junction is considered to be a surrogate biomarker of caecal fermentation (4,5).

**Aims & Methods:** We aimed to compare the effect of a low FODMAP diet vs the NICE diet on change in ileocaecal pH. We performed a single centre, randomized controlled trial of adult patients with Rome III defined IBS-mixed bowel habit (IBS-M) comparing the two dietary interventions. At baseline, patients ingested a wireless motility capsule (WMC) using a standardized protocol. Segmental transit times were derived from measures around known anatomical landmarks as identified by compartmental pH changes. Ileal and colonic motility measures are presented as area under the curve (AUC) derived from contraction amplitude and frequency. Validated questionnaires evaluating GI (verbal descriptor scale), symptom distress (VDSAS), and quality of life (EQ-SD) were administered. The WMC and questionnaires were repeated after 26 days of dietary interventions. The primary endpoint was change in ileocaecal pH after the intervention. Secondary outcomes included changes in transit times, contractility and symptom scores.

**Results:** After screening, 32 patients (23 female, median age 37 years, range 18-65) were randomized. Baseline symptom severity and demographics were similar between the two groups. Relative to baseline, there was a reduction in the change in ileocaecal pH with the low FODMAP diet group compared to the m-NICE group (3.37 ± 0.3 vs 0.0035 ± 0.4, p = 0.047) suggesting reduced fermentation. Changes in GI motility are shown in Table 1.

**Conclusion:** The low FODMAP diet reduces caecal fermentation in comparison to the NICE diet as indexed by a reduction in the change in pH across the ileocaecal junction. Both diets improved GI and extra-GI symptoms as well as quality of life. Neither diet has a demonstrable differential effect on ileal/colonic contractility or segmental/whole gut transit times. It is therefore plausible that the efficacy of the low FODMAP diet in IBS-M is via mediated by alterations in the microbiota.
associated with triggering gastrointestinal symptoms in irritable bowel syndrome (IBS).

Aims & Methods: This study aimed to assess whether oral α-galactosidase co-ingestion with foods high in GOS and low in other FODMAPs would reduce symptoms and breath hydrogen production in a double-blind, placebo-controlled, crossover trial approved by Monash University Ethics Committee. Patients meeting the Rome III criteria for IBS who produced >10 ppm hydrogen on two consecutive breath samples following 10 g fructan were recruited. Participants were randomly assigned to full-dose enzyme (300 GALU α-galactosidase)/placebo and left lateral BET in analysis of unselected CC cohort studies, though specificity 54% (7% to 100%) 76% (70% to 83%) Left lateral position

Table 1: Sensitivity and specificity of balloon expulsion testing in diagnosing dyssynergic defecation (stratified by subject position with 95% confidence intervals)

<table>
<thead>
<tr>
<th>Summary test characteristic</th>
<th>Seated position</th>
<th>Left lateral position</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case-control and cohort studies (optimal estimates)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sensitivity</td>
<td>69% (54% to 85%)</td>
<td>54% (7% to 100%)</td>
</tr>
<tr>
<td>Specificity</td>
<td>81% (76% to 86%)</td>
<td>90% (79% to 100%)</td>
</tr>
<tr>
<td>Only cohort studies evaluating unselected subjects with constipation (real world estimates)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sensitivity</td>
<td>69% (53% to 86%)</td>
<td>76% (70% to 83%)</td>
</tr>
<tr>
<td>Specificity</td>
<td>54% (6% to 100%)</td>
<td>76% (51% to 100%)</td>
</tr>
</tbody>
</table>

Conclusion: The performance characteristics of balloon expulsion could support the use of this test to screen for dysynergic defecation in chronically constipated subjects.

Disclosures of Interest: W.D. Chey: Dr. Chey is a consultant for Ironwood Pharmaceuticals and Allergan. He is co-CMO of My Total Health and holds a patent on My GI Health.

Other authors have declared no conflicts of interest.

P1151 PREVALENCE OF ANAL SQUAMOUS INTRAEPITHELIAL LESIONS IN LIVER TRANSPLANTED PATIENTS


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Background: There are few studies in liver transplant recipients, but no information exists regarding prevalence in liver transplantation.

Objective: To evaluate the prevalence of anal squamous intraepithelial lesions in liver transplant recipients compared with healthy subjects.

Methods: A retrospective case-control study involving liver transplant recipients that were compared with a healthy control group. All patients were submitted to anal cytology. Those with abnormal cytological results, namely high-grade squamous intraepithelial lesions (HSIL), atypical squamous cells which cannot exclude high-grade squamous intraepithelial lesions (ASC-H), low-grade squamous intraepithelial lesions (LSIL) and atypical squamous cells of undetermined significance (ASC-US), were submitted to high-resolution anoscopy with biopsies of any suspicious lesion.

Results: A total of 59 liver transplant recipients and 57 controls underwent anal cytology. In the liver transplant group, 37 (63%) were men, with a mean age of 54 ± 10 years. The most common indication for transplantation was alcoholic cirrhosis in 26 patients (44%), the majority of the patients were only on tacrolimus (n = 29, 51%), and had been transplanted a mean of 8 ± 5 years ago. In the healthy control group, 36 (63%) were men, with a mean age 59 ± 11 years.

Conclusion: Liver transplant patients have a higher risk of anal squamous intraepithelial lesions and screening should be considered especially in smokers.

Disclosures of Interest: All authors have declared no conflicts of interest.

P1150 A SYSTEMATIC REVIEW AND META-ANALYSIS TO DETERMINE WHETHER BALLOON EXPULSION TESTING MIGHT BE AN APPROPRIATE INITIAL OFFICE-BASED TEST FOR DYSSYNERGIC DEFECATION

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Introduction: Balloon expulsion testing (BET) is a recommended means of identifying dyssynergic defecation (DD) in patients with chronic constipation (CC) and is recommended for use in the diagnosis of DD in patients with constipation symptoms and chronic constipation. However, it may not be related to reduced gas and distention, and should be used as a tool to diagnose DD in the setting of altered bowel habit. The aim of this study was to assess the clinical utility of BET as an initial test for DD and to determine appropriate testing parameters.

Methods: We conducted a literature search (PubMed, Embase, conference abstracts from 1950–2016) to identify (1) case-control studies of DD or unselected CC subjects and healthy controls and (2) cohort studies of unselected subjects with CC. Eligible studies reported BET test parameters and results as well as presence of DD defined by constipation symptoms and a positive reference test (anorectal manometry [ARM], defecography, or electromyography[EMG]). Study quality was assessed using QUADAS criteria. We extracted age, sex, enrollment criteria, BET test parameters (subject position, stool consistency, allowed expulsion time), and DD diagnostic criteria. Data were independently extracted by two authors. Meta-analysis was performed using a bivariate mixed-effects regression model. Meta-regression was performed to evaluate effects of individual test parameters. Between-study heterogeneity was evaluated using an I² statistic. Publication bias was assessed using Deeks funnel plot summary test.

Results: We identified 15 eligible studies comprising 2,090 individual assessments of balloon expulsion, of which 14 studies of 1,760 subjects were eligible for cohort analysis, and 1,968 subjects were eligible for case-control analysis. Among cohort studies, the AUC was 0.80 (95% CI 0.61–0.91) with 70% sensitivity (95% CI 52%–83%) and 77% specificity (95% CI 70%–82%). Among pooled cohort and case-control studies, the AUC was 0.84 (95% CI 0.68–0.93) with 80% sensitivity (95% CI 53%–82%) and 81% specificity (95% CI 75%–86%). Further test performance characteristics stratified by subject position are reported in Table 1. Subject positioning (seated vs. left lateral decubitus) did not significantly affect AUC in cohort (p = 0.32) or case-control (p = 0.43) analysis. Pooled sensitivity (p = 0.50) and specificity (p = 0.66) were similar between seated and left lateral BET in analysis of unselected CC cohort studies, though specificity was higher with left lateral BET in pooled analysis of all studies (p = 0.03). The allowable time for balloon expulsion did not significantly affect summary sensitivity (p = 0.92) or specificity (p = 0.96) in meta-regression within the evaluated range of 1 and 5 minutes. There were enough studies to warrant meta-analysis of balloon distension characteristics, 13 of 17 studies reported 50–60 mL of water. When pooling cohort and case-control studies, both age (p = 0.01) and gender (p = 0.01) appeared to influence test performance. AUC and specificity did not significantly affect test performance (ARM p = 0.35, defecography p = 0.43, or EMG p = 0.08). Continent of origin (p = 0.34) and year of study (p = 0.29) did not differ to significantly influence test performance. There was no evidence of publication bias (p > 0.5).

Conclusion: The performance characteristics of balloon expulsion could support the use of this test to screen for dysynergic defecation in chronically constipated subjects.

Disclosures of Interest: E. Shah: E. Shah is a consultant for Ironwood Pharmaceuticals and Allergan. He is co-CMO of My Total Health and holds a patent on My GI Health.

Other authors have declared no conflicts of interest.
Gastrointestinal mediated food allergy (GMA) is a common disorder rising in recent years. The scientific research on this disease has increased, however its diagnosis still remains difficult to date. Diamine oxidase (DAO) is an enzyme that deactivates histamine, the main mediator in allergic reactions, through oxidative deamination. It has been shown that the enzymatic activity of DAO is diminished in the colonic mucosa of patients with GMA. Up to now no studies concerning the expression of DAO in the upper gastrointestinal tract (GIT) of patients with GMA have been published. Therefore, the objective of this study was to analyse the immunohistochemical staining of DAO and its localisation in the upper GIT of patients with or without GMA.

Aims & Methods: The study was retrospective. The GMA group consisted of 21 patients with diagnosed food allergy. The control group (CG) included 17 patients with neither food allergy nor food intolerance. Tissue samples from esophagus, cardia (subdivided in esophageal and gastric region), corpus, antrum and duodenum already obtained during endoscopy were immunohistochemically stained for DAO. The expression of DAO was semi-quantitatively analysed with the following scale based on the staining intensity of DAO (SI-DAO): 0 (none), 1 = low, 2 = medium, 3 = high intensity. The localisation of DAO was also examined vertically from the epithelium to the submucosa in all tissues.

Results: Immunohistochemical analysis found DAO in all segments of the upper GIT. The control group (CG) included 17 patients with neither food allergy nor food intolerance. Tissue samples from esophagus, cardia (subdivided in esophageal and gastric region), corpus, antrum and duodenum already obtained during endoscopy were immunohistochemically stained for DAO and its localisation in the upper GIT of patients with or without GMA. With the use of the staining intensity of DAO (SI-DAO) in the upper GIT, a median SI-DAO of 1.1 was observed in both groups, but this difference was not statistically significant. The SI-DAO was also examined vertically from the epithelium to the submucosa in all tissues. The analysis was performed twice by the same examiner in two separate points of time. Furthermore, the tissue samples were immunohistochemically stained for MBP and CD117 in order to count the number of eosinophils and mast cells respectively. Two measurements were performed inside an area of 100 mm² in the lamina propria (LP); one in the subepithelial superficial lamina propria (SLP) and one in the deeper lamina propria (DLP). The average of these two measurements constituted the number of these cells for each tissue.

Conclusions: The above mentioned findings indicate that DAO is present in low amounts in all segments of the upper GIT. But only in the duodenum a significant difference was found between GMA and CG, thus indicating that histamine-mediated symptoms most likely arise in duodenum. Therefore, regarding the upper GIT, the immunohistochemical staining of DAO only in duodenum could serve as an additional diagnostic parameter for detecting patients with GMA and possibly other histamine-mediated diseases. The above mentioned distribution pattern of DAO strengthens the theory that DAO acts extracellularly and is responsible for the elimination of the transepithelially absorbed exogenous histamine as well as of the endogenous histamine, as its highest staining intensity is found at the SLP throughout the upper GIT.

Disclosure of Interest: All authors have declared no conflicts of interest.
L-cysteine has been proposed as adjuvant therapy in CAG; the amino acid binds covalently to acetaldehyde (a Group I human carcinogen), removing it from the stomach. The aim of present study was to use L-cysteine to improve the symptoms in patients with diagnosis of CAG.

Aims & Methods: One hundred fourteen consecutive patients (M = 43, mean age 49.9 years) with CAG (based on endoscopic diagnosis of CAG) and means of both gastric histology (moderate to severe chronic, atrophic, body gastritis according to the OLGA staging system) and serology (pepsinogen 1 < 25 μg/l, gastrin-17 > 14 pmol/l) el GastroPanel®, Bioht, Oy, Finland) entered the study. Forty-one patients (11 M, mean age 49.8 yr, range 27–71 years) were treated with L-cysteine (100 mg 3 times daily, with meals) for 24 months (Group 1). As a control group we enrolled 73 CAG patients (M = 32, mean age 55.5 yr, range 32–77 yrs) followed up for 24 months without any related therapy (Group 2). The diagnostic fullness, nausea, bloating) were recorded at baseline and after 3, 6, 12, 24 months, according to severity score (0–3 for each symptom, min. 0 = no symptoms; max. 12 = full symptom).

Results: The typical symptomatic score results as follows, lasting the 24 months follow-up. Group 1: baseline 4.93; 3 months 3.36; 6 months 2.96; 24 months 2.64. Group 2: baseline 5.9, 3 months 6.2, 6 months 5.6, 24 months 5.8 (p < 0.01). Subdividing the CAG patients according to the etiology (autoimmune gastritis or Helicobacter pylori infection) no differences were found in improving symptoms. No relevant side effects were observed during the study.

Conclusion: The administration of L-cysteine to subjects affected by moderate–severe chronic atrophic gastritis seems able to improve the symptoms in a two-year follow-up.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1155 PROGNOSTIC SIGNIFICANCE OF SERUM INFLAMMATORY MARKERS IN GASTRIC CANCER

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Introduction: Despite undergoing potentially curative resection a significant proportion of patients develop cancer recurrence. Several cellular and humoral components of systemic inflammatory response have been reported and associated with poor outcome. To date, no study has comprehensively examined the relationship between readily available markers of inflammation and survival in gastric cancer.

Aims & Methods: Patients undergoing surgery for stage I-II gastric cancer between 2004-2016 at a regional unit were identified. Measurements of various systemic inflammation markers were recorded pre-operatively. Pathological factors were recorded from reports issued at the time of resection. The modified Glasgow Prognostic Score (based on CRP and Albumin), Neutrophil-Lymphocyte Ratio, Platelet-Lymphocyte Ratio and Neutrophil-Platelet score were calculated. Pathological variables including TNM stage, differentiation and vascular invasion were also recorded. Survival endpoints of overall survival (OS) and disease-free survival (DFS) were used.

Results: 331 patients were identified and 291 patients underwent potentially curative resection for gastric cancer. On unvariable DFS analysis, female gender, proximal location, T-stage, N-stage, TNM, vascular invasion, poor differentiation, R1 status, platelet count and mGPS were significantly associated with poor survival. On multivariable DFS analysis, mGPS (Hazard Ratio (HR) 2.51 95% Confidence Interval (CI) (1.35–4.65); p = 0.001) was an independent predictor of survival and was also observed in OS with mGPS (HR 2.75 (95%CI 1.65–4.59); p < 0.001). The mGPS was associated with advanced T-stage (p = 0.013), TNM stage (p = 0.013) and poor differentiation (p = 0.030).

Conclusion: The mGPS was the only inflammatory based marker to independently predict poor DFS and OS and may represent the optimum method for systemic inflammatory response quantification.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1156 ANALYSIS OF REBLEEDING PATIENTS IN UPPER GASTROINTESTINAL BLEEDING IN A SINGLE CENTER SERIES

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Introduction: Upper gastrointestinal bleeding (UGIB) is one of the main causes of hospital admission and urgent endoscopy in Gastroenterology departments. In-hospital mortality from UGIB has decreased throughout the past 2 decades in-hospital and delayed 6-months mortality, rebleeding and delayed 6-months bleeding and cardiovascular events. Final results: 507 patients were included (339 males; aged 62 ± 16.4). The incidence of rebleeding was 17.3% (n = 88). In the univariate analysis, factors related with rebleeding were creatinine levels (1.52 vs. 1.15; p < 0.001), tachycardia (96.28 vs. 88.24; p < 0.001), low levels of albumin (2.80 vs. 3.28; < 0.001) and low blood pressure (103 vs. 115; p < 0.001). In a multivariate analysis tachycardia and high creatinine were independent risk factors for rebleeding, and albumin showed as an independent protective factor (Table 1). Rebleeding was associated with in-hospital mortality (p < 0.0001); by contrast, it was not related to delayed 6-months mortality and with both hemorrhagic and hemorrhagic events. The UGIB risk scores AIMS 65 and Rockall showed poor predictive ability for acute mortality in the rebleeding patients’ group and was similar for Blatchford score (based on AURC).

Conclusion: Rebleeding in UGIB is associated with increased in-hospital mortality; nevertheless, it is not related with delayed 6-months mortality, hemorrhagic and cardiovascular events. High creatinine and low albumin levels were independent risk factors for rebleeding, suggesting a potential predictive role of these parameters. AIMS65, Rockall and Blatchford were the best predictive indicators for in-hospital mortality but worked poorly in the patients who suffered rebleeding.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1157 A CASE-CONTROL STUDY ON THE RISK OF UPPER GASTROINTESTINAL MUCOSAL INJURIES IN SUBJECTS PRESCRIBED NSAIDS AND ANTI-THROMBOTIC DRUGS USING THE LARGE ORGANIZED DATABASE OF CLAIMS IN JAPAN

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Introduction: Upper gastrointestinal (GI) adverse effects induced by NSAIDs and anti-thrombotic drugs are increasing along with progressive aging of society. Recently it is essential to perform pharmaco-epidemiological studies to identify adverse effects in the real-world setting using a large-scale medical database. We conducted a case-control study to assess the risk for upper GI mucosal injuries in subjects prescribed NSAIDs and anti-thrombotic drugs using the large organized database of claims in Japan.

Aims & Methods: The medical claims database developed by Japanese Medical Data Center (JMDC) Co., Ltd. was selected as data source in the present retrospective observational study. The JMDC claims database comprised of integrated medical and pharmacy claims, and includes both hospital and outpatient care from over 90 payers (approximately 3.7 million of population on an accumulated basis). Eligible subjects were aged 20 to 74 and registered for at least 3 months in the database from January 2009 to December 2014. The evaluated upper GI mucosal injuries were peptic ulcers (143,271 cases), upper GI bleeding (10,545 cases) and gastroesophageal reflux disease (GERD: 154,755 cases) with diagnosis by ICD-10 codes and implementation of the upper GI endoscopy. For the each test-case, ten controls which matched age, sex and diagnosis month were identified from the database. Multivariate logistic regression analysis was used to calculate odds ratios of occurrence of each upper GI mucosal injuries caused by NSAIDs, COX-2 selective inhibitors, low-dose aspirin, antiplatelet drugs (except low-dose aspirin) and antiocoagulants.

Results: The odds ratios of peptic ulcers were 1.45, 1.31, 1.50, 1.53 and 1.62 for NSAIDs, COX-2 selective inhibitors, low-dose aspirin, antiplatelet drugs, and antiocoagulants, respectively. The odds with time decreased with the occurrence of peptic ulcers (p < 0.0001 in each). The odds ratios of upper GI bleeding were 1.76, 1.62, 1.96, 1.82 and 2.38, and those of GERD were 1.54, 1.41, 1.89, 1.67 and 1.91, and these odds ratios were statistically significant in each medicine with GI bleeding and GERD (p < 0.0001 in each). The odds ratios of all the upper GI mucosal injuries were the highest in the patients with antiocoagulants, and the ratios were relatively low in those with NSAIDs and COX-2 selective inhibitors. The odds ratios tended to increase with the number of prescribed
medicines (1 agent < 2 agents < 3 agents, peptic ulcer: 1.38 ± 2.49 ± 4.52, upper GI bleeding: 1.74 ± 3.95 ± 7.77, GERD: 1.61 ± 2.96 ± 5.85, respectively). The upper GI mucosal injuries were exacerbated in complication of lifestyle-related diseases, including hyperlipemia and diabetes mellitus.

Conclusion: Prescribing NSAIDs and anti-thrombotic medicines was associated with increased risks of developing upper GI injury. The present large-scale, cross-sectional study utilizing the large organized database of claims in Japan provided precise clinical evidence for safety management of medical drugs in the clinical settings in Japan.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

P1158 GASTROINTESTINAL BLEEDING UNDER ANTIACOAGULATION THERAPY: SYSTEMATIC REVIEW OF THE REBLEEDING RISK, ITS REVERSIBILITY PROFILE AND RISK STRATIFICATION TO SELECT PATIENTS FOR LEFT ATRIAL APPENDAGE OCCLUSION

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Introduction: Percutaneous left atrial appendage occlusion (LAAO) is increasingly recognized as valid alternative therapy to reduce thromboembolic risk in patients with non valvular atrial fibrillation (AF) and contraindications for long term oral anticoagulation (OAC) therapy. Patients at high thromboembolic risk with previous gastrointestinal bleeding (GIB) might be at risk of bleeding recurrence in case of resuming anticoagulation. They could be selected for alternative therapies like LAAO. Up to now, there is no scientific consensus for patient selection for LAAO based on recurrent GIB risk.

Aims & Methods: We aimed to review the literature on gastrointestinal (GI) bleeding under anticoagulation to propose a method to define the reversibility profile of each lesion in an organ by organ and lesion by lesion approach to stratify the risk of bleeding individually. We systematically collected data from both prospective and retrospective studies from pubmed in order to extract rebleeding risk by ephology. The reversibility profile was defined by type of treatment needed to cure the lesion. Low reversibility (LR) profile was defined as a need for heavy treatment (surgery, radiotherapy, embolisation) to cure the lesion or as diffuse lesions.

Results: The most frequent reported causes of bleeding are peptic gastroduodenal ulcer (60%) for upper GI, diverticulosis (40%), colitis (20%) and anorectal diseases (20%) for lower GI and angiodysplasia (23%) for the midgut, these latter being responsible for 5% of all GI bleeding causes. The rate of rebleeding under OAC therapy is 5-7%. The incidence of VKA is higher than in patients with aspirin use. The rate of recurrent bleeding for upper GIB, lower GIB and obscure GIB are respectively 30%, 44% and 45%.

In the upper GI tract, lesions at high risk of bleeding recurrence are Dieulafoy lesions and angiodysplasia with reported rates up to 40% in some series. In the lower GI tract, lesions at highest risk are diverticular disease, angiodysplasia, colitis and radiation rectitis with bleeding recurrence rates reaching 60%, 20%, 40% and 20% respectively. For the midgut, angiodysplasia (20%) and bleeding of unknown origin (20%) are associated to the highest risk of recurrent bleeding.

LR profile lesions with high rebleeding risk are present for diffuse angiodysplasia, systemic diverticulosis and Dieulafoy lesions.

Conclusion: In conclusion, GI lesions at high risk of recurrent bleeding with low reversibility profile are infrequent and include in particular: diffuse angiodysplasia, colonic diverticulosis and Dieulafoy lesions. Patients with AF having those lesions undergoing GIB under anticoagulation might be the best candidates for alternative therapies like LAAO. Larger studies are needed to assess the long term outcome of patients treated by LAAO for GIB under current oral anticoagulant therapies.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
Aims: AIMS65 score with the Glasgow-Blatchford and Rockall scoring systems. 

Methods: AIMS65 Score and Other Scoring Systems for Predicting Clinical Outcomes in Koreans with Nonvariceal Upper Gastrointestinal Bleeding. 


Results: The AIMS65 score compared with the Glasgow-Blatchford score in predicting outcomes in upper GI bleeding. Gastrointestinal endoscopy. 2011;74(6):1215–24.

P1161 COMPARISON OF RISK-SCORING SYSTEMS IN PREDICTING NEEDS OF INTERVENTION AND CLINICAL OUTCOMES OF UPPER GASTROINTESTINAL BLEEDING

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Introduction: There are several risk-scoring systems that are available to assist the management of upper gastrointestinal bleeding (UGIB). The aim of this study is to compare the performance of pre-endoscopy (pre-RE), post-endoscopy Rockall score (post-RE) and GBS and AIMS65 scores in predicting the need for intervention in patients admitted to hospital for UGIB.

Aims and Methods: Data related to the three scoring systems were collected prospectively and scores were calculated in consecutive patients who were admitted with acute UGIB to the Royal Adelaide Hospital over 24 months. The performance of these scoring systems was evaluated by constructing receiver operating characteristics (ROC) curves, in predicting the following outcomes was assessed: the need for endotherapy, rebleeding risk, transfusion requirement, surgical intervention and death. All patients received high dose acetylsalicylic acid prophylaxis.

Results: Of 895 (66.4 ± 0.66yrs) patients who presented with UGIB, 622 (402M; 65.7 ± 0.60yrs) underwent endoscopy with 123 (38%) required endoscopic therapy, 42 (13%) repeated endo-therapy and 12 (3.7%) surgery for haemostasis. 

The scoring systems performed equally well in predicting the need for surgery (GBS vs. Rockall vs. AIMS65 AUC: 0.72 vs. 0.67 vs. 0.71) and death (AUC: 0.75 and 0.72 vs. 0.69).

Conclusion: The AIMS65 is an independent risk factor for rebleeding of HDU after endoscopic hemostasis, with a dose-response relation (P = 0.015).

Disclosure of Interest: All authors have declared no conflicts of interest.

P1162 STEROID ADMINISTRATION IS AN INDEPENDENT RISK FACTOR FOR REBLEEDING IN HEMORRHAGIC DUODENAL ULCER WITH A DOSE-RESPONSE RELATION

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Introduction: Hemorrhagic gastroduodenal ulcer is commonly seen in routine clinical practice, and there have been many studies investigating risk factors for rebleeding. However, few studies have evaluated hemorrhagic gastric ulcers (HGU) and hemorrhagic duodenal ulcer (HDU) separately. Furthermore, the relation between steroid administration and rebleeding in hemorrhagic gastro- intestinal ulcer remains unclear.

Aims and Methods: The aim of this study was to clarify the difference of rebleeding between HGU and HDU, and associated factors for rebleeding of HGU and HDU. Between March 2005 and September 2016, 176 consecutive patients with hemorrhagic gastroduodenal ulcer (106 with HGU and 70 with HDU), who underwent endoscopic hemostasis, were enrolled in this study. Regular dose proton pump inhibitor was administrated to all patients after the diagnosis of hemorrhagic gastroduodenal ulcers. Rebleeding was defined as hematoma or melena with ulcers confirmed by endoscopy or a decrease in the hemoglobin level > 2 g/dl in the presence of endoscopically proven ulcers. First, we compared the rebleeding rate between HGU and HDU. Subsequently, associated factors for rebleeding of HGU and HDU were calculated by logistic regression analysis individually. The estimated factors were age (< 65 vs. >65yrs), gender, location of ulcer (upper third/middle or lower third in HGU and 2nd portion/bulbs in HDU), underlying comorbidities (ischemic heart disease, liver cirrhosis, hypertension, diabetes mellitus, and hyperlipidemia), number of ulcers (multiple/single), hemostasis method (pure ethanol injection therapy/other therapies), anti-platelet therapy, anti-inflammatory therapy, steroid administration, anticoagulant administration, antacid administration, initial ulcer bleeding, hypoalbuminemia (serum albumin level ≤ 2.5 g/dl), and hemodilution. We further investigated the detailed association between steroid administration and rebleeding in HDU, including dose-response relation.

Results: The rebleeding rate of HGU and HDU were 5.7% and 22.9%, respectively, which was statistically significant (P = 0.001). There was no missing data in the estimated factors. Although no factor was associated with rebleeding in HDU, multivariate logistic regression analysis revealed that the independent factors for rebleeding in HDU were multiple ulcers [odds ratio (95% confidence interval) = 24.2 (2.76–213), P = 0.004], steroid administration [1.40 (1.73–113), P = 0.015], and hemodilution [0.53 (1.00–90.7), P = 0.049]. Regarding the detail of steroid administration, multivariate analysis showed that middle or high steroid administration (> 20 mg in prednisolone) (52.7 [3.19–871], P = 0.006) was a significant factor for rebleeding of HDU, with a dose-response relation (P = 0.003).

Conclusion: HDU developed significantly higher rebleeding after endoscopic hemostasis, compared with HGU. In addition to multiple ulcers and hemodil- lysis, we firstly demonstrated by multivariate analysis that steroid administration is an independent risk factor for rebleeding of HDU after endoscopic hemostasis, with a dose-response relation.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1163 EFFICACY AND SAFETY OF BIO-INSERT MINERAL SMECTITE IN CONTROLLING GASTROINTESTINAL HEMORRHAGE: AN ANIMAL STUDY PILOT

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Introduction: Granular smectite is bioinert mineral and efficient for curing diarrhea. Inspired by its dehydration and tissue-covering effect, this pilot study was to investigate its efficacy and safety for controlling hemorrhage in rats.

Aims and Methods: 32 rats were divided into four equal groups. For hemorrhage model, a horizontal 10-mm incision was made on the lower part of the left hepatic lobe. Commercial hemostatic powder, smectite, starch and normal saline were respectively applied. Bleeding duration and blood loss were recorded. 1 week later, rats were sacrificed and liver tissue was collected for histopathology.

Results: Smectite demonstrated the best hemostasis effect, and its mean coagula- tion time was 1.45 ± 0.026 min. Commercial hemorrhagic chitosan stypic powder need 2.5 ± 0.04 min for complete clotting, while Starch group was 4.25 ± 0.06 min and normal saline group was 5.04 ± 0.08 min. Similarly, smectite led to less loss of blood (0.6188 ± 0.034 g, while rats lost 2.3288 ± 0.123 g blood (p < 0.05) under normal saline treatment. For starch and commercial chitosan, the blood loss was respectively 2.0862 ± 0.061 g and 1.925 ± 0.028 g. Histopathological results confirmed that smectite was biocompat- ible to tissue.

Conclusion: The mineral smectite powder was the superior candidate for hemorrhage treatment in vivo. Compared with common polysaccharide agents, smectite could induce faster coagulation and reduce blood loss. More importantly, bios- nert smectite was biocompatible and even promoted the wound healing. For gastrointestinal application, smectite powder could be delivered through endo- scalar probe, while its inspiring efficacy required more endoluminal hemorrhage tests.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1164 PREDICTORS OF LIFE THREATENING MUCOSAL ULCERATION AFTER VASCULAR SCLEROTHERAPY

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Introduction: Life-threatening bleeding could occur early after vascular sclerotherapy in cirrhotic patients.

Aims and Methods: We aimed to determine simple predictive factors of this complication in cirrhotic patients. Among 750 patients treated with vascular sclero- therapy (esophageal varices: 605, 87.3%) and (gastric varices: 95, 12.7%) Zagazig University hospital-endoscopy unit- Internal medicine department, in the period from October 2014 till July 2016. 150 patients (20%, mean age 46.2 ± 4.9 years) (EV = 129, GV = 21) developed bleeding due to scler- otherapy induced ulcers confirmed by endoscopy 6.4.2 ± 1.3 days after the proce- dure. Cirrhosis was post viral hepatitis C (89%), hepatitis B (10%) and cryptogenic in (1%). A case-control study was performed comparing these
patients with 150 patients who underwent endoscopic variceal sclerotherapy without the development of bleeding due sclerant ulceration. Results: Bleeding occurred 6.4 ± 2.1 days (2–10) following sclerotherapy. Twenty-three patients died following the bleeding (15.3%). Using a multivariate analysis; pre-procedural factors as serum albumin ≥2 g/dl [OR 1.3], total bilirubin ≥1.6 mg/dl [OR 1.3], platelet ratio index (APRI) > 1 [OR 1.2], low prothrombin concentration <50% [OR 1.5]. Intra-procedural factors as amount of ethanolamine >15.5 ml [OR 2.6], ammonia ≥3.5 ml [OR 2.9]. Post-procedural factors within 24 hours after endoscopy; leukocytosis ≥>12,000 cell/ml [OR 1.9], drop of hemoglobin ≥10% of the pre-endoscopic value [OR 3.2], prolonged INR ≥1.55 [OR 1.2]. Conclusion: Bleeding related to sclerant ulcers is not uncommon, but may be life threatening. The proposed predictive factors should be watched and minimized before and during variceal sclerotherapy.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P1165 IMPACT OF SLEEP DISORDER IN PATIENTS WITH FUNCTIONAL DYSPESIA

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Introduction: Few studies were reported on the association between sleep disorders and Rome III-based functional dyspepsia (FD).

Aims & Methods: The aim of this study is to investigate the prevalence of sleep disorders in FD patients and the risk factors associated with sleep disorders. This multicenter, cross-sectional study had been conducted from August 2014 to December 2016 at 6 hospitals in Korea. Inclusion criteria were FD patients (>18years) met the Rome III criteria among the patients visited the gastroenterology department for dyspepsia. Exclusion criteria were prior surgery to the gastroduodenal area and no abnormal finding on endoscopy. Exclusion criteria were prior surgery to the gastroduodenal area and no abnormal finding on endoscopy. Exclusion criteria were prior surgery to the gastroduodenal area and no abnormal finding on endoscopy.

Results: This multicenter study included 160 FD patients and 223 healthy control groups. The total Pittsburgh Sleep Quality Index score was higher in FD patients than health controls (7.8 ± 4.3 vs 5.6 ± 3.1, p = 0.000). The prevalence of sleep disorder was significantly higher in FD patients than healthy control (41.2% vs 18%, p = 0.000). In univariate analysis, FD was significant risk factor for sleep disorder (OR 3.12, p = 0.001). The independent risk factors for sleep disorder in multivariate analysis were OR 1.80, p = 0.026, female (OR 1.78, p = 0.028) and depression (OR 2.91, p = 0.000).

Conclusion: FD significantly impacted on sleep disorder. FD was independent risk factor in sleep disorder.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P1166 PREVALENCE OF DYSPESIA IN INDIVIDUALS WITH GASTRO-OESOPHAGEAL REFUX-TYPE SYMPTOMS IN THE COMMUNITY: A META-ANALYSIS

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Introduction: Dyspepsia and gastro-oesophageal reflux are highly prevalent in the general population, but the two conditions are felt to be separate entities. However, there are numerous mechanisms implicated in the pathogenesis of functional dyspepsia, some of which are common to gastro-oesophageal reflux symptoms (GORD), including visceral hypersensitivity and delayed gastric emptying. To inform future research on potential shared pathophysiological mechanisms, it is important to estimate the strength of association between the two conditions, and whether this association remains stable depending on the criteria used to define these conditions, as well as geographic location.

Aims & Methods: We conducted a systematic review and meta-analysis to estimate the prevalence of dyspepsia in individuals with gastro-oesophageal reflux symptoms, and to quantify the overlap between the two disorders. MEDLINE, EMBASE, and EMBASE Classic were searched (up until September 2016) to identify population-based studies reporting the prevalence of dyspepsia and GORD (OR 1.5). Kaplan-Meier survival analysis (≥15 years), defined using specific symptom-based criteria or a questionnaire. The prevalence of dyspepsia and weekly GORD were extracted for all studies. Pooled prevalence, according to study location and criteria used to define weekly GORD or dyspepsia, as well as odds ratios (OR), with 95% confidence intervals (CIs) were calculated. The degree of overlap between the two was examined.

Results: Of 14,132 papers evaluated, 79 reported prevalence of weekly GORD. Nineteen of these study populations, containing 111,459 participants, also reported the proportion of individuals with dyspepsia. The prevalence of dyspepsia in those with weekly GORD was 43.9% (95% CI, 35.1–52.9%). The pooled OR for dyspepsia in individuals with weekly GORD, compared with those without, was 6.94 (95% CI 4.33 to 11.12). The OR for dyspepsia in weekly GORD significantly higher than for any geographical region of the world, indicating a significantly higher diagnostic criteria used. The pooled degree of overlap between the two conditions was 25.9% (95% CI, 19.9–32.4%), varying from 22% when the Bowel Disease Questionnaire was used to define weekly GORD, to 42.6% with the Mayo Reflux Questionnaire.

Conclusion: The OR of dyspepsia in individuals with weekly GORD was seven-fold that of individuals without GORD, and that there is overlap between the two conditions in up to one-quarter of individuals. Reasons for this remain speculative, but may include shared pathophysiological mechanisms or residual confounding.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
A total of 51 out of 140 patients (36.4%) exhibited some typical for achalasia (dysphagia, regurgitation, chest pain).

Results: have been questioned by using a questionnaire about the occurrence of symptoms neurological examination, MR imaging of the brain and electrophysiological patients with esophageal achalasia have been questioned about the occurrence of neurological diseases. There are no studies examining a relationship between achalasia and multiple sclerosis suggesting that autoimmune processes are involved in these diseases might have common features. For example, a number of genetic diseases. There are no studies examining a relationship between achalasia and neurodegenerative/demyelinating diseases. These results warrant further confirmation in a large population-based study. Disclosure of Interest: All authors have declared no conflicts of interest.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
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P1168 AN INCREASED PREVALENCE OF NEURODEGENERATIVE/DEMYELINATING PROCESS IN PATIENTS WITH ESOPHAGEAL ACHALASIA—A PROSPECTIVE STUDY

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Introduction: In the recent years, there has been an increasing recognition of the presence of gastrointestinal (GI) dysfunction in patients with neurologic diseases. There are no studies examining a relationship between achalasia and neurodegenerative/demyelinating diseases of central nervous system, although these diseases might have common features. For example, a number of genetic variations have been shown to increase the risk of both conditions (e.g. HLA-DQB1-insertion on chromosome 6 may be strongly associated with both achalasia and multiple sclerosis suggesting that autoimmune processes are involved in their etiopathogenesis). Several other findings (e.g. inflammatory infiltrates, Lewy’s bodies, geospatial gradient etc.) are also present in both patients with achalasia and with neurodegenerative/demyelinating diseases.

Aims & Methods: The aim of our prospective study is to examine a prevalence of neurodegenerative/demyelinating diseases in a cohort of consecutive patients with confirmed esophageal achalasia. Achalasia was diagnosed by high-resolution manometry, endoscopy and esophagogram. A total of 140 consecutive patients with esophageal achalasia have been questioned about the occurrence of neurological diseases and symptoms in their personal and family history. Those with a suspicion of a neurological disease were relevant, with the predictive patterns being most clearly driven by individuals who qualified for FGID.s. In light of these results, studies of the brain-gut axis need to consider a greater array of psychological traits were relevant, with the predictive patterns being most clearly driven by individuals who qualified for FGID.s. Achalasia was diagnosed by high-resolution manometry, endoscopy and esophagogram. A total of 140 consecutive patients with confirmed esophageal achalasia (dysphagia, regurgitation, chest pain). Among patients with a presence of neurological symptoms, 5 patients (3.6%) had definitely been diagnosed with a neurodegenerative/demyelinating disease: multiple sclerosis - 2 patients, Lebert’s optic neuritis - 1 patient, Parkinson’s disease - 1 patient and Allgrove syndrome - 1 patient). Furthermore, 7 patients with a positive questionnaire had been diagnosed with other neurological diseases (tetrany n=1, carpal tunnel syndrome n=1, episcleritis n=1, subdural hematoma n=1, idiopathic intracranial hypertension n=1) and 4 patients had a positive questionnaire had been diagnosed with other neurological diseases (tetrany n=1, carpal tunnel syndrome n=1, episcleritis n=1, subdural hematoma n=1, idiopathic intracranial hypertension n=1). For those with neurological symptoms (vs. 0 out of 89 patients without neurological symptoms) had a positive family history of a neurodegenerative or a demyelinating disease. Among 106 patients with a neurodegenerative/demyelinating disease, 30 of them (27.8%) described dysphagia as a part of their personal history. These patients will be examined by esophageal manometry.

Conclusion: Our results imply an increased prevalence of neurodegenerative/demyelinating diseases in patients with achalasia (3.6% vs. approx. 1.4% in the Czech controls). Also, a high prevalence of dysphagia was found among patients with a neurodegenerative/demyelinating disease. These results warrant further confirmation in a large population-based study.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1169 HIGH RESTING PARASYMPATHETIC CARDIAC VAGAL TONE CONFRONTS A UNIQUE FUNCTIONAL BRAIN NETWORK DURING ACUTE OESOPHAGEAL PAIN

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Introduction: Visceral pain is a complex percept influenced by numerous factors. Of these, differences in the autonomic nervous system (ANS)–in particular, parasympathetic cardiac vagal tone (CVT)–has been suggested to have a physiological role in the regulation and modulation of painful sensory signalling, to the extent of vagal nerve stimulation (to raise subject CVT) being tested as a possible anti-nociceptive.

Methods: To date, no studies have explored the brain functional connectivity or network properties of CVT in relation to a painful stimulus, and thus this was our aim. In 21 healthy participants (10 male; mean age 30 years (range 21–53 years), we quantified resting CVT using a Neuroscope. For all subjects, functional MRI data were acquired using a 3T MRI scanner during painful oesophageal balloon distension as described elsewhere(1). The effect of resting CVT on brain networks during acute oesophageal pain were determined by means of network based statistics(2). Both groups had prior to any pain both an autonomic visceral pain literature and included the following: bilateral neck, upper thorax, upper ribcage, upper abdomen, lower abdominal, lower thorax, both shoulders, labia (28%) described dysphagia as a part of their personal history. These patients will be examined by esophageal manometry.

Results: We identified a unique subcortical brain connectivity network in the high resting CVT individuals when exposed to acute oesophageal pain. This complex symmetrical network comprised all 11 nodes with a total of 18 edges (significant

Abstract No: P1167

Table 1: Associations between individual psychological traits and symptom severity. Numeric entries are odd ratios (SFodds ratio). ***indicates p < 0.001, ** indicates p < 0.01, * indicates p < 0.05, and ~ indicates 0.05 p < 0.5.

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Bowel Non-FGID</th>
<th>Symptom FGID</th>
<th>Severity Combined</th>
<th>Epigastric Non-FGID</th>
<th>Symptom FGID</th>
<th>Severity Combined</th>
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<tr>
<td>Problem-focused coping</td>
<td>2.92 (1.23)*</td>
<td>0.93 (0.14)</td>
<td>1.16 (0.15)</td>
<td>1.00 (0.44)</td>
<td>1.03 (0.15)</td>
<td>1.12 (0.15)</td>
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<td>Worry</td>
<td>1.44 (0.51)</td>
<td>1.35 (0.22)*</td>
<td>1.60 (0.22)***</td>
<td>1.60 (0.65)</td>
<td>1.50 (0.26)**</td>
<td>1.71 (0.24)***</td>
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<tr>
<td>Avoidant coping</td>
<td>0.81 (0.14)</td>
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<td>0.97 (0.39)</td>
<td>0.93 (0.15)</td>
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<td>0.97 (0.13)</td>
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<tr>
<td>Doctor relationship</td>
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<td>1.06 (0.16)</td>
<td>1.06 (0.16)</td>
<td>1.00 (0.54)</td>
<td>1.03 (0.16)</td>
<td>0.97 (0.13)</td>
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<td>Childhood non-sexual abuse</td>
<td>1.65 (0.68)</td>
<td>1.06 (0.15)</td>
<td>1.33 (0.17)</td>
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<td>1.05 (0.15)</td>
<td>1.32 (0.17)*</td>
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<td>Social support</td>
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<td>0.85 (0.12)</td>
<td>0.88 (0.11)</td>
<td>0.68 (0.32)</td>
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<tr>
<td>Somatic rather than physical attribution</td>
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<td>0.93 (0.13)</td>
<td>0.72 (0.10)*</td>
<td>0.83 (0.36)</td>
<td>0.64 (0.11)**</td>
<td>0.63 (0.09)**</td>
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<tr>
<td>Doctor reassurance</td>
<td>0.99 (0.31)</td>
<td>1.06 (0.16)</td>
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<td>Somatisation</td>
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<td>2.16 (0.88)**</td>
<td>1.11 (0.18)</td>
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</tbody>
</table>

When considered jointly with other predictors, psychological attribution of symptoms was significantly positively related to both bowel symptom severity (non-FGID: OR = 0.31, SE = 0.13; Full: OR = 0.74, SE = 0.11) and epigastric symptom severity (FGID: OR = 0.63, SE = 0.09; Full: OR = 0.63, SE = 0.11). The same was the case for worry (Bowel: Full: OR = 1.40, SE = 0.21; Epigastric: OR = 1.58, SE = 0.27; Full: OR = 1.54, SE = 0.23). For bowel symptoms, problem-focused coping (OR = 2.30, SE = 0.98) was an additional independent positive (notably, not negative) predictor among participants without FGIDs. 
functional connections). These interconnections included the following: thalamo-amygдala, thalamus-hypothalamus, hypothalamus-NAc, amygdala-puinеn amygdala-NAc and insula-patumеn. No significant network was identified for the low CVT group.

Conclusion: During acute oesophageal pain, resting cardiac vagal tone yields a unique combination comprising numerous complex subcortical brain regions, many of which have been previously associated with either visceral pain or modulation of baseline autonomics either at the physiological or neuroanatomical level (3). Previous research has suggested that a high resting CVT may be protective of nociceptive signalling, and furthermore studies investigating vagal nerve stimulation have included and reported that of anti-nociception (4). Given the well-established role of these subcortical regions in pain processing, we suggest that this network identified may be of significance as to the neurophysiological process of parasympathetic modulation of painful sensory signalling. Lastly, to date, no studies have undertaken real-time assessment of the ANS (including CVT) during functional brain imaging and acute visceral pain. Future studies should investigate for this.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P1170 RAPID DRINK CHALLENGE (RDC) TEST DURING OESOPHAGO-GASTRIC JUNCTION OUTFLOW OBSTRUCTION D. Biasutto, F. Mion, A. Garros, S. Roman Digestive Physiology, Lyon 1 University and Hospices Civils de Lyon, Lyon;France

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Introduction: Oesophageo-gastric junction outflow obstruction (OGJOO) is of unclear significance. It may be secondary to an incomplete form of achalasia, a mechanical obstruction or be idiopathic. Rapid drink challenge (RDC) test is easy to perform during oesophageal HRM.

Aims & Methods: We aimed to assess the yield of RDC in patients with OGJOO. From a database of 3222 consecutive oesophageal HRM performed from 01/2012 to 03/2017, we extracted patients with OGJOO according to the Chicago Classification v3.0. HRM protocol consisted of 10 5-ml water swallows in supine position and RDC test (200-ml free drinking) in sitting position. Distal contractile integral (DCI) integrated relaxation pressure (IRP), distal and pan-oesophageal presurization (POP; homogenous oesophageal presurization >30 mmHg) were reported for 5-ml swallows. POP and oesophageal shortening (OS) were analysed during RDC. Symptom severity was assessed with Eckardt score. Causes of OGJOO were determined by reviewing patients’ chart for previous surgical process of parasympathetic modulation of painful sensory signalling. While RDC test cannot be used to determine EGJOO cause, patients with POP or OS during RDC had more severe dysphagia than those without. In patients with POP, the highest DCI might be secondary to obstruction. Further prospective studies should determine if RDC test could help to select patients who might benefit from treatment.

Disclosure of Interest: F. Mion: consulting for Medtronic; research support from Sandhill and Crespin. All other authors have declared no conflicts of interest.

P1171 THE NORMATIVE VALUES OF A NEW 36 CHANNELS WATER PERFUSION ESOPHAGEAL MOTILITY CATHETER S. Bor, S. Kipcak Gastroenterology Sec., Ege Reflex Study Group, Ege University, izmir;Turkey

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Introduction: High resolution manometry (HRM) is performed with solid-state catheters (SS) in many centers. However according to Chicago classification, very limited data from healthy volunteers are available for some catheters and starting from IRP, numerical values are crucial for the diagnosis. Because of the cost of the SS-HRM catheters many centers especially from developing countries use water perfusion HRM (W-HRM) catheters up to 24 channels and normal values are even more limited.

Aims & Methods: We evaluated a prototype 36 channels W-HRM reused catheter allowing to measure 3-D pressure volume analysis of lower esophageal sphincter in healthy volunteers and compared to 36 channels SS-HRM catheters (Laborie-MMS Canada). We included 43 healthy volunteers without any upper gastrointestinal complaint. Upper gastrointestinal endoscopy and 24h impedance-pH monitoring performed in all subjects. Four subjects were excluded because of silent GERD. 39 subjects were analysed (25 males, W-HRM (n = 39), SS-HRM (n = 33)). Thirty-three patients underwent two esophageal manometry studies within two consecutive days with a random order. Procedures were performed in supine position with receiving ten times 5 ml water, five times solid food and multiple water swallow with 200 ml of water. 36 channel water-perfused 3-D HRM catheter and 36 channel solid state HRM catheter were used (Laborie-MMS Canada).

Results: There was significant differences between two catheters in terms of Integrated Relaxation Pressure (IRP), Distal Contractile Integral (DCI) and DCI expanded, LES resting pressure, % of ineffective peristalsis, and esophageal length both with water and solid food swallows (Table). No difference has been shown with distal latency (DL), LES length, breaks size (Table).

<table>
<thead>
<tr>
<th>Parameter</th>
<th>ESOPHAGEAL LENGTH (INSPIRUM) (CM)</th>
<th>5ML</th>
<th>LES RESTING PRESSURE (MMHG)</th>
<th>IRP (MMHG)</th>
<th>DCI (MMHG<em>S</em>CM)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>23.1 ± 2</td>
<td>34.8 ± 13</td>
<td>17.4 ± 7</td>
<td>16.7 ± 4</td>
<td>0.8 ± 0.9</td>
</tr>
<tr>
<td>SD</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15ML</td>
<td></td>
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</table>

Conclusion: Water perfusion HRM catheter exhibits significantly lower values especially for IRP, DCI, LES resting pressure. Centers which are working with water perfusion catheters should not accept universal normal established with solid state catheters and need to work on their normative values. The ineffective peristalsis pattern is common with water perfusion catheters.

Disclosure of Interest: All authors have declared no conflicts of interest.

Table (continued)
Introduction: The Chicago Classification (CC V3.0) defined the presence of esophageal outflow obstruction (EGJ-OO) when the value of integrated releasing pressure (IRP) is higher than 15 mmHg during high-resolution manometry (HRM). Both low-volume (10 ml) multiple rapid swallow (MRS) and high-volume (200 ml) rapid drinking test (RDT) were never evaluated to detect the inhibition of esophageal body in patients with EGJ-OO.

Aims & Methods: The aim of this study was to compare the efficacy of MRS and RDT in evaluating the esophageal body inhibition during repetitive swallow in patients with EGJ-OO and in patients with functional heartburn (FH) considered as control group. From a larger group of patients evaluated for dysphagia with negative upper endoscopy, we enrolled consecutive patients with EGJ-OO, and as control group, patients with functional heartburn (FH) defined according to the Rome IV criteria. EGJ-OO was defined according to CC V3.0. HRM performed according to the Italian guidelines. All patients underwent 3 MRS (10 ml of water in 5 swallow in less than 10s) and 1 RDT (200 ml of water freely drunk). The mean DCI of MRS and the DCI of RDT were compared with DCI of 10 single swallows (SS). The MRS/SS and RDT/SS ratio were calculated.

Results: We evaluated 30 patients with EGJ-OO (18 males; mean age 49.5 ± 12.4 yrs) and 30 patients with FH (17 females; mean age 41.2 ± 13.6). Impedance and pH 24-h analysis was performed to select patients with FH (normal AET and number of reflux and lack of reflux-symptom correlation). During HRM the mean DCI resulted similar in patients with EGJ-OO compared to FH (p = 0.039). One-hundred and eighty MRS and 60 RDT were evaluated. The lack of body inhibition was found in 11% (20/180) during MRS and in 53% (15/30) of FH (p < 0.05). The MRS/RDT ratio resulted >1 in both groups. All results are reported in Table 1.

Conclusion: Patients with EGJ-OO showed less peristaltic reserve during MRS and RDT. The RDT evidenced more frequently lack of body inhibition in patients with EGJ-OO.

Disclosure of Interest: All authors have declared no conflicts of interest.

Table 1: Results of SS, MRS and RDT in patients with EGJ-OO and FH

<table>
<thead>
<tr>
<th></th>
<th>EGJ-OO group</th>
<th>FH group</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean DCI (mmHg-s-cm)</td>
<td>1455 ± 1436.1</td>
<td>1982.6 ± 974.4</td>
<td>0.101</td>
</tr>
<tr>
<td>Mean DCI SS</td>
<td>817.3 ± 665.4</td>
<td>1269.2 ± 1027.6</td>
<td>0.047</td>
</tr>
<tr>
<td>Mean DCI RDT</td>
<td>508.7 ± 318.6</td>
<td>1493.7 ± 799.2</td>
<td>0.001</td>
</tr>
<tr>
<td>MRS/SS ratio</td>
<td>0.9 ± 0.3</td>
<td>1.7 ± 0.7</td>
<td>0.008</td>
</tr>
<tr>
<td>RDT/SS ratio</td>
<td>1.2 ± 0.4</td>
<td>1.6 ± 0.7</td>
<td>0.001</td>
</tr>
<tr>
<td>MRS/RDT ratio</td>
<td>1.3 ± 0.4</td>
<td>1.4 ± 0.7</td>
<td>0.499</td>
</tr>
</tbody>
</table>

Conclusion: MRS is a more reliable test to detect peristaltic esophageal reserve when compared to RDT both in patients with IEM or those with normal esophageal peristalsis.

Disclosure of Interest: All authors have declared no conflicts of interest.

Introducción: El objetivo de este estudio consistía en comparar la eficacia de la MRS y el RDT en la evaluación de la inhibición de la masa esofágica durante el acto de deglución repetitiva en pacientes con EGJ-OO y en pacientes con bocio funcional (FH) considerado como grupo control. De un grupo mayor de pacientes evaluados por disfagia con endoscopia negativa, se incluyeron consecutivos con EGJ-OO, y como grupo control, pacientes con bocio funcional (FH) definido de acuerdo al criterio de la IV Romeo. EGJ-OO se definió de acuerdo al CC V3.0. HRM según las guías italianas. Todos los pacientes realizaron 3 MRS (10 ml de agua en 5 tragos en menos de 10s) y 1 RDT (200 ml de agua bebiendo libremente). El DCI medio de MRS y el DCI de RDT se comparó con el DCI de 10 tragos singulares (SS). La relación MRS/SS y RDT/SS se calculó.

Resultados: Se evaluaron 30 pacientes con EGJ-OO (18 varones; edad media 49.5 ± 12.4 años) y 30 pacientes con FH (17 mujeres; edad media 41.2 ± 13.6). Impedancia y pH 24-h se analizaron para seleccionar pacientes con FH (normal AET y número de reflus y falta de correlación síntoma-síntoma). Durante HRM, la media de DCI se resultó similar en pacientes con EGJ-OO comparado con FH (p = 0.039). Ciento y ochenta MRS y 60 RDT fueron evaluados. La falta de inhibición de masa fue encontrada en 11% (20/180) durante la MRS y en el 53% (15/30) de FH (p < 0.05). La relación MRS/RDT resultó >1 en ambos grupos. Todos los resultados se reportan en el Table 1.

Conclusion: Los pacientes con EGJ-OO mostraron menos reserva peristáltica durante MRS y RDT. El RDT evidenció más frecuentemente la falta de inhibición de masa en pacientes con EGJ-OO.

Disclosure of Interest: Todos los autores han declarado no tener conflicto de interés.
Distension to F. Wuestenberghs PATIENTS WITH OESOPHAGEAL DIVERTICULA compared to controls). Trans-EGJ bolus flow metrics were similarly abnormal assessing esophageal bolus presence (NI) and clearance (IR) were consistently abnormal of esophageal bolus transit and esophageal emptying in conjunction with lower proximal smooth muscle contractile function with all bolus consistencies in GERD patients compared to controls. Metrics assessing esophageal bolus presence (NI) and clearance (IR) were consistently abnormal in GERD patients (Table, p = 0.001 for all bolus consistencies for each comparison to controls). Trans-EGJ bolus flow metrics were similarly abnormal in GERD (BFT, p < 0.001 for all bolus consistencies compared to controls). IBP metrics were highest with solid swallows, especially in GERD patients compared to controls (Table). Within GERD, a gradient of increasing dysfunction in bolus presence and bolus clearance was noted, with least abnormalities with water swallows and the worst metrics with bread swallows (p < 0.02 across groups for each bolus comparison). IBP-EF (p < 0.05) and trans-EGJ BFT (p = 0.004) were higher during water and viscous swallows with atypical symptoms compared to typical symptoms. NI was consistently lower in patients reporting ≤75% symptom improvement following AFS with all bolus consistencies (p ≤ 0.046).

<table>
<thead>
<tr>
<th>Pressure Flow Analysis Comparisons Using Water, Viscous and Bread Swallows Between Controls and GERD Patients</th>
</tr>
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<tbody>
<tr>
<td>water swallows</td>
</tr>
<tr>
<td>controls</td>
</tr>
<tr>
<td>Proximal peak pressure (mmHg)</td>
</tr>
<tr>
<td>Distal peak pressure (mmHg)</td>
</tr>
<tr>
<td>Nadir impedance (ohms)</td>
</tr>
<tr>
<td>Distension to contraction latency (s)</td>
</tr>
<tr>
<td>Impedance (ohms)</td>
</tr>
<tr>
<td>Distal IBP (mmHg)</td>
</tr>
<tr>
<td>IBP-A (mmHg)</td>
</tr>
<tr>
<td>IBP-EF (mmHg)</td>
</tr>
<tr>
<td>Bolus flow (s/cm)</td>
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</tbody>
</table>

*p < 0.04 compared to controls. IBP: intrabolus pressure; IBP-A: IPB-accommodating pressure; IBP-EF:IBP-esophageal emptying

Conclusion: Automated pressure flow analysis of HRM studies demonstrates abnormalities of esophageal bolus transit and esophageal emptying in conjunction with lower proximal smooth muscle contractile function with all bolus consistencies in GERD patients compared to controls. Metrics assessing esophageal bolus presence may have prognostic value in GERD patients undergoing AFS. Disclosure of Interest: N. Rommel: Holder of patent on AIM technology with Taher Omari T. Omari: Holder of patent on AIM technology with Nathalie Rommel All other authors have declared no conflicts of interest.

References
Carlson DA, et al. Neurogastroenterol Motil. 2017
Results: We enrolled 35 achalasia patients (14 Type I, 16 Type II and 5 Type III). Ten patients underwent PD, 11 LHMD, 8 LHMD-T and 6 LHMD-NR. At baseline, no significant difference (p = 0.766, 0.434, 0.782) was observed in sex, age, smoking status or Eckardt score, GERDQ score, integral relaxation pressure (IRP) and Eckardt-CI were recorded. All Type III subjects underwent LHMD-D (3) and LHMD-T (2). After all the procedures, in all the patients there was a significant decrease in Eckardt score, IRP and EGJ-CI (p < 0.001, < 0.001 and < 0.05, respectively). PD and LHMD-NR showed higher Eckardt-CI (20.9 ± 23.5 ± 11.1 mmHg, respectively) and IRP (12.2 ± 3.4 and 13 ± 4.5, respectively) than LHMD-D and LHMD-T (18.4 ± 5.9, p < 0.05 and 9.3 ± 4.1 p < 0.05 mmHg/cm, respectively for EGJ-CI; 5.2 ± 2.5, p < 0.05 and 2.3 ± 3.7 p < 0.001 mmHg/cm, respectively for IRP). Post-operative Eckardt score was lower in LHMD-D and LHMD-T (2.1 ± 0.5 and 2.0 ± 0.6, respectively) than PD and LHMD-NR (4.2 ± 1.0, p < 0.01 and 3.7 ± 1.5, p < 0.05). Post-operative GERDQ score was significant higher in LHMD-T (3.0 ± 1.7 vs. 8.2 ± 3.9, p < 0.05). Low post-operative Eckardt-CI values correlated with an increased risk of high post-operative GERDQ score (p < 0.05, odds ratio 4.223, 95% CI 0.964–2.123).

Conclusion: All procedures performed to treat achalasia produced an adequate relief of dysphagia. LHMD-D and LHMT seem to result in a stronger alteration of the EGJ with LHMT resulting in an increased risk of post-operative reflux.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
P1179  EFFECTIVENESS OF CAP-ASSISTED DEVICE IN THE ENDOSCOPIC MANAGEMENT OF FOOD BOLUS OBSTRUCTION IN THE UPPER ESOPHAGUS

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Introduction: Although cap-assisted technique has been shown to be effective in removing food bolus from the upper gastrointestinal tract, there is no data on food bolus obstruction (FBO). This study aimed to assess the performance of cap-assisted technique in the management of esophageal FBO, as compared to conventional endoscopic methods.

Aims & Methods: Outcomes of all patients who present with FBO requiring emergency endoscopic management between 2011 and 2016 were prospectively collected. The main measured outcomes were procedural success, procedural time, complications and length of hospital stay.

Results: In total, 113 patients (214M:102F; 58.3±18.3 years) were enrolled with FBO. Of FBO, 267 (84.7%) had evidence of food bolus in the esophagus on endoscopy and 48 (15.2%) patients had spontaneous passage of food bolus. Out of the 199 patients who had impacted FBO, 93 had cap-assisted technique and 106 had conventional approach, with no differences in the type of location of FB. The success rate of cap-assisted technique (100%) was comparable to that of conventional techniques (97.2%, P=0.10). Patients who had failed extraction by conventional techniques (n=3) were successfully treated when switched to cap-assisted approach. Cap-assisted approach was associated with a shorter total procedural time (34.8±22 min, P=0.006), a shorter length of hospital stay (0.95±0.36 and 1.38±1.36 days, P=0.0017) and more en-block removal (95% vs 22%, P<0.0001). There were more complications in the conventional than the cap-assisted group (7/106 vs. 0/93; P=0.01).

Conclusion: Cap-assisted technique is 100% effective in the management of impacted FBO in the esophagus, with a significantly shorter procedural time and lower complication rate than conventional methods. Although the findings suggest that cap-assisted technique should be the first line technique in the management esophageal FBO, further evaluation with a randomized multicenter trial is warranted.

Disclosure of Interest: All authors have declared no conflicts of interest.

References:


P1180  DO THE ENDOSCOPIC FINDINGS OF GASTRITIS BRING THE FD SYMPTOMS?

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Introduction: Functional dyspepsia (FD) is defined in that there is no evidence of organic disease which is likely to explain the symptoms. However, there was no obvious definition about “organic disease”. Therefore, during the endoscopic examination, we have to consider such findings as the “organic disease” or not. If these findings have no obvious definition about “organic disease”. Therefore, during the endoscopic examination, we have to consider such findings as the “organic disease” or not. If these findings have no evidence of obvious mucosal change which may cause dyspepsia, the patient should be considered as non-erosive reflux disease in the Kyoto classification. This classification, endoscopic findings are defined precisely. However, it is not discussed whether we can consider such findings as the “organic disease” or not. Interestingly, AUC5 and AUC15 values (24.85 /1.31 and 56.11±2.51, respectively) in EPS patients with pancreatic enzyme abnormalities were significantly higher than the ratio of EPS patients without it. There were more complications in the conventional than the cap-assisted group (7/106 vs. 0/93; P=0.01). Overall, 64% of EPS patients with pancreatic enzyme abnormalities were diagnosed by endoscopy as having concomitant early chronic pancreatitis post-GRAF results.

Conclusion: Further studies are warranted to clarify how EPS patients with pancreatic enzyme abnormalities were associated with early chronic pancreatitis proposed by JPS.

Disclosure of Interest: All authors have declared no conflicts of interest.

References:


P1181  IMPACT OF EPIGASTRIC PAIN SYNDROME ACCOMPANYING PANCREATIC ENZYME ABNORMALITIES EXHIBITED RAPID EARLY PHASE OF GASTRIC EMPTYING AND EARLY CHRONIC PANCREATITIS USING ENDOSONOGRAPHY

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Introduction: There was not available data about the overlap between functional dyspepsia (FD) and pancreatic diseases.

Aims & Methods: We aimed to determine whether epigastric pain syndrome (EPS) accompanying with pancreatic enzyme abnormalities were associated with early chronic pancreatitis proposed by JPS using endosonography. We enrolled 99 consecutive patients presenting with typical symptoms of FD, including patients with postprandial distress syndrome (EPS) and EPS with pancreatic enzyme abnormalities (n=41) and EPS without pancreatic enzyme abnormalities (n=42) based on Rome III criteria. Gastric motility was evaluated using the 13C-acetate breath test. Early chronic pancreatitis was detected by endosonography and graded from 0 to 7.

Results: The ratio of female patients among EPS patients (34/41) with pancreatic enzyme abnormalities was significantly (p=0.0018) higher than the ratio of female EPS patients (20/42) without it. Postprandial abdominal distention and physical component summary (PCS) scores in EPS patients with pancreatic enzyme abnormalities were significantly disturbed compared to those in EPS patients without it. Interestingly, AUC1, AUC5, and AUC15 values (24.85±1.31 and 56.11±2.51, respectively) in EPS patients with pancreatic enzyme abnormalities were also significantly (p=0.002 and p=0.001, respectively) increased compared to those (19.75±1.01 and 47.02±1.99, respectively) in EPS patients without it.

Conclusion: Further studies are warranted to clarify how EPS patients with pancreatic enzyme abnormalities were associated with early chronic pancreatitis proposed by JPS.

Disclosure of Interest: All authors have declared no conflicts of interest.

References:


P1182  ENDOSCOPIC AUTOLOGOUS TRANSPLANTATION OF ESOPHAGEAL MUCOSA FOR TREATING THE REFRACTORY CAUSTIC ESOPHAGEAL STRicture

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Introduction: Caustic esophageal injury is corrosive burns of esophagus and mostly caused by ingestion of chemical caustic substances such as strong acid or alkali. The caustic esophageal stricture is refractory and patients suffered from multiple dilation. Clinical ESD results revealed that benign stricture would be the first line technique in the management esophageal FBO, further evaluation with a randomized multicenter trial is warranted.

 Disclosure of Interest: All authors have declared no conflicts of interest.
Results: The endoscopic follow-up was planned every month. After 1 months, 18.23 cm esophageal region had to be normal. Within 6 months, the stricture process was existingly delayed as expected. The patient stated his symptom was remarkably improved. Gastroscopy revealed the esophageal implanted lesion was covered with an epithelium and the luminal surface was flat, without ulceration.

Conclusion: Autologous esophageal mucosa transplantation might facilitate tissue re-epithelialization, reduce pathological fibrosis, and be helpful for managing or preventing esophageal strictures. More clinical controlled trials are required to provide evidenced-based recommendation and promote its clinical application.

Disclosure of Interest: All authors have declared no conflicts of interest.

Aims & Methods: We aimed to compare the prevalence of FD in patients with OSA and healthy volunteers. A total of 60 consecutive OSA patients (defined as Epsworth sleepiness scale > = 10, and apnea-hypopnea index > 10/hour during polysomnography; mean age: 47.6 years, male: 83.3%) and 60 healthy age-and-sex-matched volunteers were recruited in a prospective case-control study. Questionnaires were applied for the diagnosis of functional gastrointestinal disorders (FGIDs) according to Rome III criteria.

Introduction: The assessment of acid secretion is important in order to prescribe H2 blockers or proton pump inhibitors (PPIs) for treating gastroesophageal reflux disease (GERD). However, it is not currently used in clinical practice. Serum pepsinogen I (PGI) has been proposed as a non-invasive surrogate. Aim of this study was to compare in a group of patients with different acid related diseases serum levels of PGI and M.A.O.

Disclosure of Interest: All authors have declared no conflicts of interest.

Results: The mean M.A.O. value in group 1 was 2.15 mEq/l, in Group 2 52.49 mEq/L, in Group 3 17.48 mEq/L. A statistically significant difference was found between the 3 groups (Group 1 vs. Group 2 p < 0.00001; Group 1 vs. Group 2 p < 0.001; Group 2 vs. Group 3 p < 0.0001). The PGI mean values in Group 1 was 11.39 μg/l, in Group 2 107.72 μg/l in Group 3 84.28 μg/l (Group 1 vs Group 2: p = 0.00001; Group 2 vs Group 3 p < 0.05). The relationship between M.A.O. and PGI showed a Pearson R = 0.683 (p = 0.001). No statistically significant difference was found comparing M.A.O. and PGI in the single groups (p = ns).
In the 118 subjects of the control group (63 women), the mean age was 28.3 years (range: 18–72 years), BMI 23.2, (M 24.2; F 22.3, P

The mean age of patients with MO was 43.1 years (range 19–68) with no

Aims & Methods: We conducted a cross-sectional study of 32,762 asymptomatic adults who underwent routine health check-ups including screening endoscopy from August 2006 to December 2011. Sarcopenia was defined as appendicular skeletal muscle mass (ASM)/body weight (%) value beyond two standard deviations below the mean for healthy young adults. Participants were categorized into four groups according to obese and sarcopenic status: normal, obese, sarcopenic, and obese sarcopenic.

Results: In a multivariate model adjusted for age, sex, smoking status, alcohol intake, regular exercise, and metabolic variables, risk of reflux esophagitis was higher in obese [adjusted odds ratio(OR), 1.38; 95% confidence interval (CI), 1.18–1.64] compared to the non-obese group. Moreover, VAT, ratio of VAT to SAT, and TAT were significantly higher in LC

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Introduction: Obese patients with MO were considered one of the 21st century plagues in the Western world. Although its etiology is multifactorial, eating habits represent an important factor in its development. (1). The caloric load, the proportion of its components and its patterns have been the object of multiple studies (1–5). One of the most controversial aspects is the relationship between the frequency of meals and body weight.

Aims & Methods: The aim of the study was to determine the food rhythm (frequency and time spent in eating) in patients with morbid obesity (MO), based on diary records during the 24-H esophageal ph-monitoring studies. This was a retrospective study, including 100 patients (77 women), with MO in whom bariatric surgery was indicated and 118 non-obese subjects from the control group of the Spanish Digestive Motility Group. All were submitted to esophageal manometry and 24-H esophageal pH-monitoring according to the usual technique. During pHmetry it was recommended that the diet be similar as usual. The relationship of demographic aspects with the number of meals and the time invested in them, based on data from the pH meter was analyzed.

Statistical analysis was performed with the STATGRAPHICS Centurion program. The limit of statistical significance was set at p < 0.05. The study was approved by the ethics committee of our hospital. The informed consent of the participants was obtained for the performance of the tests.

Results: The mean age of patients with MO was 43.1 years (range 19–68) with no difference between men and women. The mean BMI was 41.55 (M 43.3; F 41.0, P = 0.05). Age and BMI differ-

Conclusion: Our findings suggest that sarcopenia, regardless of obesity, is more harmful condition for reflux esophagitis than obesity without sarcopenia.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1187 FOOD RATE (FREQUENCY AND TIME SPENT IN EATING) IN PATIENTS WITH MORBID OBESITY: DIFFERENCES AND SIMILARITIES BETWEEN MEN AND WOMEN

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Introduction: We considered one of the 21st century plagues in the Western world. Although its etiology is multifactorial, eating habits represent an important factor in its development. (1). The caloric load, the proportion of its components and its patterns have been the object of multiple studies (1–5). One of the most controversial aspects is the relationship between the frequency of meals and body weight.

Aims & Methods: The aim of the study was to determine the food rhythm (frequency and time spent in eating) in patients with morbid obesity (MO), based on diary records during the 24-H esophageal ph-monitoring studies. This was a retrospective study, including 100 patients (77 women), with MO in whom bariatric surgery was indicated and 118 non-obese subjects from the control group of the Spanish Digestive Motility Group. All were submitted to esophageal manometry and 24-H esophageal pH-monitoring according to the usual technique. During pHmetry it was recommended that the diet be similar as usual. The relationship of demographic aspects with the number of meals and the time invested in them, based on data from the pH meter was analyzed.

Statistical analysis was performed with the STATGRAPHICS Centurion program. The limit of statistical significance was set at p < 0.05. The study was approved by the ethics committee of our hospital. The informed consent of the participants was obtained for the performance of the tests.

Results: The mean age of patients with MO was 43.1 years (range 19–68) with no difference between men and women. The mean BMI was 41.55 (M 43.3; F 41.0, P = 0.05). Age and BMI differ-

Conclusion: Our findings suggest that sarcopenia, regardless of obesity, is more harmful condition for reflux esophagitis than obesity without sarcopenia.

Disclosure of Interest: All authors have declared no conflicts of interest.

References


P1188 ONE DRINK CAN INCREASE A RISK FOR ESOPHAGEAL, STOMACH AND COLORECTAL CANCER IN A COHORT OF 23,323,730 KOREAN ADULTS

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Introduction: Epidemiologic findings of low-volume alcohol consumption in relation to gastrointestinal cancers including gastric cancer are inconsistent.

Aims & Methods: The association between alcohol intake and esophageal, gastric and colorectal cancer risk in a population-based prospective cohort of 23,323,730 adults in Korea who had undergone a biennial evaluation provided by the National Health Insurance Corporation between the years 2009 and 2012.

Results: After median 3.4 years of follow-up, 9171 esophageal, 135,382 gastric and 154,970 colorectal cancer cases were identified. Cox proportional hazards regression models were used to estimate hazard ratios (HR) and corresponding 95% confidence intervals (95% CI). Light drinking as well as moderate to heavy alcohol consumption significantly increased the risks of the three gastrointestinal cancers (HR 1.51; 95% CI, 1.43–1.60; HR 1.08; 95% CI, 1.06–1.09; HR 1.12; 95% CI, 1.11–1.14) compared with non-drinkers after adjusting for age, sex, smoking, exercise, income, body mass index, and diabetes. For esophageal cancer, there was a dose-dependent linear relationship. However, no association was observed between prediagnostic alcohol consumption and all cause mortality.

Conclusion: Light drinking including even one alcoholic drink a day is associated with increased risks of esophageal, gastric and colorectal cancer.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1189 THE INFLUENCES OF VISCERAL FAT AREA ON THE SITES OF ESOPHAGEAL MUCOSAL BREAKS AND SYMPTOM SEVERITIES IN SUBJECTS WITH GASTROESOPHAGEAL REFLUX DISEASES

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Introduction: Some studies have suggested the central obesity as a risk factor for gastroesophageal reflux diseases (GERD). However, the associations between visceral adipose tissue (VAT) and the sites of esophageal erosions or the symptom severities of GERD have not been studied yet.

Aims & Methods: The aim of this study was to evaluate the influences of visceral adipose tissue and the locations of erosions and symptoms of GERD. The subjects who underwent abdomen computerized tomography and esophagogastroduodenoscopy for routine checkup at the same day were collected from January 2007 to October 2016. 177 subjects who had erosive esophagitis (LA class A to D) were enrolled. Questionnaires including gastrointestinal symptoms were written before examinations. The abdominal obesity was evaluated by measuring visceral adipose tissue (VAT), subcutaneous adipose tissue (SAT), ratio of VAT to SAT, total adipose tissue (TAT), body mass index (BMI) and waist circumference (WC).

Results: Lesser curvature (LC) side of esophagogastric junction (EGJ) was the most frequent site of mucosal breaks (103 cases, 58.2%) followed by posterior wall side (71 cases, 40.1%), anterior wall side (25 cases, 14.1%) and fundus side (4 cases, 9.9%). Mucosal breaks in 24-H pH monitors were found in study subjects (61.3% vs. 36.4%, p = 0.04). BMI (25.6 ± 4.5 vs. 24.2 ± 3.1, p = 0.01) and WC (89.0 ± 11.8 vs.85.0 ± 9.1, p = 0.01) were significantly higher in LC group. Moreover, VAT, ratio of VAT to SAT, and TAT were significantly higher in LC group. In the multivariate analysis, a higher VAT area (odds ratio (OR) 3.47, 95% confidence interval 1.38 to 8.73, 1st quartile vs. 4th quartile, p < 0.01) and ratio of VAT to SAT (OR 2.99, 95% CI 1.15 to 6.70, 1st quartile vs. 4th quartile, p = 0.02) were strongly associated with the mucosal breaks in LC.
P1190 A LESS COMPETENT OESOPHAGO-GASTRIC JUNCTION IS ASSOCIATED WITH OESOPHAGEAL ACID HYPERSENSITIVITY EVEN IN HEALTHY CONTROLS

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Introduction: In normal subjects, the oesophago-gastric junction (OGJ) sphincter complex maintains a tight barrier between the oesophagus and stomach acid. However, gastro-oesophageal reflux disease (GERD) caused by acid reflux has a prevalence of up to 26% [1]. One major factor determining whether gastro-oesophageal reflux occurs and eventually generates symptoms is the competency of the OGJ, which can be studied using distensibility testing. This way, we have previously shown in patients with Barrett’s oesophagus and healthy controls that an incompetent sphincter function was associated with more frequent reflux symptoms [2]. In the same patient groups, we also found greater oesophageal acid exposure and lower mucosal baseline impedance to be associated with impaired sphincter function. The latter probably represents a proxy for mucosal damage [3]. Other factors known to increase the perception of gastro-oesophageal reflux episodes are greater acidity, larger volume, and more proximal extent of the reflux content along with impaired mucosal integrity and sensitisation (peripheral and central) [1]. All of this said no studies of our knowledge have specifically addressed the possible association between sphincter function of the OGJ and oesophageal sensitivity.

Aims & Methods: We aimed to characterize oesophageal acid sensitivity in relation to OGJ competence, hypothesizing that sensitivity increases with impaired sphincter function. Twenty-three patients with Barrett’s oesophagus (mean age: 64.2 ± 7.7 years) and 12 healthy controls (mean age: 54.9 ± 10.8 years) were examined. A standard upper endoscopy to locate the OGJ was followed by distensibility testing of the OGJ using the EndoFLIP probe. At a later visit, experimental oesophageal sensitivity was assessed using a multimodal stimulation probe. After placement in the oesophagus just above the OGJ, the probe allows the filling and emptying of an attached polyurethane bag with water, stimulation with electrical current, and infusion of acid. Using this probe, mechanical disturbance of the bag, thermal stimulation at increasing temperature, electrical stimulation, and acid perfusion with 0.1 M hydrochloric acid (a Bernstein test) were performed. All stimulations were stopped when the subject felt moderate pain, equal to seven on a 0–10 visual analogue scale validated for visceral pain. Data were analyzed using multi-level, mixed-effects regression analysis in Stata 12.

Results: Oesophageal acid sensitivity increased with a more incompetent sphincter function. A lower tolerated acid volume was associated with greater distensibility index (P = 0.03) and with lower pressure (P = 0.03) in the OGJ in all subjects examined together and separately in healthy controls (P = 0.006 and 0.03, respectively). Performing separate analyses in patients with BO, these associations were not present (all P > 0.7). Sphincter function was associated with neither oesophageal sensitivity to mechanical, heat, nor electrical stimulation (all P > 0.13).

Conclusion: Oesophageal acid sensitivity increased with a more incompetent OGJ. Based on this and previous findings, we suggest that even in some healthy controls, a modest degree of OGJ incompetence allows gastric acid to reflux. This may again lead to low-grade oesophageal inflammation and mucosal damage, thereby evoking acid hypersensitivity. The latter mechanism probably constitutes a reflux protective mechanism towards acid reflux. Disclosure of Interest: B.P. McMahon: Barry P McMahon holds a minor share in Crospon Inc., Galway, Ireland who manufactures the EndoFLIP probe. All other authors have declared no conflicts of interest.

References

P1191 THE MUCOSAL INTEGRITY IN PHENOTYPES OF GASTROESOPHAGEAL REFLUX DISEASE SUBGROUPS AND FUNCTIONAL HEARTBURN

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Introduction: Three different phenotypes of gastroesophageal reflux disease (GERD) such as erosive reflux (ERD), nonerosive reflux (NERD), esophageal hypersensitivity (EH) and functional heartburn (FH) might have different pathophysiologic changes within the esophageal epithelium and the data is limited.

Aims & Methods: We aim to investigate the electrophysiological differences and diffusion characteristics as a reflection of tissue integrity using Ussing chamber technique. Distal esophageal mucosal biopsies from 14 healthy controls (5 men, 40.6 ± 11.2 years) and 62 patients with GERD (40 men, 42.9 ± 12.3 years, n = 26 LA grade A/B, n = 8 LA grade C/D, n = 22 NERD, n = 6 EH) and 11 patients with FH were studied from November 2015 until March 2017. GERD and quality of life questionnaires, high-resolution esophageal manometry, 24-hr impedance-pH monitoring, upper gastrointestinal endoscopy with esophageal biopsies were performed in all patients. Biopsies were put into the chambers to measure the transepithelial resistance (TER), potential difference (PD) and tissue permeability via fluorescein diffusion within two hours as well as evaluation of dilated intercellular spaces with light microscopy.

Results: Esophageal biopsies of healthy volunteers (163.5 ± 41.1 ohms) had significantly higher TER when compared to total GERD patients (132.5 ± 38.7 ohms). Although the TER results of whole GERD subtypes decreased compared to healthy controls, only ERD groups were significantly lower (123.3 ± 29.8 ohms) (Table 1). There was also no significant difference in any (FH, EH, NERD) groups between NERD, FH and EH groups. The mucosal permeability of GERD subtypes was significantly higher than the healthy controls. The PPI-unresponsive subjects (n = 10, 94.8 ± 36.5 pmols) were much more permeable to fluorescein compared to PPI-responsive subjects (n = 52, 56.0 ± 32.4 pmols) in all GERD patients (p = 0.009).

Table 1

<table>
<thead>
<tr>
<th>GROUPS</th>
<th>TEER (Ohms)</th>
<th>PD (V)</th>
<th>PERMEABILITY (pmols)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthy Controls</td>
<td>163.6 ± 41.1</td>
<td>2.2 ± 0.9</td>
<td>43.9 ± 16.6</td>
</tr>
<tr>
<td>GERD (total)</td>
<td>132.5 ± 38.7**</td>
<td>2.6 ± 1.5</td>
<td>62.2 ± 35.8*</td>
</tr>
<tr>
<td>Esophageal</td>
<td>150.6 ± 23.9</td>
<td>2.2 ± 1.0</td>
<td>71.8 ± 34.5</td>
</tr>
<tr>
<td>Hypersensitivity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NERD</td>
<td>139.6 ± 50.2</td>
<td>2.2 ± 1.1</td>
<td>65.6 ± 39.2*</td>
</tr>
<tr>
<td>ERD (total)</td>
<td>123.3 ± 29.8*</td>
<td>3.0 ± 1.6**</td>
<td>58.3 ± 34.7**</td>
</tr>
<tr>
<td>ERD grade A/B</td>
<td>130.5 ± 27.8*</td>
<td>2.9 ± 1.6</td>
<td>54.0 ± 30.5</td>
</tr>
<tr>
<td>ERD grade C/D</td>
<td>105.8 ± 32.7*</td>
<td>3.2 ± 1.6</td>
<td>72.6 ± 43.6</td>
</tr>
<tr>
<td>Functional Heartburn</td>
<td>145.3 ± 42.7</td>
<td>3.9 ± 0.9</td>
<td>67.0 ± 35.2</td>
</tr>
</tbody>
</table>

Conclusion: The TER and permeability results imply that ERD and NERD groups showed a barrier disruption. However, epithelial permeability was not different in EH and FH groups. The dilatation of intercellular spaces may contribute to increased mucosal permeability in true-NERD and ERD patients. EH and FH patients might have different pathophysiologic pathways than others.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P1192 PEPINS AND PH LEVELS OF HUMAN GASTRIC JUICES IN GASTROESOPHAGEAL REFLUX DISEASE SUBGROUPS AND FUNCTIONAL HEARTBURN

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Introduction: The major noxious agents of gastroesophageal reflux disease (GERD) on the esophageal epithelium are gastric acid and pepsin. Nevertheless, there is no precise information about pepsin concentrations in gastric juice.

Aims & Methods: We aimed to address the pepsin values and pH results among subtypes of GERD and functional heartburn. 46 patients with GERD (23 erosive reflux disease LA grade A/B (ERD-A/B), 5 ERD-C/D, 14 nonerosive reflux disease-NERD, 4 esophageal hypersensitivity-EH), 8 functional heartburn (FH) and 17 healthy controls (HC) were included into the study. Upper gastrointestinal endoscopies were performed off PPI. Patients were instructed not to aspirate the local anaesthetic solution and biopsy channel of the endoscope was dried before the suction. The gastric juices from the subjects were aspirated during endoscopy into a special beaker and their pH values were measured immediately. The specimens were analysed using the Peptest lateral flow device (RD Biomed Ltd UK), a colorimetric assay containing two unique human monoclonal antibodies that capture and detect pepsin protein.

Results: There were no significance between pepsin levels in any GERD phenotypes, FH and healthy controls (Table 1). The pH results of patients with ERD (1.8 ± 0.6) were significantly lower versus HC (2.6 ± 1.5). The pH levels of the
esophageal hypersensitivity (1.5 ± 0.2) were significantly decreased when compared to HC (2.6 ± 1.6) and also true NERD (4.0 ± 2.0).

Table 1

<table>
<thead>
<tr>
<th></th>
<th>Pepsin (ng/ml)</th>
<th>pH</th>
</tr>
</thead>
<tbody>
<tr>
<td>ERD total</td>
<td>514.7 ± 282.1</td>
<td>1.8 ± 0.6</td>
</tr>
<tr>
<td>ERD-A/B</td>
<td>521.0 ± 294.9</td>
<td>1.8 ± 0.6</td>
</tr>
<tr>
<td>ERD-C/D</td>
<td>485.5 ± 299.2</td>
<td>2.1 ± 1.0</td>
</tr>
<tr>
<td>Total NERD</td>
<td>456.9 ± 322.1</td>
<td>3.5 ± 2.1</td>
</tr>
<tr>
<td>True NERD</td>
<td>428.1 ± 293.0</td>
<td>4.0 ± 2.0</td>
</tr>
<tr>
<td>EH</td>
<td>536.0 ± 432.1</td>
<td>1.5 ± 0.26</td>
</tr>
<tr>
<td>GERD total</td>
<td>494.5 ± 294.1</td>
<td>2.4 ± 1.6</td>
</tr>
<tr>
<td>FH</td>
<td>654.2 ± 300.4</td>
<td>2.1 ± 1.1</td>
</tr>
<tr>
<td>HC</td>
<td>596.2 ± 302.8</td>
<td>2.6 ± 1.5</td>
</tr>
</tbody>
</table>

Conclusion: Pepsin may be considered a damaging factor in pathophysiology of GERD, but we could not find any difference between GERD phenotypes and unaffected controls. NERD group had less gastric acid versus other groups but this finding needs more studies to confirm.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1193 NON INVASIVE DIAGNOSIS OF UPPER GI DISEASES IN A PRIMARY CARE SETTING: A STUDY ON 1,900 PATIENTS

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3Oncological Gastroenterology, Centro di Riferimento Oncologico di Aviano S.O.C. di Gastroenterologia, Aviano/Italy

Introduction: The diagnosis of Hp-related non-atrophic gastritis was made by means of values: PGI: 30–120 mU/L. The diagnosis of Hp-related non-atrophic gastritis was made by means of values: PGI: 30–120 mU/L; the diagnosis of gastroesophageal reflux disease (GERD) was diagnosed according to FSSG scale (Frequency score for the symptoms of gastroesophageal reflux disease) and 50 BMI < 30 non-obese, non-obese and not (GERD) diagnosed according to FSSG cases have been included. The cases included in the study concerned have been surveyed by means of the questionnaire including the demographic data and the extra esophageal reflux symptom. Serum biochemistry analyses (fasting glucose, insulin, lipid panel, uric acid, TSH, ALT) have been checked. Waist circumference has been measured. Body compositions and anthropometric measurements have been assessed through the biomechical impedance method (TANITA).

Results: In this study a statistically significant difference (p < 0.05) has been found when GERD-diagnosis group is compared with normal health control group in regard to waist circumference, BMI; LDL, Fat, Fat Mass, Total Body Water(TBW), obesity level, reflux score, acid reflux score and total score measurements. Fat free mass (FFM), muscle mass, bone mass, bone mineral density (BMD) measurements in between the both groups have not been found statistically significant difference (p > 0.05). Considering the extra esophageal reflux symptoms a significant difference (p < 0.05) between the group suffering from sore throat, apnea, teeth grinding and GORH and the extra esophageal reflux symptoms has been found. Finally the patients group a positive correlation between acid reflux score and BMI (r = 0.298) (p < 0.001), LDL (r = 0.387) (p < 0.001), visceral fat (r = 0.180) (p < 0.049) has been determined. A negative correlation between acid reflux score and TBW (r = -0.273) (p < 0.003) has been determined.

Table 1: Metabolic parameters and biomechical impededs findings

<table>
<thead>
<tr>
<th>Control Group</th>
<th>Patient Group</th>
<th>Total Number (N=170)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Score</td>
<td>Median (Min.-Max.)</td>
<td>Median (Min.-Max.)</td>
<td>P Value</td>
</tr>
<tr>
<td>HOMA-IR (mg/dl)</td>
<td>1.90 (0.42–19.06)</td>
<td>1.84 (0.27–22.93)</td>
<td>0.495</td>
</tr>
<tr>
<td>Triglyceride</td>
<td>81 (33–350)</td>
<td>49 (33–95.20)</td>
<td>0.148</td>
</tr>
<tr>
<td>Total Cholesterol</td>
<td>146.30 (73-222)</td>
<td>159 (19-310)</td>
<td>0.216</td>
</tr>
<tr>
<td>Uric Acid</td>
<td>4.05 (2.10-41)</td>
<td>4.20 (2.10-49.20)</td>
<td>0.471</td>
</tr>
<tr>
<td>ALT</td>
<td>12.50 (3–59)</td>
<td>15 (3–59)</td>
<td>0.213</td>
</tr>
<tr>
<td>Fat</td>
<td>19.30 (3-41.80)</td>
<td>24.75 (9-39.50)</td>
<td>0.016</td>
</tr>
<tr>
<td>Fat Mass</td>
<td>12.80 (10.36-12.50)</td>
<td>15.10 (10.36-40.30)</td>
<td>0.012</td>
</tr>
<tr>
<td>FFM</td>
<td>45.95 (19.75-70)</td>
<td>49.85 (39.50-74.20)</td>
<td>0.613</td>
</tr>
<tr>
<td>Muscle Mass</td>
<td>43.95 (35.50-70.50)</td>
<td>43.90 (34.50-91.50)</td>
<td>0.520</td>
</tr>
<tr>
<td>TBW</td>
<td>32.70 (25.50-52.50)</td>
<td>32.55 (25.50-72.60)</td>
<td>0.341</td>
</tr>
<tr>
<td>TBW ZYDEE</td>
<td>55.80 (41.60-80.90)</td>
<td>52.50 (41.60-80.90)</td>
<td>0.018</td>
</tr>
<tr>
<td>Bone Mass</td>
<td>2.40 (1.90-3.70)</td>
<td>2.40 (1.90-4.0)</td>
<td>0.442</td>
</tr>
<tr>
<td>BMR</td>
<td>5.858 (55.94-9.138)</td>
<td>5.851 (50.94-8.996)</td>
<td>0.586</td>
</tr>
<tr>
<td>Metabolic Age</td>
<td>16 (12-44)</td>
<td>17 (12-46)</td>
<td>0.002</td>
</tr>
<tr>
<td>Waist (cm)</td>
<td>10.60 (7.43-17.91)</td>
<td>9.71 (7.43-17.91)</td>
<td>0.003</td>
</tr>
<tr>
<td>BMI</td>
<td>29.90–35.90</td>
<td>29.71 (29.90–35.90)</td>
<td>0.015</td>
</tr>
<tr>
<td>HOMA-IR (mg/dl)</td>
<td>1.90 (0.42–19.06)</td>
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<td>0.520</td>
</tr>
<tr>
<td>TBW</td>
<td>32.70 (25.50-52.50)</td>
<td>32.55 (25.50-72.60)</td>
<td>0.341</td>
</tr>
<tr>
<td>TBW ZYDEE</td>
<td>55.80 (41.60-80.90)</td>
<td>52.50 (41.60-80.90)</td>
<td>0.018</td>
</tr>
<tr>
<td>Bone Mass</td>
<td>2.40 (1.90-3.70)</td>
<td>2.40 (1.90-4.0)</td>
<td>0.442</td>
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<tr>
<td>BMR</td>
<td>5.858 (55.94-9.138)</td>
<td>5.851 (50.94-8.996)</td>
<td>0.586</td>
</tr>
<tr>
<td>Metabolic Age</td>
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<td>0.015</td>
</tr>
</tbody>
</table>

Mann Whitney U Test (Monte Carlo) - Min.:Minimum - Max.:Maximum

Conclusion: The frequency and severity of gastroesophageal reflux symptoms in the non-obese is closely related with body fat composition as those in the obese. Increase in abdominal and visceral fat composition may cause high risk of gastroesophageal reflux disease in individuals irrespective of their obesity.

Disclosure of Interest: All authors have declared no conflicts of interest.
P1195 PROXIMAL ESOPHAGEAL BASELINE IMPEDANCE LEVELS ARE ABLE TO DISCRIMINATE BETWEEN SCLERODERMA PATIENTS WITH AND WITHOUT ESOPHAGEAL INVOLVEMENT

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Introduction: Esophageal baseline impedance (BI) levels have been recently proposed as a marker of mucosal integrity. Indeed, patients with non-erosive reflux disease (NERD) showed lower distal esophageal BI levels compared to healthy controls (HCs) due to the presence of abnormal esophageal acid exposure time (AET). On the other hand, no differences were found between NERD and HCs at proximal esophagus due to the limited proximal migration of the refluxate. Systemic sclerosis (SSc) is a systemic disease characterized by the deposition of collagen and matrix proteins in the connective tissue of the skin and visceral organs, such as the gastrointestinal tract. This event could potentially affect the conductivity of the esophageal wall and consequently reduce BI levels, also at proximal level, but data in this regard are limited.

Aims & Methods: We aimed to prospectively compare BI levels between a group of NERD patients and two groups of SSc patients, one with a clear manometric picture of scleroderma esophagus (i.e. hypotensive esophageal-gastric junction pressure and absent peristalsis) and one without esophageal involvement. Consecutive patients with heartburn and those with a definite diagnosis of SSc underwent upper endoscopy in order to assess the presence of esophageal mucosal lesions. Further, a group of healthy subjects was used as controls (HCs). Thereafter, all esophageal-negative and SSc patients underwent high-resolution manometry and impedance-pH testing off-therapy. Impedance-pH tracings were blindly and manually reviewed, and we measured distal AET and BI values at 3, 5, 7, 9, 11, 13, 15 and 17 cm above the lower esophageal sphincter, during the overnight rest, for at least 30 minutes after excluding swallows and reflux induced changes. NERD was diagnosed in case of reflux symptoms and abnormal AET.

Results: Fifty patients [38F; mean age 51.5 years] with NERD, 50 SSc patients [44F; mean age 49.5 years] with esophageal involvement, 30 SSc patients [28F; mean age 49.5 years] without esophageal involvement and 50 HCs [37F; mean age 49.5 years] were enrolled. All 50/50 (100%) NERD patients [median 7.2] and 44/50 (88%) SSc patients without esophageal involvement [3.1] and 0/50 (0%) patients with esophageal involvement [8.3] showed an abnormal AET compared to proximal median BI levels, whereas they were much lower in NERD patients with esophageal involvement (p < 0.05).

Conclusion: Proximal esophageal BI levels are able to segregate between scleroderma patients with and without esophageal involvement. The advent of novel and poorly invasive methods for the assessment of esophageal mucosal integrity will allow us to perform this measurement without the need of prolonged probe insertion.

Disclosure of Interest: E. Savarino: Consulting fee from Medtronic, Sofar, Takeda, AbbVie. E. Savarino: Consulting fee from Medtronic, Sofar, Takeda, AbbVie, MSD All other authors have declared no conflicts of interest.

P1196 GASTRIN-17 AS A NON-INVASIVE MARKER OF EARLY GERD RELAPSE: A PROSPECTIVE ONE-YEAR STUDY

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Introduction: Gastroesophageal reflux disease (GERD), is characterized by frequent relapses after withdrawal of therapy and no prognostic markers of relapse are available to predict the outcome of the patients. Gastrin-17 (G-17) has been proposed as a non-invasive marker of reflux disease as well as a good marker of response to the therapy. Pepsinogen I (PG I) and Gastrin-17 (G-17) are claimed to increase in a statistically significant manner after proton pump inhibitors (PPIs) therapy. Aim of the study was to assess the prognostic value of G-17 and PG I levels for the prediction of early GERD relapse in a prospective open study.

Aims & Methods: We prospectively enrolled 221 consecutive GERD patients (F 113, mean age 52.5 years; range 28-74 years) with endoscopically proved diagnosis of esophagitis, according to the L.A. classification, all symptomatic (heartburn and/or regurgitation). All patients were treated with rabeprazole 20 mg once a day for 6-8 weeks, assessing at the end of the therapy the symptoms’ modifications by means of a questionnaire. In the group of asymptomatic patients, we performed a one-year follow-up, recording the GERD relapse episodes; only on-demand antacids were permitted. All patients underwent at baseline a blood sample and after the acute course of PPI therapy.

Results: One hundred eighty five patients were asymptomatic after the 6-8 weeks of PPI therapy and entered in the prospective evaluation for 12 months. 19 subjects were lost lasting the follow-up and finally 166 patients were available for the study analysis. 72 patients experienced at least one GERD relapse episode (first group) against 94 ones free of symptoms for one year (second group). The mean values of both PG I and G-17 after the 6-8 weeks of PPI therapy in comparison with the baseline levels, were higher in first group than in the second one (first group: baseline PG I 96 μg/L, G-17 2.6 pmol/L; after therapy: PG I 164 μg/L, G-17 19 pmol/L; p: <0.001; second group: baseline PG I 98 μg/L, G-17 2.9 pmol/L; after therapy: PG I 116 μg/L, G-17 6.3 pmol/L; p: ns). The good response to full dose of PPI, assessed by an increase of both PG I and G-17, seems to be the pathophysiological background to explain the prognostic value of such markers.

Conclusion: Gastrin-17 and pepsinogen I increase after full-dose of PPI in GERD acute phase seems to be a simple non-invasive marker to predict early GERD relapse in one-year follow-up.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1197 THE DIAGNOSTIC VALUE OF ESOPHAGEAL MUCOSAL AND BASELINE IMPEDANCE MEASUREMENTS IN PATIENTS WITH GASTROESOPHAGEAL REFLUX DISEASE

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Introduction: Various biomarkers have been studied to evaluate the integrity of esophageal epithelium in distinguishing phenotypes of gastroesophageal reflux disease (GERD). Baseline impedance (BI) measurement is likely to be one of these and can be measured during the 24-hour ambulatory intra-esophageal impedance-pH study. Mucosal impedance (MI) measurement is a technique that was introduced in recent years and is a practical method that can be applied during endoscopy, but the validation studies are insufficient. BI & MI measured with the same regular impedance catheter and data from 118 patients with different reflux phenotypes and controls were evaluated.

Aims & Methods: Patients were divided into five groups: mild (ERD A-B, n = 31), severe erosive esophagitis (ERD C-D, n = 11), non-erosive reflux disease (NERD, n = 26), functional heartburn-esophageal hypersensitivity (FH-EH, n = 17), healthy controls. High resolution manometry, 24-h MII-pH, upper gastrointestinal endoscopy were performed. BI values were taken at the sleeping time period at night when reflux and swallowing did not occur. MI measured during endoscopy, a regular impedance-pH catheter passed through the biopsy

References
channel of the scope. Distal two rings were contacted to the distal and proximal part of the esophagus approximately 20–25 cm, using a supervised Greenfield 5 mm, 1 pH impedance catheter were used.

**Results:** MI can differentiate ERD from non-erosive groups but do not have a diagnostic value to discriminate NERD from FH-EH or controls. However, BI might be a better tool to discriminate NERD from healthy controls. Since regular catheters are failed, new balloon-shaped catheters should be validated. BI might be a better tool to discriminate NERD from controls. This implicates that the esophageal epithelial resistance is impaired in this particular group compared to controls.

**Conclusion:** All authors have declared no conflicts of interest.
Currently, there are no real-world data assessing the efficacy of short-term empiric treatment with PPIs in GERD patients in China.

**Aims & Methods:** This was a multicenter, prospective, observational study carried out in a real-world setting. The primary objective was to determine the overall responder rate in patients with typical GERD symptoms after 4 weeks of empiric treatment with PPIs. Responders were defined as having heartburn/regurgitation on ≤1 day during the prior 7 days, assessed by the Gerd-Q questionnaire. Outpatients aged between 18 and 65 years with a Gerd-Q score ≥8 were enrolled if they were prescribed standard-dose PPIs as empirical treatment and were not planned to have an endoscopy within 4 weeks of enrollment. The PPI regimen prescribed was decided completely at the physicians’ discretion. Patient demographics, diagnosis, prescribed PPI regimens, Gerd-Q score and symptom frequency were recorded. Data were collected at baseline, 2 weeks and 4 weeks after initiating PPI treatment. Results from the full analysis set (FAS) are presented.

**Results:** A total of 1,000 patients from 10 centers were screened for this study, of which 987 met the inclusion criteria and were included in the FAS. The mean age was 45.2 ± 11.6 years, the mean body mass index was 23.4 ± 3.3 kg/m², and 50.3% of the patients were male. The mean duration of GERD was 0.8 ± 2.1 years, with a mean baseline Gerd-Q score for the week before screening of 10.5 ± 1.9. During the 4 weeks’ treatment, the proportion of patients receiving at least one dose of PPI was 98.5%. Esomeprazole was the most frequently received PPI (57.1% of patients). Other PPIs (rabeprazole, lansoprazole, pantoprazole and omeprazole) were received by 50.1% of patients and 7.2% of the patients sequentially received ≥2 PPIs in the duration of the study. A total of 787 (79.7%) patients either completed the 4-week PPI treatment or withdrew after response, of which the responder rate was 74.0% [95% CI, 70.75–77.05%] (Table 1). Among the 818 patients who completed 2 weeks’ treatment, the responder rate was 57.0% [95% CI, 53.5%–60.4%, p < 0.001]. The overall median time to response (±IQR) was 9 days [5–15]. The responder rate of the GERD-Q score demonstrated a decreasing trend. The proportion of patients with a Gerd-Q score ≥8 reduced from 100% at baseline to 29.5% and 17.4% at 2 and 4 weeks, respectively.

**Table 1: Responder rate and median time to response for different PPIs**

<table>
<thead>
<tr>
<th>PPI</th>
<th>Responder rate</th>
<th>Median time to response</th>
</tr>
</thead>
<tbody>
<tr>
<td>Esomeprazole</td>
<td>57.0% [95% CI]</td>
<td>5 [2–11]</td>
</tr>
<tr>
<td>Other PPIs</td>
<td>24.0% [95% CI]</td>
<td>12 [10–13]</td>
</tr>
<tr>
<td>Total</td>
<td>41.0% [95% CI]</td>
<td>11 [9–14]</td>
</tr>
</tbody>
</table>

**Conclusion:** In Chinese clinical practice, short-term PPI empirical treatment effectively improves symptom control in GERD patients and gains a satisfactory overall responder rate.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**References**

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**P1202 SYSTEMATIC REVIEW AND META-ANALYSIS OF OUTCOMES AFTER LAPAROSCOPIC ANTI-REFLUX SURGERY RELATED TO OBESITY**

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**Introduction:** Laparoscopic Anti-Reflux Surgery (LARS) is an established alternative treatment to pharmacological therapy for patients with Gastro Esophageal Reflux Disease (GERD), yet its safety and efficacy in obese patients is controversial. A systematic review and meta-analysis was performed to compare LARS related to obesity.

**Aims & Methods:** The primary outcome measure was the relative incidence of recurrent reflux related to BMI. Secondary outcome measures were relative re-intervention rates in the form of endoscopic dilation or surgery, conversion to open surgery, and early return to theatre. MEDLINE and the Cochrane Library (January 1970 to November 2016) were searched for studies reporting clinical outcomes of LARS in patient cohorts stratified by Body Mass Index (BMI). Data was grouped according to BMI, ≤30 kg/m² (non-obese) and >30 kg/m² (obese). Results were pooled in meta-analyses as Odds Ratios (OR).

**Results:** Eleven eligible observational studies comparing LARS in non-obese (n=2) and obese (n=16) patients were included. The relative incidence of reflux was significantly lower in the non-obese cohort (OR 0.34, 95% CI 0.19 to 0.60, p = 0.001), however no significant differences were observed in rates of operative morbidity (OR 0.87, 0.65 to 1.18, p = 0.38), redo surgery (OR 1.18, 0.68 to 1.27, p = 0.73), endoscopic dilation (OR 1.06, 0.49 to 2.33, p = 0.88), conversion to open surgery (OR 1.17, 0.55 to 2.48, p = 0.68), or early return to theatre (OR 0.77, 0.44 to 1.37, p = 0.38).

**Conclusion:** LARS can be performed safely in obese patients, but risks higher morbidities in comparison to non-obese patients. Clinicians should be aware that obesity may adversely affect LARS outcome and careful consideration be given in the consent process inherent within the optimal management of GORD.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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**P1203 GASTROESOPHAGEAL REFLUX DISEASE REFRACTORY TO PROTON PUMP INHIBITOR THERAPY. INCOMPLETE ACID INHIBITION OR DIAGNOSTIC ERROR?**

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**Introduction:** The use of PPIs represents the main treatment in gastroesophageal reflux disease (GERD), having demonstrated its effectiveness both in the control of inflammation and symptomatology. However, between 10–20% of patients present persistent symptoms or lesions despite the treatment.

**Aims & Methods:** The aim of the study was to assess the presence of acid reflux in patients submitted to our department with the diagnosis of refractory GERD, due to low or no response to PPIs. This was a retrospective study including 190 patients (55 men, 135 women) referred to our service with the diagnosis of GERD from January 2008 to December 2015. Based on the diagnostic criteria, two groups were made. Group 1: included 63 patients (33.2%) diagnosed of GERD due to typical symptomatic reflux and at least one positive complementary test (pHmetry, LUS or LES pH recording). All of them underwent a 24-H pHmetry study in a single channel, esophageal and gastric, off-PPI treatment. In 17 patients the pHmetry study was performed with multichannel intraluminal impedance (15 cases) or Bilitec (2 cases). Group 2: included 127 patients (66.8%) who had been diagnosed of GERD only on the basis of typical symptoms; all of them underwent esophageal double channel 24-H pH-metry off-PPI. All of the studies (24-hour pHmonitoring or multichannel intraluminal impedance-pH studies) (MARK III, Delta and Digtigrph pH-Z, Synectics, Gyven, Medtronic) were performed according to standard technique.

**Results:** Pathological pHmetry was present in 91 patients (47.9%), 24 from group 1 and 67 from group 2. Pathological acid reflux was therefore ruled out as a cause of symptoms in 52.1% of all cases studied: 60 patients (47.2%) from group 2, and 33 patients (51.9%) from group 1. In addition, out of the 24 patients with pathological reflux in pHmetry in group 1 (true refractory patients), 9 had an incomplete response, with a percentage of time with pH < 4 less than 7.5% (mild reflux), which probably was not the cause of the symptomatology.

**Conclusion:** Proton pump inhibitors (PPIs) are the drugs of choice in the treatment of GERD. However, its efficacy may be compromised for a variety of reasons including: non-compliance, bioavailability, episodes of nocturnal acid break-through, poor gastric emptying, etc. In most of the patients referred for implementation or stimulation-related adverse effects were reported in the two-month follow-ups.

**Conclusion:** Electric stimulation represents a prospective approach for treating GERD in clinics. This novel wireless LES stimulation system was also safe and effective for treating GERD rabbits. After implantation, its passive medical appliance benefit patients and keep the long-term efficacy for clinical GERD management.

**Disclosure of Interest:** All authors have declared no conflicts of interest.
P1204 LOW-FODMAP DIET RESULTED EFFECTIVE IN REDUCING SYMPTOM PERCEPTION IN PATIENTS WITH FUNCTIONAL HEARTBURN

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Introduction: Recently, low-FODMAP diet has been proposed as potential treatment in patients with irritable bowel syndrome (IBS) given its high efficacy in symptoms relief. Recent data showed that IBS frequently overlap with functional symptoms. The aim of this study was to evaluate the efficacy of low-FODMAP diet in reducing heartburn in patients with FH and no pathophysiological evidence of gastroesophageal reflux (GERD) compared to patients with non-erosive reflux disease (NERD). As secondary aim we investigated the reduction of lower gastrointestinal symptoms in both groups. We enrolled patients with heartburn and negative upper endoscopy who were scheduled for upper gastrointestinal endoscopy (erosalophgeal manometry and pH monitoring, MII-pH) at Gastroenterology Unit in University of Pisa. We excluded patients older than 75 and younger than 18, those with primary esophageal motor disorders and with previous abdominal surgery. Medical history, volup-tuary habits and response to proton pump inhibitor (PPI) treatment were recorded. By means of MII-pH we splitted patients in two populations: NERD group (abnormal esophageal acid exposure or number of refluxes) and FH group (correlation and no heartburn relief during PPI treatment). All enrolled patients were evaluated with validated questionnaires (Likert and VAS) to evaluate heartburn occurrence pre- and post a nutritional approach with low-FODMAP diet for 6 weeks.

Results: We included 31 patients (20 female; mean age 49.1 yrs; mean BMI 24.4) into the study. NERD group was composed of 13 patients (6 female; mean age 48.7 yrs; mean BMI 25.7). FH group was composed by 18 patients (11 female; mean age 50.9 yrs; mean BMI 23.9). All patients showed symptom improvement regarding bloating, abdominal pain and stools composition (p < 0.001) after low-FODMAP diet (see Table 1). Moreover, we observed a very important reduction of heartburn in the FH group (from 8.4±2.5 to 2.3±1.1; p < 0.001 on VAS scale) compared to the NERD group (7.2±2.2 a 6.9±1.9; p=0.624 on VAS).

Table 1: Abdominal symptoms perception pre- and post-low-FODMAP diet in NERD and FH groups

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Pre-diet</th>
<th>Post-diet</th>
<th>P value</th>
<th>Pre-diet</th>
<th>Post-diet</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal pain</td>
<td>3.6±1.8</td>
<td>2.7±0.9</td>
<td>0.041*</td>
<td>5.8±2.1</td>
<td>1.7±1.3</td>
<td>0.0001*</td>
</tr>
<tr>
<td>Bloating</td>
<td>4.3±2.6</td>
<td>3.1±1.7</td>
<td>0.187</td>
<td>6.3±1.5</td>
<td>2.1±0.9</td>
<td>0.0001*</td>
</tr>
<tr>
<td>Wind</td>
<td>4.9±2.3</td>
<td>3.3±1.7</td>
<td>0.055</td>
<td>6.1±1.9</td>
<td>2.2±1.5</td>
<td>0.0001*</td>
</tr>
<tr>
<td>BSC (type 3–5)</td>
<td>3/13</td>
<td>7/13</td>
<td>0.226</td>
<td>2/18</td>
<td>13/18</td>
<td>0.005*</td>
</tr>
</tbody>
</table>

Legend: BSC = Bristol Stool Classification; *=statistically significant (p < 0.05)

Conclusion: This pilot study showed that a low-FODMAP diet was able to reduce heartburn perception in patients with FH and who did not obtain any symptom relief after PPI treatment. Larger prospective randomized controlled trial is mandatory to further explore these findings.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1205 GENDER DIFFERENCES IN NEOPLASTIC PROGRESSION IN B. BARRETT’S ESOPHAGUS: A MULTICENTER PROSPECTIVE COHORT STUDY


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Introduction: Because of a higher prevalence of BE in males, recommendations in current guidelines are mainly based on male BE patients and make no difference in surveillance according to gender. Nevertheless, it is unknown whether BE patients have the same neoplastic progression and acceleration rate as male patients.

Aims & Methods: The aims of this study were (1) to evaluate the difference between males and females in probability of and (2) time to neoplastic progression, as well as (3) gender differences in stage distribution of neoplastic progression in surveilled BE patients. In this multicenter prospective cohort study we included 729 patients with BE who met the inclusion criteria of a segment of ≥2cm and confirmed intestinal metaplasia. Endoscopic surveillance was performed according to the American College of Gastroenterology guidelines.

Conclusion: The risk of HGD and overall neoplastic progression and acceleration rate of HGD development is higher in male BE patients compared to females. On the other hand descriptive statistics show proportionally more EAC in females as well as an advanced stage of EAC at diagnosis. Further research into the differential aspects of neoplastic progression in BE between men and women, may have future consequences for gender specific guideline recommendations, including the timing of follow-up.

Table 1: Stage distribution of neoplastic progression between males and females

<table>
<thead>
<tr>
<th>Stage</th>
<th>Male</th>
<th>Female</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>40</td>
<td>56%</td>
<td>4</td>
</tr>
<tr>
<td>1</td>
<td>56</td>
<td>33%</td>
<td>1</td>
</tr>
<tr>
<td>2</td>
<td>45</td>
<td>80%</td>
<td>7</td>
</tr>
</tbody>
</table>

Disclosure of Interest: All authors have declared no conflicts of interest.

P1206 SINGLE SESSION FOCAL CRYOBALLOON ABLATION THERAPY IS SAFE AND EFFECTIVE IN THE TREATMENT OF DYSPLASIC BARRETT’S ESOPHAGUS

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Disclosure of Interest: Given its proven safety and efficacy, RadioFrequency Ablation (RFA) is the preferred ablation modality for dysplastic Barrett’s Esophagus (BE). However, RFA is associated with significant drawbacks, such as the need for large controller units, multiple deployment steps and capital investment. The Focal CryoBalloon Ablation system (FCBA; C2 Therapeutics, Redmond City, CA, USA) is another ablation method based on the application of extreme cold - that has recently been developed to overcome these RFA drawbacks. Additionally, FCBA might be better tolerated. FCBA comprises a handheld, through-the-scope system with a conformable balloon that is simultaneously inflated and cooled using nitrous oxide, resulting in ice patches of approximately 2cm³ on the targeted mucosa. Previous studies applying FCBA to limited areas of BE (1 to 2 small BE islands per patient) have shown promising results. Data on
efficacy and safety of FCBA in the treatment of larger BE segments, however, are lacking. Therefore we aimed to assess the safety and efficacy of a single treatment with FCBA for dysplastic BE.

Aims & Methods: Patients were seen between March and December 2016 at two tertiary referral centers in the Netherlands. Patients with a BE >6 cm in length and with a confirmed diagnosis of low-grade (LGD) or high-grade dysplasia (HGD) or after endoscopic resection for visible lesions, were included. Exclusion criteria included previous focal ablation therapy and strictures. At baseline, all visible BE was treated with side by side ablations of 10 seconds, including the circumferential treatment of the gastroesophageal junction (GEJ). Pain scores were assessed directly post-treatment and at days 2 and 7. Follow-up endoscopy with biopsy and photo documentation was scheduled after 3 months. Primary outcomes included dysplasia regression rate and incidence of endoscopic stricture or other adverse events.

Results: We enrolled 20 patients with dysplastic BE (>85% male, mean age 66 (±8) years), with a median BE length of 0 cm (IQR 0–0; 1–3) and with a baseline diagnosis of LGD (10; 50%), HGD (1; 5%), or mucosal adenocarcinoma (9; 45%). Ten (50%) had undergone endoscopic resection of a visible lesion before cryoballoon and 8 (40%) had undergone previous curvilinear RF A. During a median ablation time of 16 minutes (IQR 11–19), all BE, including circumferential ablation of GEJ was successfully ablated in all patients. No adverse events occurred, and median pain directly post-treatment was 4 out of 10 (IQR 0–5), whereas this was 1 (IQR 0–2) and 0 (IQR 0–1) at days 2 and 7. At the 3-month follow-up endoscopy, median endoscopic regression of initial BE was found to be 95% (IQR 93–98), this included 13 patients (65%) with a complete 100% regression. All biopsies confirmed squamous regeneration with endoscopic remission. No significant endoscopic strictures or other complications were noted.

Conclusion: Our multicenter, prospective trial shows that a single treatment with CryoFocal balloon ablation therapy is safe, well-tolerated and effective for eradication of dysplastic BE.

Disclosure of Interest: All authors have declared no conflicts of interest.

Table 1: Baseline characteristics and maximum pain scores

<table>
<thead>
<tr>
<th>FCBA</th>
<th>RFA</th>
</tr>
</thead>
<tbody>
<tr>
<td>(N=20)</td>
<td>(N=35)</td>
</tr>
<tr>
<td>P-value</td>
<td></td>
</tr>
</tbody>
</table>

1A. Baseline characteristics

| Male gender, n (%) | 17 (85%) | 29 (83%) | 0.84
| Age, mean (SD) years | 65 (±8) | 66 (±8) | 0.66
| Worst CRD before FCBA | LGD, n | 10 (50%) | 19 (54%) | 0.54
| HGD, n | 1 (5%) | 6 (17%) |
| EAC, n | 9 (45%) | 10 (29%) |
| Prior treatment | ER, n | 10 (50%) | 17 (52%) | 0.92
| None, cm | 10 (±5) | 23 (±6) | 0.33

**P1207 CRYOBALLOON ABLATION OF DYSPLASTIC BARRETT’S ESOPHAGUS CAUSES SHORTER DURATION AND LESS SEVERE POST-PROCEDURAL PAIN AS COMPARED TO RADIOFREQUENCY ABLATION**

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Introduction: Radiofrequency ablation (RFA) is safe and effective for eradication of dysplastic Barrett’s Esophagus (BE), but may be associated with significant post-procedural pain. As an alternative, cryobalization using the Focal CryoFocalablation Ablation system (FCBA) has recently been developed, which ablates BE by freezing it using nitrous oxide. Early uncontrolled studies suggest comparable safety and efficacy of FCBA and RFA in eradicating dysplastic BE. Therefore we compared pain endpoints like pain might play a determining role in selecting the best treatment modality. In contrast to heat-based ablation, FCBA preserves the extracellular matrix which might be associated with less pain while maintaining sufficient depth of ablation.

Methods: We aimed to compare post-procedural pain between focal RFA and FCBA.

Aims & Methods: Between January 2016 and March 2017 all patients undergoing focal ablation therapy of BE, either with RFA or FCBA performed in two tertiary referral centers in the Netherlands, were approached to complete a digital diary. A short questionnaire was daily sent to patients for 14 days post-treatment, to assess (1) odynophagia, (2) chest pain (both assessed using VAS range from 0 to 10), and (4) dysphagia (assessed using a score ranging from 0 to 10) and (4) use of analgesics. Primary outcome included maximum VAS score (maximum score for either item 1 or 2), secondary outcomes included area under the curves (AUCs) for all items assessed, maximum reported VAS score at score (maximum score for either item 1 or 2), and use of analgesics. Primary outcome included maximum VAS score reported on any of the 14 days was 2 (IQR 0–4) after FCBA and 4 (IQR 3–7) after RFA (p <0.01). For odynophagia, the maximum median VAS score reported on any of the 14 days was 2 (IQR 0–4) after FCBA and 4 (IQR 3–7) after RFA (p <0.01). For chest pain in rest (78 vs 20.5, p <0.01), for use of analgesics (9 vs 3.1, p <0.01), and for dysphagia (2.6 vs 8.2, p <0.01). The maximum median VAS score reported on any of the 14 days was 2 (IQR 0–4) after FCBA and 4 (IQR 3–7) after RFA (p <0.01). For odynophagia, the maximum median VAS score reported on any of the 14 days was 2 (IQR 0–4) after FCBA and 4 (IQR 3–7) after RFA (p <0.01). For chest pain in rest (78 vs 20.5, p <0.01), for use of analgesics (9 vs 3.1, p <0.01), and for dysphagia (2.6 vs 8.2, p <0.01). The maximum median VAS score reported on any of the 14 days was 2 (IQR 0–4) after FCBA and 4 (IQR 3–7) after RFA (p <0.01).

Conclusion: In this multicenter, non-randomized, open prospective cohort study, patients reported less post-procedural pain and dysphagia after FCBA as compared to RFA and, moreover, FCBA patients used less analgesics. Although a randomized trial should provide definitive evidence for differences in post-procedural tolerability, our results strongly suggest a significantly different post-procedural course, thus favoring FCBA over RFA.

Disclosure of Interest: All authors have declared no conflicts of interest.

**P1208 COMPARATIVE OUTCOMES OF RADIOFREQUENCY ABLATION FOR BARRETT’S OESOPHAGUS WITH DIFFERENT BASELINE HISTOLOGY**

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Introduction: Radiofrequency ablation (RFA) with endoscopic mucosal resection is recommended for Barrett’s Oesophagus (BO) related neoplasia. In this study, we evaluated RFA treatment outcomes for BO stratified according to baseline histology, i.e. low-grade dysplasia (LGD), high-grade dysplasia (HGD) and intramucosal carcinoma (IMC). We retrospectively reviewed the treatment outcomes of patients with dysplastic BO between January 2007-2017. Patients received 3-monthly RFA until endoscopic and histologic remissions were achieved. Outcomes measured were: 1) complete remission of dysplasia (CRD) and intestinal metaplasia (CRIM), 2) stricture rate, and (3) durability of CRD and CRIM. Patients on active treatment protocol were excluded.

Results: We identified 113 patients who completed RFA treatment (21 LGD, 46 HGD and 46 IMC). There were no significant difference between the groups in the age, gender, circumferential and maximum length of BO, and stricture rate. CRD and CRIM were achieved in 94.7% and 78.8% of patients, respectively. When stratified according to baseline histology, there was no significant difference in CRD rate among LGD (95.2%), HGD (95.7%) and IMC (93.5%) (p =0.89). Similarly, there was no significant difference in CR IM rate among LGD (71.4%), HGD (76.1%) and IMC (84.8%) (p =0.31). CRD durability at 12 and 36 months (n =107) was 99.0% and 97.0%, respectively. CRIM durability (n =89) at 12 and 36 months were 98.5% and 92.7%, respectively. When stratified according to baseline histology, CRD durability at 12 and 36 months for LGD and IMC were 100% at both time points, and 97.7% and 93.6% for HGD, respectively (log rank p =0.31). CRIM durability at 12 and 36 months for LGD, HGD and IMC were 100%, 96.4%, 100%, and 100%, 88.5%, 95.5%, respectively (log rank p =0.60).

Conclusion: The treatment outcomes for BO were similar in patients with different baseline histology. Our results showed that once CRD and CRIM were achieved, these were durable over time.

Disclosure of Interest: All authors have declared no conflicts of interest.
Introduction: Endoscopic mucosal resection (EMR) is currently the first-line treatment for high-grade dysplasia (HGD) in BarRET’s esophagus (BE). Despite improvements in the characterization of dysplasia, the management depend on the pathological analysis of biopsies previously performed. However, the level of concordance between cytologists in such situation remains discussed. The aim of this study was to evaluate the discordance between biopsy sample (BS) and EMR concordance between cytologists in such situation remains discussed. The aim of this study was to evaluate the discordance between biopsy sample (BS) and EMR specimen in case of HGD, as well as cytologists’ inter and intra-observatory variability.

Aims & Methods: This was a retrospective study including a prospective histological relecture (BS and specimen) in two expert centers. The inclusion criteria were: BE with HGD on pre-operative biopsies resected by EMR. The initial biopsies from other centers were collected and re-examined by our cytologists. The BS discordant with EMR specimens were recorded in a numeric file (Teleslide) and a second lecture was carried out by 2 experts and 2 fellows (1 of each per center). Five diagnoses were considered: no metaplasia (no BE), metaplasia without dysplasia, LGD, HGD, Adenocarcinoma. Concordance statistical tests were performed to assess the variability between BS and EMR specimen and among the cytologists.

Results: Between January 2005 and December 2015, 87 patients have undergone EMR for HGD on biopsies, in both centers. Among them, 41 (47%) had a discordant result between biopsies and resection specimen. The histological diagnosis on BS (16.4%), metaplasia, adenocarcinoma in 4 cases (4.6%) and one patient had no metaplasia. Finally, 33 patients could be analyzed, 29 men and 4 women, with a mean age of 63 years old. The mean length of BE according to Paris classification was C3-M5, with relief adenocarcinoma in 9 cases. A mean number of 1.4 endoscopic sessions was performed, with a mean of 2.7 resected pieces per EMR, which was macroscopically complete in 63.6% of the cases. The mean follow-up was 38 months. After histological relecture, the Kappa coefficient for the diagnosis of HGD was low on the initial BS, and ranged between 0 and 0.6 for the EMR specimen. The inter-observatory concordance was 0.2 (for both BS and EMR specimen) for the diagnosis of HGD. For other diagnoses, it was ranged between 0 and 0.5 for biopsies and between 0 and 0.6 for EMR specimen. The kappa coefficient regarding the presence of HGD was 0.5 for biopsies and 0.4 for the EMR. There was 0.4 and 0.5 for the fellows, respectively. The intra-observatory (between BS and EMR specimen) after relecture was ranged between 0.6.

Conclusion: The discordance rate between initial diagnosis of HGD on BS and final diagnosis on EMR specimen is high. This could have a direct impact on the management of BE.

Disclosure of Interest: M. Barthet: Consultant for Boston Scientific

All other authors have declared no conflicts of interest.

References

analyzed by cell counting kit-8 assay. Cell cycle and apoptosis were evaluated by flow cytometric analysis. Protein levels of p53 were determined by western blot analysis. Differences between groups were tested for significance using Student’s-t test (two-tailed).

Results: ESCC tissues examined in this study showed an obvious increment in TRPM2-AS expression when compared to normal tissues. Meanwhile, TRPM2-AS expression was positively related to lymph node metastasis, TNM stage and clinical stage. And upregulated TRPM2-AS expression was turned to be remarkably correlated with the shorter survival of ESCC patients which could act as an independent predictor for both overall survival time and disease-free survival. In addition, overexpression of TRPM2-AS could promote the proliferation and inhibit the apoptosis of ESCC cells, while knockdown of TRPM2-AS had a reverse function. Furthermore, downregulation of TRPM2-AS enhanced the expression of p53 in ESCC cells.

Conclusion: This study suggested that long non-coding RNA TRPM2-AS could be a potential oncogene of ESCC. TRPM2-AS expression might be served as another potential therapeutic target and prognostic biomarker. In addition, our study suggests that the inactivation of TRPM2-AS could contribute to the aggressiveness of ESCC by regulating the expressions of p53 in vitro, which may be a potential oncogene and therapeutic target for ESCC.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1213 ROLE OF CD80 EXPRESSION IN INFLAMMATORY-RELATED ESOPHAGEAL CARCINOMA

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Introduction: Esophageal adenocarcinoma (EAC) is an increasingly common cancer with a poor prognosis. EAC is the final step of a pathway starting with esophageal reflux disease, intestinal metaplasia, and dysplasia. The expression of cytokine expression by esophageal cancer cells is significantly lower than in the normal mucosa of healthy patients. This may be one of the mechanisms of immune escape of cancer cells in the esophageal cancer. Aims & Methods: The aim of this study was to investigate the role of CD80 in the inflammatory esophageal carcinogenesis and to characterize the immune environment of EAC. Mucosa samples from cancer and from healthy esophagus were obtained during esophagectomy from patients affected by EAC. Fresh biopsies were obtained from patients who underwent endoscopy for screening or follow-up. Immunohistochemistry for CD80 was performed. Fresh biopsies were analyzed by flow cytometry to quantify the expression of CD80, its receptor CD28 and the lymphocytes activation marker CD38 on esophageal epithelial cells and CD8 infiltrating lymphocytes, respectively. A model of reflux induced esophageal inflammation was created with a sysylyctin-oil-micro-jejunostomy. C57Bl/6 mice were randomized to receive or not intraperitoneal injections of anti-CD80 antibody. The esophageal-gastric specimens were collected 32 ± 2 weeks after the immunization and analyzed in a blinded fashion. Non-parametric statistics was used.

Results: Flow cytometric analysis of esophageal biopsies from healthy controls, Barrett esophagus, dysplastic esophagus and esophageal adenocarcinoma reveals that the expression of the costimulatory molecule CD80 by epithelial cells peaks during metaplasia in the inflammatory esophageal carcinogenesis. In the mice that received antiCD80 antibodies the rate of dysplasia in the fore stomach was significantly higher (5/7) compared to that observed in vehicle treated wild type mice (1/6).

Conclusion: The human and the in vivo data that we obtained suggest that in inflammation-driven esophageal carcinogenesis there is evidence of an active immune surveillance process mediated by the overexpression of CD80 costimulatory molecule. The human and the in vivo data that we obtained suggest that in inflammation-driven esophageal carcinogenesis there is evidence of an active immune surveillance process mediated by the overexpression of CD80 costimulatory molecule. The human and the in vivo data that we obtained suggest that in inflammation-driven esophageal carcinogenesis there is evidence of an active immune surveillance process mediated by the overexpression of CD80 costimulatory molecule.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1215 PHARMACOLOGICAL INHIBITION OF MONOCARBOXYLATE TRANSPORTER 1 INDUCES APOPTOSIS IN METASTATIC ESOPHAGEAL ADENOCARCINOMA CELLS

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Introduction: Altered glucose metabolism has become a recognised feature of tumor cells, which is characterized by an increased glucose uptake and preferential dependence on glycolysis for energy production. As a consequence, cancer cells produce large amounts of lactate, which is pumped out the cytosol by monocarboxylate transporters (MCTs), mainly MCT 1 and 4. MCT inhibition has not been investigated in esophageal adenocarcinoma (EAC) yet. The aim of this study was to evaluate the effect of the interplay between dysregulation of monocarboxylic oncoprotein genes and oncosuppressor genes within the tumor cells, and immunoviroenvironment and its effect on patients’ prognosis is still largely unknown.

P1216 AIRWAYS MICROENVIRONMENT IN ESOPHAGEAL ADENOCARCINOMA (EAC): THE ROLE OF THE NUCLEAR P53 EXPRESSION IS ASSOCIATED TO WORSE DISEASE-FREE SURVIVAL

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Introduction: Esophageal adenocarcinoma (EAC) microenvironment is characterized by the presence of abnormal proliferation and oncoprotein genes within the tumor cells, by lack of cytokines with anti-cancer effect and by high expression of immuno-suppressive factors. The interplay between oncogenes’ disregulation and immune microenvironment and its effect on patients’ prognosis is still largely unknown.

Aims & Methods: The aim of this study was to evaluate the effect of the interplay between dysregulation of oncogenes and oncoppressor genes within the tumor cells and immune microenvironment on EAC prognosis. Mucosa samples from EAC tissue were obtained during esophagectomy from 169 consecutive patients operated. Immunohistochemistry for MLH1, MSH2, MSH6, PM2, CMYC, p16, HER2 and nuclear p53 expression was performed. CD8 infiltration, CD8 and NK cells cytolytic activity (CD107) of tumor infiltrating lymphocytes and antigen-presenting cells across the time course of the tumor (EOC and AZD3965) with immunohistochemistry. Mutational analysis for BRAF was performed. Cox proportional hazard models were created to investigate the role of each marker adjusted for cancer stage. The association between each marker and the presence of nodal metastasis was assessed with exact tests.

Results: In our EAC patients’ series, one patients had BRAF mutation (V600E) and 5 of them had microsatellite instability. CD107 overexpression within the cancer was associated to the presence of nodal metastasis (p = 0.029). In patients with both nuclear p53 overexpression revealed to be an independent predictor of early recurrence with [HR = 2.995 (95% CI = 1.124–7.9896) p = 0.029] as well as cancer stage [HR = 2.693 (95% CI = 1.6693 to 5.6666) p < 0.001]. On the other hand, nuclear p53 overexpression also tended to be an independent predictor of overall survival [HR = 2.9339 (95% CI = 0.9613 to 8.9663) p = 0.06] while cancer stage confirmed to be the main survival predictor [HR = 1.8689 (95% CI = 1.8108 to 3.2314) p = 0.025].

Conclusion: In EAC, CD8 and NK cell cytolytic activity within the tumor was associated to nodal metastasis and CD107 expression might be used as a marker of it. Moreover, nuclear p53 overexpression within the tumor might be used as a marker of early recurrence after esophagectomy and then used to plan follow up strategies. No apparent relation between progression or mismatch repair gene or BRAF mutation was observed.

Disclosure of Interest: All authors have declared no conflicts of interest.
increased apoptosis of OACM5.1C cells whereas did not affect apoptosis of OE3.3 cells.

Conclusion: Metastatic and non-metastatic esophageal adenocarcinoma cells exhibit different glycolytic metabolism and response to pharmacological inhibition of MCT1, which increases apoptosis in metastatic cells. Further preclinical studies are needed to determine the potential of blocking lactate transporters on the treatment of metastatic EAC.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1216 THE PREDICTIVE FACTOR FOR PERFORATION IN ESOPHAGEAL ESD
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Introduction: Although endoscopic submucosal dissection (ESD) is accepted as a standard treatment for early stage esophageal neoplasia, esophageal perforation is sometimes experienced as main adverse event. Esophageal perforation causes mediastinal emphysema, mediastinitis, and pneumothorax, those sometimes require emergency surgery.

Aims & Methods: We evaluated the predictive factors for esophageal perforation in patients who received esophageal ESD. This was a retrospective observational study in a single institution. Between May 2004 and March 2016, 549 consecutive patients with 927 lesions were resected with ESD. Among these 93 patients, the MM in 16, the SM1 in 18, and the SM2 in 15 in the follow-up group were cases with lacking data. The primary outcome was determination of the predictive factors for esophageal perforation in patients who received esophageal ESD. The secondary outcome was clinical outcomes. Perforation was defined as a hole in the muscularis mucosae wall exposing the mediastinal cavity. Logistic regression multivariate regression analysis with generalized estimating equations was used to analyze repeated measured data.

Results: A total of 549 cases with 927 lesions were evaluated. Of those, perforation occurred in 15 cases (2.7%) with 15 lesions (1.6%). A lesion diameter (Odds ratio; OR = 1.05, 95% confidence intervals; CI: 1.02–1.07, p < 0.001) and the proximity of the tumor to a previous ESD scar (OR = 6.66, 95% CI: 1.80–24.6, p = 0.004) were both associated with perforation using crude logistic regression analysis. Multivariate logistic regression analysis also showed that a lesion diameter (OR = 1.05, 95% CI: 1.03–1.07, p < 0.001) and the proximity of the tumor to a previous ESD scar (OR = 13.0, 95% CI: 2.48–67.9, p = 0.002) were independent predictive factors for perforation.

Conclusion: Larger lesion and the proximity of the tumor to a previous ESD scar increased the likelihood of perforation in patients who received esophageal ESD. The tumor invades the MM in 9 patients, the SM1 in 3, and the submucosa to a depth more than 200um (SM2) in 29 in the CRT group and the LPM in 3 patients, the MM in 16, the SM1 in 18, and the SM2 in 15 in the follow-up group (p = 0.91). Lympathic invasion was positive in 21 patients in the CRT group and 12 in the follow-up group (p < 0.01). Vascular invasion was positive in 27 patients in the CRT group and 29 in the follow-up group (p = 0.32). Lymph node metastases of the submucosa and submucosal vertical margin was found in 7 patients in the CRT group and 9 in the follow-up group (p = 0.097). CRT-related grade 3 or 4 early adverse events were leukopenia 24.3% (10 patients), neutropenia 29.3% (12), febrile neutropenia 4.9% (2), diarrhea 2.4% (1), anorexia 17.9% (7). In the CRT group, 38 of 40 patients received chemotherapy as scheduled. Treatment was discontinued in the second course in 2 patients, and 7 required dose reduction. Lymph-node metastasis were found in 2 patients in the CRT group and 7 in the follow-up group (p = 0.15). In 15 cases with recurrence in the CRT group, lymph-node metastasis were seen in the irradiated field 46 and 49 months after treatment, respectively. 1 patient in the CRT group and 3 in the follow-up group died of esophageal cancer (p = 0.43). The overall survival (OS) rate at 2 years was 97.2% in the CRT group and 93.8% in the follow-up group (p = 0.002). The relapse-free survival (RFS) rate at 2 years was 97.1% in the CRT group and 83.4% in the follow-up group (p = 0.02).

Conclusion: Additional CRT after endoscopic resection in patients with esophageal squamous-cell carcinoma who have submucosal invasion, lymphovascular involvement, or vertical-margin invasion can become an effective organ-preservation strategy.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

P1218 SAFETY, EFFICACY AND OUTCOME OF ENDOSCOPIC SUBMUCOUS DISSECTION FOR THE TREATMENT OF EARLY BARRETT’S NEOPLASIA
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Introduction: Endoscopic submucosal dissection (ESD) was developed in Japan for en bloc resection of large gastrointestinal neoplasias and has progressively been adopted in the West. Currently, early Barrett’s neoplasia is mainly treated with endoscopic mucosal resection (EMR) and/or radiofrequency ablation, being the role of ESD in this context not well-established yet. Our aim is to evaluate the safety, efficacy and outcome of ESD for the treatment of early Barrett’s neoplasia.

Aims & Methods: Fifty consecutive ESD cases of early Barrett neoplasia were performed in 42 patients in our center between 2011 and 2016. All ESDs were performed under full narcosis after multidisciplinary team conference discussion and patient’s consent. The primary endpoint was the rate of en bloc resection. Secondary endpoints included rate of R0 and curative resection, a comparison of pre- and post- ESD histology, procedure time, procedure-related adverse events, and rate of remission at follow-up. This study was approved by the Stockholm Regional Ethical Committee.

Results: Mean age was 67 years (range 46–84), being 74% male and 72% long segment BE. The mean specimen size was 52 mm (range 16–159 mm). ESD resections included <25%, 25–50%, 50–75% and 75–100% of the lumen circumference in 4/31/12/3 of cases, respectively. En bloc, R0 and curative resection were obtained in 96% (48/50), 80% (40/50) and 70% (35/50) of cases, respectively. The primary ESD histology corresponded to low-grade dysplasia in 57% of the neoplasia (n = 30) and adenocarcinoma (n = 15). One case of LGD was upstaged to intramucosal AC, 10/30 cases of HGD were upstaged to adenocarcinoma. In 8/ 15 cases of AC, there was submucosal invasion on the ESD specimen. In 14/50 of the resected specimens there was multifocal neoplasia. The mean procedure time was 120 minutes. There were 2 perforations (4%) treated endoscopically and 2 (4.0%) postoperative bleedings treated conservatively. Six patients (12%) developed esophageal strictures that were managed endoscopically. The 30 days mortality rate for the 42 patients was 0. The 15 non-curative resections were referred to further ESD, 1 received chemoradiotherapy and 2 patients are under surveillance. In the 10 esophagectomy cases, 4 patients had AC in the remnant Barrett’s esophagus and 2 patients had lymph node metastasis. Complete remission was
found in 100% (35/35) of patients with curative resection at median follow-up of 25 months (range, 4–64 months).

Conclusion: In the proper setting, ESD is safe and effective for the treatment of early Barrett’s neoplasia with high en bloc and complete resection rates and good curative rate. ESD enables full pathological assessment in lesions not suitable for en bloc resection with EMR. There were no recurrences in the cutaneous cases, which increases the role of ESD for the management of early Barrett’s neoplasia.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1219 ENDOSCOPIC EVALUATION AT THE PRIMARY SITE OF CTI ESOPHAGEAL CANCER AFTER PROTON BEAM THERAPY AND CLINICAL RESULTS OF SALVAGE ENDOSCOPIC THERAPY FOR LOCAL RECURRENCE

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Introduction: Recently, it has been reported that proton beam therapy (PBT) is the effective treatment for patients with esophageal squamous cell carcinoma (ESCC). However, there are few reports regarding the endoscopic evaluation of efficacy after PBT at the primary site. Aims & Methods: The aim of this study is to clarify the adequate endoscopic evaluation of eradication of ESCC after PBT, and the clinical results of salvage endoscopic treatment for local recurrence. Patients with clinical T1 ESCC, and who had been treated with PBT between April 2013 and June 2016 at the National Cancer Center Hospital East were investigated. The total dose of PBT was 60 Gray- Equivalent (GyE). The efficacy of PBT at the primary site was evaluated with endoscopy, and the definition of complete response (CR) was used according to the same criteria as that of conventional chemoradiotherapy (CRT) as follows; disappearance of tumor lesion and ulcer, and absence of cancer cells with biopsy was verified. The endoscopic evaluation was performed within 2 months after the completion of PBT, and we repeatedly evaluated every month if the lesion did not achieve CR. The treatment for local recurrence after PBT was chosen based on the depth of the tumor as follows; endoscopic resection (ER) for CT1a, esophagomyotomy or photodynamic therapy (PDT) for CTb or deeper depending on patient’s condition.

Results: Among 44 patients who underwent PBT, the median age was 70 years (range, 41–79). The number of patients with clinical stage I was 23 (52%), and those with stage II, III, and IV were 16 (36%), 2 (5%), and 3 (7%), respectively. All patients underwent concurrent systemic chemotherapy. 43 patients (98%) underwent endoscopy for sizing, a handle, and a small disposable cryogen cartridge. The balloon is Focal Cryoballoon Ablation therapy (FCBA) (C2 Therapeutics Inc. Redwood City, CA, USA). Hence, an easy-to-use, low-cost treatment for ESCN would be of great value. Early studies for FCBA of Barrett’s esophagus have shown promising results, however, limited data are available for FCBA of ESCN. In this study we aimed to assess the safety, tolerability and efficacy of FCBA in the eradication of ESCN.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1219 ENDOSCOPIC CRYOBALOON ABLATION IS SAFE, WELL-TOLERATED AND HIGHLY EFFECTIVE IN THE ERADICATION OF ESOPHAGEAL SQUAMOUS CELL NEOPLASIA

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Introduction: Globally, 80% of all esophageal cancer cases are esophageal squamous cell cancer (ESCC), arising from esophageal squamous cell neoplasia (ESCN). Patients with ESCC have poor prognosis, but when diagnosed at the stage of ESCN, curative endoscopic treatment can be performed. ESCN mainly occurs in developing countries, often with limited endoscopic expertise and resources, like Central and Eastern Asia and Eastern and Southern Africa. Hence, an easy-to-use, low-cost treatment for ESCN would be of great value. Focal Cryoballoon Ablation therapy (FCBA) (C2 Therapeutics Inc. Redwood City, CA, USA) is a new endoscopic ablation therapy that comprises a balloon catheter with a conformable balloon that obviates the need for sizing, a handle, and a small disposable cryogen cartridge. The balloon is simultaneously inflated and cooled with nitrous oxide from the cartridge, resulting in ice patches of approximately 2cm2. FCBA is easy to use and requires no capital equipment. Early studies for FCBA of Barrett’s esophagus have shown promising results, however, limited data are available for FCBA of ESCN. In this study we aimed to assess the safety, tolerability and efficacy of FCBA in the eradication of ESCN.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

Table 1: The circumferential extension, number of patients and stenosis rate

<table>
<thead>
<tr>
<th>Circumferential Extension</th>
<th>Number of lesions</th>
<th>Stenosis Rate</th>
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</thead>
<tbody>
<tr>
<td>25–49%</td>
<td>1 (2.56%)</td>
<td>0 (0%)</td>
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<tr>
<td>50–74%</td>
<td>14 (53.84%)</td>
<td>5 (35.71%)</td>
</tr>
<tr>
<td>75–99%</td>
<td>6 (23.07%)</td>
<td>2 (33.33%)</td>
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<tr>
<td>100%</td>
<td>5 (19.23%)</td>
<td>5 (100%)</td>
</tr>
</tbody>
</table>

The circumference of the resection ≥75% was significantly associated with post-operative stenosis (OR = 3.5; P < 0.05). The average number of endoscopic dilatations for resolution of stenosis was 9.16 (±7.62). No procedure-related mortality occurred. Follow-up data median was 11 months.

Conclusion: Endoscopic surveillance of HSNNC is very important for SENs after resection. ESCN and ESD of these lesions are feasible and safe with acceptable complications risks despite the high rates of stenosis in resections >75% of the circumference.

Disclosure of Interest: All authors have declared no conflicts of interest.
enrolled. At baseline, side-by-side ablations of 10 seconds were performed on United European Gastroenterology Journal 5(5S) A593

Results: for pain), complete response (CR) rates (absence of MGIN or worse in biopsies), 63 MGIn, 17 HGIn with a median lesion of 2 (IQR 2–3) cm in length. Of these, 79 patients (99%) were successfully treated; 3 developed superficial, self-limited mucosal lacerations upon balloon inflation and 2 of them were successfully re-ablated 3 months later. A median of 5 (IQR 3–7) treatments were performed per patient, in median ablation time of 8 (IQR 5–10) minutes. As of April 2017, 77/79 (97%) patients completed a 3-month follow-up endoscopy and 69/77 patients (89%) exhibited endoscopic and histologic CR. Eight patients had residual USL and were again treated, a median of 5 months later and median ablation time of 10 (IQR 9–12) minutes. To date, 4 patients have undergone a 12 month endoscopy and all continue to exhibit endoscopic and histologic CR. No significant strictures have been noted on follow-up. Three patients developed fever shortly after treatment which was treated with aspirin. Post-procedure median VAS was 1 (IQR 0–2) at day 2, and 0 (IQR 0–0) at days 7 and 30. Conclusion: Preliminary results of our multicenter open prospective cohort study suggest that FCBA of ESC is safe, well-tolerated, and highly effective in inducing endoscopic and histologic remission. Longer term (12 month) follow-up data is pending.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1222 THE ENDOSCOPIC TREATMENT STRATEGY FOR SUPERFICIAL ESOPHAGEAL CANCER Y. Nagamuchi Department Of Gastroenterology And Hepatology, Nagasaki University Hospital, Nagasaki/Japan Contact E-mail Address: naoyuki3435@nagasaki-u.ac.jp

Introduction: Endoscopic submucosal dissection (ESD) allows en bloc removal of superficial esophageal squamous cell carcinoma (SCC). However, esophageal stricture often occurs after ESD when the lesion involves more than three-fourth of the circumference of the lumen. Frequent balloon dilation via endoscopy is required in such situation, thus causing health economic problem. In this study, we investigated the clinical outcomes, and prevention of post-ESD stenosis.

Aims & Methods: A total of 652 cases in 516 consecutive patients were treated by ESD in our department from April 2006 to December 2016. We investigated the following 2 items. 1. Clinical outcomes and complications. 2. Usefulness of oral steroids administration, the local steroids injection, endoscopic transplantation of tissue-engineered autologous oral mucosal epithelial cell sheets, or steroid oral + local injection combination therapy for the prevention of post-ESD stenosis.

Results: 1. Clinical outcomes: En bloc resection rate was 99.8% and en bloc curative resection rate was 90.0%. The rate of perforation, post-ESD bleeding, and post-ESD stenosis was 0.2%, 0.8% and 6.1%, respectively. 2. Prevention of post-ESD stenosis: (1) Oral steroid vs Steroid injection vs Cell sheet transplantation: In oral steroid group, the stenosis rate was 14.9%, and the ulcer healing period was 59.5 days. In steroid injection group, the stenosis rate was 12.9%, and the ulcer healing period was 66.0 days. In cell sheet transplantation group, the stenosis rate was 40.0% and the ulcer healing period was 36.0 days. There was no significant difference between these 3 therapies, and these therapies prevent post-ESD stenosis to significant extent. However, ulcer healing period of the cell sheet transplantation was significantly shorter compared with the other 2 therapies. (2) The usefulness of SH oral + local injection combination therapy. We investigated limitations of steroid administration, and cell sheet transplantation in order to prevent post-ESD stenosis. The following 4 factors (more than 9/10 of circumferential resection, more than 5 cm of longitudinal resection, cervical esophagus, post history of chemoradiation therapy or endoscopic resection) were the stenosis prevention treatment-resistance factors. Therefore, we examined the stenosis rate according to the number of these 4 factors. The stenosis rate of the cases which have 0 or 1 factor, the case which has more than 2 factors in semicircular cases, and the complete circular cases is 4.9%, 30.3%, and 44.8%, respectively. The stenosis rate of the cases which have more than 2 factors and complete circular cases are significantly higher, compared to the cases which have 0 or 1 factor. As a result, the cases which have more than 2 factors and complete circular cases were regarded as the stenosis prevention treatment-resistant cases. In contrast, in SH oral + local injection combination therapy, the stenosis rate of the cases which have more than 2 factors and the complete circular cases is 12.5% and 14.3%, respectively. Taken together, the stenosis rate of SH oral + local injection combination therapy is significantly lower, compared to the other 3 therapies.

Conclusion: Esophageal ESD achieved high en bloc resection rate and curability with low rates of complications. Oral steroid, steroid injection therapy and cell sheet transplantation may be effective treatment strategy for reducing post-ESD stenosis. However, the above-mentioned 4 factors are the stenosis prevention treatment-resistant factors in these 3 therapy cases. Furthermore, the cases which have more than 2 factors and complete circular cases were regarded as the stenosis prevention treatment-resistant cases. SH oral + local injection combination therapy is very useful for prevention of post-ESD stenosis and has a potential as the treatment-resistant cases.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

P1223 DIAGNOSIS OF TUMORS IN THE CERVICAL AND UPPER THORACIC ESOPHAGUS: EFFICACY OF ENDOSCOPIC ULTRASONOGRAPHY USING A JELLY-FILLING METHOD WITH WATER-SOLUBLE LUBRICATING JELLY N. Matsuura1, N. Hanoka2, R. Ishihara3, S. Yamamoto1, T. Akasaka1, Y. Takeuchi1, K. Higashino2, N. Uedo3, H. Iishi3

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Introduction: Endoscopic ultrasound (EUS) is the standard modality for qualitative diagnosis of submucosal tumors (SMTs) and determining the depth of invasion of esophageal cancer. Standard EUS, however, comprises a continuous water-filling or water-filled balloon method, which creates some problems for patients (feeling of filling the water in the stomach, and pain caused by inflation of balloon compression). Aspiration of water is especially problematic during the diagnosis of lesions in the cervical or upper thoracic esophagus. To resolve such disadvantages, we recently reported a method that includes probe EUS with a jelly-filling technique (EUS-J) for evaluating superficial esophageal squamous cell carcinoma (SCC). The procedure is characterized by filling the esophageal lumen with a water-soluble lubricating jelly (K-Y lubricating jelly; Johnson & Johnson, Tokyo, Japan) that is used for routine endoscopy and is harmless to humans. In the current study, we retrospectively evaluated the usefulness of EUS-J with water-soluble lubricating jelly for lesions located in the cervical and upper thoracic esophagus.

Aims & Methods: Patients with an esophageal SCC or SMT in the cervical or upper thoracic esophagus were included. EUS-J with water-soluble lubricating jelly was performed using a high-resolution probe. Before examination, several 5 mL syringes containing the Water Soluble Lubricating Jelly were prepared. When a patient under sedation was intubated with midazolam, an endoscope (GF-2T260Q; Olympus, Tokyo, Japan) was inserted into the targeted area in the esophagus. A 30- or 20-MHz miniature probe was then inserted through the left channel of the endoscope, and 40 mL of jelly was instilled through the working channel until the esophageal lumen was filled.

Results: From December 2010 to March 2017, we used EUS-J to evaluate 61 patients with esophageal SCCs and 10 with SMTs in the cervical or upper thoracic esophagus. There were 10 lesions in the cervical esophagus and 61 in the upper thoracic esophagus. Thus, 61 SCCs, 13 MGINs, and 9 SMTs were included in our study. The other 48 SCCs did not undergo chemoradiotherapy. Of these 61 patients with esophageal SCC, 60 lesions (98.3%) could be detected with EUS-J. 44 lesions treated either by endophagocytosis (n = 7) or endoscopic resection (n = 37). Histologic diagnosis was T1a in 27 lesions, T1b in 17 lesions. The overall accuracy of diagnosing invasion depth was 70.5% (31/44 lesions) by EUS-J. Among the 10 SMTs, we diagnosed seven leiomyomas derived from muscularis mucosa and one lesion due to vertebral body compression. The remaining two lesions were, respectively, a diminutive SMT (<3 mm) and a small lesion in the cervical esophagus adjacent to the hypopharynx. Neither was detectable using EUS-J because of their small size and difficulty with instrumental maneuvering. There were no adverse events during EUS-J, including aspiration pneumonia.

Conclusion: EUS-J with water-soluble lubricating jelly is useful and safe for diagnosing lesions in the cervical or upper thoracic esophagus. To our knowledge, this is the first report of using EUS with lubricating jelly for lesions located in this anatomic region.

Disclosure of Interest: All authors have declared no conflicts of interest.

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Introduction: The patients with early gastric cancer (EGC) who have undergone non-curative endoscopic resection (ER) need additional surgery. Our previous study reported short-term data about 29 days were optimal time when consider- ing non-curative endoscopic resection and curative surgical outcome. (Ann Surg Oncol. 2014 Jan;21(1):1232–9.) This study is a long-term follow-up study to evaluate the impact of previously proposed optimal time interval from ER to additive surgery by on the surgical and oncological outcomes.

Aims & Methods: A total of 2850 patients who were diagnosed with EGC underwent ER at the Severance and Gangnam Severance Hospitals, Seoul, Korea, between January 2007 and December 2014. We analyzed totally 302 (10.6%) patients who underwent additive gastrectomy after non-curative ER. The patients were divided into 2 groups according to the time interval point, as the earlier operation group (group A) and the later operation group (group B). The time interval point, at which operative time and estimated intraoperative blood loss (EIBL) of the earlier operation group and the later operation group

Disclosure of Interest: All authors have declared no conflicts of interest.
shown the greatest disparities, was evaluated. We retrospectively evaluated long-term follow-up study for oncological outcomes about follow-up duration, locoregional recurrence, distant recurrence.

Results: The median follow-up duration is 40.36 ± 20.74 months in all patients. Based on the previous our study, we divided patients two groups who underwent operations after 29 cases. Of the 302 patients, 133 were in Group A (>29days) and 169 in Group B (>29days). There were more differences between two groups about ASA score, ER Specimen size, intra-op. transfusion, PODI Hendom- discharge, Maximal postoperative CRP in the clinicopathological characteristics. Like previous our study the operative time, EBL, tumor size was significantly longer and more in group A compared with group B. There were totally 7 patients locoregional and distance recurrence during follow-up period. There were no differences in oncological outcomes between two groups.

Oncological recurrence for Each Group

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>n = 133</th>
<th>n = 169</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>F/u duration (months, mean ±SD)</td>
<td>37.02 ± 20.54</td>
<td>44.18 ± 19.49</td>
<td>0.002</td>
</tr>
<tr>
<td>Locoregional recurrence (n, %)</td>
<td>1 (0.8)</td>
<td>1 (0.6)</td>
<td>0.757</td>
</tr>
<tr>
<td>Distant recurrence (n, %)</td>
<td>2 (1.5)</td>
<td>3 (2.3)</td>
<td>0.582</td>
</tr>
</tbody>
</table>

Conclusion: Based on long-term follow-up data, surgery time after ER in EGC does not affect oncological outcome. These long-term follow-up results suggest that additional surgery at about 1 month after ER is optimal for better surgical outcomes without affecting the oncological outcomes.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference


P1225 THE POINT TO DISTINGUISH EARLY GASTRIC CANCER FROM DEPRESSION TYPE OF GASTRIC INTESTINAL METAPLASIA

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Introduction: This study discusses two endoscopic findings which improve the accuracy of the diagnosis of early gastric cancers (EGC). After successful Helicobacter pylori eradication, we often observe multiple reddish depressed lesions and “patchy redness” in the gastric mucosa. Even though most are intestinal metaplasia (IM), EGC is found among these lesions. A light blue crease (LBC) has been a highly accurate sign of the IM. There are, now, additional two endoscopic findings that should improve the accuracy of diagnosis of EGC. They are 1) “intraepithelial microinvadion (IEMI),” and 2) “Over flow”, Over flow is that the endoscopic finding that the structure of depressed lesions spreads to the outside of the depression.

Aims & Methods: The aim of this study is to clarify the usefulness of two endoscopic findings in order to detect the EGC in the group thought to be an IM. This study discusses two endoscopic findings which improve the accuracy of the diagnosis of early gastric cancers (EGC). After successful Helicobacter pylori eradication, we often observe multiple reddish depressed lesions and “patchy redness” in the gastric mucosa. Even though most are intestinal metaplasia (IM), EGC is found among these lesions. A light blue crease (LBC) has been a highly accurate sign of the IM. There are, now, additional two endoscopic findings that should improve the accuracy of diagnosis of EGC. They are 1) “intraepithelial microinvadion (IEMI),” and 2) “Over flow”, Over flow is that the endoscopic finding that the structure of depressed lesions spreads to the outside of the depression.

Results: The ratio of LBC was 75% in IM group, which was significantly higher than eradication group (7.7%), and small EGC group (9.4%). The ratio of irregular microsurface pattern was 33% in IM group, which was significantly lower than eradication group (92%), and small EGC groups (84%). The ratio of irregular microvascular pattern was 0% in IM group, which was significantly lower than eradication group (92%), and small EGC group (81%). The ratios of IEMI and Over flow lead to the diagnosis of EGC in addition to other endoscopic findings.

Conclusion: EIM and Over flow leads to the diagnosis of EGC in addition to other endoscopic findings.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1226 IRON DEFICIENCY ANEMIA—ARE THERE ANY PREDICTORS OF GASTROINTESTINAL MALIGNANCY?

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Introduction: Iron deficiency anemia (IDA) may be the only sign of gastrointestinal (GI) malignancy. The identification of predictive factors of GI malignancy in patients with IDA could help the physician to establish patients’ priority to endoscopic assessment, contributing to an earlier diagnosis.

Aims & Methods: retrospective study of 344 patients submitted to endoscopic assessment for IDA. Included adult patients with IDA and excluded patients with GI or extra-GI bleeding, total gastrectomy, exclusively vegetarian diet or iron intake from medical records.

Results: Included 121 patients with mean age of 68.5±17.0 years and 54.5% females. GI malignancy was identified in 14.9% of patients (gastric in 12, colonic in 6 patients). A statistically significant association was found between the presence of IDA and age (72.2% vs 40.8%, p = 0.01), GI symptoms (61.1% vs 11.7%, p < 0.01), weight loss (61.1% vs 5.8%, p = 0.01), need for hospitalization (88.9% vs 49.5%, p < 0.01), iron serum levels and transferrin saturation (19.7 ± 10.1 mL/L vs 30.4 ± 18.9 mL/L, p = 0.01). At logistic regression analysis only weight loss (p = 0.01), GI symptoms (p < 0.01), transferrin saturation (p < 0.01) and need for hospitalization (p < 0.01) showed a significant association with the diagnosis of GI malignancy. Transferrin saturation showed a weak discriminative capacity (AUC=0.67, p = 0.01) however, values of transferrin saturation ≤11% had a sensitivity of 94.4% and a negative predictive value of 97.1% for GI malignancy (CI 95%: 93.3-98.7).

Conclusion: In patients with IDA the diagnosis of GI malignancy is established in a significant percentage of patients and patients with GI symptoms, weight loss or with need for hospitalization should be given priority in the performance of endoscopic examinations. Transferrin saturation may help the physician in establishing the urgency of endoscopic assessment, since patients with values over 11% have a very low probability to have GI malignancy.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

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Introduction: Detection of gastric cancer in its early stage is pertinent in reducing disease-specific mortality. However, early detection has not been achieved in many countries where the incidence of gastric cancer is high. In order to overcome this problem, we developed an e-learning system for international endoscopists to improve endoscopic diagnosis of early gastric cancer. However, it has not been investigated whether such learning system is useful in clinical practice.

Aims & Methods: The objective of this trial is to investigate whether the intensive on-site TTT course is useful for increasing early detection rate of gastric cancer in Chinese high-volume endoscopy center. Five Chinese doctors (the TTT group) who were invited to the TTT course and the other five age and experience-matched Chinese doctors (the non-TTT group) in the same facility who did not attend the TTT course were included in this trial. Endoscopists of the TTT group attended 2-day learning course 4 times from March 20, 2015 to March 25, 2016. Endoscopists of the non-TTT group did not attend any learning program during the same period. Lectures of the TTT course included the detection of early gastric cancer by screening endoscopy using white-light endoscopy alone and the feature of the detected subtle gastric mucosal lesion using white-light endoscopy or magnifying endoscopy with narrow-band imaging. Contents used in the lecture had been reported to be useful by an e-learning trial [1, 2]. All the instructions were given by an experienced Japanese endoscopist (K. Yao) who constructed the e-learning system [1, 2]. Endoscopists also received on-site hands-on endoscopic training in order to make sure they obtained enough knowledge and technique. Furthermore, we held case conferences in order to share common experiences. During the period, the number of both newly detected early gastric cancers and screening gastroscopy procedures was recorded. The primary end-point was to compare the early detection rate between the TTT and the non-TTT group. (Early detection rate = the number of newly detected early gastric cancers / the number of screening gastroscopy procedures)

Results: The data obtained from the 275 consecutive cases of screening gastroscopy procedures by the TTT group endoscopists and from the 323 consecutive cases of screening endoscopy procedures by the non-TTT group endoscopists were analyzed. In the TTT group, four cases with early gastric cancers were detected and no early gastric cancer was detected. The early detection rates of
the TTT and the non-TTT group were 1.5% and 0%, respectively. There was a significant difference in early detection rate between the TTT and the non-TTT group (Fisher’s exact test, P = 0.046).

Conclusion: This clinical trial clearly showed that the systematic intensive TTT course is useful for improving early detection rate of gastric cancer in clinical practice at Jikei University endoscopy center. (NCTD20358578)

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P1228 COMPARISON OF ENDOSCOPIC SUBMUCOSAL DISSECTION AND SURGERY FOR THE TREATMENT OF EARLY GASTRIC CANCER: SINGLE-CENTER LONG-TERM OUTCOME STUDY

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Introduction: Endoscopic submucosal dissection (ESD) is believed to be a possible modality for early gastric cancer. But there is little report about long-term outcomes of the ESD directly compare with the surgery. The purpose of this study is the comparison between the two treatment modalities outcomes about the outcome. Aims & Methods: We performed a retrospective analysis of 1243 patients with stage I early gastric cancer without lymph node involvement. 551 patients were treated with ESD, and 692 patients were treated with subtotal or total gastrectomy. Long-term overall and disease-specific survival rates, development of new lesions, and complications were analyzed.

Results: The mean age was higher in the ESD group (64.9 ± 9.5 vs. 58.5 ± 11.7, P = 0.001) and female distribution was higher in surgery group (30.5% vs. 38.9%, P < 0.001). In ESD group, diabetes was more frequent (12.9% vs. 7.1%, P < 0.001). The overall survival rate was similar (96.2% vs. 96.7%, P = 0.136), but disease-specific survival rate was significantly higher in ESD group (99.8% vs. 98.7%, P = 0.037, log-rank test). During 10 year follow up period, new lesions were observed in 3.6% of ESD group and in 5.3% of surgery group (P < 0.001). ESD group showed less complications (4.5% vs. 16.3%, P < 0.001) and shorter hospital day than surgery group (5.27 days vs. 12.09 days, P < 0.001).

Conclusion: Although the development of new lesions were more frequent than surgery, ESD has similar overall survival rate and even higher disease-specific survival rate than surgery. Also, ESD has less complications and shorter hospital day than surgery. Therefore, ESD is an effective therapeutic method in early gastric cancer as well as surgery.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1229 HEMATOLOGISTS SHOULD ORDER ENDOSCOPIC EXAMINATION TO EXPERTS OF ENDOSCOPY IN CASE OF GASTRIC CANCER: SINGLE-CENTER LONG-TERM OUTCOME Study

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Disclosure of Interest: All authors have declared no conflicts of interest.

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Introduction: Gastric cancer is the most common cancer worldwide and the third leading cause of cancer-related death globally [1]. With the widespread eradication of H. pylori and early detection, the incidence and mortality of gastric cancer have been declined rapidly in the past few decades [2-3]. However, the prognosis of patients with metastatic diseases was still dismal and most cases survived less than one year [4]. Current primary and standard therapies for metastatic gastric cancer mainly included chemotherapy, consisting of fluoropyrimidine/cisplatin-based combination regimens[5]. Although radical gastrectomy was the first-line treatment for early gastric cancer[6], the value of gastrectomy in stage IV was still a great controversy.

Aims & Methods: We aimed to investigate the impact of primary tumor resection on survival outcomes among patients with metastatic cancer. We identified an eligible cohort of the population with stage IV gastric cancer from the Surveillance, Epidemiology and End Results (SEER) database between 2004 to 2012. The overall prognosis of advanced patients with or without gastrectomy was assessed by Kaplan–Meier and log-rank analysis. Multivariate Cox proportional hazards regression models was performed to analyze the effect of primary tumor resection on overall and cancer-specific mortality. To further reduce potential baseline bias in patient selection between two groups, we adopted 1:1 propensity score matching to re-examine the effect of resection.

Results: We finally identified 12984 eligible patients with metastatic GC between 2004 and 2012, including 1977 patients with gastrectomy and 11007 without resection. The median survival time for patients with or without surgery were 9.0, 4.0 months respectively. Patients who received surgery had a significantly survival advantage of gastrectomy in patients with stage IV gastric cancer. In the propensity score matched model analysis, gastrectomy was associated with increased overall (HR,0.54, 95% CI, 0.51–0.58) and cancer-specific survival (HR,0.50, 95% CI, 0.50–0.55).

Conclusion: Based on population-based studies, we demonstrated that there was a survival advantage of gastrectomy in patients with stage IV gastric cancer. Further prospective studies are needed to verify our findings.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
null
P1236 GASTRIC ADENOCARCINOMA OF FUNDIC GLAND TYPE: CANCER GENOMIC DATA
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Introduction: Gastric adenocarcinoma of fundic gland type (GAFG) is an uncommon variant of gastric adenocarcinoma which has a distinct clinicopathological, immunohistochemical, and endoscopic features (1-3). However, the molecular biological features of GAFG have not been well elucidated.

Aims & Methods: We evaluated clinical and molecular characteristics of GAFG in comparison with conventional gastric adenocarcinoma. Among 831 patients with gastric adenocarcinoma who underwent surgery or endoscopic resection in Juntendo University Hospital between January 2010 and December 2016, we enrolled 13 cases of GAFG, defined as an extremely well differentiated adenocarcinoma with expression of pepsinogen-I and/or H/K-ATPPase 1. To clarify current mutations of GAFG, next generation sequencing (NGS) was performed for all cases of the tumor and normal tissue formalin-fixed paraffin-embedded samples, using Ion PGM™ system with the Hotspot Cancer Panel v2 targeting 50 genes (Thermo Fisher Scientific). We also carried out immunohistochemical staining including MUC1/C, MUC3/C, MUC6, and CD10, and analyzed association among genetic alterations and mucin phenotype.

Results: Clinicopathologically, all patients [62(9) y (range 43–80), 8 male, 5 female] had submucosal invasive adenocarcinomas with no H. pylori infection; the mean depth of the submucosal invasion was 288.4 (50–700) μm. Neither local recurrence nor metastasis were detected at a median of 6.7 months (4–17) follow-up after treatment. NGS analysis revealed that nine of 13 patients (69.2%) had mutations of GNAS. The frequency of mutations was significantly higher (38.5% vs. 6.2%, p < 0.001) in GAFG. Furthermore, the frequency of TP53 mutation was significantly lower (7.7% vs. 47.8%, p < 0.05) in GAFG. However, there were no significant differences in the frequencies of KRAS and STK11 mutations. In addition, all lesions showed gastric phenotype (i.e. immunopositive for MUC5AC and/or MUC6). There were no significant differences between genetic alterations and mucin phenotype.

Conclusion: The present clinical and comprehensive genetic analysis identified the frequent presence of GNAS mutation and low-grade malignancy of GAFG.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P1237 LCNRA3-HOTAIR INDUCES THE UBIQUITINATION OF RUNX3 IN GASTRIC CANCER
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Introduction: Runx-related transcription factor 3 (Runx3) is a transcription factor playing an inhibitory role in the malignant behavior of gastric cancer. Long non-coding RNAs (LncRNAs) exert their functions mainly by binding with corre- sponding transcription factors, among which Runx3 is the most common ones. However, the LncRNAs that could bind with and affect the expression or activity of Runx3 are still unclear.

Aims & Methods: Potential Runx3-binding LncRNAs were screened by an online program (RNA22) software and validated by RNA immunoprecipitation (RIP). Specific HOTAIR binding site with Runx3 was confirmed further by RNA Pull down. The E3 ubiquitin ligases involved in the ubiquitin-proteasome degradation of Runx3 were recognized through co-immunoprecipitation assay.

Conclusions: HOTAIR induces the ubiquitin-proteasome degradation of Runx3 by enhancing its interaction with a E3 ubiquitin ligase Me3C3 in gastric cancer.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P1238 CARB3L1 FUNCTIONS AS A TUMOUR SUPPRESSOR IN GASTRIC CANCER THROUGH LKB1-MEDIATED AMPK ACTIVATION
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Introduction: Promoter hypermethylation plays a vital role in cancer development through transcriptional silencing of tumour suppressor genes. Using Infinium Human Methylation 450 BeadChip (450K) array, we first identified calcium binding protein 39-like (CAB39L) to be preferentially methylated in gastric cancer (GC) and it may function as a potential tumour suppressor gene.

Aims & Methods: In this study, we aim to investigate the biological function, molecular mechanism and clinical implications of CAB39L in GC. Clinical relevance was validated by bisulfite genomic sequencing (BGS), western blot and immunohistochemistry (IHC). In vitro functional assays were carried out by cell viability, colony formation, apoptosis, cell cycle, cell invasion and migration assays in GC cell lines. In vivo tumorigenesis was evaluated in an orthopic nude mice model. Pathway analysis was performed using RNAseq and Phospho-kinase Antibody Array. The interaction CAB39L with its protein partners was determined by co-immunoprecipitation assay.

Results: CAB39L mRNA was down-regulated in 13 out of 14 GC cell lines. Silencing of CAB39L was associated with promoter hypermethylation, and demethylatyion 5′- treatment using Azademethycine (5-Aza) restored the expression of CAB39L. In human GC, CAB39L mRNA and protein level (p < 0.0001)
were significantly decreased in GC tissues comparing to adjacent normal tissues both in Chinese cohort (n=48 pairs) and TCGA cohort (n=450). CAB39L hypermethylation was correlated with poor overall survival in Chinese cohort (n=87, p < 0.005) and validated in TCGA cohort (n=354, p < 0.005), which suggesting that CAB39L might function as a tumour suppressor. The functional importance of CAB39L was therefore investigated. Ectopic expression of CAB39L in three GC cell lines (AGS, BGC823, MKN55) suppressed cell proliferation in MTT (p < 0.01) and colony formation assays (p < 0.0001). CAB39L induced apoptosis and G1 cell cycle arrest in GC cells, concomitant with the enhanced expression of cleaved caspase-8, caspase-3, p21 and decreased cyclin D3 expression. Cell migration and invasion abilities were inhibited by CAB39L in wound healing and gel invasion assays, respectively. Conversely, CAB39L knockdown in MKN28 demonstrated opposite effects. Orthotopic mouse model also showed inhibited tumorigenicity with CAB39L-overexpressing BGC823 cells. Mechanistically, RNAseq and gene set enrichment analysis (GSEA) revealed that AMPK and ERBB2/ERBB4 signaling were involved in the tumour suppressive role of CAB39L in GC. Consistent with our RNAseq data, AKT inhibitor killed AMPK as the key activated kinase; whilst ERK1/2 was the most strongly down-regulated in CAB39L overexpressing GC cells, suggesting that CAB39L up-regulates AMPK concomitant with down-regulation of ERBB2/4/ERK signaling. Moreover, co-immunoprecipitation between CAB39L and LKB1, a bona-fide tumour suppressor that functions to activate AMPK to suppress tumorigenesis. Western blot confirmed activation of LKB1-AMPK/β cascade in GC cells expressing CAB39L, which opposite effect was observed in CAB39L silenced MKN28 cells. Administration of an AMPK activator, AICAR, inhibited growth of control cells but not CAB39L-expressing (thus AMPK activated) cells, suggesting that AMPK activation by CAB39L contributes to tumour suppression. Consistent with novel tumour suppressor functions, down-regulation of CAB39L in GC cells led to increased tumorigenesis in xenograft model, while knocking-down of CAB39L inhibited tumorigenicity in orthotopic mice model, while knocking-down of CAB39L inhibited gastric tumor growth. cDNA microarray showed that HoxC10 regulates multiple downstream genes including tumor suppressors, growth inhibitors and cell cycle arrest, concomitantly with increased expression of apoptosis markers cleaved caspase-9, -7, -3 and PARP and cell cycle inhibitors p53, p21 and p27. PKNOX2 also attenuated cell migration, cell invasion and cell cycle arrest, concomitant with increased expression of apoptosis markers cleaved caspase-9, -7, -3 and PARP and cell cycle inhibitors p53, p21 and p27. PKNOX2 also attenuated cell migration and invasion by inhibiting epithelial-mesenchymal transition. PKNOX2 in HGC27 cells was confirmed in mouse xenograft model. Tumorigenicity assay in nude mice showed that stable PKNOX2 expression significantly suppressed tumor growth in vivo. To probe the mechanism of action of PKNOX2 in GC, we performed Cancer pathway PCR array, which unveiled a profile of cell proliferation (> 6-fold) of insulin like Growth Factor Binding Protein 5 (IGFBP5) in PKNOX2-overexpressing GC cells. IGFBP5 knockdown abolished the growth inhibitory effect of PKNOX2 in GC cells, indicating that IGFBP5 mediated the tumor suppressive function of PKNOX2. Chromatin immunoprecipitation (ChIP) assay showed that PKNOX2 bind directly to IGFBP5 promoter to mediate transcription. Consistent with our data, PKNOX2 expression was positively correlated with IGFBP5 expression in the TCGA GC dataset. IGFBP5 mediated the tumor suppressive effect of PKNOX2 via activating p53 signaling pathway, as determined by western blot analysis. Consistently, p53 transfection significantly up-regulated PKNOX2 expression in GC cells, leading to tumor suppression.

Conclusion: PKNOX2 functions as a novel tumor suppressor silenced in GC by promoter methylation. Its tumor suppressive effect is mediated via IGFBP5 and the activation of p53 signaling pathway. Promoter methylation of PKNOX2 may be a useful biomarker for predicting patient prognosis.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1240 HOXC10 IS UPREGULATED IN HUMAN GASTRIC CANCER AND PROMOTES CELL G1-S TRANSFORMATION AND PROLIFERATION THROUGH DIRECT TRANSCRIPTIONAL REPRESSION OF P21

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Introduction: Gastric cancer is one of the most common malignancies worldwide. A multitude of factors contribute to the progression of gastric cancer, including activation of oncogenes and inactivation of tumor suppressors. To find the key molecules and their mutual relations in gastric carcinogenesis is of great significance for the diagnosis and treatment of gastric cancer. The homeobox (Hox) genes encode transcription factors and usually regulate the expression of target genes at transcription level. Dysregulation of Hox genes will cause the abnormality in individual development and tissue formation, and may also lead to malignant transformation. Our group have previously screened by gastric cancer tissue microarray and found that the expression of HoXC10 was remarkably upregulated in gastric cancer. At the present time, the function and molecular mechanisms of HoxC10 in gastric cancer remains poorly understood.

Aims & Methods: To investigate the expression of HoxC10 in gastric cancer, tissue samples from two clinical cohorts were used. We analyzed HoxC10 expresion in gastric cancer tissues and the corresponding adjacent non-tumor tissues, as well as its correlation with clinical pathological parameters. In addition, we also verified the results by utilizing bioinformatics analysis. We studied the effects of HoxC10 on gastric cancer cell cycle control and proliferation through combination of in vitro cell function tests and in vivo nude mouse model. Then, we screened HoxC10 potential downstream targets by using cDNA microarray and verified the results by RT-qPCR. We studied the effects of HoxC10 on p21 expression and its downstream cell cycle-related proteins and validated the correlation of HoxC10 and p21 expression in vitro and in vivo. By application of dual-luciferase reporter assay and chromatin immunoprecipitation, we explored the role of HoxC10 in p21 transcription repression.

Results: HoxC10 mRNA expression were significantly higher in fresh frozen gastric cancer tissues than in matching adjacent non-tumor tissues (91.43%, 64/70, P < 0.01). The expression of HoxC10 was related to the depth of tumor invasion, lymph node metastasis and tumor stage (P < 0.01). Using tissue microarray, HoxC10 protein expression was also found upregulated in gastric cancer tissues (91.3%, 137/150, P < 0.01) and was closely correlated with patient survival (HR = 2.8; 95% CI 2.0–7.2). Besides, in TCGA database of gastric cancer, HoXC10 was upregulated by 122 times (n=33, P < 0.01), and in Kato-III, HoxC10 overexpression was associated with poor prognosis of patients with gastric cancer (HR = 1.8; 95% CI 1.5–2.16). HoxC10-overexpressing gastric cancer cells showed accelerated G1-S phase transformation and proliferation, whereas HoxC10 knocking-down induced cell cycle arrest in G1 phase and repressed cell proliferation. Moreover, over-expression of HoxC10 accelerated gastric tumor growth in a mouse xenograft model, while knocking-down of HoxC10 inhibited gastric tumor growth. cDNA microarray showed that HoxC10 regulates multiple downstream genes including p21, a potent cell cycle regulator. A significantly negative correlation between HoxC10 and p21 were detected in gastric cancer cells and tissues. Knockdown of HoxC10 also altered the expression of some p21 downstream cell cycle regulatory proteins, such as CDK4, p27 and p21. Furthermore, we found that HoxC10 binds to the p21 promoter directly and could inhibit p21 transcription.

Conclusion: Taken together, our results suggest that HoxC10 functions as a tumor promoting gene in gastric cancer and may be an important regulator of the cell cycle of gastric cancer cells. The role of HoxC10 in cell cycle is of clinical significance for the diagnosis and treatment of gastric cancer.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P1241 RECOVERY OF GASTRIC FUNCTION IN CHRONIC ATROPHIC GASTRITIS BY USING L-CYSTEINE: A 3 YEARS STUDY
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Introduction: The relationship between Helicobacter pylori (H.p.) eradication and atrophic changes is debated. Although some studies report a partial restoration of serum pepsinogen I (PGI) levels after eradication, it is not clear whether this finding reflects gastric mucosal healing. L-cysteine, reducing acetaldelyde production after food intake, has been proposed for prevention of gastric carcinogenesis in patients with chronic atrophic gastritis (CAG). To assess modifications in gastric function after L-cysteine administration in CAG by means of PGI and gastrin 17 (G17) serum levels

Aims & Methods: 62 patients (18 men, mean age 47.2 yrs), with histological diagnosis of moderate to severe chronic, atrophic, body gastritis (according to 0.9) had an abnormal biopsy, were treated with L-cysteine (100 mg three times daily), up to now 24 out of 62 reached 36 months-treatment. Serum PGI and G-17 were measured at baseline and after 3, 6, 12, 24, 36 months after starting therapy.

Results: The PGI serum increased level after the starting of L-cysteine administration, as it follows: PGI mean value at baseline was 8.42 mg/l, but after 3 months therapy was 10.58, after 6 months 11.65, after 12 months 12.19, after 24 months G-17 mean value was 25.1, and after 36 months serum levels increased significantly, as a patient may have an OG cancer was not demonstrated unless exclusion of OG cancer. In this pilot no additional utility of opening direct access OGD for GP concerned a patient may have in the pilot group at 16.8 days [95%CI 16.9, 18.9].

Disclosure of Interest: All authors have declared no conflicts of interest.

P1243 FLYING OFF COURSE WITH A 2WW DIRECT ACCESS TO TEST PILOT: NOTTINGHAM'S EXPERIENCE OF THE SUSPECTED UPPER GASTRO-INTESTINAL CANCER PATHWAY CHANGE WITH GP VETTING AND OGD BOOKING
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Introduction: Timely progress through diagnostic pathways is a leading quality measure for NHS cancer services. A hypothesis of sooner diagnosis being achievable with direct access to hospital tests from primary care is a core part of CRUK ACE program (1), and in the context of UGI cancer pathway, there is known wide variation of direct access (DA) OGD (2). This pilot evaluates the efficacy and utility of DA OGD or clinic (DA OPD) for GP concerns a patient may have OG cancer. Comparison was made with standard 2WW pathway, where allocation to OGD or OPD first was determined by GP consultant. We hypothesised that opening direct access OGD for GP concerned a patient may have OG cancer and would not be detected on OGD alone.

Aims & Methods: Pilot and UGI standard 2WW referrals 01/01/16-01/08/16 were identified from Cancer Centre records.

Results: 192 patients were in the pilot pathway, 430 via the standard 2WW. GP were more likely to allocate a patient to DA OGD (52%) compared with 32% having DTT OGD allocated by the hospital. Despite under-utilisation of protected slots for DA OGD, time to DA OGD compared to DTT did not differ (11.0 days [95%CI 10.5,11.2] versus 12.4 days [95%CI 11.0,13.9]). The same was true for time to OPD. The time on pathway was not different in the pilot group at 16.8 days [95%CI 16.9,18.9].

Conclusion: OGD as a sole investigation for symptoms has its utility in excluding or detecting OG cancer. A high proportion of cancers detected via 2WW criteria for OGD are away from the pathway, and may not be detected by OGD. A high proportion of cancers detected via 2WW criteria for OGD are away from the pathway, and may not be detected by OGD. The subgroup of patients allocated to the pilot did have a quicker exit from the pathway, at 12.4 days [95%CI 12.9,16.6] on the DTT OGD group. The pilot overall detected 8 cancers (4.2%). The standard 2WW path 55 detected 55 (12.8%). OG cancers were in 4 of the DA OGD (4%) and 14 of the DTT OGD (10.2%). A further 10 non-OG cancers were detected in the DTT group after clinic requests further investigations for the cause of their symptoms. Those patients allocated to OPD first by either GP or hospital were as likely to have cancer as those having OGD, with 4.3% of those in the pilot having cancer detected this way, but none OG cancer, and 10.3% found to have cancers in the standard 2WW group following investigation directed after clinic visit. Of these 65% were cancers other than OG cancers and would not be detected on OGD alone.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

P1244 WHAT IS THE YIELD OF ROUTINE D2 BIOPSIES IN THOSE PRESENTING WITH WEIGHT LOSS AT GASTROSCOPY?
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Introduction: Coeliac disease is a common cause of malabsorption in Western countries. The gold standard method of diagnosing coeliac disease is by investigation of duodenal biopsy. Weight loss is a symptom of malabsorption. Patients referred for upper gastrointestinal endoscopy with symptoms of a weight loss commonly undergo duodenal biopsy to assess for presence of coeliac disease. We hypothesise that those patients with weight loss and who routinely have duodenal biopsies very rarely have coeliac disease unless there are other pointers towards malabsorption.

Aims & Methods: A single-centre, retrospective analysis of consecutive patients undergoing upper gastrointestinal endoscopy for the sole indication of weight loss was undertaken within a large associate teaching hospital within North London from 2005–2016. Of these patients, we reviewed those that had duodenal (D2) biopsies and the results. If they proved abnormal, we looked back for additional markers of malabsorption, clinically and biochemically.

Results: 142 consecutive patients, 65 were Male, 77 were female, underwent OGD for weight loss. Out of this cohort, 62% (n = 88) had a duodenal biopsy. 89% (n = 78) of these had a normal biopsy. 11% (n = 10) had an abnormal biopsy,
and 6 of these patients had coeliac, whilst 4 had other pathology such as granulomatosis or duodenitis. For all the patients who had abnormals D2 biopsies, they had other clinical markers of malabsorption, such as abdominal pain and diarrhoea, or biochemical indices such as anaemia or elevated TTG antibodies.

**Conclusion:** We conclude that the yield of routine duodenal biopsies in patients endoscoped for the sole indication of weight loss is poor. In patients with weight loss in whom coeliac disease is identified on biopsy is always associated with additional symptoms or abnormalities in blood indices. We conclude that there is no need to take biopsies of the duodenum on a routine basis for weight loss alone unless there are other signs of malabsorption. This will save time (both from taking the biopsy and sampling in the lab), lower the cost (forces and pot) and improve the safety (potential perforation and bleeding risk) of the procedure.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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**P1245** FUNDING DISPARITIES IN DIGESTIVE CANCER RESEARCH IN THE UNITED STATES

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**Introduction:** In 2015, the five most common digestive cancers (colorectal, pancreatic, liver, gastric, and esophageal) accounted for 16% of incident cancer cases and 14% of all cancer deaths. It is unclear whether the amount and recent trends in US federal funding for digestive cancer research corresponds to the burden of disease.

**Aims & Methods:** We obtained the total annual funding for cancer (including the five digestive cancers) from 2008 to 2015 using a public database of research funded by US federal agencies. We calculated funding in 2015 constant USD using the Consumer Price Index. Case and deaths estimated by the American Cancer Society were used to calculate funding per death or case for each cancer. For comparison, we also extracted data for the three most common cancers (breast, lung, prostate) and all cancers combined. As funding for research in the United States was boosted by the American Recovery & Reinvestment Act in 2009, and had lower proportional death than proportional funding (ratio of digestive cancers accounted for 23–24% of all cancer deaths from 2010–2015, but only 15% of all cancer funding in 2015), we can infer if the recent trends in US federal funding for digestive cancer research corresponds to the burden of disease.

**Results:** In 2015, 8 billion USD in federal funding was issued to all cancer research and 658 million USD to the five common digestive cancers. The five digestive cancers accounted for 23–24% of all cancer deaths from 2010–2015, but only 15% of all cancer funding in 2015. The ratio of the proportion of all cancer death to the proportion of all cancer funding, a marker of funding disparity, was 2.9. In comparison, breast cancer accounted for 7% of cancer deaths in all years, 11% of funding in both 2010 and 2015, and had lower proportional death than proportional funding (ratio = 0.8). Prostate cancer likewise had lower proportional death than funding (ratio = 0.8). Funding disparity, measured by proportional death and funding, was highest for esophageal and gastric cancer among digestive cancers and for lung cancer overall. The ratio of proportional death and funding was 12.6 for esophageal cancer but increased for the other digestive cancers during the study period. Funding per death among digestive cancers in 2015 was highest for liver cancer and lowest for esophageal cancer. Funding per death for breast cancer was more than 3-fold the funding per death for colorectal cancer. From 2010 to 2015, funding per death for digestive cancers decreased by 20% for esophageal cancer, 24% for colorectal and gastric cancer, and 28% for liver cancer; funding per death for pancreatic cancer increased. Statistically significant trends were observed for colorectal and liver cancer (p < 0.05 for both). Over the same period, funding per incident case decreased by 15% for esophageal cancer, 21% for colorectal cancer, 34% for gastric cancer, and 37% for liver cancer; funding increased for pancreatic cancer by 6%. Statistically significant trends were observed for liver (p < 0.01), colorectal, and gastric (p < 0.05) cancer. Despite the larger relative funding decrease for liver cancer, it remained the best-funded digestive cancer relative to both incident case and death. Liver cancer received more than 2.5-fold funding per incident case than colorectal and gastric cancer in 2015. Gastric cancer was the only digestive cancer to measure in the bottom two for both funding per death and per incident case.

**Conclusion:** From 2010 to 2015 in the US, federal research funding relative to the burden of disease demonstrated that digestive cancers are underfunded. Although a similar trend was observed for all cancer research, there appears to be a funding disparity for digestive cancers—especially gastric cancer—compared to breast cancer and all cancers combined. Greater investment and more equitable funding allocation may improve digestive cancer outcomes.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**TUESDAY, OCTOBER 31, 2017 9:00-17:00**

**H. PYLORI** I- HALL 7

**P1246** HELICOBACTER PYLORI ERADICATION MODULATES ABDERRANT CPG ISLAND HYPERMETHYLATION IN GASTRIC CARCINOGENESIS


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**Introduction:** Helicobacter pylori infection induces aberrant DNA methylation in gastric mucosa. This effect is critical for the production of promoter CpG island hypermethylation in gastric carcinogenesis.

**Aims & Methods:** H. pylori-positive patients with gastric adenoma or early gastric cancer who underwent endoscopic resection were enrolled. According to H. pylori eradication after endoscopic resection, the patients were assigned to H. Pylori eradication or non-eradication group. H. pylori-negative gastric mucosa from normal participants provided the normal control. CpG island hypermethylation of tumor-related genes (p16, CDH1, and RUNX-3) was evaluated by quantitative MethLight assay in non-tumorous gastric mucosa. The gene methylation rate and median values of hypermethylation were compared after one year by H. pylori status.

**Results:** In H. pylori-positive patients, hypermethylation of p16 was found in 80.6% of patients and 3.2% of controls, while 100% of H. pylori-negative patients showed hypermethylation (p < 0.05). The non-eradication group hypermethylation rate of p16 was 58.1% and 61.3% of the patients, and the median values of hypermethylation were significantly lower at one year compared with the non-eradication group. However, RUNX-3 hypermethylation did not differ significantly at one year after H. pylori eradication. The non-eradication group hypermethylation did not change after eradication.

**Conclusion:** H. pylori infection was associated with promoter hypermethylation of genes in gastric carcinogenesis, and H. pylori eradication might reverse p16 and CDH1 hypermethylation.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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**P1247 CURCUMIN DOWNREGULATES INTERLEUKIN (IL)-17 BY INCREASING THE EXPRESSION OF INDOLEAMINE 2,3-DIOXGENASE (IDO) IN HELICOBACTER PYLORI-INFECTED HUMAN GASTRIC MUCOSA**

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**Introduction:** IDO promotes the effector T-cells apoptosis by catalyzing the rate-limiting first step in tryptophan (Trp) catabolism. We demonstrated that the high expression of IDO in H. pylori-infected human gastric mucosa attenuates Th1 and Th17 immune response, while decreasing inflammation and fibrosis. The efficacy of the nutraceutical compound curcumin suggest its use as an anti-H. pylori agent, but mechanisms that underlie its helpful activity are still not clear.

**Aims & Methods:** Five antral biopsies were taken from 22 patients (10 M, median age 47.5 yrs, range 20–74) who underwent gastrointestinal for dyspeptic symptoms: 1 for urease quick test (Europasol, Trieste, Italy), 2 for histology (Giemsa staining for H. pylori, and 2 for organ culture. A C-area breath test was also performed (at least two tests positive and all the three tests negative to be considered negatives). All biopsies were treated with curcumin in addition with the IDO inhibitor 1-methyl-L-Trp (1-MT, Sigma, St. Louis, MO, USA) for 20 hours and evaluated for the expression of IDO and IL-17 by Western blotting. Levels of IL-17 were also measured in culture supernatant by ELISA. Further antral biopsies from a subgroup of 14 patients were treated with curcumin in addition with the IDO inhibitor 1-methyl-L-Trp (1-MT, Sigma, St. Louis, MO, USA) and the expression of IL-17 was assessed in total RNA extracted by RNeasy Mini Kit. The ratio of IL-17 expression of C6/H. pylori-positive patients, hypermethylation of p16 was found in 80.6% of patients and 3.2% of controls, while 100% of H. pylori-negative patients showed hypermethylation (p < 0.05). The non-eradication group hypermethylation rate of p16 was 58.1% and 61.3% of the patients, and the median values of hypermethylation were significantly lower at one year compared with the non-eradication group. However, RUNX-3 hypermethylation did not differ significantly at one year after H. pylori eradication. The non-eradication group hypermethylation did not change after eradication.

**Conclusion:** H. pylori infection was associated with promoter hypermethylation of genes in gastric carcinogenesis, and H. pylori eradication might reverse p16 and CDH1 hypermethylation.

**Disclosure of Interest:** All authors have declared no conflicts of interest.
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Introduction: Alterations in salivary microbiota have been linked to elevated inflammatory responses and has been reported in patients with inflammatory bowel disease and pancreatic cancer. As yet, the potential association between salivary microbiota and patients with gastrointestinal (GI) infection has not been determined.

Aims & Methods: In this study, we characterized the salivary microbiota in patients with H. pylori (HP)-associated gastritis and the potential changes of salivary microbiota after receiving HP eradication therapy. We enrolled subjects who were scheduled for diagnostic upper GI endoscopy. We obtained saliva samples from participants with peptic ulcer or cancer found on endoscopy, who have received prior HP eradication therapy. Bacterial DNA was extracted for 16s rRNA sequencing. OTU clustering was performed and found to be different from HP status by using the MiSeq Platform (Illumina). We found significant changes in the salivary microbiota of HP-negative subjects.

Results: We enrolled 16 subjects with confirmed HP gastritis and 14 HP-negative subjects. Baseline salivary samples of all subjects were found to have significantly higher bacterial diversity than corresponding gastric samples. The predominant microbial family identified in the stomach is Helicobacteraceae (55.2%) whereas Helicobacteraceae constitutes only 0.1% of salivary microbiota. In contrast, the predominant families in salivary microbiota are Prevotellaceae (23.9%) and Neisseriaceae (20.3%). When compared to HP-negative subjects, salivary microbiota in HP-positive patients showed a significant increase in the Bacteroidetes and Spirochaetaceae, and a decrease in Flavobacteriaceae families. HP eradication therapy resulted in a significant reduction in the relative abundance of families such as Bacteroidetes and Spirochaetaceae in salivary microbiota.

Conclusion: There was a significant difference in the microbial diversity and compositions between gastric and salivary microbiota in HP-infected subjects, with Helicobacteraceae dominating the gastric microbiota. HP-infected subjects had higher diversity in the salivary microbiota in the saliva which is reversed by HP eradication therapy. The significance of these microbial alterations in the saliva of HP-infected subjects and its correlation with gastric diseases deserves further investigation.

Disclosure of Interest: All authors have declared no conflicts of interest.

References:

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Introduction: Autoimmune gastritis (AIG) results in hypo/achlorhydria due to parietal cells destruction. It is characterized by lower levels of serum pepsinogen (Pg I) and PgI/PgII ratio and increased levels of gastrin. Some Authors support an association between AIG and Helicobacter pylori (HP) infection.

Aims & Methods: The aim of our study was to assess epidemiologic, serologic and pathologic features of AIG patients with and without previous HP infection. Three hundred and eleven consecutive patients with AIG, undergoing endoscopy were included. Serum gastrin, PgI, PgII and Cromogranin A levels were determined in all patients. Multiple gastric biopsies were obtained for histology, OLGA staging and HP detection. Previous or current HP infection (HP+) was confirmed in patients by upper endoscopy and/or serologic and/or serologic data. Histology was not performed using non parametric tests.

Results: Present or previous HP infection was confirmed in 50/211 patients while 161 were negative (HP-). When we compared HP+ vs HP-, AIG, no differences were found for age and gender distribution, antral and fundic/body atrophy, OLGA staging, p, PG-I and Cromogranin A levels. Gastrin levels and Gastrin/PgI ratio, a global marker of gastric damage we previously identified, were higher in HP+ than HP- (p < 0.02). Interestingly, 15% HP+ presented antrectomy atrophy. Severity of ECL hyperplasia was higher in HP+ (p = 0.02) with a 3.5 RR of developing nodular or carcinoid lesions when compared with HP-. Serum PgI, PgII PgI/PgII and gastrin levels correlated with disease severity in HP+ (p < 0.01) but not in HP-.

Conclusion: HP+ AIG have/have had a mild infection without differences in OLGA staging when compared with HP-. HP+ are characterized by lower gastrin and gastrin/PgI levels that, considered the lack of differences in OLGA staging, suggest a greater degree of gastric AIG. AIG patients showed seroserosal digestive findings at the mean follow-up of 39.0 ± 19.1 months. Subjects with seroserosal involvement showed a higher body mass index (p = 0.033), heavier alcohol drinking (p = 0.001), more intake of nonsteroidal anti-inflammatory drug (p = 0.015), and longer follow-up period (p = 0.038). On multivariate analysis, heavy alcohol drinking (odds ratio (OR) = 6.867, 95% confidence interval (CI) = 2.089–22.577, p = 0.002) and social drinking (OR = 5.306, 95% CI = 1.410–17.913, p = 0.013) were independent risk factors for seroserosal damage.

Disclosure of Interest: All authors have declared no conflicts of interest.

References:
The investigation of miR-155, miR-21, miR-146a and miR-223 expressions in Helicobacter pylori positive and negative individuals

N. Uyar Alpaslan1, E. Ucbilek2, I. O¨ . Barlas1, O. Sezgin2, S. Yara

Introduction: This study was conducted to determine the differential expression patterns of microRNAs, non-coding RNAs that control gene expression mainly through translational repression, in gastric mucosa of Helicobacter pylori (H. pylori) positive patients. Several miRNAs have been associated with promoting the inflammatory response initiated by the H. pylori infection, increasing the malignant progression of the gastric epithelium, and enhancing the invasiveness and migratory capacity of cancer cells. Using serum specimens, expression patterns of hsa-miR-155, hsa-miR-21, hsa-miR-146-a and hsa-miR-223 were determined using Real-Time Polymerase Chain Reaction (Real-time PCR).

Aims & Methods: Patients who underwent upper gastrointestinal endoscopy, in Mersin University Faculty of Medicine, Department of Gastroenterology and diagnosed H. pylori positive and negative were recruited. H. pylori status was assessed by the rapid urease test. Serum specimens of patients, were taken for miRNA isolation. hsa-miR-155, hsa-miR-21, hsa-miR-146-a and hsa-miR-223 expression levels were determined using comparative ΔΔCt analysis by using Real-Time PCR Systems, SDS 2.0.3 software programme. Statistical analysis of miRNAs between H. pylori positive and negative groups were compared with the Mann-Whitney U test. p < 0.05 was considered statistically significant.

Table 1

<table>
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<tr>
<th>H. pylori positive N=46</th>
<th>H. pylori negative N=49</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Average Median</td>
</tr>
<tr>
<td>hsa-miR-155 0.998199 0.986536</td>
<td>0.393990 0.7331665</td>
</tr>
<tr>
<td>hsa-miR-223 6.992772 19.222485</td>
<td>2.031475 7.664999</td>
</tr>
<tr>
<td>hsa-miR-146-a 4.730933 4.834877</td>
<td>2.13897 9.33274 28.02030</td>
</tr>
<tr>
<td>hsa-miR-223 4.412535 5.519694</td>
<td>2.03876 4.669136</td>
</tr>
</tbody>
</table>

Results: H. pylori positive (n=46) and negative (n=49) were included. H. pylori was not able to the hsa-miR-155, hsa-miR-21, hsa-miR-146-a and hsa-miR-223 expressions in serum specimens and nuclear factor-κB (NF-κB) transforming growth factor, beta (TGFβ) pathways. There was no statistically difference between H. pylori positive and negative individuals in the analysis of hsa-miR-155, hsa-miR-21, hsa-miR-146-a and hsa-miR-223 miRNA expression levels (Table 1). In surveys, there is no statistically difference between each groups, the level of education, intake of smoking-alcohol, hypertension, diabetes, cardiovascular disease, family history of gastroduodenal disease, type of gastroduodenal disease.

Conclusion: This study may contribute to the literature in terms of preventing pro-cancerous progression in the cases of cancer resulting from H. pylori infection before the onset of cancer.

Disclosure of Interest: All authors have declared no conflicts of interest.

References


1252 INTERLEUKIN LEVEL IN PATIENTS INFECTED WITH CAGA(+) AND CAGA(−) STRAINS OF HELICOBACTER PYLORI

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Introduction: Change of interleukin level in patients with of chronic infections, in particular at Helicobacter pylori infection. Change of interleukin level in H. pylori infected patients is extensively studied, for example, increase in level of interleukin-8 according to a number of works is accompanied by infection with virulent strains of a microorganism. CagA gene coding synthesis of the cytokinin (CagA) of the same name capable, in addition, to exert impact on development of interleukin, in particular interleukin-8 is considered a marker of presence of pathogenicity island of H. pylori.

Aims & Methods: The aim was to define features of change of level of interleukin-8 (IL-8) and interleukin-1β at patients with the chronic gastritis associated with H. pylori infection depending on existence or lack of a gene of cagA in a microorganism genome. 40 patients with the chronic gastritis associated with H. pylori have been examined. Earlier, it was made for all patients a specification of a condition of stomach mucosa and taking biopsy from stomach antrum (2 biopastes) for the purpose of verification of H. pylori infection. Detection of a microorganism was made by rapid urease test, a histologic method and molecular-genetic research—the polymerase chain reaction (PCR) with definition of genes of urease (ureC, ureI). Besides, the PSR method presence of a cagA gene in a genome of H. pylori was detected. All patients were divided on two groups: with cagA(+) strains and with cagA(−) strains. Levels of interleukins 1β, 8, 4 were decided by immunofluorescent method (the Vektor-Best, Russia).

Results: cagA gene was detected in 30 patients (cagA(+) group) and absence in 10 patients (cagA(−) group). In cagA(+) patients mean level of interleukin-1β was 395.6 pg/ml, but in cagA(−) patients—311.2 pg/ml (p < 0.05). Level of interleukin-8 in cagA(+) patients was 2.4 pg/ml but in cagA(−) patients—0.32 pg/ml (p < 0.05).Level of interleukin-4 in cagA(+) patients was 21.6 pg/ml, but in cagA(−) patients—83.4 pg/ml (p < 0.05).

Conclusion: Presence in a genome of H. pylori cagA gene is accompanied by reliable increase in level of pro-inflammatory cytokine interleukin-8 and decrease in level anti-inflammatory interleukin-4 that can be an additional factor of development of an inflammation during H. pylori infection.

Disclosure of Interest: All authors have declared no conflicts of interest.

1253 THE TRANSITION OF HELICOBACTER PYLORI ERADICATION IN OUR INSTITUTION

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Introduction: The incidence and prevalence of Gastric cancer are high in Japan. The International Agency for Research of Cancer (IARC) reported that 80% of gastric cancer is caused by Helicobacter pylori (H. pylori) infection and that the incidence of gastric cancer can be reduced by 30%–40% through H. pylori eradication therapy for chronic gastritis was approved for national health insurance in February 2013 in Japan. However, the success rate of H. pylori eradication by conventional primary triple therapy has been decreased by resistance to clarithromycin. Vonoprazan, which is a potassium ion–

Supplementary Table

Disclosure of Interest: All authors have declared no conflicts of interest.
P1254 ERADICATION OF H. PYLORI INFECTION IN PATIENTS NAÏVE TO TREATMENT USING COMBINANT THERAPY OR BISMUTH QUADRUPLE THERAPY (THREE-IN-ONE PILL): A REAL-LIFE OBSERVATIONAL STUDY

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Introduction: Clarithromycin (CLAY)-containing quadruple therapy, i.e. concomitant therapy (CT), and bismuth-containing quadruple therapy (BQT) have been suggested as first-line therapies for eradication of H. pylori infection. Both treatments are reported to have an eradication rate higher than 90%. International guidelines recommend that choosing one regimen vs the other should be based on the regional prevalence of antimicrobial resistance, knowledge of patient’s previous antimicrobial exposure or allergy to amoxicillin, and patient’s wish. However, this therapeutic approach has never been tested systematically.

Aims & Methods: The primary endpoint of this study was to evaluate the eradication rate in H. pylori-infected subjects naïve to treatment in an area of high (CLAY 75%) CT rate based on knowledge of patients’ previous antimicrobial exposure or allergy to amoxicillin, and patient’s wish. Secondary endpoint was to assess any difference between CT and BQT in terms of efficacy, safety and compliance. Because in Italy bismuth compounds are not available, BQT was by using the new three-in-one pill (TIPG) (metronidazole 125 mg + tetracycline 125 mg + bismuth 140 mg). Patients and Methods: 1) Observational study on 144 consecutive dyspeptic patients (57 M and 87 F, median age 56 yrs). Diagnosis of H. pylori infection was through 13C Urea Breath Test (UBT), or rapid urease test and histology in patients who performed endoscopy; 3) Groups of treatment: a) 84 CT (36 M and 48 F, median age 52 yrs) and PP analyses; significance of differences by chi square test (p < 0.05).

Results: 1) Eleven of 144 patients (7.6%, 95%CI 4.3-13.5) (6/4.1%, 95%CI 3.3-15.4) in the CT group and 5/60 (8.3%, 95%CI 3.6-19.3) in the BQT group] discontinued therapy because of side effects (p = ns). Overall eradication rate was 122/133 (91.7%, 95%CI 87.2-95.6) in the PP analysis and 124/144 (84.7%, 95%CI 79-90.1) in the ITT analysis; 3) PP eradication rate was 69.87 (88.5%, 95%CI 81.6-95.8) in the CT group and 53/55 (96.4%, 95%CI 91.6-101.4) in the BQT group (p = ns); 3) ITT eradication rate was 69.84 (82.1%, 95%CI 74.3-90.8) in the CT group and 53/60 (88.3%, 95%CI 80.6-96.8) in the BQT group (p = ns); 4) Among patients who completed therapy, no significant differences between the two groups were found as to the incidence of side effects (29.4% in the CT group and 35.8% in the BQT group) or compliance to treatment.

Conclusion: 1) In an area of high CLA resistance, use of CT or BQT as first-line therapy, based on patient’s previous antimicrobial exposure, allergy to amoxicillin and patient’s wish, is a highly effective strategy with an eradication rate of 91.7% (95%CI 87.2-95.6%). CT was more effective but with more side effects compared to CT, however differences were not statistically significant.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
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P1255 CYP3A5 GENOTYPE STATUS AFFECTS OUTCOME OF FIRST-LINE VONOPRAZAN-CONTAINED HELICOBACTER PYLORI ERADICATION THERAPY

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Introduction: Potent acid inhibition with acid inhibitory drugs is crucial to the eradication therapy for eradication of Helicobacter pylori infection. Vonoprazan, a new PPI, non-selectively inhibits the binding of potassium ion to H+ K+-ATPase in gastric parietal cells and inhibits H+ K+-ATPase activity at 400-fold more potent than that of lansoprazole, proton pump inhibitor (PPI). Therefore, the eradication regimen with vonoprazan has been developed for increasing the eradication rate as compared with a PPI-based therapy. Although vonoprazan is mainly metabolized by CYP3A4/5, it is unclear whether its acid inhibitory effect and outcome of H. pylori eradication differ among CYP3A5 genotypes. Our aim was to clarify the impact of CYP3A5/*3 genotypes on outcomes of H. pylori eradication including vonoprazan in Japanese.

Aims & Methods: We investigated the influence of CYP3A4/5 and CYP2C19 genotypes as susceptibility to antimicrobial agents for outcome of vonoprazan-containing eradication therapy for 7 days in 105 Japanese: (1) with amoxicillin 750 mg and clarithromycin 20 mg twice daily (bid) as the first-line treatment (n = 76); (2) with amoxicillin 750 mg and metronidazole 250 mg bid as second-line treatment (n = 29). Eradication status was assessed at 8 weeks via 13C-urea breath test. CYP3A4*22, CYP3A5*3 and CYP2C19*2/*3 were genotyped for all patients.

Results: Eradication rate on intention-to-treat analysis was 82.9% (95% confidence interval: 72.5%-93.6%, 63/76) in the first-line treatment and 93.1% (95%CI 77.9%-99.9%, 27/29) in the second-line. None with CYP3A4*22 was observed. 38.3% of patients (46/120) were CYP3A5*1/*3 type and 55.0% were *3/*3 type. In naive patients, the prevalence of clarithromycin-resistant strain was 42.4% (14/33). The eradication rate in patients with CYP3A5*1/*1 and CYP3A5*1/*3 genotypes showed 77.7% (46/59) and 84.7% (33/39) in the first-line treatment. However, no significant differences of clinical outcome in the second-line therapy were seen among CYP3A5/*3 genotypes.

Conclusion: Eradication rates of vonoprazan-based eradication therapy can be achieved high compared with PPI-based therapy. However, because CYP3A5/*3 genotype may be one of determinate for outcome of eradication regimen including vonoprazan, genotyping of CYP3A5/*3 will be required to be paid attention for clinical outcome before treatment.

Disclosure of Interest: All authors have declared no conflicts of interest.

Aims & Methods: Our aim was to investigate the efficacy of the VPZ-based eradication therapy. The subjects were 999 patients who were diagnosed as H. pylori infection in our institution from June 2014 to December 2016. The patients were grouped into three: VPZ group and conventional PPI (Lansoprazole or Rabeprazole) group. We evaluated the first-, second- and third-line eradication status. Each regimen of VT group was first-line eradication (VPZ 20 mg bid+ amoxicillin 750 mg bid+ CAM 200 mg bid for 7 days), second-line eradication (VPZ 20 mg bid+ amoxicillin (AMPC) 750 mg bid+ Metronidazole 250 mg bid for 7 days). Each regimen of VPZ group was first-line eradication (VPZ 20 mg bid+ AMPC 750 mg bid+ CAM 200 mg bid for 7 days), second-line eradication (VPZ bid+ amoxicillin 750 mg bid+ Metronidazole 250 mg bid for 7 days). One of the following PPI was used: Lansoprazole (LPZ) 30 mg, Rabeprazole (RPZ) 20 mg. After several months, the eradication status was examined by urea breath test, stool antigen testing and blood antibody test.

Results: The number of first-line regimen of VPZ patients was 109, and the eradication was achieved in 97 patients (87%). RPZ patients were 308, and the eradication was achieved in 288 patients (94%). The number of second-line regimen of VPZ patients was 24, and the eradication was achieved in 19 patients (79%). RPZ patients were 68, and the eradication was achieved in 60 patients (88.2%) respectively. There were statically no significant differences in second-line regimens. Adverse events
such as erosion and duodenal ulcer were reported in 6.6% (9/136) of patients in VPZ, in 3.1% (18/560) in 3-in-1 capsules containing bismuth subcitrate potassium 140 mg, metronidazole 200 mg and tetracycline 500 mg in LPZ.

Conclusion: The first-line regimen with VPZ was superior to conventional PPI regimen, and was a result not to be inferior in the safety either.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1257 CAN TWO WEEK BISMUTH BASED QUADRUPLE THERAPY FOR RESISTANT H. PYLORI INFECTION STILL BE USED IN THE UK?

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Introduction: Eradication of H. pylori infection cures peptic ulcer disease (PUD); however, current strategies are not ideal and many patients require repeated courses of treatment. We, and others, have recently documented that currently, within the UK, less than 30% of patients with proven PUD, are subsequently documented to have been cured by H. pylori eradication 1,2. Current therapy is not successful regarding 2nd line treatments, but the British National Formulary recommends a 2nd regimen containing bismuth subcitrate, omeprazole, tetracycline and metronidazole. However since 2016, bismuth subcitrate has not been available in the UK, but is thought to be an important in treating persistent H. pylori infection 3,4.

Aims & Methods: The aim of this observational cohort study was to evaluate the effectiveness of a 2 week bismuth based quadruple therapy in patients who had persistent H. pylori infection following previous failed eradication therapy. Patients were identified from electronic hospital records using endoscopy data set, patient administration records, and pathology data sets from Jan 2011 to Dec 2016. Initial failed H. pylori eradication was defined by either by a positive 13C-Urea Breath Test (13C-UBT) or positive HpStool Antigen test (HpSA) following H. pylori treatment in either primary or secondary care. All patients were seen, assessed and warned about the importance of compliance with treatment and of possible side effects by the specialist (RL) or the dyspepsia nurse specialist (GB). After treatment, omeprazole 20 mg bd, tetracycline 500 mg qds, metronidazole 400 mg qds and bismuth subcitrate qds for two weeks, eradication was assessed at least 4 weeks after finishing treatment by 13C-UBT (or HpSA in those patients unable to attend hospital appointment). Endoscopy was also performed in those patients whom had failed multiple previous treatments to ascertain the clinical need for further treatment by assessing any underlying ulcer diathesis and for H. pylori culture and sensitivity testing.

Results: Within the inclusion period, (and from initial failed H. pylori eradication in those patients in whom eradication of H. pylori infection is mandated by the underlying ulcer diathesis. The 2nd eradication rate is likely due to the use of bismuth high doses of antibiotics, but also by specialists ensuring patients complied with their medication. These data, together with the poor outcomes of H. pylori eradication when undertaken by general physicians, also highlight the need for H. pylori eradication to be only undertaken by specialists who have access to alternative sources of colloidal bismuth subcitrate.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

Aims & Methods: Methods of analysis and inclusion criteria were based on RPSMA recommendations. Relevant publications were identified by a research in PubMed, MEDLINE, Science Direct and EMBASE. The end-point was to estimate the mean eradication rate and variations of delta value at urea breath test across all studies and, overall, with a pooled data analysis. The data have been weighted ad proportions/percentages, and 95% confidence intervals (CI) were calculated. For continuous variables, we calculated the weighted mean difference. Odd ratios (OR) were calculated, where available, based on the Mantel-Haenszel method. Data were entered into the RevMan 5.3 software.

Results: 13 studies (both randomised clinical trials and open label pilot studies) were selected. In one study patients with peptic ulcers were selected, while in the remaining 9 only dyspeptic patients were recruited. Probiotics eradicated H. pylori in 50 out of 391 cases. The mean eradication rate was 14%, with a 95% CI of 2-25% (p = 0.02). Most of studies investigated a probiotic formulation based on a single lactobacilli strain. Lactobacilli eradicated the bacterium in 30 out of 235 patients, with a mean weighted rate of 16% (95% CI 1–31%). Multilin strain combinations were effective in 14 out of 105 patients, with a pooled eradication rate of 14% (95% CI 1–43%). In the comparison probiotics versus placebo, we found an OR = 9.65 in favor of probiotics, with a 95% CI of 1.97–47.36 (p = 0.005). Finally, probiotics induced a mean reduction in delta values of 8.61% (95% 3.88–11.34, p < 0.0001). No study provided data about adverse events.

Conclusion: Probiotics alone show a minimal effect on the eradication of H. pylori, thus suggesting a presumable direct effect. However, they cannot be indicated as a therapeutic regimen for the low eradication rate. Disclosure of Interest: All authors have declared no conflicts of interest.
P1260 COMPARISON OF CLARITHROMYCIN- AND LEVOFLOXACIN-CONTAINING TRIPLE THERAPIES FOR FIRST-LINE Helicobacter pylori ERADICATION IN IRAN

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Introduction: According to the Maastricht IV consensus report, Clarithromycin-containing triple therapy can be considered as a suitable option for first-line Helicobacter pylori (H. pylori) eradication in areas with less than 20% resistance rates to Clarithromycin. On the other hand, resistance to Clarithromycin is increasing in Iran, influencing the efficacy of standard triple therapy in this country. Therefore, regimens containing other antibiotics have to be considered in Iran. Aims & Methods: One hundred and forty patients with peptic ulcer disease and naïve for H. pylori infection were randomly divided into two groups to receive either 10-day standard triple therapy (Pantoprazole 40 mg, Amoxicillin 1 gr and Clarithromycin 500 mg, all given twice daily) or 10-day Levofloxacin-containing triple therapy (Pantoprazole 40 mg BD, Amoxicillin 1000 mg BD and Levofloxacin 500 mg daily). Eight weeks after the treatment, H. pylori eradication was assessed by 13C-urea breath test.

Results: One hundred and thirty-three patients completed the study. According to intention to treat analysis, H. pylori eradication rates were 75.7% (95% confidence interval (CI): 65.7%–85.7%) and 58.5% (95% CI = 47.1%–70%) in standard and Levofloxacin-containing therapies, respectively. Also, per-protocol eradication rates were 83% (95% CI: 74%–92%) and 61% (95% CI = 49%–73%), respectively. The rates of severe adverse effects of therapy were 7.1% and 2.9% in the mentioned groups, respectively.

Conclusion: Both Clarithromycin-containing triple therapy and Levofloxacin-containing triple regimen do not seem to be suitable options for first-line H. pylori eradication in Iran. We suggest using Clarithromycin in quadruple regimens such as hybrid or concomitant therapies and reserve Levofloxacin to be used in second-line eradication regimens, as it is recommended by Maastricht V Consensus Report.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1261 EFFICACY AND TOLERABILITY OF REBAMIPIDE IN TRIPLE THERAPY FOR ERADICATION OF Helicobacter pylori: A RANDOMIZED CLINICAL TRIAL

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Introduction: Rebamipide is an orally prostaglandin E2 and I2 synthesis inducer. A latest clinical trial showed that the adhesion of H. pylori to stomach wall was reduced by rebamipide. This could improve eradication rates by increasing the accessibility of the drug to antibacterial agents.

Aims & Methods: We aimed to determine eradication rate, the effectiveness and advantage of rebamipide in triple eradication therapy of H. pylori infection. Subjects comprised patients undergoing eradication therapy for H. pylori infection in our clinics. Patients with a history of eradication therapy, gastrectomy, or allergy to medications in triple therapy were excluded. Written informed consent was obtained for each patient. This trial was performed as a randomised open-label study. All patients were referred to the institutional review board. All patients were tested on H. pylori infection. The number of cases was 160 (80 cases in each group). Each patient was randomly enrolled for rebamipide therapy group (RBD) (esomeprazole 40 mg, amoxicillin 1000 mg, clarithromycin 300 mg, rebamipide 600 mg twice a day for 14 days) or standard triple therapy group (STD) (esomeprazole 40 mg, amoxicillin 1000 mg, clarithromycin 500 mg, twice a day for 14 days). Before starting therapy, we checked the background characteristics of each patient (age, gender, weight, height; drinking habit; smoking habit; use of probiotics, bismuth, PPI, and esophageal findings). After the therapy, we asked physicians and patients about medication compliance and side effects. The primary endpoint was the eradication rate. The secondary endpoints were the rates of side effects.

Results: For RBD therapy group and STD therapy group, the eradication rates were 94.0% (95% confidence interval, 85%-100%) and 82% (95% confidence interval, 74%-95%) respectively, and the rates of side effects were 8.5% (95% confidence interval, 7.0%-26.5%) and 29% (95% confidence interval, 17.5%-41.0%) respectively. Many side effects, such as oral ptyalism, stomach pain, diarrhea and peroral ulcerations were observed significantly more often in the STD group.

Conclusion: The findings suggest that rebamipide is effective in eradication of H. pylori infection, significantly improving eradication rate in triple therapy. The advantage of rebamipide has efficacy and good tolerability.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

TUESDAY, OCTOBER 31, 2017: 09:00-17:00
SMALL INTESTINAL II - HALL 7_

P1262 OBSERVER AGREEMENT FOR DIAGNOSIS OF ACUTE GRAFT-VERSUS-HOST DISEASE AFTER ALLOGENEIC STEM CELL TRANSPLANTATION WITH MICROVILLI ATROPHY IN THE TERMINAL ILEUM

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Introduction: Intestinal graft-versus-host disease (GVHD) represents one of the most serious complications of allogeneic stem cell transplantation (allo-SCT). Almost 10%–40% of patients who undergo allo-SCT develop significant clinical acute graft-versus-host disease (GVHD) [1]. Endoscopic and histological proofs are required because of the number of differential diagnoses manifesting as diarrhea. Previous studies reported that endoscopic features, such atrophied terminal ileum, are useful in predicting acute GVHD. However, these previous studies did not address details of the random sequence, and were performed in a single centre.

Aims & Methods: The present study investigated the incidence of the characteristic finding, particularly microvilli atrophy of the terminal ileum, of colonscopic, and inter-observer agreement of the finding among experienced endoscopists in multiple centres. Concurrent cases who underwent allo-SCT with the permission of the institutional review board were selected. Patients were tested on the terminal ileum is present. Demographic information, disease, symptoms, and histological finding were obtained from the patients’ medical records retrospectively. All study participants provided informed consent. The local ethics review committee granted ethical approval (approval 1610-013), and was registered in the University Hospital Medical Network Clinical Trials Registry (UMIN-CTR) as number UMIN 000025390.

Results: Definitive pathological and non-pathological GVHD were found in 22 patients, and 32 patients, respectively, a significantly higher proportion of patients with definite GVHD found in this study compared to previous studies [2,3]; are useful in predicting acute GVHD. However, these previous studies did not address details of the random sequence, and were performed in a single centre.

Conclusions: Microvilli atrophy in the terminal ileum is an effective character finding for real-time predictive histological diagnosis of acute intestinal GVHD. We achieved substantial inter-observer agreement for the analysis of microvilli atrophy in the terminal ileum and excellent agreement for predictive histological diagnosis.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
findings showed that crypt dilatation, villus stunting, and villus atrophy were of immune cell distribution by LAZ, hematopoietic cells in the lamina propria metabolites were analyzed by a CE-TOFMS platform. To examine the changes collected before and after LAZ administration. Genomic DNA of the gut microflora instilled intraperitoneally for two weeks. The ileal contents and feces were collected WBC count was performed with whole blood from Inferior vena cava of mice. The end points were villus height, villus/crypt ratio, histologic characteristics, and mRNA expression of tumor necrosis factor (TNF-α), and interleukin (IL)-6. Results: In 5-FU group, neutropenia was confirmed by laboratory test (5-FU, 0.650 K/μL), Control, 5.317 K/μL, indicating sufficient 5-FU effect. Histologic findings showed that crypt dilatation, villus stunting, and villus atrophy were reduced in EGCG plus 5-FU group than in 5-FU group (Figure 1). Quantitative mRNA expression (EGCG, 352 μm; 5-FU, 319 μm) and villus/crypt ratio (EGCG plus 5-FU, 3.26; 5-FU, 2.31) in EGCG plus 5-FU group, compared with 5-FU treated group, were significantly higher. mRNA expression of TNF-α was significantly lower in EGCG plus 5-FU group compared with 5-FU group (P < 0.05)(Figure 2). Figure 1. Effects of EGCG administration on intestinal epithelial cells in mice jejunum (Figure (B) control (B) 5-Fluorouracil (5-FU) group with significant villus atrophy and crypt dilatation (c) EGCG group (d) EGCG plus 5-FU group with mild villus destruction and less crypt dilatation). Unlike 5-FU, mRNA expression of TNF-α, IL-6, and TNF-α in the Peyer’s patch along with an increase in the cell infiltration after the administration of 5-FU significantly enhanced the immune response associated with the inflammatory cytokine production. Furthermore, on investigating the mRNA and protein expressions of LAT1 and LAT2 in the small intestines, we observed that LAT1 expression significantly increased and LAT2 expression decreased after the administration of 5-FU. Conclusion: It was considered that the uptake capacity of amino acids, such as L-type amino acid transporter (LAT) transports a wide range of nonselective amino acids, including essential amino acids, it is considered to be a gastrointestinal transporter that is important for nutrient absorption. Furthermore, the involvement of other amino acid transporters in inflammation has been reported by several studies. Aims & Methods: We aimed to clarify the pathophysiologic role of an amino acid transporter in gastrointestinal tract inflammation caused by an antitumor agent in this study. The antitumor agent fluorouracil (5-FU) was orally administered to mice. The severity of mucositis was assessed based on the length, villus height, mucus production, cell infiltration, and immune response of the intestinal tract. We measured the mRNA expressions of LATs in the tissues of the small intestines. In addition, we analyzed the protein expressions among the small intestines using anti-LAT antibodies.

Results: After the administration of 5-FU, the body weight, food intake, water consumption, and fecal volume decreased; thus, a systemic influence was observed. The length and villus height of the intestinal tract decreased because of the administration of 5-FU, and mucosal damage with histological change was observed. The number of PAS-positive cells decreased in the small intestinal mucosa, and it was assumed that the defensive function of the epithelial cells had decreased. In addition, an increase in the mRNA expression of IL-1β, IL-6, and TNF-α in the Peyer’s patch along with an increase in the cell infiltration after the administration of 5-FU significantly enhanced the immune response associated with the inflammatory cytokine production. Furthermore, on investigating the mRNA and protein expressions of LAT1 and LAT2 in the small intestines, we observed that LAT1 expression significantly increased and LAT2 expression decreased after the administration of 5-FU. Conclusion: It was considered that the uptake capacity of amino acids, such as Gly, Ala, Ser, Thr, Cys, Asn, and Gin, that transported through LAT may be decreased in case of small intestinal mucosal injuries. On the other hand, LAT1 expression associated with the production of inflammatory cytokines suggested that LAT1 is a gastrointestinal inflammatory marker.

Disclosure of Interest: All authors have declared no conflicts of interest.
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**P1266 A MUCOUS DEPENDENT MECHANISM OF ACETYL SALICYLIC ACID-INDUCED SMALL INTESTINAL MUCOSAL INJURY IN RATS**

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**Introduction:** Acetyl salicylic acid (ASA) has been used for the secondary prevention of cardiovascular diseases. Especially, the enteric coated ASA is widely used to prevent ASA-induced gastric mucosal injury. Recent technology such as video capsule endoscopy and balloon endoscopy enabled us to look inside the small intestine in more detail. Consequently, not a few cases of ASA-induced small intestinal mucosal injury have been reported. However, the effective prophylaxis and treatment is not clear yet. Previously, we reported direct detrimental effect of ASA on small intestinal epithelial cells using an *in vitro* model [1]. However, there are the thick mucus layer between intestinal lumen and epithelial cells. The mucus has been reported to prevent foreign objects such as bacteria, medicine and food from epithelial cells.

**Aims & Methods:** This study was conducted to clarify the role of mucus on ASA-induced small intestinal mucosal injury using a rat model. Male Sprague-Dawley rats, 9 weeks old was used. These rats were divided into four groups; group 1: sham (carboxy methyl cellulose: CMC alone), group 2: polysorbate-80 (P80) alone, group 3: ASA alone, and group 4: P80 plus ASA. CMC and/or 50-200 mg/kg ASA was injected into the proximal duodenum of rats. P80, an emulsifier, which has been reported to reduce mucosal thickness [2], was administered via drinking water for 2 weeks before ASA treatment. Indeed, P80 also reduced the thickness of mucosal layer in our analyses. One hour after ASA treatment, blue color was injected into a vein of rats to visualize small intestinal lesions. Ninety minutes after ASA treatment, the entire small intestine was removed for histological assessment. To further investigate the importance of mucus, rebamipide (Reb, 300 mg/kg) or saline were orally administered for one week prior to ASA administration. Reb is a gastric mucoprotective drug widely used for the treatment of gastric ulcer, and increases mucus secretion by small intestinal goblet cell.

**Results:** Evans blue method suggested that high-dose ASA (200 mg/kg) induced severe mucosal lesions, which was further confirmed by the histological examination. Although lower doses of ASA (50 and 100 mg/kg) did not cause mucosal damage, P80 significantly induced Evans blue exudate and severe mucosal lesions in jejunum at these concentrations, suggesting the pivotal role of mucus in these lesions. Moreover, P80-administered Reb significantly suppressed reducing small intestinal mucus and the exacerbation of ASA-induced mucosal lesions by P80, indicating that mucus is inevitable in the protection of ASA-induced small intestinal mucosal injury.

**Conclusion:** Mucus secretion increasing therapy might be a useful strategy for the prevention of ASA-induced small intestinal mucosal injury.

**Disclosure of Interest:** Y. Naito: Contribution and lecture fee from Otsuka Pharmaceutical Co. Inc., Y. Itoh: Encouragement and research support from Otsuka Pharmaceutical Co. All other authors have declared no conflicts of interest.

**References**


**P1267 ANTIBIOTIC-INDUCED DYSBIOSIS IN THE MOUSE SMALL INTESTINE PROMOTES ALLERGIC SENSITISATION**

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**Introduction:** Food allergy is characterised by a T helper type-2 immune response against a food antigen, manifesting as symptoms including nausea, diarrhoea, vomiting or anaphylactic events. It is estimated that 10% of the Australian population have a food allergy, and common allergens include cow’s milk, shellfish and peanuts. Epidemiological studies have identified antibiotics as a significant risk factor for food allergy in infants.

**Aims & Methods:** We examined how the broad spectrum antibiotic amoxicillin influenced mucosal immune responses to peanut proteins and the development of peanut allergy in mice. Balb/C mice were treated daily with 5 mg/kg amoxicillin or PBS for 5 days (days 0-4). On days 5 and 6 animals received 0.2 mg peanut extract or PBS vehicle by oral gavage. Animals were rechallenged with peanut on days 11 and 13 and sacrificed on day 16. Immune responses to peanut challenge in blood and intestinal tissues were assessed by protein, mRNA and histological analysis.

**Results:** The proportion of circulating eosinophils was increased in the blood of mice treated with both antibiotics and peanut. Histological examination revealed an increase in small intestinal eosinophils, predominantly at the villous tips, indicating recruitment to the mucosa. RNA and protein analysis revealed an increase in IL-5 associated with increased Nod-Like Receptor Protein 3 (NLRP3) inflammasome activation.

**Conclusion:** These studies demonstrate that antibiotic treatment prior to food antigen challenge can lead to altered mucosal immune homeostasis, facilitating IL-5-mediated eosinophil recruitment, characteristic of allergic responses. Importantly, we have demonstrated an adjuvant-free model of food sensitisation and small intestinal eosinophilia. These findings contribute to a better understanding of how disruption of mucosal homeostasis by antibiotics contributes to the development of allergic sensitisation and reaction.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**P1268 PREBIOTIC EFFECTS ON HEALTHY AND CHEMOTHERAPY-INDUCED SMALL BOWEL INJURY IN RATS**

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**Introduction:** Intestinal mucositis is a severe side-effect of chemotherapy. We investigated the potential to reduce the severity of 5-Fluorouracil (5-FU)-induced intestinal mucositis in rats. Female Dark Agouti rats (n=8/group) were orally gavaged with either 5% FOS, GOS, MOS or water (controls) for 16 days, and received an intraperitoneal injection of 5-Fluorouracil (5-FU: 150 mg/kg) or saline (controls), on day 13. Rats were housed in metabolic cages for the duration of the study, and metabolic data was recorded daily. Rats were killed on day 16 and visceral organ weights and lengths were analyzed post mortem. CRYPT depth, villus height and histological severity scores were quantified in haematoxylin & eosin stained sections. Sucrase and myeloperoxidase [MPO] activity were quantified by biochemical assay. White and red blood cell types were quantified by whole blood analysis. Fecal volatile fatty acids (VFAs), acetic, propionic, isobutyric, butyric, isovaleric and valeric acid were also measured. Statistical analysis was by one-way ANOVA or Kruskal Wallis and Mann Whitney U test, where p < 0.05 was considered statistically significant. Data are expressed as mean ± standard error of the mean

**Results:** %Bodyweight loss was significantly decreased in all treatment groups following 5-FU injection. The fecal output was increased in rats treated with MOS or FOS, pre and post 5-FU compared to saline treated controls (p < 0.05). Leal villus height was significantly higher in GOS treated rats pre 5-FU (284.16 ± 11.95 μm) compared to respective water controls (240.40 ± 8.33 μm; p < 0.05). A villus height and crypt depth was significantly decreased in all treatment groups after 5-FU injection (p < 0.05) and prebiotic treatment did not significantly modify this parameter. Similarly, jejunal and ileal sucrase activity was decreased in all groups after 5-FU injection (p < 0.05), correlating with histological measurements. Tissue MPO activity was significantly increased post 5-FU injection, reflecting increased neutrophil activation, and was unchanged by prebiotic treatment. Interestingly, MOS and GOS both lowered %circulating neutrophils pre 5-FU compared to water controls (p < 0.05). Pre 5-FU treatment with GOS significantly increased the fecal VFAs acetic acid (16.76 ± 1.22 mM/L) and propionic acid (4.60 ± 0.99 mM/L) compared to saline treated controls (7.7 ± 0.92 mM/L) and 3.05 ± 0.28 mM/L respectively; p < 0.05). MOS and GOS treatment also significantly increased fecal acetic and propionic acid post 5-FU compared to water control (p < 0.05).

**Conclusion:** Our study has found that prebiotics, MOS, GOS and FOS modified some parameters of intestinal health and immune regulation in healthy rats; however, these prebiotics were not protective against 5-FU-induced intestinal damage. Furthermore, our findings have demonstrated that prebiotic treatment significantly increases VFA production, suggesting functional changes to the intestinal microbiome. Further studies are indicated to investigate prebiotics, both alone and in combination, during the repair phase of intestinal mucositis, and to determine their effect on gut microbial composition.

**Disclosure of Interest:** All authors have declared no conflicts of interest.
P1269 THE RELATION OF CHEMKINE RECEPTOR CXCR3 AND GIT-HOMING MARKERS ON SMALL INTESTINAL LAMINA PROPRIA-T-LYMPHOCYTES IN CROHN’S DISEASE PATIENTS

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Introduction: Crohn’s disease has been thought to be caused by abnormal immune responses affecting many parts of digestive tract in which Th1 cells and M1 macrophages predominates. The recruitment of Th1 cells is regulated by interaction of their expression of chemokine receptor CXCR3 and its ligands. There have been many IBD murine models showing the increase of CXCR3 expression and its role in the disease promotion. However, there are limited evidences in the roles of CXCR3 in human IBD. In fact, a small study in large bowel in a cohort of 10 Crohn’s disease patients showed lower expression of CXCR3 on T lymphocytes, compared to colon cancer patients. In terms of inhibition of T-lymphocyte migration into intestine in IBD patients, anti a4β7 (Vedolizumab) therapy is currently shown to be effective.

Aims & Methods: Our study aimed to assess expression of CXCR3 by different subsets of small intestinal lamina propria T-cells and its association with a4 and b7 integrin expression in CD patients. Total of 56 duodenal biopsies were obtained from CD (n = 15), functional dyspepsia (FD)/irritable bowel syndrome (IBS) (n = 24) or iron deficiency patients (n = 17) with ethical approval. Lamina propria (LP) cells were isolated from biopsies using EDTA, collagenase and gradient density centrifugation with Ficoll. Expression of CXCR3, a4, and b7 on isolated T-lymphocytes was examined by flow cytometry. Statistical significance was assessed using T-test or Spearman correlation.

Results: The expression of CXCR3 on CD4 lymphocytes was significantly lower (p < 0.05) compared to 61.6% in control group (FD/IBS deficiency). Although the expression of CXCR3 on CD8 lymphocytes was higher than CD4 lymphocytes, it was not different between CD and other group (75.8% in CD patients vs 82.2% in controls). Similar observation was obtained on the double positive a4 CD4 and CD8 lymphocytes. Interestingly, only expression of CXCR3 on CD4 lymphocytes positively correlated with expression of the gut-homing integrins, a4 and b7.

Conclusion: These observations showed significant expression of CXCR3 across different patient groups, with consistently higher expression seen in CD8 lymphocytes compared to CD4 lymphocytes. An unexpected reduction of CXCR3 expression was seen in small intestinal of CD patients, which associated with gut-homing integrins. This result showed CXCR3 expression may play a role in migration of CD4 lymphocytes but not CD8 lymphocytes into duodenum in relation with integrins, a4 and b7. However, CXCR3 expression on CD4 lymphocytes in CD patients’ small intestine may have protective role. This propose further study to clarify.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P1270 METHODOLOGICAL QUALITY OF CLINICAL PRACTICE GUIDELINES ON PROBIOTICS IN ACUTE GASTROENTRITIS IN CHILDREN FROM 2000 TO 2014: AN APPRAISAL OF THE GUIDELINES FOR RESEARCH & EVALUATION II INSTRUMENT (AGREEII)

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Introduction: Acute Gastroenteritis (AGE) is one of the diseases that most frequently affects paediatric population. Successful treatment in AGE has been demonstrated to be effective in reducing its duration. The role of probiotics in the management of AGE in children under 5 years and 5. Use of probiotics for management of AGE. A position paper by the ESPGHAN Working Group for Probiotics and Prebiotics. All of the CPG consider that the administration of Lactobacillus rhamnosus GG and Saccharomyces boulardii should be considered in the management of children with AGE as an adjunct to rehydration therapy with different level of evidence. The concordance between evaluators was >0.9 and <1.0 for all guideline positions. Four CPG had probiotics among higher than 60% in 4 or more domains and one in only one domain. Only a CPG was greater than 60% in all domains. Four had an overall score greater than or equal to 5 and were recommended, and one with modifications, according to the instrument AGREE II. The CPG is a Position Paper of a Working Group, not a Guideline, and its the reason for the lower rates obtained.

Conclusion: Conclusions: The selected CPG have good methodological quality, but are not specific to probiotics. Despite, they should be spread for better decision making.

Disclosure of Interest: A. Maruy Saito: CONSULTANT BIODECODE SPEAKER MEAD JOHNSON NUTRITION

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References

P1271 COMBINATION OF TWO IN VITRO MODELS TO STUDY THE IMPACT OF CHRONIC CO-EXPOSURE OF A PESTICIDE WITH A PREBIOTIC ON THE INTESTINAL ENVIRONMENT

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Introduction: The excessive use of pesticides, often found as residues in our diet and as contaminants in drinking water, has become a public health problem. Most of these substances are considered as endocrine disruptors and their daily exposure is likely to have severe and irreversible consequences. Indeed, preliminary studies have shown that chronic exposure to low doses of chlorpyrifos (CPF) causes intestinal imbalance (dysbiosis) in vitro.

Aims & Methods: The objective of this study is to evaluate the preventive potential of a prebiotic (mulin) in co-exposure with the CPF on the intestinal dysbiosis, the bacterial translocation and the integrity of the intestinal mucosa. For this we used an in vitro system: the SHIME® (Simulator of the Human Microbial
Intestinal Ecosystem). The SHIME® consists of series of fermenters, mimicking the gastrointestinal environment from the mouth to the colon. The SHIME® was exposed to a daily dose of 3.5 mg of CPF- combined with 10 g of inulin for 30 days. The samples were collected at day 0 (baseline, without CPF or inulin), D15 and D30 to determine the profile and microbial metabolism.

Results: Contrary to the previous results with CPF alone showing dysbiosis, prebiotic supplementation seems to reestablish CPF-induced imbalance, particularly in the potentially pathogenic microflora (Staphylococcus), which is suppressed. A significant increase in pathogenic microflora (3.44-12.73) in controls. Regardless of the diagnostic modality, prevalence of SIBO is significantly higher in IBS-P than IBS-N (47.19 ± 2.62% vs. 40.74 ± 1.68%), significantly higher than that of HC (39.8% vs. 12.5%, P=0.005). IBS-D patients with high fat diet had higher LMBHT positive rate than that of non-high fat diet patients (54.2% (13/24) vs. 17.2% (11/64), P=0.001). The baseline of breath methane in IBS-P was significantly higher than that of in IBS-N (8.6 ± 0.39) vs. (6.39 ± 0.47) ppm, P=0.002. Breath methane peak value was positively related with the fat proportion of diet (r=0.413, P=0.022).

Conclusion: The CPF/inulin co-exposure therefore had a positive impact on bacterial profile and metabolism, suggesting that prebiotic supplementation could reduce some intestinal damages caused by an exposure to CPF.

Disclosure of Interest: All authors have declared no conflicts of interest.

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Reynger J, Lichtenberger L, Elmghri G, Dou S, Bahi-Jaber N, Rahlzi N, Khorsi-Caet H. Inulin Supplementation Lower the Metabolic Defects of Prolonged Exposure to Chlorpyrophyrin from Gestation to Young Adult Stage in Offspring Rats

P1273 SYSTEMATIC REVIEW AND META-ANALYSIS: PREVALENCE OF SMALL INTESTINAL BACTERIAL OVERGROWTH IN CHRONIC LIVER DISEASE
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Introduction: Alterations to the gut microbiota and bacterial translocation have been implicated as relevant factors for the progression of chronic liver disease (CLD). While the results of events leading to translocation remain unclear, deficiencies in local host immune defences, increased permeability of the intestinal mucosal barrier and dysbiosis of the gut microbiota are suggested to play a role. Small intestinal bacterial overgrowth (SIBO), in which an excessive and/or abnormal type of bacteria is present in the small intestine has been implicated as a potential factor in translocation. However, systematic assessments of the extent of SIBO in CLD remain limited. We therefore aimed to compare the prevalence of small intestinal bacterial overgrowth (SIBO) in patients with chronic liver disease (CLD) and controls.

Aims & Methods: Using the search terms ‘small intestinal bacterial overgrowth (SIBO)’ and ‘chronic liver disease (CLD)’ or ‘small intestinal bacterial overgrowth (SIBO)’ and ‘cirrhosis’, 19 case-control studies that met inclusion criteria were identified. Data were extracted to calculate prevalence rates and 95% confidence intervals (CI).

Results: The final dataset included 1,000 adult patients with CLD and 488 controls. Nine studies employed glucose breath tests (GBT), four lactulose breath tests and one hydrogen breath test (HBT). All studies employed a 13C-labelled glucose or xylose breath test. Five studies utilised culture methods and one quantitative PCR. Across all testing methods, the prevalence of SIBO in patients with CLD was 38.9% (95% CI 36.9-40.9) compared to 9.8% (95% CI 7.5-12.8) in controls. Regardless of the sample size of SIBO in CLD was increased as compared to controls (RR =7.15, 95% CI 4.9-10.4). In patients with cirrhosis the prevalence of SIBO was 40.1% (95% CI 36.6-43.8) compared to 7.3% (95% CI 4.9-10.8) in controls. The majority of researchers employed breath tests to detect SIBO, regardless of the diagnostic modality, prevalence of SIBO in CLD was 35.8% (95% CI 32.6-39.1) compared to 8.0% (95% CI 5.7-11.0) in controls. In contrast, based upon culture techniques, the prevalence of SIBO in CLD was 68.3% (95% CI 59.6-76.0) vs 7.94% (95% CI 3.44-12.73) in controls.

Conclusion: Regardless of the diagnostic modality, prevalence of SIBO is significantly increased in patients with CLD when compared to controls. It is notable that culture-based detection leads to a higher prevalence in CLD, suggesting breath tests may underestimate overall prevalence. Given the levels of SIBO detected, further studies need to explore the role of intestinal dysbiosis for the progression of CLD.

Disclosure of Interest: All authors have declared no conflicts of interest.

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P1274 IS THERE AN ASSOCIATION BETWEEN ENTERIC METHANE (C14) PRODUCTION AND SYMPTOMS IN PATIENTS WITH UNEXPLAINED GI SYMPTOMS?
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Introduction: Enteric methane (C14) production is a common gastrointestinal symptom reported by patients. While the relationship between enteric methane production and symptoms is unclear, there is evidence suggesting that enteric methane production is associated with small intestinal bacterial overgrowth (SIBO). In this study, we aimed to assess the relationship between enteric methane production and SIBO in patients with unexplained GI symptoms.

Methods: Patients with unexplained GI symptoms who were referred to a tertiary gastroenterology centre were recruited. Enteric methane production was measured using a 13C breath test. SIBO was diagnosed using a breath test in patients with a positive result. Patients were classified into two groups: SIBO and non-SIBO. The relationship between enteric methane production and SIBO was assessed using a Chi-square test.

Results: A total of 100 patients were recruited. Of these, 50 patients had SIBO and 50 patients did not. The prevalence of SIBO was 50% (50/100). There was no statistically significant difference in enteric methane production between patients with SIBO and those without SIBO (50% vs. 47.5%, P=0.23).

Conclusion: There was no statistically significant association between enteric methane production and SIBO in patients with unexplained GI symptoms. Further studies are needed to explore the role of enteric methane production in the pathogenesis of unexplained GI symptoms.

Disclosure of Interest: All authors have declared no conflicts of interest.
Introduction: In humans, enteric methane (CH₄) production is highly variable and related to the gastrointestinal microbiome and diet. Previous work suggests that CH₄ production is more common in patients with ‘constipating’ conditions such as encopresis and diverticulosis. We aimed to explore the link between gastrointestinal symptoms breath CH₄ exhalation in patients with unexplained GI symptoms.

Aims & Methods: Consecutive patients (n = 100) with unexplained GI symptoms underwent a combined H₂/CH₄ breath test after ingestion of 75 g of glucose. H₂ and CH₄ were measured by Breathtracker microlyser (Quintron, USA). Gastrointestinal symptoms were assessed utilising the Structured Assessment of Gastrointestinal Symptoms Instrument (SAGIS). The association between methane exhalation and symptoms during the 2 weeks prior the test were evaluated using non parametric test.

Results: 100 consecutive patients (55f), aged 52.2 ± 15.7 yrs (mean ± SD) were included. Of these, 14 with positive GBT and 19 without SAGIS data were excluded, resulting in 67 data-sets available for analysis. Methane peak and baseline values were highly correlated (r all = 0.96, p < 0.001). Methane peak (and baseline) were inversely correlated with the SAGIS diarrhoea score (r = -0.35, p < 0.01, Figure 1). Contrary to current opinion, CH₄ exhalation was not associated with constipation (r = 0.1, P > 0.4). In addition, excessive belching and acid eructation were significantly associated with the baseline and peak CH₄ exhalation (r all >0.3, p all <0.04).

Conclusion: There is an inverse association between CH₄ exhalation and diarrhoea symptoms. At the same time, CH₄ is associated with bloating and acid eructation. These data suggest that CH₄ or metabolic products from CH₄ production microbes modulate human gut function.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

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conditions [4]. Although other Authors described similar patients [2,3], it is still unclear whether CRSs are two independent conditions or whether they are two faces of the same coin. Alternatively, they could be umbrella terms covering one or more atopic enteropathies still awaiting to be identified, as was the case of olmsartan-associated enteropathy until a few years ago. 

Our aim was to clarify the nature of these forms of FA. We retrospectively re-evaluated the clinical notes of patients referred to our Clinic from January 1999 to October 2016 with a previous diagnosis of refractory CD. Patients with VA in whom CD could not be confirmed and in whom other causes of malabsorption were not identified were selected.

**Results:** 7 patients (2F, age at diagnosis of VA 46 ±26 years, all with severe malabsorption) were identified, 3 were DQ2 positive and so were diagnosed as UC: case 1 (F, 32 years) died of ulcerative jejunitis 8 years later; case 2 (M, 38) died of pulmonary embolism complicating systemic candidiasis 1 year later and case 3 (M, 71) died of intestinal lymphoma after 4.5 years. The remaining 4 patients were HLA DQ2/DQ8 negative, so a diagnosis of NCRS was made. DQ2:5.4 positive: case 4, (F, 61) died of EATL type 2 after 4.5 years; case 5 (M, 64) died of intestinal lymphoma 10 years after diagnosis and in good conditions; case 6 (M, 69) is still alive but could be affected by a form of enteropathy due to celiac disease. He is in good clinical condition and has been refusing follow-up. The last patient, case 7 (M, 29) is DQ7.3 positive. He is still alive 11 years after the diagnosis of VA, although complains of diarrhoea.

**Conclusion:** We described 7 patients with VA unrelated to CD or other known enteropathies. Although overall mortality among them is very high (57%) and mainly due to lymphoproliferative disorders, 3 of the 4 DQ2/DQ8 negative patients are alive many years after the diagnosis of VA with no evidence of malignancy. This suggest that these 7 patients are not affected by the same condition. We speculate that DQ2 positive patients who died of lymphoma could have been affected by a form of CD who escaped diagnosis or get complicated. However, we feel that the 3 DQ2:8 negative patients with long survival are affected by a still unidentified form of VA.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**References**


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**P1278 EVERYDAY LIFe RESTRICTIONS CAUSED BY LONG-TERM TREATED CELIAC DISEASE: PREVALENCE AND ASSOCIATED FACTORS**

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**Introduction:** Strict gluten-free diet (GFD) in celiac disease is burdensome and difficult to maintain, which might predispose to poor dietary adherence and impaired quality of life. We aimed to evaluate adult patients’ experience of living with celiac disease diagnosed in childhood, and identify factors associated with possible everyday life restrictions caused by the disease.

**Aims & Methods:** 232 adults (women 69%, median age 27.0 yr) with a childhood diagnosis of celiac disease fulfilled a questionnaire evaluating their experiences about their social and lifestyle, possible co-morbidities, adherence and attitudes towards GFD and long-term follow-up of celiac disease. In addition, they were asked to rate the development of MS. The intergroup comparison among HS patients showed that those patients had significantly lower PGWB vitality scores (median 17 vs 23, p = 0.001) and had significantly lower PGWB vitality scores (median 17 vs 23, p = 0.001) and had significantly lower PGWB vitality scores (median 17 vs 23, p = 0.001) and had significantly lower PGWB vitality scores (median 17 vs 23, p = 0.001) and had significantly lower PGWB vitality scores (median 17 vs 23, p = 0.001) and had significantly lower PGWB vitality scores (median 17 vs 23, p = 0.001) and had significantly lower PGWB vitality scores (median 17 vs 23, p = 0.001) and had significantly lower PGWB vitality scores (median 17 vs 23, p = 0.001) and had significantly lower PGWB vitality scores (median 17 vs 23, p = 0.001) and had significantly lower PGWB vitality scores (median 17 vs 23, p = 0.001) and had significantly lower PGWB vitality scores (median 17 vs 23, p = 0.001). Patients reporting restrictions had more often anemia (38% vs 22%, p = 0.013) and severe symptoms (16% vs 6%, p = 0.047) at diagnosis, whereas the groups did not differ in age, gender or other clinical and histological presentation. Current age (median 33 vs 28 years, p = 0.015) and time since diagnosis (18.6 vs 7.9 years, p = 0.468) were also comparable, as well as were self-reported general health and concern about health, presence of co-morbidities and complications, smoking, physical exercise, socioeconomic status, membership of celiac society and presence of celiac disease in relatives. There was no difference in specific gastrointestinal symptoms as measured by GRS1 scores, but patients considering the disease restrictive reported more overall symptoms possibly related to celiac disease than those without restrictions (32% vs 17%, p = 0.007). Furthermore, disease severity (suffering from severe symptoms) (32% vs 28%, p = 0.770) and experienced adhering to the diet more challenging (somewhat difficult 33% vs 7%, p < 0.001) and had significantly lower PGWB vitality scores (median 17 vs 18, p = 0.023).

**Conclusion:** Almost half of the patients diagnosed in childhood experienced celiac disease to cause marked restrictions in adulthood. This was associated with current symptoms, lower vitality scores and difficulties to maintain GFD. Patients with severe symptoms and anemia at diagnosis might require special attention and tailored follow-up in these circumstances.

**Disclosure of Interest:** All authors have declared no conflicts of interest.
the severe grade of HS was more frequently observed in GG than in CC carriers (57% vs. 37%, p < 0.01). There were 192 patients with CD of whom, 160 fulfilled the inclusion criteria. 72 (23.9%) patients had developed MS (4.3% vs 23.9%; p < 0.001) of cases, and 37.5% (n = 60) were actually never referred for DEXA scan according to guidelines2,3, and 68% (n = 81) did not fulfil criteria for a DEXA scan. The use of PPI in patients with CD on GFD is unclear due to conflicting recommendations in current guidelines. The indication for a DEXA scan is unclear due to conflicting recommendations in current guidelines. The aim of our study was to audit our practice, with a focus on requests for DEXA scans where needed. Aims & Methods: This was a single-centre, retrospective study of CD patients under the care of 3 consultants. We reviewed the electronic records to identify if haematological and biochemical profiles were being monitored. We also identified patients who had their first DEXA scans and whether or not they were indicated.2,3 Results: Data were collected on 160 patients (Female = 107 [67%]), Annual checks of FBC occurred in 94% of patients, vitamin B12 in 74%, folic acid in 77%, calcium in 88%, and vitamin D in 69%. DEXA scans occurred in 74% of patients (n = 119), including 65% (n = 77) who were screened around the time of diagnosis. However, only 24% (n = 28) actually warranted the scan according to guidelines.2,3, and 68% (n = 81) did not fulfill criteria for a DEXA. In 8% of patients (n = 10), there was inadequate data. Of the 81 patients who did not warrant a DEXA scan, 77 results were available: normal in 48% (n = 37), osteopenia in 43% (n = 33) and osteoporosis in 9% (n7). Of the 7 patients that had osteoporosis, 4 patients were under 50 years old (57%). Of the appropriate DEXA requests, 25% (7) were normal, 39% (n = 11) had osteopenia and 36% (n = 10) had osteoporosis. Conclusion: Most CD patients require very little clinical input at their routine appointments. Annual blood checks and adherence to a gluten-free diet are standard enquiries. However, there is a cohort of patients who are not getting their regular blood tests: 33% for bone profile and 25% for haematinsics. Clinicians tend to order a DEXA in most CD patients because it is easier than attempting to judge an individual’s risk in the setting of conflicting guidelines. The pick-up rate of osteoporosis in 36% of appropriately screened patients (vs 9% in inappropriate scan requests) suggests that targeted screening allows for a more rational and cost-effective use of a limited resource. We hope that the guidelines can now be updated with more clarity for the practitioners who request DEXA scans in CD patients.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P1284 CELIAC DISEASE AND ADHERENCE TO THE GLUTEN-FREE DIET: A 30-YEAR FOLLOW-UP STUDY

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2Department Of Pathophysiology And Transplantation, Università degli Studi di Milano, Milan/Italy
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Introduction: Patients with celiac disease (CD) should be seen annually for a clinical review, blood tests and a DEXA scan if needed1,2. The indication for a DEXA scan is unclear due to conflicting recommendations in current guidelines2,3,4. The aim of our study was to audit our practice, with a focus on requests for DEXA scans where needed. Aims & Methods: This was a single-centre, retrospective study of CD patients under the care of 3 consultants. We reviewed the electronic records to identify if haematological and biochemical profiles were being monitored. We also identified patients who had their first DEXA scans and whether or not they were indicated2,3. Results: Data were collected on 160 patients (Female = 107 [67%]). Annual checks of FBC occurred in 94% of patients, vitamin B12 in 74%, folate in 77%, calcium in 88%, and vitamin D in 69%. DEXA scans occurred in 74% of patients (n = 119), including 65% (n = 77) who were screened around the time of diagnosis. However, only 24% (n = 28) actually warranted the scan according to guidelines2,3, and 68% (n = 81) did not fulfill criteria for a DEXA. In 8% of patients (n = 10), there was inadequate data. Of the 81 patients who did not warrant a DEXA scan, 77 results were available: normal in 48% (n = 37), osteopenia in 43% (n = 33) and osteoporosis in 9% (n7). Of the 7 patients that had osteoporosis, 4 patients were under 50 years old (57%). Of the appropriate DEXA requests, 25% (7) were normal, 39% (n = 11) had osteopenia and 36% (n = 10) had osteoporosis. Conclusion: Most CD patients require very little clinical input at their routine appointments. Annual blood checks and adherence to a gluten-free diet are standard enquiries. However, there is a cohort of patients who are not getting their regular blood tests: 33% for bone profile and 25% for haematinsics. Clinicians tend to order a DEXA in most CD patients because it is easier than attempting to judge an individual’s risk in the setting of conflicting guidelines. The pick-up rate of osteoporosis in 36% of appropriately screened patients (vs 9% in inappropriate scan requests) suggests that targeted screening allows for a more rational and cost-effective use of a limited resource. We hope that the guidelines can now be updated with more clarity for the practitioners who request DEXA scans in CD patients.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
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**Introduction:** A life-long gluten-free diet (GFD) is the only available treatment for patients with celiac disease (CD). Adherence to the GFD is associated with symptoms remission, reversal of mucosal atrophy and, possibly, prevention of CD-related complications. However, data on the long-term effects of a good or poor adherence to the GFD are limited.

**Aims & Methods:** The aim of this study was to assess the rate and accuracy of compliance to a strict GFD in patients with a CD history of more than 30 years and to compare endpoints such as complications, symptoms and histology between patients following a strict GFD and patients not compliant to the diet. Between 2015 and 2016, data from all patients diagnosed with CD at the Fondazione IRCCS Ca’ Granda before 1985 were retrieved. Patients not undergoing regular follow-up at the clinic were contacted in order to collect recent clinical data, especially at a known time for symptoms, adherence to the GFD, laboratory data, and complications occurrence. All patients were asked to fill in a questionnaire investigating their knowledge on gluten free products and behavioral rules; in case of patients with CD diagnosis in childhood, the same questionnaire was administered to their parents.

**Results:** Clinical data from 196 patients were collected and analyzed. Patients were divided into 3 groups according to their adherence to GFD: 133 patients reporting a lifelong strict GFD, 29 patients on GFD at the time of follow-up but with a history of at least 5 years of gluten-containing diet (GCD), and 35 patients who reported to be on a GCD. No significant differences were found between groups regarding symptoms and histology at diagnosis, onset of associated autoimmune disorders, family history of CD and compliance to follow-up. The onset of complications at follow-up did not significantly differ in the three as well. Follow-up histology was available in 63 patients (32.1%). Persistence of villous atrophy was as expected more frequent in patients on GCD as on GFD (41% vs 7%, p = 0.008) however 20 patients showed normal histology during long-term GCD. The questionnaire was returned by 90 patients and 66 parents: a slightly better knowledge about the GFD and its behavioral rules was found between patients on lifelong GFD and patients with ongoing or past GCD (p = 0.03).

**Conclusion:** Poor adherence to the GFD is reported by almost one-third of patients with a long-term history of CD, confirming the high rate of poor compliance to such a strict diet among patients. Poor adherence to the GFD was confirmed as a major predictor of persistence of villous atrophy, but this does not necessarily imply the development of CD complications. Moreover, results from follow up biopsies showed that a GCD does not imply recurrence of villous atrophy in all patients, attesting the possibility that some CD patients may maintain a gluten tolerance over time.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**References**


**P1285 PATIENTS WITH SHORT BOWEL SYNDROME STRATIFIED BASELINE PARENTERAL SUPPORT VOLUME: POSThoc ANALYSIS OF THE CLINICAL EFFECT OF TEGLDULURATE**

P.B. Jeppesen

**Introduction:** A life-long gluten-free diet (GFD) is the only available treatment for patients with intestinal failure (IF). The aim of this study was to assess the rate and accuracy of compliance to a strict GFD in patients with a CD history of more than 30 years and to compare endpoints such as complications, symptoms and histology between patients following a strict GFD and patients not compliant to the diet. Between 2015 and 2016, data from all patients diagnosed with CD at the Fondazione IRCCS Ca’ Granda before 1985 were retrieved. Patients not undergoing regular follow-up at the clinic were contacted in order to collect recent clinical data, especially at a known time for symptoms, adherence to the GFD, laboratory data, and complications occurrence. All patients were asked to fill in a questionnaire investigating their knowledge on gluten free products and behavioral rules; in case of patients with CD diagnosis in childhood, the same questionnaire was administered to their parents.

**Results:** Clinical data from 196 patients were collected and analyzed. Patients were divided into 3 groups according to their adherence to GFD: 133 patients reporting a lifelong strict GFD, 29 patients on GFD at the time of follow-up but with a history of at least 5 years of gluten-containing diet (GCD), and 35 patients who reported to be on a GCD. No significant differences were found between groups regarding symptoms and histology at diagnosis, onset of associated autoimmune disorders, family history of CD and compliance to follow-up. The onset of complications at follow-up did not significantly differ in the three as well. Follow-up histology was available in 63 patients (32.1%). Persistence of villous atrophy was as expected more frequent in patients on GCD as on GFD (41% vs 7%, p = 0.008) however 20 patients showed normal histology during long-term GCD. The questionnaire was returned by 90 patients and 66 parents: a slightly better knowledge about the GFD and its behavioral rules was found between patients on lifelong GFD and patients with ongoing or past GCD (p = 0.03).

**Conclusion:** Poor adherence to the GFD is reported by almost one-third of patients with a long-term history of CD, confirming the high rate of poor compliance to such a strict diet among patients. Poor adherence to the GFD was confirmed as a major predictor of persistence of villous atrophy, but this does not necessarily imply the development of CD complications. Moreover, results from follow up biopsies showed that a GCD does not imply recurrence of villous atrophy in all patients, attesting the possibility that some CD patients may maintain a gluten tolerance over time.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**References**


**P1206 POST-HOC ANALYSIS OF THE RELATIONSHIP BETWEEN PLASMA CITRULLINE AND PARENTERAL SUPPORT NEEDS IN PATIENTS WITH SHORT BOWEL SYNDROME WITH INTESTINAL FAILURE RECEIVING TEGLDULURATE**


**Introduction:** Plasma citrulline has been proposed as a biomarker for remnant intestinal length, but it is unclear if plasma citrulline levels reflect intestinal absorptive function.

**Aims & Methods:** This post hoc analysis investigated the relationship between reductions in parenteral support (PS) volume and changes in plasma citrulline levels with tegldulutide (TED) in patients with intestinal failure associated with short bowel syndrome (SBS-IF). STEPS (NCT00798967; EudraCT2008-006193-15) was a 24-week, placebo-controlled study of teduglutide (TED) in patients with intestinal failure associated with short bowel syndrome (SBS-IF). STEPS (NCT00798967; EudraCT2008-006193-15) was a 24-week, placebo-controlled study of TED 0.5 mg/kg/day in patients with SBS-IF. Plasma citrulline levels were assessed at baseline and Week 24 in all patients randomised to TED and in patients stratified by bowel anatomy.

**Results:** In the TED arm (n = 42), plasma citrulline levels at baseline were significantly correlated with remnant small bowel length (R2 = 0.14; p = 0.02; n = 36) but not with baseline PS volume (R2 = 0.03; p = 0.30; n = 39). The correlation between baseline plasma citrulline and plasma citrulline change at Week 24 was significant (R2 = 0.80; p < 0.0001; n = 39). No correlation was found between change in plasma citrulline levels and change in PS volume at Week 24 with TED (R2 = 0.05; p = 0.16; n = 39). When patients were analysed by bowel anatomy subgroups, significant increases in Plasma citrulline were seen with TED but not placebo (Table).

**Table:** Mean (SD) Change From Baseline in Week 24 Volume and Plasma Citrulline Stratified by Bowel Anatomy

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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volume reductions with TED. Plasma citrulline changes with TED may reflect increased enterocyte mass. This research was funded by Shire International GmbH, Zug, Switzerland.

Disclosure of Interest: P.B. Jeppesen: I have served as a consultant and on the speaker bureau for Shire.

S.M. Gabe: I have served as a consultant for Shire. D.L. Seidner: I have served as a consultant for Shire.

H. Lee: I am an employee for Shire.

C. Olivier: I am an employee for Shire.

P1228 PATIENTS WITH SHORT BOWEL SYNDROME STRATIFIED BY DIAGNOSIS: POST HOC ANALYSIS OF TEGDULITIDE ON FLUID COMPOSITE EFFECT

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Introduction: Inflammatory bowel disease (IBD) and mesenteric vascular (Vasc) disease are underlying conditions for intestinal failure associated with short bowel syndrome (SBS-IF). Fluid balance, urine production, and parenteral support (PS) volume are variable among patients with SBS-IF.

Aims & Methods: This is a post hoc analysis of the impact of tegdulitide (TED) on fluid composite effect (FCE = sum of urine volume output increase, oral fluid intake reduction, and PS volume reduction) in patients stratified by diagnosis. STEPS (NCT01790967; EudraCT2008-006193-15) was a 24-week, placebo-controlled study of TED 0.05 mg/kg/day in patients with SBS-IF. Three groups were evaluated: SBS-IBD, SBS-Vasc, and Other.

Results: The SBS-IBD group included more patients with stoma (95%; SBS-Vasc, 19%; Other, 41%) and fewer with colon-in-continuity (11%; SBS-Vasc, 78%; Other, 62%). At Week 24 (Table), PS volume reductions were significantly higher in SBS-IBD patients treated with TED vs placebo (P = 0.02) and vs TED patients in the SBS-Vasc (P = 0.04) and Other (P = 0.02) groups. Change in FCE was greater in SBS-IBD patients treated with TED vs placebo (P < 0.02) and vs TED patients in the SBS-Vasc (P < 0.01) and Other (P = 0.05) groups.

Table: Components of Fluid Composite Effect at Baseline and Week 24 and Fluid Composite Effect at Week 24 by Diagnosis

Table:

![Table Image]

Disclosure of Interest: P.B. Jeppesen: I have served as a consultant and on the speaker bureau for Shire.

S.M. Gabe: I have served as a consultant for Shire.

K. Iyer: I have served as a consultant for Shire.

U. Pape: I have received grant/research support from and served as a consultant for on the speaker bureau for Shire.

D.L. Seidner: I have served as a consultant for Shire.

H. Lee: I am an employee for Shire.

C. Olivier: I am an employee for Shire.

P1229 RESULTS OF A POST HOC ANALYSIS OF BASELINE CHARACTERISTICS AND CLINICAL RESPONSE TO TEGDULITIDE IN PATIENTS WITH SHORT BOWEL SYNDROME BASED ON RESIDUAL BOWEL ANATOMY

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2St Mark’s Hospital, Northwick Park, London/United Kingdom

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Shire Human Genetic Therapies, Inc., Lexington/United States of America/MA

Shire International GmbH, Zug/Switzerland

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Introduction: Intraepithelial lymphocytic (IEL) and lamina propria (LP) T cells are increased in patients with celiac disease (CD) and may play a role in the development of intestinal inflammation in patients with short bowel syndrome (SBS). This research was funded by Shire International GmbH, Zug, Switzerland.

Disclosure of Interest: P.B. Jeppesen: I have served as a consultant and on the speaker bureau for Shire.

R. Pape: I have received research support from and served as a consultant for on the speaker bureau for Shire.

H. Lee: I am an employee for Shire.

C. Olivier: I am an employee for Shire.

Table 1: Induction of Gastrointestinal Symptoms with Lactulose, Lactose and Fructose

Table:

![Table Image]
were evaluated: Group 1 (no colonic/stoma present/no colonic-in-continuity), Group 2 (≥50% colonic/stoma present/colonic-in-continuity), and Group 3 (other bowel anastomoses). Clinical response was defined as ≥20% reduction from baseline in weekly parental support (PS) volume at Weeks 20-24. Data presented as mean (SD).

Results: The predominant diagnosis in Group 1 was Crohn’s disease, whereas the predominant diagnosis in Group 2 was vascular complications (Table). Group 1 patients required the highest baseline PS volumes compared with Group 2 or Group 3. TED-induced PS volume reduction (change in L/week) took longer to be realised in Group 2 (Week 12, -0.9 [1.2]; Week 24, -2.5 [2.1]) compared with Group 1 (Week 12, -5.5 [3.8]; Week 24, -6.4 [4.5]) or Group 3 (Week 12, -2.7 [1.2]; Week 24, -5.1 [3.7]). Response rates were higher with TED versus placebo in all groups, but the difference was significant only in Group 1 (76% vs 19%, P = 0.001; Group 2, 56% vs 40%, P = 0.36; Group 3, 57% vs 29%, P = 0.03). Adverse events were reported by 94%, 72%, and 86% of Group 1, Group 2, and Group 3 patients receiving TED, respectively.

Conclusion: Patients with SBS needs and responded most and fastest to TED with PS volume reductions, compared with patients in Group 2 or Group 3. This research was funded by Shire.

Disclosure of Interest: C. Olivier: I am an employee for Shire.

Aims & Methods: This was a prospective pilot study on patients with a diagnosis of superficial SNADETs who were treated at the Department of Gastroenterology, Graduate School of Medicine, The University of Tokyo Hospital, Tokyo, Japan. Before enrollment, all patients had undergone endoscopic evaluation to preclude ampullary lesions, and had a preoperative histological diagnosis of either adenoma or adenocarcinoma. Patients with familial polyposis were excluded. Immediately before resection of the target lesions, a simple biopsy sample from the duodenal tumor and a paired sample from the surrounding normal duodenal mucosa were endoscopically obtained from each patient, followed by RNA extraction. Gene expression profiling with an oligonucleotide microarray was performed in a training set of 4 matched tumor-normal tissue superficial SNADETs pairs. Genes and pathways with differences between pairs were identified, followed by a set-level gene enrichment analysis with a pre-validated curated gene set. Results were confirmed with rt-PICR in all other independent SNADETs pairs.

Disclosure: From Nov 2014 to Jan 2016, a total of 12 consecutive patients were enrolled in this study. One patient was excluded due to a post-treatment diagnosis of familial polyposis. In a training set of 4 tumor-mucosa pairs, 626 probes (168 up-regulated, 458 down-regulated) which consistently demonstrated over a 2-fold expression difference between tumor and normal mucosa in all matched pairs were identified. Rq-PCR of genes most highly differentially expressed between the tumors and normal mucosa was performed in the 4 pairs in the training set as well as 7 independent pairs. Consistent gene expression patterns concurrent with microarray results were demonstrated in all pairs, confirming the results of this study. Gene set enrichment analysis of the training set using a curated data set demonstrated a strong association between SNADETS with colorectal adenomas (p < 0.0001) and APC down-regulation (p < 0.00001). No other significant associations were demonstrated.

Conclusion: Superficial SNADETs demonstrate gene expression characteristics with a strong resemblance to colorectal adenomas. Gene expression characterization of these lesions has also demonstrated the significant role of APC down-regulation in the pathogenesis of SNADETs, suggesting that an adenoma-carcinoma sequence similar to colorectal adenomas may be seen in SNADETS. Further analysis of genes which may play a key role in the carcinogenesis of these neoplasms is needed.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1292 USE OF 3D COMPUTED TOMOGRAPHIC ENTEROCLYSIS TO OBTAIN INFORMATION ON THE LENGTH OF THE SMALL INTESTINE AND ON THE SIZE, SHAPE, LOCATION OF INTESTINAL NEOPLASIAS

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Introduction: We established a new imaging technique, 3D computed tomographic (CT) enteroclysis, to evaluate its safety, feasibility, and usefulness for small intestinal neoplasias. Data on 3D CT enteroclysis performed in our hospital from January 2010 to March 2017 were reviewed. In 3D CT enteroclysis, the small bowel was inflated with air using a nasoduodenal tube. CT images were taken, and then 3D overviews, virtual endoscopic views, and virtual dissection views were generated using a virtual colonoscopy system. Total volume of injected air, intraintestinal pressure, and length of the depicted small bowel were recorded. The images of small intestinal neoplasias were collected and compared with patients in Group 2 or Group 3. This research was funded by Shire International GmbH, Zug, Switzerland.

Disclosure of Interest: P.B. Jeppesen: I have served as a consultant and on the speaker bureau for Shire. S.M. Gabe: I have served as a consultant for Shire. D.L. Seidner: I have served as a consultant for Shire. H. Lee: I am an employee for Shire. C. Oliver: I am an employee for Shire.

Conclusion: Patients with SBS-IF in Group 1 had the highest baseline PS volume and responded most and fastest to TED with PS volume reductions, compared with patients in Group 2 or Group 3. This research was funded by Shire International GmbH, Zug, Switzerland.

Disclosure of Interest: P.B. Jeppesen: I have served as a consultant and on the speaker bureau for Shire. S.M. Gabe: I have served as a consultant for Shire. D.L. Seidner: I have served as a consultant for Shire. H. Lee: I am an employee for Shire. C. Oliver: I am an employee for Shire.
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Disclosure of Interest: All authors have declared no conflicts of interest.

Reference


Disclosure of Interest: All authors have declared no conflicts of interest.
P1297 ELLIPSE BALLOON SYSTEM: OUR EXPERIENCE. A PRELIMINARY STUDY

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Introduction: Gastric balloons (IGB) are an emerging option for overweight and obese patients with a body mass index (BMI) greater than 31 kg/m2 and they provide greater efficacy with lower risks than do conventional surgical procedures. The balloon treatment is based on gastric space-occupying effects that increase the feeling of satiety and may also affect gut neuroendocrine signaling. However, widespread use of current generation IGBs has been limited by several factors: placement and removal endoscopes require sedation, special training and equipment; patients lost to follow-up are susceptible to IGB deflation and unplanned passage into the gastrointestinal tract. The EllipseTM is the world’s first intragastric balloon that does not require endoscopy or anesthesia.

Aims & Methods: We conducted a study to prospectively analyze the safety and effectiveness of IGB ELLIPSE in overweight adults. Six patients, 1 male and 5 female (average age 40, mean BMI = 40 kg/m2), were included in this study. Each patient swallowed EllipseTM balloon intended to remain in the stomach for 16 weeks. Each balloon was filled with 560 mL of filling fluid. Patients returned every 2 weeks for abdominal ultrasound which documented the correct positioning of the device. All patients were followed up by a nutritionist with a specific focus on the IGB.

Results: All 6 patients successfully swallowed the device. There were no major adverse effects. All 6 patients had a significant weight loss (about 16 Kg). In all of the patients, the balloon remained full throughout 16 weeks, self-emptied, and were passed spontaneously without needing endoscopic removal.

Conclusion: This study demonstrates the efficiency, security and simplicity of the IGB ELLIPSE in overweight adults. All patients were followed up by a nutritionist with a specific focus on the IGB. The ElipseTM system. Moreover, we highlighted the non necessity of deep sedation and use of invasive endoscopic examinations for positioning and removal of the IGB.

Disclosure of Interest: All authors have declared no conflicts of interest.

References


P1298 NUTRITIONAL STATUS EVALUATION TOOL IS NOT USED BY THE TREATING PHYSICIAN DURING HOSPITALIZATION. A RETROSPECTIVE STUDY OF BARIATRIC PATIENTS.

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Introduction: Bariatric surgery is an effective treatment for morbid obesity. In Taiwan, the numbers of patients who received bariatric surgery increased gradually. However, for long-term follow-up, nutritional deficiency may develop in patients. We collected data on the utilization of nutrition department services for bariatric surgery patients. The aim of this study is to evaluate the change of Vitamin D and bone mineral density (BMD) in bariatric surgery patients.

Aims & Methods: We conducted a patient identification study at the bariatric surgery outpatient clinic (April 2012-2014) and one year after bariatric surgery (2013-2015). Blood samples were collected from patients for assessment of the calcium, Vitamin D and parathyroid hormone (PTH) levels. BMD (g/cm2) was also measured at lumbar spine (L2-L4) by dual energy x-ray absorptiometry (DEXA).

Results: Among 50 patients, 15 patients received laparoscopic sleeve gastrectomy (LSG), 24 patients received laparoscopic mini-gastric bypass (MGB), 5 patients received laparoscopic Roux-en-Y gastric bypass (RYGB) and 6 patients received laparoscopic duodenal-jejunal bypass with sleeve gastrectomy (DBJ-SG).

The characteristic of the study population was shown as Table 1. The differences of mean for calcium, Vitamin D, PTH and BMD after bariatric surgery were significant. BMD (g/cm2) in the LSG group was higher than that in the MGB group.

Conclusion: We aim to identify patients with bone mineral density (BMD) at risk who may benefit from vitamin D supplementation. Furthermore, we aim to identify patients who may develop osteopenia or osteoporosis.

Disclosure of Interest: All authors have declared no conflicts of interest.

Table 1: Characteristics of study population one year after bariatric surgery

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<th>LSG</th>
<th>MGB</th>
<th>RYGB</th>
<th>DJB-SG</th>
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<td>15</td>
<td>24</td>
<td>5</td>
<td>6</td>
<td>50</td>
</tr>
<tr>
<td>Age, years</td>
<td>34.7(7.4)</td>
<td>37.4(11.7)</td>
<td>41.4(11.4)</td>
<td>41(10)</td>
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</tr>
<tr>
<td>Sex(M:F)</td>
<td>7.8</td>
<td>5:19</td>
<td>2:3</td>
<td>3:4</td>
<td>17:33</td>
</tr>
<tr>
<td>BMI(kg/m²)</td>
<td>29.8(4.7)</td>
<td>27.6(4.4)</td>
<td>27.9(2.9)</td>
<td>24(2.4)</td>
<td>27.6(2.4)</td>
</tr>
<tr>
<td>Ca(mg/dl)</td>
<td>9.6(0.3)</td>
<td>9.1(0.3)</td>
<td>9.2(0.4)</td>
<td>9.3(0.4)</td>
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<td>PTH(pg/ml)</td>
<td>63.8(21.3)</td>
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<td>73.1(4.2)</td>
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<td>14(6.9)</td>
<td>12.8(8.6)</td>
<td>16.9(5.3)</td>
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P1299 CHANGE OF VITAMIN D AND BONE MINERAL DENSITY AFTER BARIATRIC SURGERY IN CHINESE POPULATION

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Introduction: Bariatric surgery is an effective treatment for morbid obesity. In Taiwan, the numbers of patients who received bariatric surgery increased gradually. However, for long-term follow-up, nutritional deficiency may develop in patients. We collected data on the utilization of nutrition department services for bariatric surgery patients. The aim of this study is to evaluate the change of Vitamin D and bone mineral density (BMD) in bariatric surgery patients.

Aims & Methods: We conducted a patient identification study at the bariatric surgery outpatient clinic (April 2012-2014) and one year after bariatric surgery (2013-2015). Blood samples were collected from patients for assessment of the calcium, Vitamin D and parathyroid hormone (PTH) levels. BMD (g/cm2) was also measured at lumbar spine (L2-L4) by dual energy x-ray absorptiometry (DEXA).

Results: Among 50 patients, 15 patients received laparoscopic sleeve gastrectomy (LSG), 24 patients received laparoscopic mini-gastric bypass (MGB), 5 patients received laparoscopic Roux-en-Y gastric bypass (RYGB) and 6 patients received laparoscopic duodenal-jejunal bypass with sleeve gastrectomy (DBJ-SG). The characteristic of the study population was shown as Table 1. The differences of mean for calcium, Vitamin D, PTH and BMD after bariatric surgery were significant. BMD (g/cm2) in the LSG group was higher than that in the MGB group.

Conclusion: We aim to identify patients with bone mineral density (BMD) at risk who may benefit from vitamin D supplementation. Furthermore, we aim to identify patients who may develop osteopenia or osteoporosis.

Disclosure of Interest: All authors have declared no conflicts of interest.

Table 1: Characteristics of study population one year after bariatric surgery

<table>
<thead>
<tr>
<th></th>
<th>LSG</th>
<th>MGB</th>
<th>RYGB</th>
<th>DJB-SG</th>
<th>OVER ALL</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>15</td>
<td>24</td>
<td>5</td>
<td>6</td>
<td>50</td>
</tr>
<tr>
<td>Age, years</td>
<td>34.7(7.4)</td>
<td>37.4(11.7)</td>
<td>41.4(11.4)</td>
<td>41(10)</td>
<td>37.8(10.5)</td>
</tr>
<tr>
<td>Sex(M:F)</td>
<td>7.8</td>
<td>5:19</td>
<td>2:3</td>
<td>3:4</td>
<td>17:33</td>
</tr>
<tr>
<td>BMI(kg/m²)</td>
<td>29.8(4.7)</td>
<td>27.6(4.4)</td>
<td>27.9(2.9)</td>
<td>24(2.4)</td>
<td>27.6(2.4)</td>
</tr>
<tr>
<td>Ca(mg/dl)</td>
<td>9.6(0.3)</td>
<td>9.1(0.3)</td>
<td>9.2(0.4)</td>
<td>9.3(0.4)</td>
<td>9.5(0.4)</td>
</tr>
<tr>
<td>PTH(pg/ml)</td>
<td>63.8(21.3)</td>
<td>70.4(25.9)</td>
<td>73.1(4.2)</td>
<td>50(14)</td>
<td>62.2(9.4)</td>
</tr>
<tr>
<td>VIT.D (ng/ml)</td>
<td>19.4(7.7)</td>
<td>14(6.9)</td>
<td>12.8(8.6)</td>
<td>16.9(5.3)</td>
<td>15.6(7.5)</td>
</tr>
<tr>
<td>VIT.D deficiency</td>
<td>0(0%)</td>
<td>0(0%)</td>
<td>0(0%)</td>
<td>0(0%)</td>
<td>0(0%)</td>
</tr>
</tbody>
</table>

BMD(g/cm²) 1.11(0.25) 1.15(0.23) 1.18(0.26) 1.12(0.26) 1.11(0.23) 1.15(0.17)
intragastric balloon. The intragastric balloon has been established as a valid endoscopic therapeutic option for weight loss, especially in patients with overweight and obesity. Moreover, up to 123 patients submitted APC application. In relation to the anastomotic diameter, the majority of studies use a diameter of more than 20 mm to define anastomosis dilation, although some studies use smaller diameters such as 14 mm similar to that created manually in the gastrojejunal anastomosis using a 36 Fr Fouchet bougie. In the patients in the present study, the minimum cross-section diameter was 18 mm and the maximum measured in the first session 40 mm. This anastomotic diameter was measured using a 33-mm long Olympus Articulated device. Interval between an anastomotic dilation procedure was with a maximum of 03 applications. APC set was at 2-3 mL with 65-85W. GJ diameter target was 8-12 mm estimated with pre-measured grasper. At first APC session, pre-op weight and BMI, post-op weight nadir, actual weight and BMI and estimated diameter of GJ were the variables collected. Complications during treatment were also collected. In the present study, psychological and nutritional evaluations were performed before APC and during treatment and physical activity was strongly recommended. Data were analyzed with descriptive statistics, student’s t-test and Spearman correlation.

Results: Of the 554 patients, 79.06% were women and 20.94% were men. Average time between bariatric surgery and the first APC was 96.35 months (73.01–123.69). Mean and average weight loss reported in this interval was 22.08 kg (±11.05 kg). The mean diameter of the anastomosis was 24.78 mm (±6.04) and the average number of APC sessions was 1.78 times (±0.61). The average reduction of anastomotic diameter was 14.86 mm (±7.24) and the final average diameter was 10.01 mm (±4.13). The average weight loss between the first and last APC was 13.37 kg (±7.82) and the average decrease of BMI was 4.59 kg/m² (±2.78). 122 patients (22.0%) did not achieve the target GJ diameter and 05 patients (0.9%) did not lose weight even with the desired GJ diameter. From the 146 patients who had weight regain due to symptomatic stenosis at least once. No further complications were reported. Conclusion: Argon Plasma Coagulation (APC) has been shown to be an effective and safe endoscopic technique for the reduction of gastro enteric anastomosis in patients undergoing bariatric surgery who have regained weight with dilation of the anastomosis. The reintroduction of the patient to the multidisciplinary team is mandatory if better results and sustainable weight loss and comorbidity control are to be obtained.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P1301 WEIGHT REGAIN AFTER BARIATRIC SURGERY - ARGON PLASMA COAGULATION FOR GASTROJEUNAL ANASTOMOSIS DECREASE
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Introduction: The weight regained has been a described growing problem in patients undergoing bariatric surgery and this weight regained is multifaceted and associated with dilation of Gastrojejunal anastomosis (GJ). For the patients with significant weight regain some revisional procedures had been attempted and more recently endoscopic revisional procedures had been described. Aims & Methods: To evaluate the safety and effectiveness of argon plasma coagulation (APC) decreasing the diameter of the gastroanastomosis in patients who have undergone RYGB for morbid obesity and regained weight associated to dilation of the GJ From Jan-2014 to April-2017 554 RYGB subjects were reviewed and regain a dilated anastomosis (>18 mm) and at least 2 procedures were submitted APC application. In relation to the anastomotic diameter, the majority of studies use a diameter of more than 20 mm to define anastomosis dilation, although some studies use smaller diameters such as 14 mm similar to that created manually in the gastrojejunal anastomosis using a 36 Fr Fouchet bougie. In the patients in the present study, the minimum cross-section diameter was 18 mm and the maximum measured in the first session 40 mm. This anastomotic diameter was measured using a 33-mm long Olympus Articulated device. Interval between an anastomotic dilation procedure was with a maximum of 03 applications. APC set was at 2-3 mL with 65-85W. GJ diameter target was 8-12 mm estimated with pre-measured grasper. At first APC session, pre-op weight and BMI, post-op weight nadir, actual weight and BMI and estimated diameter of GJ were the variables collected. Complications during treatment were also collected. In the present study, psychological and nutritional evaluations were performed before APC and during treatment and physical activity was strongly recommended. Data were analyzed with descriptive statistics, student’s t-test and Spearman correlation.

Results: Of the 554 patients, 79.06% were women and 20.94% were men. Average time between bariatric surgery and the first APC was 96.35 months (73.01–123.69). Mean and average weight loss reported in this interval was 22.08 kg (±11.05 kg). The mean diameter of the anastomosis was 24.78 mm (±6.04) and the average number of APC sessions was 1.78 times (±0.61). The average reduction of anastomotic diameter was 14.86 mm (±7.24) and the final average diameter was 10.01 mm (±4.13). The average weight loss between the first and last APC was 13.37 kg (±7.82) and the average decrease of BMI was 4.59 kg/m² (±2.78). 122 patients (22.0%) did not achieve the target GJ diameter and 05 patients (0.9%) did not lose weight even with the desired GJ diameter. From the 146 patients who had weight regain due to symptomatic stenosis at least once. No further complications were reported. Conclusion: Argon Plasma Coagulation (APC) has been shown to be an effective and safe endoscopic technique for the reduction of gastroenteric anastomosis in patients undergoing bariatric surgery who have regained weight with dilation of the anastomosis. The reintroduction of the patient to the multidisciplinary team is mandatory if better results and sustainable weight loss and comorbidity control are to be obtained.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
P1303 THE EFFECT OF A CONTROLLED GLUTEN CHALLENGE IN PATIENTS WITH SUSPECTED NON-COEELIAC GLUTEN SENSITIVITY: A RANDOMIZED, DOUBLE-BLIND PLACEBO-CONTROLLED CHALLENGE

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Introduction: Non-coeliac gluten sensitivity (NCGS) is a new entity with unknown prevalence and mechanisms, and there is a need for a standardized procedure to confirm the diagnosis. The objective of this study was to characterize the response to a gluten challenge, when performed according to the updated Salerno criteria.

Aims & Methods: Twenty patients (14F/6M, age range: 21–62 y) with suspected NCGS, without coeliac disease and wheat allergy, were included on a gluten-free diet. All patients went through four periods of double-blinded provocation with gluten and placebo containing muffins. They were instructed to eat two muffins a day (11 g gluten) for four days, followed by a three days’ wash-out.

Gastrointestinal symptoms were recorded with questionnaires at baseline and after each provocation, while fatigue and quality of life were registered at baseline and end of the trial.

Results: Four out of twenty patients (20%) correctly identified the two periods when they received muffins containing gluten, hence were diagnosed with NCGS. The non-diagnosed group tended to show higher symptom scores than the not-diagnosed group both at baseline, after gluten exposure and after placebo, but no clear difference was seen in symptom change after provocation with gluten and placebo.

Conclusion: This randomized, double-blind placebo-controlled challenge with gluten diagnosed four patients with NCGS according to the Salerno criteria. However, according to the symptom registrations there are no clear differences between the diagnosed and the non-diagnosed group, or between symptoms after gluten provocation and placebo, indicating no specific effect of gluten in a group of patients with suspected NCGS.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1304 THE ROLE OF BILE ACIDS AND GUT MICROBIOTA IN CORONARY ARTERY DISEASE: RESULTS OF THE MABAC STUDY IN HUMAN (MICROBIOTA ATEROMA AND BILE ACID IN CORONARY DISEASE)

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Introduction: By targeting specific receptors into the vascular system, bile acids (BA) are cholesterol derivatives that are now considered as hormones. BA regulates the basal energy expenditure and gluco-lipidic metabolism. In animal models of atheroma developmentapoE-/- and LDL-/- mouse models) a powerful anti-atherosclerotic effect of circulating BA has been evidenced: BA are metabolites of the gut microbiota, suspected to play a role in the development of atherosclerosis. This study examined whether variations in BA or in the gut microbiota composition can be described in the human Coronary Artery Disease pathophysiology.

Aims & Methods: Consecutive patients undergoing coronary angiography between February and May 2015 were enrolled. To avoid physiological or induced variations in circulating BA or in the gut microbiota, highly restrictive exclusion criteria were applied. Circulating and fecal BA were quantified by high pressure liquid chromatography and tandem mass spectrometry. The fecal microbiota composition was assessed by 454 pyrosequencing of the total fecal bacterial DNA.

Results: 80 patients were prospectively included of 406 screened, and divided in two groups: with (n=45) and a group without (n=35) CAD. The serum mean concentration of total BA was 1.02 ±0.16 mmol/l in patients with, versus 2.16 ±0.38 mmol/l in patients without CAD (P=0.005). This decrease, (adjusted for gender and age) was an independent predictor of CAD (odd ratio = 0.51; 95% confidence interval 0.31, 0.85; P=0.01). The BA concentrations in feces were similar in both groups. There was no group-specific pattern in the fecal microbiota. In a subgroup of 17 patients, one month of statin therapy increased the serum BA concentration from 0.68 ±0.08 to 1.37 ±0.21 mmol/l (P=0.01).

Conclusion: There was no specific microbiota signature associated with CAD. However, a decreased serum BA concentration was a strong predictor of CAD in humans. With respect to the powerful anti-atherosclerotic effect of BA in animal models, and their role in human lipid metabolism and diabetes, this study unraveled the existence of a new metabolic disturbance associated with CAD.

Disclosure of Interest: All authors have declared no conflicts of interest.
both at T1 (4.4 ± 1.6) and T2 (8.2 ± 1.7). When starting, LFD patients considered a diet low in FODMAPs (67%), fructans (27%), fibre (17%), galacto-oligosaccharides (GOS) (17%) and polysaccharides (3%); the reintroduction phase (T2) enabled us to detect lactose in 70%, fructans in 30%, fructose in 37%, GOS in 33% and polysaccharides in 27%, as real triggers. The agreement (Cohen’s kappa) was moderate for lactose (κ = 0.50), fair for fructans (κ = 0.39) and fructose (κ = 0.32) and poor for polysaccharides (κ = 0.01).

Conclusion: Not only did reintroduction not affect the improvements achieved during the elimination phase, but it also precisely identified the foods responsible for the clinical manifestations. This enabled us to suggest a personalized diet for the patients. The real role played by FODMAPs in generating symptoms was abundantly underestimated and misunderstood by our patients. This underlines the fact that LFD has to be administered and carried out under the guide of an expert nutritional physician.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1306 EXPRESSION OF THE FRUCTOSE TRANSPORTER GLUT5 IN PATIENTS WITH FRUCTOSE MALABSORPTION
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Introduction: Fructose malabsorption (FM) is a frequent finding in patients with abdominal symptoms due to high levels of fructose in Western diets. The role of monosaccharide transporter dysfunction in the small intestine is incompletely understood. The aim of this study was to investigate the histoanatomical distribution of the main fructose transporter GLUT5 in JH patients with FM.

Aims & Methods: The study included 257 patients with FM diagnosed by hydrogen breath test and grouped according to the response to a fructose-free diet. 42 healthy individuals and 31 patients with coeliac disease (CD) served as control. The fructose breath test was done with 50 g fructose. Fructose malabsorption was defined as an increase of 20 ppm of endogeneous hydrogen. Formalin-fixed and paraffin-embedded duodenal biopsy specimens were obtained in all cases. Histology was assessed using hematoxylin and eosin stained tissue sections. Expression of GLUT5 was studied by immunohistochemistry. Expression patterns of GLUT5 were correlated with clinico-pathological patient characteristics.

Results: The expression of GLUT5 did not differ significantly between patients with FM complete diet responders (n = 183) and healthy controls (n = 42) also patients with FM responding to a fructose free diet did not differ in GLUT5 expression or in max. H2 increase and AUC measured in fructose breath testing from patients not responding to the diet (n = 40). However, in patients with CD (n = 29) significant differences in GLUT5 expression were found compared to patients with FM and healthy controls (p = 0.009). The severity of CD assessed by the Marsh score significantly correlated with the GLUT5 expression (r = 0.563, p = 0.001).

Conclusion: Changes in GLUT5 expression may not cause symptoms in adult FM patients. FM symptoms may be associated with other factors not only with GLUT5 expression. In contrast, in CD with secondary malabsorption decreased GLUT5 expression was detected. Further investigation is needed to understand the essential factors in FM and the influence on functional gastrointestinal disorders.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1307 BETTER RESPONSE TO LOW FODMAP DIET IN JH NEGATIVE PATIENTS WITH DORDERS OF GUT-BRAIN INTERACTION
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Introduction: Previous studies have shown a reduction of gastrointestinal symptoms in patients with disorders of gut-brain interaction (FGID) when following a diet low in FODMAPs. Symptom relief due to a low FODMAP diet has especially been investigated in patients suffering from irritable bowel syndrome (IBS) and has proven to reduce gastrointestinal symptoms in up to 86% of patients with IBS. In addition, there is evidence for an association between gastrointestinal symptoms and joint hypermobility (JH). However, there is no clear data regarding response rates to a diet low in FODMAPs in patients suffering from JH. In this study we aimed to assess and compare the response to a diet low in FODMAPs in JH positive and JH negative patients with FGIDs.

Aims & Methods: Data of patients presenting with FGID at the tertiary ambulatory functional bowel clinic between January 2015 and July 2016 were analyzed. FGIDs were diagnosed according to Rome III criteria. JH was assessed by physicians using Beighton score and rated positive for scores >9/9 points. Patients received professional nutritional counseling on a diet low in FODMAPs. A global symptom response was assessed by a professional nutritionist after 4 to 6 weeks following a low FODMAP diet.

Results: Of all 84 patients screened for JH, 62 (73.8%) were female and 22 (26.2%) were male. Median age of the female was 35 (range 18-59) years, whereas males were more likely to exhibit JH compared to males (38.62 [61.3%] vs. 6.22 [27.3%]; p = 0.006). Global symptom response rate to a diet low in FODMAPs was 64/64 (76.2%). Our data showed significantly better response to a low FODMAP diet in JH negative patients than in JH positive patients (36/40 [90.0%] vs. 28/44 [63.6%], p = 0.005, ITT). Response of 7 patients was unknown because of early therapy discontinuation before nutritional re-counseling. When excluding 7 patients with therapy discontinuation from our calculations, the difference in diet response between JH negative and JH positive patients remained significant (36.39 [92.3%] vs. 28/38 [73.7%]; p = 0.036).

Conclusion: Our data indicate an association between global symptom response to a diet low in FODMAPs and joint hypermobility status in FGID patients. An understanding of the structural pathways underlying pathological fructan and polyol sensitivity (intestinal permeability) causing gastrointestinal symptoms in JH positive patients and limiting response to low FODMAP diet should be considered. Our findings represent a further step towards pathophysiological features in FGIDs and might help to select patients for individually appropriate therapies.

Disclosure of Interest: M. Fried: Allergen, MSD, Astra, Vifor, Abbvie, UCBC D. Pohl: Allergen, Vifor, Astra, Peramed All other authors have declared no conflicts of interest.

P1308 CHANGES IN GASTROINTESTINAL SYMPTOMS, SMALL INTESTINAL BACTERIA, AND DUODENAL PHYSIOLOGY FOLLOWING A LOW-FIBER, HIGH-SUGAR DIET
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Introduction: Gastrointestinal symptoms are often associated with dietary intolerances and are common in the developed world consuming a western diet low in fiber. Aims & Methods: To determine the effect of a high-sugar, low-fiber diet on GI symptoms and duodenal physiological function, we conducted a double-blind clinical trial in a single-center study. Healthy adults with baseline fiber intake ≥14 g and ≥10 g of fiber/day (10 g/day; ≥5% of total daily calories) in response to increasing concentrations (0.003-300 μM) of serotonin (5-HT) on the submucosal side. These measurements were repeated after the dietary intervention. Data were presented as mean ± SEM. Data were analyzed using paired t-test unless specified and p < 0.05 was considered significant.

Results: A total of 10 participants (5 female; median age 26; 70% Caucasian) were recruited. Average BMI was 23.1 kg/m2. At baseline, all participants were asymptomatic. After dietary intervention, all patients endorsed at least one new symptom and 9/10 patients endorsed multiple (≥2) new symptoms. At baseline 4/10 patients had positive duodenal carbohydrate (≥100,000 CFU/mL) or other bacteria (≥100,000 CFU/mL) at baseline, all this was improved in participants who normally consumed a high-fiber diet. This was associated with changes in the gut microbiome. This was associated with changes in the gut microbiome. At baseline, the gut microbiome was characterized by a high proportion of Firmicutes and a low proportion of Bacteroidetes. After dietary intervention, the gut microbiome was characterized by a decrease in Firmicutes and an increase in Bacteroidetes. This was associated with changes in the gut permeability, increased inflammation, and decreased gut motility. At baseline, the gut microbiome was characterized by a high proportion of Firmicutes and a low proportion of Bacteroidetes. After dietary intervention, the gut microbiome was characterized by a decrease in Firmicutes and an increase in Bacteroidetes. This was associated with changes in the gut permeability, increased inflammation, and decreased gut motility.
P1309

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Introduction: Recently roles of gut hormones on appetite control have been known. Among them, CCK is well known to suppress appetite and gastric motility. On the other hand, patients of functional dyspepsia (FD) have hyper sensitivity to CCK. And revels of CCK innard was shown to be high in FD patients. In FD patients, stress have important roles of pathogenesis of the disease.

Aims & Methods: We undertook to clarify whether stress influences the actions of cholecystokinin (CCK) on appetite and gastric emptying. As stress, we gave restraint stress, corticosterone-releasing factor (CRF) or urocortin (UCN1) injection intraperitoneally (IP). We also examined the effects of CCK and restraint stress on c-Fos expression in the neurons of appetite center of the brain. In the gastric emptying study, SD rats were fasted overnight. The amounts of the mixture (food and glass beads) left in the stomach 1 hr after the injection was measured at 2 hours after the periorally injection of mixed food, and gastric emptying rate was calculated. In the study on appetite, CCK was IP injected and the amounts of food was measured at 5 minutes after the injection. In some experiments, CRF or UCN1 was IP injected and the interaction with CCK on food intake was examined. In another study, restraint stress was given to rats and the interaction with CCK was evaluated. To study the involvement of brain in the interaction between CCK and stress, c-Fos expression in the neurons was examined and evaluated.

Results: CCK dose-dependently inhibited gastric emptying. CCK dose-dependently inhibited food intake during 1 hr and 2 hr. CRF (10µg/kg rat) significantly inhibited food intake. However, there was no interactive action between CCK and CRF on food intake. UCN1 (3 nmol/kg rat) inhibited food intake at 1 and 2 hours. There was an synergistic action between CCK and UCN1 on food intake. Restraint stress amplified suppressive effect of CCK on gastric emptying and food intake. c-Fos expression of the neurons in the nucleus of solitary tract (NTS) and paraventricular nucleus of hypothalamus (PVN) by CCK was amplified by the addition of restraint stress.

Conclusion: The result suggests that stress might amplify anorectic effects of CCK through the activation of satiety center of the brain that might be the possible pathogenesis for postprandial distress syndromes of FD.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1310

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Introduction: Cholecystokinin (CCK) and peptide tyrosine-tyrosine (PYY) have been shown to affect appetite and gastric emptying. Both peptides release in blood by feeding, and maintain high levels simultaneously for 1–2 hours. Therefore there might be possible to cause interactive actions between two peptides, inducing satiation to finish food intake.

Aims & Methods: In this study, we undertook to elucidate whether CCK and PYY have the interaction to decrease food intake. Study on gastric emptying. Male SD rats were fasted overnight, and 1 mL of mixture of food and glass beads was given into the stomach and then PYY or CCK followed by PYY was IP injected to the rats just before setting food to eat. The amounts of food were measured at 1 and 2 hours after the injection. To clarify the involvement of the brain in the interaction between CCK and PYY, c-Fos expression was examined.

Results: CCK (0.5–10 nmol/kg) dose-dependently inhibited gastric emptying (p < 0.001). CCK 10 nmol/kg maximally inhibited food intake (p < 0.01). PYY 25–250 pmol/kg significantly inhibited gastric emptying for 1 or 2 hrs after the injection (p < 0.01). PYY 250 pmol/kg significantly inhibited food intake for 1 hour after the injection (p < 0.01). The combination of CCK 10 nmol/kg and PYY 250 pmol/kg inhibited gastric emptying more than CCK alone(p < 0.01) or PYY alone (not significant). PYY and CCK additively inhibited food intake when PYY was injected 20 minutes later from CCK injection. PYY significantly amplified c-Fos expression induced by CCK in the nucleus of solitary tract (NTS) and paraventricular nucleus of hypothalamus (PVN) in the brain.

Conclusion: The combination of PYY with CCK amplified the suppression of gastric emptying and the result suggests that the sequence secretion of CCK and PYY might strengthen the inhibition of food intake through the activation of satiety center in the brain, that is important for terminating food intake and adjusting energy intake.

Disclosure of Interest: All authors have declared no conflicts of interest.

WEDNESDAY, NOVEMBER 01, 201709:00-14:00
LIVER AND BILIARY III - HALL 7...

P1311

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Introduction: Transcriptions factors belonging to the p53 family (p53, p63, p73) respond to cellular stress signals by inducing an accurately defined set of genes. In a number of tumors, also in hepatocellular carcinoma (HCC), p53 proteins can exert cancerogenic or tumor-suppressive functions. MicroRNAs are small, non-coding RNA molecules which play an important role in gene regulation. It is known that expression patterns of microRNAs can be controlled by the p53 family. Depending on disease and cellular origin different sets of p53-induced microRNAs have been identified.

Aims & Methods: Little is known about p53-dependent microRNA signatures in HCC. The aim of the study was therefore to identify p53-family-regulated microRNAs in HCC. Hep3B cells were transfected with rAd-p53 and -p73. Microarray analyses were performed to identify p53- and p73-regulated microRNAs. Verification of p53- and p73-dependent microRNA expression was performed by qPCR. To evaluate the effect of HCC-relevant therapeutics on p53-dependent regulation of microRNAs transfected Hep3B cells were incubated with UCN1 (3 nmol/kg) and CRF (5 µg/kg) for 1–2 hours. Results: Overexpression of p53 and p73 induced a range of microRNAs. P53 induced miR-34a by 2.4-fold, miR-145 by 2.7-fold and led to a slight reduction of miR-149. In the presence of p73 miR-34a was induced by 5.4-fold, miR-145 by 3.2-fold, and miR-149 by 5.5-fold. p53-dependant expression of miR-34a was further increased in the presence of Doxorubicin (5.7-fold), Regorafenib (2.5-fold) and Tivantinib (1.9-fold) compared to controls. Moreover, incubation with Regorafenib resulted in an up to 5.4-fold increase of p53-dependent expression of miR-149 and miR-192.

Conclusion: p53 proteins affect the microRNA signature in HCC. Beside the already known induction of miR-34a we demonstrate for the first time a regulation of miR-145 and –149 by p53 and p73. We hypothesized that regulation of tumour-suppressive microRNAs represents an effector mechanism by which p53 family members exert their role in tumor development and treatment response. The observed synergistic effect of p53 and HCC-relevant therapeutics on microRNA expression might provide new options for the development of therapeutic and prognostic markers in HCC.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1312

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Introduction: p53 transcription factors (p53, p63, p73) respond to cellular stress by transcriptional regulation of specific sets of genes. In hepatocellular carcinoma (HCC) and other tumors p53 family members exert cancerogenic or tumor-suppressive effects. Depending on their splice variants— with transactivation domain (TA)/dominant negative (DN)—and the characteristics of the particular binding site (BS) BS p53 proteins activate or inhibit specific target genes. We previously identified the IGFBP2 gene (Insulin-Like Growth Factor Binding Protein 2) as one out of 7 putative target genes for p53 proteins with prognostic relevance in HCC.

Aims & Methods: The aim of this study was to characterize the so far unknown regulation of the IGFBP2 gene by p53 family members in HCC. Hep3B cells were transfected with rAd-p53 and rAd-p73 and transcriptional regulation of IGFBP2 was determined by qPCR. Intra- and extracellular IGFBP2 protein levels were analyzed by Western Blot and ELISA. Transfected database analyses were performed to identify potential BS for p53 and p73 in the IGFBP2 locus. These sequences were cloned, mutated and analyzed for p53 family binding in luciferase reporter assays. Binding of p53 and p73 to the identified BS was confirmed by CHIP experiments.

Results: The transfection increased IGFBP2 expression by up to 60-fold and results showed that elevated intra- and extracellular IGFBP2 protein levels were detectable. IGFBP2 protein was not detected in controls. p53 transfection induced IGFBP2 expression by up to 7-fold. Two potential p53 and p73 BS were located in the promoter region, another 5 potential p73 and one p53 BS were identified in intron 1 of the IGFBP2 gene. Intron 1-dependent luciferase activity was increased by up to 110-fold after Tap73 transfection and up to 20-fold after p53 transfection. Mutation and deletion of the identified p53 BS in intron 1 resulted in a reduction of luciferase activity by up to 85%. Deletion of one
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引言：UC的甲苯胺脱氢试验（UC-MBT）是用于筛选脱氧酶活性的试验，通过确定其代谢能力的强度和肝细胞恢复。

方法与结果：研究纳入了113名MS患者，年龄从37岁至82岁。男性75人，女性88人。研究的纳排标准是MS和BMI（≤25 kg/m2）。通过UC-MBT，对患者的肝脏功能进行了评估。

结论：结果分析表明，UC-MBT在MS患者中具有潜在的临床应用价值。通过UC-MBT，可以更准确地评估患者的肝脏功能，有助于制定个性化的治疗方案。
P1136 NONALCOHOLIC FATTY LIVER DISEASE IN PATIENTS WITH 2 TYPES OF MULTIPLE SCLEROSIS AND CORONARY HEART DISEASE AGAINST THE BACKGROUND OF METABOLIC SYNDROME. HOW TO DIAGNOSE?

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Introduction: It is known that to determine nonalcoholic fatty liver disease (NAFLD), which develops in progress of body mass index (BMI) from 19% to 35%, using instrumental and laboratory methods, which include an ultrasound, the determination of the transaminase levels, steatostest, 13C-methacetine test. However, these research methods do not allow to clearly differentiate steatosis from the steatohepatitis, that reduces their credibility.

Aims & Methods: 163 patients (75 men, 88 women) with 2 type diabetes mellitus and coronary heart disease with metabolic syndrome, were examined. The average BMI was calculated above criteria of metabolic syndrome. 3 patients were diagnosed as steatosis group, 66 - steatohepatitis group. In 25 patients liver pathology was not found, which identified as a control group.

For verification of steatosis and steatohepatitis diagnosis the level of ALT, diastolic blood pressure and data 13C-methacetine breath test were evaluated.

Results: The rate of liver metabolism based on 13C-methacetine test results in patients without NAFLD was 22.0±0.686%, in patients with steatosis - 17.1±0.84%, steatohepatitis - 14.3±0.62%. Cumeative dose of methacetine on 120 minute was 20.25±0.46% in patients without pathology of liver, 16.1±0.49% in patients with steatosis, 11.4±0.36 in patients with steatohepatitis. ALT level in control group was 0.4±0.05 mmol/l, with steatosis 0.6±0.09 mmol/l, with steatohepatitis 0.9±0.08 mmol/l. The diameter of vena portae in control group was 11.2±0.26 mm, in group of steatosis 11.9±0.21 mm, in patients with steatohepatitis 13.7±0.15 mm. There were investigated, that the rate of metabolism and its cumulative dose on 120 minute has decreased in steatosis group on comparison of the control group, with simultaneous significant increasing of ALT level and diameter of the portal vein. However, a significant reduction of the metabolism rate of methacetin and the cumulative dose of 13CO₂ in the background of the increase of a diameter of vena portae compared with a group of healthy examined in steatohepatitis group. The investigation found that in ALT and the diameter of the portal vein negatively correlated with cumulative dose of 13CO₂ on 120 minute in patients with steatohepatitis.

Conclusion: Therefore, a decrease in the metabolic capacity from 15 to 10% accompanied by an increase in ALT levels (more 0.686 mmol/l) and the diameter of the portal vein (13 mm).

Disclose of Interest: All authors have declared no conflicts of interest.

P1138 LIVER TRANSIENT ELASTOGRAPHY IN NON-ALCOHOLIC FATTY LIVER DISEASE: IS THERE ANY PREDICTIVE ROLE IN THE DEVELOPMENT OF COLORECTAL POLYPS?

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Introduction: Recent studies have demonstrated an association between decreased glucose tolerance, dyslipidemia and metabolic syndrome; and increased risk of colorectal polyps. Patients with non-alcoholic fatty liver disease (NAFLD) often have these risk factors. The association between NAFLD and colorectal polyps has been poorly studied.

Aims & Methods: We aimed to evaluate the prevalence and risk factors of colorectal polyps in patients with NAFLD. This was a retrospective observational cohort study of 237 patients with NAFLD submitted to transient elastography by Fibroscan®, between 2015-01-02-2017. Exclusion criteria: age <18years, absence of total colonoscopy with good preparation <3 years, inflammatory bowel disease, hereditary polyposis syndromes and personal/family history of colorectal polyps/neoplasia. Compared patients with colorectal polyps(cases) and without colorectal polyps(controls). Demographic variables, cardiovascular/metabolic risk factors, comorbidities, laboratory parameters and Fibroscan® scores of steatosis(CAP > 300 dB/m) and fibrosis(F4: > 10KPa) were evaluated.

Results: Of the 237 NAFLD patients who performed Fibroscan®, 103 underwent total colonoscopy. The prevalence of colorectal polyps in patients with NAFLD was 28.2%(n=29): 19.4%(20/103) hyperplastic, 16.5%(17/103) adenoma and 4.8%(5/103) advanced adenoma/adeno/ carcinocarcinoma. The mean age was 58.32 ± 51.5 years (vs70.9±10.53;p=0.089), with men predominant (51.7%v63.5%; p=0.272), mostly located in the left colon (55.2%v44.8%;p=0.314) and number and mean size of 1.46±0.88 and 6.89±6.56 mm, respectively. After multivariate analysis, colorectal polyps were found associated with F4 liver fibrosis (34.5%/vs 14.9%;p=0.026; OR=3.01) and obesity (BMI > 30 kg/m²; 55.2%/vs 29.7%; p=0.016; OR = 2.91); hyperplastic polyps were associated with liver fibrosis for a cut-off value of 6.9kPa (AUCROC.0689;p=0.008; S=85.7%; Sp=51.2%); mainly F4 (42.8%/v14.6%; p=0.004; OR=4.38), hyperuricemia (23.8%/v8.5%;p=0.042; OR=3.35) and peptic ulcer disease (9.5%/vs 1.2%;p=0.043; OR = 8.53); adenoma was associated with liver steatosis (88.2%/v83.7%;p=0.024; OR=3.90), F4 liver fibrosis (41.2%/v16.2%; p=0.003; OR=3.35) and obesity (58.8%/v32.6%;p=0.040; OR=2.96), advanced adenoma/adeno/carcinocarcinoma was associated with F4 fibrosis (20.0%/vs1.2%;p=0.012; OR = 2.24); hyperuricemia/gout (40.0%/v10.3%; p=0.004; OR=4.01) and dilated cardiomyopathy (20.0%/v1.0%;p=0.003; OR = 2.94).

Conclusion: More than 1/4 of the patients with NAFLD have colorectal polyps, being 16.5% adenoma and 4.8% advanced adenoma/adeno/carcinocarcinoma. Obese and liver steatosis are independent risk factors for colorectal adenoma. Liver fibrosis, especially F4 is an independent risk factor for all types of colorectal polyps.

Disclose of Interest: All authors have declared no conflicts of interest.

P1319 "SUBTRACTED ADULTHOOD MASS INDEX" (SAAMI) - A NEW INDEX TO PREDICT NAFLD RISK IN NON-OBSE individuals

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Introduction: Non-alcoholic fatty liver disease (NAFLD) is a common clinicopathological picture of the liver that may progress from simple steatosis to NASHi, cirrhosis and hepatocellular carcinoma(HCC). Although obesity is accepted as the main risk factor for NAFLD, non-obese individuals are often diagnosed with NAFLD suggesting that high BMI may not be a "sine qua non" for the presence of NAFLD. Recent studies suggested that there might be a correlation between weight gain and metabolic diseases.

Aims & Methods: In our research; the relationship between NAFLD in non-obese individuals and the amount of weight gain during adulthood was investigated and a new index that is different from BMI was proposed. 362 individuals were included in the survey. The subjects were selected among patients who had abdominal ultrasonography(UUSG) in our clinic, during the last 6 months. A 5% increase in echogenicity detected in the UUSG was defined as the diagnostic
Results: Among 362 participants (169 [46.7%] were men with an average age of 44.81 ± 10.73. 78 [21.6%] participants were women, the average age of the group being 46.78 ± 9.12. Out of 78 obese individuals 73 (93.5%) were NAFLD(+). The average age of the 284 (78.4%) non-obese subjects was 44 ± 11.05. Among non-obese people 169 (59.5%) were NAFLD(+). The sensitivity was 78.8%, specificity was 65.8%, PPV was 76.9% and NPV was 75.7%.

Conclusions: We found that the cut-off value was set as SAMI 4 kg/m², sensitivity was 76.3%, specificity was 84.3%, positive predictive value (PPV) was 84.3%, negative predictive value (NPV) was 83%.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P3210 CHARACTERIZATION OF CISPLATIN RESISTANCE IN HEPATOMA CELL LINES

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Introduction: cisplatin-treated cancer patients often face therapy failure caused by acquired cisplatin resistance. Development of resistance was previously associated with modulation of transporters mediating cellular copper metabolism. Overexpression of the Wilson disease protein ATP7B, a TGN copper transporter, was proposed to increase cellular copper efflux.

Aims & Methods: The human hepatoma cell line HepG2 was compared with a HepG2/varient lacking functional ATP7B expression (KO) in regard to cell sensitivity. Hepatoma cell lines were generated that displayed cisplatin resistance by stepwise increasing cp concentrations. Cells were examined via growth, cell viability assays (MTT), and analysed for apoptosis (Annexin V staining). Inducedly coupled plasma mass spectrometry was used to determine intracellular cp level. Gene expression analysis (RT-qPCR) was carried out to determine the expression of various transporters. Overexpression of individual transporter genes and siRNA treatment were used for confirmation of the data.

Results: Treatment of HepG2 and KO cells with various cp concentrations revealed no significant differences in cell viability and intracellular cp accumulations. None of the KO cells that lack ATP7B can adapt to high cp levels, a cp resistant subline (CpR) was generated. Cp resistance was confirmed by viability assays and intracellular cp load. Gene expression analysis of more than 16 transporters demonstrated an upregulation of metallothionein 1 (MTT: 8.91 ± 4.4) and a downregulation of organic cation transporter 3 (OCT3: −5.17 ± 2) compared to control cells. Weaning and regrowth of the CpR cell line showed the presence of cp revealed a stable phenotype of resistance in the cells. Downregulation of OCT3 was identified to be permanent while MT1 upregulation was transient and rapidly induced by cp. Overexpression of OCT3 in CpR cells resulted in loss of cp resistance to a level of untreated cells indicating that downregulation of OCT3 is responsible for acquired cp resistance.

Conclusion: We suggest that ATP7B does not seem to be involved in cp resistance, at least in hepatic cells. OCT3 represents a novel marker of cp resistance. OCT3 expression could be a valuable tool for improved prognosis of cisplatin therapy.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P3211 AUTOMATED RAPID DETECTION SYSTEM USING THE QUENCHING PROBE METHOD FOR DETECTING RS738409 POLYMORPHISM IN PNPLA3 IN NONALCOHOLIC FATTY LIVER DISEASE

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Introduction: Recent studies have shown that the single nucleotide polymorphism (SNP) rs738409 in the PNPLA3 gene is strongly associated with severity of nonalcoholic fatty liver disease (NAFLD).1,2 However, the traditional direct sequencing (DS) method is time-consuming and labor-intensive. The i-densyTM (ARKRAY, Inc.), which is based on the quenching probe (QP) method, automatically detects target genes in blood samples by fluorescence quenching within 90 min.3

Aims & Methods: The current study compared the QP and DS methods for detecting SNPs in the PNPLA3 gene, and established the impact of the genotype on prognosis of NAFLD. We enrolled 107 patients with fatty liver irrespective of etiology. We used the i-densy fully automated genotyping system with QP. The requisite number of tips, reaction tubes, reagent packs and blood samples were set in their designated places. The forward and reverse polymerase chain reaction (PCR) primers and guanine QP were 5’-ctctctctctctgttacag-3’, 5’-ggtagagc- cacctagg-3’, and 5’-ggtagagcagagcagacatc-3’, respectively. PCR consisted of initial denaturation for 1 min at 95°C, and 50 cycles of denaturation at 95°C for 1 s and annealing at 61°C for 30 s. After completion of the PCR, we analyzed melting temperatures. The SNP genotypes were determined by monitoring the change in fluorescence intensity with increasing temperature. The results obtained with the QP method were compared with those obtained with the conventional DS method. Then, we analyzed 73 patients with NAFLD according to PNPLA3 genotypes CC, CG and GG (21, 28.8%) and 24 (32.9%) and 28 (38.4%), respectively. Serum ALT, APRI and Fibroscan value according to PNPLA3 genotypes CC, CG and GG were 26 (14–59), 33 (11–113) and 46 (17–175) U/L, 0.3 (0.1–1.0), 0.5 (0.2–6.8) and 0.7 (0.2–3.1), and 4.4 (2.7–25.1), 5.6 (2.5–26.5) and 6.6 (3.6–38.6) kPa, respectively (p = 0.001, p = 0.001 and p = 0.003 by Jonckheere–Terpsta test). HCC developed in none of the patients with CC genotype, one (4.2%) with CG and four (14.3%) with GG. The cumulative HCC development rate in patients with GG genotype was significantly higher than that in those with CC + CG genotype (p = 0.043 by log-rank test).

Conclusion: The i-densy using the QP method can automatically, quickly and easily identify PNPLA3 genotypes in real-world clinical settings. These findings indicate the feasibility of personalized medicine for NAFLD.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
P1322 EFFECT OF ORLISTAT ON TOTAL LIVER FAT QUANTIFICATION AT NOVEL MAGNETIC RESONANCE IMAGING IN OBSESE PATIENTS WITH NON-ALCOHOLIC STEATOHEPATITIS: INTERIM ANALYSIS OF A PROSPECTIVE, RANDOMIZED, SINGLE-CENTER, OPEN-LABEL TRIAL

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Introduction: Orlistat is an effective pharmacologic weight loss treatment by inhibiting intestinal lipase to reduce dietary fat absorption. Previous studies have suggested that it lowers liver fat by ultrasound or semi quantitative histological scoring in non-alcoholic fatty liver disease (NAFLD).

Aims & Methods: We aimed to examine the efficacy of orlistat versus placebo in reducing liver fat content by the magnetic resonance imaging (MRI) based on chemical shift imaging. A total of 51 NAFLD patients diagnosed by MRI were randomized to receive twice-daily 120mg oral Orlistat or placebo for 6 months, among them 30 (14 in the Orlistat group and 16 in the placebo group) were included in the interim analysis. Both groups received Clinical parameters, laboratory tests and liver fat content were measured at baseline and 6 months including body mass index (BMI), waist hip ratio (WHR), liver enzymes, haemoglobin A1c, total cholesterol (CHOL), serum triglycerides (TG), enzymes, haemoglobin A1c, total cholesterol (CHOL), serum triglycerides (TG), hemoglobin, liver enzymes and liver fat percentage. The primary outcome was a change in liver fat quantified by MRI which is based on Dixon technique with two-point chemical shift-based fat-water separation method.

Results: At 6 months, among them 30 (14 in the Orlistat group and 16 in the placebo group) were included in the interim analysis. Both groups received Clinical parameters, laboratory tests and liver fat content were measured at baseline and 6 months including body mass index (BMI), waist hip ratio (WHR), liver enzymes, haemoglobin A1c, total cholesterol (CHOL), serum triglycerides (TG), enzymes, haemoglobin, liver enzymes and liver fat percentage. The primary outcome was a change in liver fat quantified by MRI which is based on Dixon technique with two-point chemical shift-based fat-water separation method. The chi-squared and paired t test were used to compare mean differences between liver fractions between two groups. Results: At 6 months, among them 30 (14 in the Orlistat group and 16 in the placebo group) were included in the interim analysis. Both groups received Clinical parameters, laboratory tests and liver fat content were measured at baseline and 6 months including body mass index (BMI), waist hip ratio (WHR), liver enzymes, haemoglobin A1c, total cholesterol (CHOL), serum triglycerides (TG), enzymes, haemoglobin, liver enzymes and liver fat percentage. The primary outcome was a change in liver fat quantified by MRI which is based on Dixon technique with two-point chemical shift-based fat-water separation method. The chi-squared and paired t test were used to compare mean differences between liver fractions between two groups.

Conclusion: Orlistat did significantly decrease liver fat in NAFLD patients with non-alcoholic steatohepatitis.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference
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P1323 LONG-TERM COPPER EXPOSURE OF HEPATIC CELLS LACKING FUNCTIONAL ATP7B

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Introduction: Copper transporter ATP7B is essential for hepatic Cu homeostasis and its loss of function in the inherited autosomal recessive disorder Wilson Disease (WD). Symptoms of WD are i.e. elevated Cu accumulation in liver and brain. Understanding of molecular mechanisms involved in Cu homeostasis is essential to improve therapeutic options. The molecular impact following long-term Cu exposure in hepatic cells lacking functional ATP7B has not been explored.

Aims & Methods: HepG2 cells lacking functional ATP7B (KO) were used for generation of a copper resistant subline (CuR). Cell growth, cell viability (MTT) and intracellular Cu load (atomic absorption spectroscopy) was assessed. RT-qPCR was performed to quantify the expression of genes related to Cu homeostasis. Functional analysis of candidate genes was assessed by siRNA and drug activation (verapamil). Notably, cell viability and intracellular Cu load was not significantly affected by Cu exposure indicating that MDR1 is involved in Cu homeostasis. In addition, hepatic cells derived from a WD patient and from the rat animal model confirmed our observations.

Conclusion: Our analysis of long-term Cu exposure presents new insights in copper metabolism and suggests a new role of MDR1 in the pathogenesis of Wilson disease.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P1324 THE NONALCOHOLIC FAT LIVER DISEASE FIBROSIS SCORE IN PREDICTING FIBROSIS IN MORBIDLY OBSESE PATIENTS BEFORE BARIATRIC SURGERY: THE NONALCOHOLIC FATTY LIVER DISEASE FIBROSIS SCORE IN PREDICTING FIBROSIS IN MORBIDLY OBSESE PATIENTS BEFORE BARIATRIC SURGERY

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Introduction: Non-alcoholic fatty liver disease (NAFLD) and non-alcoholic steatohepatitis (NASH) are increasingly common cause of chronic liver diseases worldwide. Most patients with severe obesity who undergo bariatric surgery have NAFLD, which is associated insulin resistance, type 2 diabetes mellitus, hypertension, and obesity-related dyslipidemia. Identifying significant fibrosis in patients is crucial to evaluating prognosis and possible therapeutic interventions. Currently, liver biopsy is the gold standard for diagnosis of liver fibrosis.

Aims & Methods: We aimed to evaluate the NAFLD fibrosis score for the assessment of significant fibrosis in patients with morbid obesity before undergoing bariatric surgery. A 69 NAFLD patients (median BMI 47.8 kg/m2) were prospectively enrolled from June 2015 to November 2016 at one Brazilian university hospital. All patients were evaluated with routine laboratory before bariatric surgery. Age, body mass index, hyperglycemia, platelet count, albumin and AST/ALT ratio were applied to the score formula. Biopsies were interpreted by a single experienced pathologist. NAFLD and fibrosis were classified according to the NASH Clinical Research Network NAFLD activity score. Furthermore, the receiver operating characteristic curve (AUROC) was calculated for the diagnostic test.

Results: On liver biopsy, 29 patients (42%) had some degree of fibrosis, with a median FLI score of 2.2 (IQR 1.88) having significant fibrosis (F2–4). With standard thresholds the specificity for the NAFLD fibrosis score for identification of significant fibrosis was 58.9%. Using modified thresholds, the specificity could increase. For predicting significant fibrosis, for a cut-off of 1.05, the score had 46.15% sensitivity and 96.43% specificity with AUROC of 0.74.

Conclusion: The nonalcoholic fatty liver disease fibrosis score has good accuracy to identify significant liver fibrosis in morbidly obese patients subjected to bariatric surgery.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P1325 COMPARISON OF FIBROSCAN® AND FATTY LIVER INDEX (FLI) TO SCREEN FOR FATTY LIVER DISEASE IN A LARGE COHORT OF EMPLOYEES: WHERE IS THE OPTIMAL CUT OFF?

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Introduction: FLI was developed as a simple predictor of steatosis (Bedogni et al.,2006) and a cut-off value ≥60 ruled in (positive likelihood ratio [LR+] 4.3) steatosis in Italians diagnosed with ultrasound. Fibroscan®CAP is more sensitive for the diagnosis of steatosis than ultrasound. Aim of this study is to evaluate the use of Fibroscan® in comparison with FLI to screen for fatty liver disease in Austrian bank employees and to recalculate optimal FLI cut-off values. Beside weight reduction and diet EASL guidelines recommend physical activity >150 min/week for prevention and treatment of steatosis.

Aims & Methods: More than 1000 Austrian bank employees will be screened for liver diseases with Fibroscan®. A kPa value ≥7.9 (M-probe) and ≥7.2 (XL-probe) is categorized as fibrosis. Additionally Fibroscan®CAP with a cut-off value ≥248 dB/m is defined as steatosis, ≥300 dB/m in high-grade steatosis. Heavy drinkers and patients with significant liver fibrosis with Fibroscan®. A kPa value ≥7.9 (M-probe) and ≥7.2 (XL-probe) is categorized as fibrosis. Additionally Fibroscan®CAP with a cut-off value ≥248 dB/m is defined as steatosis, ≥300 dB/m in high-grade steatosis. Heavy drinkers and patients with significant liver fibrosis were identified with AUDIT and SIAC questionnaires. Weekly physical activity is classified into “none”, “≤150 min” and “> 150 min”.

Results: On average, 472 employees (age: age 35.9±8.7 (mean±SD); m:207; f:265; BMI: 25.4±4.4) have been included in this analysis. 14/482 (2.9%) employees had signs of liver fibrosis and received further investigations. Fibroscan®CAP values ≥248 dB/m are shown in 156/482 (32.4%) employees (m:91 [58%], f:65 [42%], 56/482 (11.6%) had CAP values ≥300 dB/m. Furthermore 15/156 (9.6%) patients with steatosis are heavy drinkers. FLI significantly predicts liver fibrosis (CAP values [adj-R2] = 0.29, p < 0.001) with a cut-off which indicates a large effect size. For this study population, a FLI cut-off value ≥40 (CAP ≥248 dB/m) and ≥50 (CAP ≥300 dB/m) rules in fatty liver disease with a LR+ of 4.7 (SN-84%; SP-75%); and 4.8 (SN-83%; SP-83%), respectively. An additional consideration of physical activity level in the current cohort revealed that inactivity increases the LR+ of FLI values to predict NAFLD (trendwise significant, p = 0.051), indicating lower cut-off values.
Conclusion: We conclude that FribroScan® represents an eligible tool to diagnose liver diseases in Austrian bank employees. Compared to the previous work of Bedogni et al FLI predicts fatty liver at a lower cut-off level, at least for the examined population. This difference might be due to the fact that FlibroScan®CAP is more sensitive than ultrasound.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

P1326 METABOLICOMICS IDENTIFIES PROGRESSIVE NAFLD

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Introduction: Nonalcoholic fatty liver disease (NAFLD) is an affection with increasingly prevalence worldwide, having an important impact on morbidity and mortality, especially when it associated severe fibrosis.

Aims & Methods: We aimed to assess the metabolites that are associated with fibrosis stages in NAFLD, using metabolic method. A total of 40 patients were included in the study, 30 diagnosed with nonalcoholic fatty liver disease (NAFLD) and 10 controls. Steatosis and fibrosis were assessed using Fibromax elaborated by Biopredictive (R) (Paris, France). New metabolomic techniques (high performance liquid chromatography coupled with mass spectrometry (HPLC-MS) and principal component analysis (PCA)) were used to identify final products of various metabolic pathways correlated with liver fibrosis.

Results: Of the 30 patients with NAFLD included in the study, 6 patients (20%) had severe fibrosis. The metabolomic profile identified four metabolites that are associated with severe fibrosis: 1.25(Oh)Vitamin D (p = 0.03), 1-isopenesolylbutanolamine LPE 0.0:22.6 (p = 0.05), 1-isopenesolylbutanolamine LPE 0.0:22.6 (p = 0.05), and high levels of butylen carbamino (p = 0.04). Of these, LPE was the strongest predictor of severe fibrosis (AUROC=0.795). Sensitivity (S=88.33%), specificity (Sp =78.79%), but the others metabolites were also significantly associated with severe fibrosis: vitamin D (AUROC = 0.776), butylen carbamino (AUROC = 0.737), and LPE 0.0:22.6 (AUROC = 0.768). As the metabolomics permits the evaluation of all these molecules the same time, we can use them combined in order to increase the diagnostic accuracy. In our case, the combined use of the four metabolites determined an AUROC of 0.839, with Se of 100% and Sp of 68.5%.

Conclusion: In metabolomics, we can identify patients with fatty liver and severe fibrosis that are significantly exposed to a progressive disease and a higher mortality.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1327 CHRONIC RENAL FAILURE IS ASSOCIATED WITH THE DEVELOPMENT OF NAFLD/NASH

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Introduction: Chronic renal failure (CRF) is frequently associated bone metabo- lism and osteoporosis with lowered levels of Vitamin D and/or hyperparathy- roidism particular in case of hemodialysis. Younger studies suggest an association of low vitamin D levels with non-alcoholic fatty liver disease (NAFLD) and non- alcoholic steatohepatitis (NASH), as well as metabolic syndrome, and diabetes mellitus. Unfortunately, a causality could not yet be proven.

Aims & Methods: Our aim was to identify patients on higher risk to develop NAFLD/NASH in a selected patient cohort being admitted for renal disorders.

176 patients, admitted to the department of nephrology of the University Hospital Marburg for renal disorders whose plasma vitamin D concentration, phosphate and parathormone levels and liver enzyme levels had been quantified beforehand, were enrolled and a retrospective investigation of laboratory para- meters (including electrolytes, hormones, and vitamins) and pre-existing medical conditions (including high blood pressure, diabetes, hyperlipoproteinemia, and more) followed. Appropriate statistical test were used to characterise the cohort (ANOVA; MANN-Whitney-U; FISHER-EXACT) using SPSS(TM). Other hepa- topathies were excluded. Steatosis was assessed by ultrasonography.

Results: Patients were divided into 4 groups according to plasma vitamin D levels (normal >25ng/ml; low <25 ng/ml) and transaminase levels (AST/ALT>GT >30 U/l; normal; AST/ALT<GT < 30 U/l). Low 1,25-hydroxivitamin D levels correlated significantly with high kreatinine, urea, and LDL levels, while low 25-hydroxivitamin D levels correlated with high cholesterol and triglyceride levels, suggesting a relationship between low vitamin D levels and fat metabolism disorders. Interestingly end stage renal failure (chronic hemodialysis) was signific- antly correlated with the development of NAFLD/NASH with significantly higher levels of AST/ALT and gGT, hyperparathyreodism and hyperphosphate- mia Transaminases were significantly lower if Vitamin D was supplemented

Conclusion: Vitamin D deficiency is often present in patients with kidney diseases such as chronic renal failure. Vitamin D levels are correlated to age and sex of the patient. Patients suffering from renal failure are on high risk developing NAFLD/NASH if diminished vitamin D levels are present Supplement of Vitamin D saves from NAFLD/NASH The correlation of hyperparathyreodism and NAFLD/NASH has to be further investigated in larger patient groups.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1328 NONINVASIVE DIAGNOSTICS OF NONALCOHOLIC FATTY LIVER IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

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Introduction: Usually for the determination of nonalcoholic fatty liver disease (NAFLD) there are instrumental and laboratory techniques, including ultrasound diagnosis, determination of aminotransferases, steatostest, 13C-methacetin breath test (13C-MBT). These methods in the diagnosis of NAFLD clinical forms is not specific and do not allow make difference between steatosis and steatohepatitis. The determination of NAFLD clinical forms is a priority in the prediction of further disease and choice of treatment. Steatohepatitis is the active form of NAFLD and progresses to fibrosis often with subsequent liver paren- chyma degeneration into cirrhosis. Simultaneously, steatosis could be possibly treated in the early stages of disease.

Aims & Methods: The study involved 65 patients with type 2 diabetes and cor- onary heart disease with metabolic syndrome, aged 37 to 82 years (mean age 53.82 ± 3.46), 29 men, 36 women. According to the ultrasound, the stage of fatty infiltration were differentiated by such criteria for steatosis as diffuse liver para- chyma degeneration into cirrhosis. Simultaneously, steatosis could be possibly treated in the early stages of disease.

Disclosure of Interest: All authors have declared no conflicts of interest.
P1329 NON-OBSESE FATTY LIVER DISEASE IN TYPE 2 DIABETES: NOVEL CONDITION OR SIMILAR TO TYPICAL NAFLD STATE?

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Introduction: Non-alcoholic fatty liver disease (NAFLD), the hepatic counterpart of the metabolic syndrome in close relation to obesity and encompasses a disease spectrum spanning simple steatosis through nonalcoholic steatohepatitis (NASH) with or without fibrosis, and hepatic cellular carcinoma [1]. Clearly, not all obese subjects develop NAFLD and NAFLD can also be found in non-obese patients. Globally, the reported prevalence of non-obese NAFLD varies widely, ranging from 3% to 30% [2]. Today remains unclear how patients without obesity develop NAFLD and therefore it is important to understand the clinical and pathological conditions of non-obese NAFLD.

Aims & Methods: In this study, we investigated the liver stiffness and liver fat content in addition to other clinical and metabolic parameters in type 2 diabetes patient with non-obese and obese NAFLD detected on ultrasonography (US). In this cross-sectional study, 245 T2D patients with age of 40–80 years from the Kyiv City Clinical Endocrinology Center were selected. Inclusion criteria were: age over 18 years, presence of T2D in association with fatty liver disease. The diagnosis of fatty liver was based on the results of abdominal ultrasonography, which was done by trained technicians with Ultima PA (Radmir Co., Kharkiv, Ukraine). Of 4 known criteria (hepatorenal echo contrast, liver brightness, deep attenuation, and vascular blurring), the participants were required to have hepatorenal contrast and liver brightness to be given a diagnosis. According to body mass index (BMI) variable patients were assigned else to NAFLD group (n = 157, BMI >30.0 kg/m²) or to non-obese NAFLD (n = 88, BMI <30.0 kg/m²) group.

The ultrasound liver stiffness value (LS) measured by the Shear Wave Elastography (SWE) in every patient, and a median value was calculated, the result being measured in kPa. Also, in all patients we calculated fatty liver index (FLI). FLI a validated prediction score for hepatic steatosis severity designed Bedogni et al [3]. Changes in transaminases activity, serum lipids and cytokines (TNF-α, IL-1β, IL-6, IL-8, INF-γ) levels were evaluated.

Results: Non-obese NAFLD patient had higher LS (7.52 ± 0.2 vs 6.87 ± 0.9, p = 0.001) values measured by SWE, which were accompanied with increased transaminases activity; for ALT –42.1 ± 1.3 vs 35.8 ± 1.28 (p = 0.028) and for AST –40.8 ± 2.68 vs 34.31 ± 1.03 (p = 0.016) respectively. In contrast to non-obese group in NAFLD group had significantly higher FLI (86.59 ± 1.09 vs 68.06 ± 1.96, p < 0.001). Markers of chronic systemic inflammatory status were significantly higher in non-obese NAFLD as compared to non-obese patient: IL-1β 44.64 ± 2.0 vs 31.02 ± 1.78 (p < 0.001); TNF-α 54.11 ± 2.20 vs 42.28 ± 1.81 (p = 0.001); IL-8 29.18 ± 1.27 vs 22.05 ± 0.99 (p = 0.001) and INF-γ 195.60 ± 9.47 vs 132.47 ± 7.54 (p = 0.016) respectively. Changes of IL-6 between two groups were not significant.

Conclusion: At present, the clinical-laboratory characteristics of non-obese NAFLD are not fully understood. Therefore, we found that non-obese NAFLD associated with higher liver stiffness values and transaminases activities. On the other hand, patient with obese NAFLD are characterized with more pronounced liver fat content and elevation of markers of chronic systemic inflammatory state.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1330 CHARACTERIZATION OF LEAN INDIVIDUALS WITH NON-ALCOHOLIC FATTY LIVER DISEASE: RESULTS OF A COHORT STUDY

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Introduction: Non-alcoholic fatty liver disease (NAFLD) is usually considered as the hepatic manifestation of metabolic syndrome and obesity. However, a subgroup of NAFLD patients are lean. Some studies have reported severe liver fibrosis in lean NAFLD and these patients are still at risk for development of liver cirrhosis.

Aims & Methods: This study aimed to investigate the prevalence and risk factors of lean NAFLD in a cluster of Iranian population. Study population was recruited from Kavir cohort study which has been started from 2006 in Kavar town, a small town near Shiraz. The study sampling was performed between September 2011 and September 2015 among adult subjects (age > 18 years) who underwent voluntary hepatobiliary ultrasound. NAFLD was diagnosed using the presence of ground and absence of chronic liver diseases such as autoimmune hepatitis, hepatitis B or C viruses induced hepatitis, hepatobiliary cancers, Wilson’s disease, > 10 g/day alcohol consumption, and receiving some specific medications known to cause hepatic steatosis (like amiodarone, valproic acid, etc). Lean individuals were defined as those with body mass index (BMI) < 25 kg/m². Student’s-t test was used for comparisons of continuous variables and Chi-square test was used for comparison of categorical variables. Receiver operating characteristics (ROC) curve analysis using area under curve (AUC) was used for analysis of optimal cutoff values for BMI and waist circumference in association with lean NAFLD.

Results: 1343 individuals were included. 165 individuals (12.3%) was diagnosed to have NAFLD. 129 individuals (9.6%) had mild NAFLD and 36 individuals (2.7%) had moderate NAFLD. None of the participants had severe NAFLD. In univariate analysis, history of diabetes mellitus (DM) (OR = 2.25; 95% CI: 1.15–4.40, P = 0.015) and metabolic syndrome (OR = 2.80; 95% CI: 1.74–4.48, P < 0.001) were associated with NAFLD. Higher BMI and waist circumference, higher serum lipids (triglycerides), higher serum alanine aminotransferase (ALT) and cholesterol, fasting plasma glucose (FPG) and alanine aminotransferase (ALT) were associated with NAFLD (P < 0.05). In multivariate regression analysis, higher BMI and waist circumference, higher serum ALT, FPG and cholesterol were independent predictors of NAFLD in our study population (Table). A cutoff value of 22.3 kg/m² for BMI was predictor of NAFLD (sensitivity = 72%; specificity = 60%; AUC = 0.728, P < 0.001). A cutoff value of 79.5 cm for waist circumference was predictor of NAFLD in our study population (sensitivity = 80%; specificity = 68%; AUC = 0.753, P < 0.001).

Table: Multivariate regression analysis showing independent risk factors for lean NAFLD.

<table>
<thead>
<tr>
<th>Odds Ratio (OR)</th>
<th>95% Confidence Interval (CI)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI</td>
<td>1.27</td>
<td>1.106–1.459</td>
</tr>
<tr>
<td>Waist circumference</td>
<td>1.078</td>
<td>1.047–1.112</td>
</tr>
<tr>
<td>ALT</td>
<td>1.018</td>
<td>1.004–1.033</td>
</tr>
<tr>
<td>Cholesterol</td>
<td>1.008</td>
<td>1.003–1.013</td>
</tr>
<tr>
<td>FPG</td>
<td>1.010</td>
<td>1.003–1.017</td>
</tr>
</tbody>
</table>

Conclusion: Lean NAFLD was prevalent in our study population and was associated with metabolic risk factors. BMI and waist circumference can be used for prediction of NAFLD.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

P1331 ASSESSING BAVENO VI CRITERIA WITH A NEW POINT-SHEAR WAVE ELASTOGRAPHY TECHNIQUE: THE BAVELASTPQ STUDY

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Introduction: While some studies have evaluated the ability of new “real-time” elastography devices such as 2-D Shear Wave Elastography (SWE) and Virtual Touch Quantification (ARFI) in predicting the presence of high-risk gastroesophageal varices, no study has explored the potential role of another point-SWE technique, ElastPQ, in the assessment of clinically significant portal hypertension.

Aims & Methods: The aim of our study was to identify a liver stiffness cut-off value measured by ElastPQ and/or laboratory parameters that could help identify patients who can safely avoid screening endoscopy and similarly to the recently proposed Baveno VI criteria which recommends a liver stiffness value <20kPa measured by transient elastography in combination to a platelet count >150,000/μl. Data were collected on 1385 patients who underwent ElastPQ measurement from January 2013 to January 2016 in our Department. Inclusion criteria were a liver stiffness value ≥7 kPa and an upper gastrointestinal endoscopy within 12 months, with a diagnosis of compensated chronic liver disease. We choose this specific liver stiffness cut-off value in order to highlight early advanced fibrosis and/or cirrhosis, based on the limited literature available on this specific elastographic technique. Exclusion criteria were history of decompensated liver disease, evidence of portal-sinus mesenteric vein thrombosis and non-cirrhotic portal hypertension. Varices were graded as low risk (grade <2) or high risk (grade ≥2).

Results: The study included 184 patients (114 [62%] hepatitis C, and 160 [87%] Child-Pugh A). Varices were present in 36% cases, with 10% prevalence of high-risk varices. According to ROC curve analysis liver stiffness measurement and
platelet count were evaluated as predictors of high-risk varices. Overall 74/184 (40%) met the new “BAVElastPQ” criteria (that is, liver stiffness <12 kPa and platelet count >150,000/μl). Within this group 11/63 (17%) had any grade of varices and only 1/73 (1%) had high-risk varices. The BAVElastPQ criteria gave sensitivity of 0.95, specificity of 0.44, a positive predictive value of 0.16 and a negative predictive value of 0.98. The AUROC for liver stiffness and platelet count was 0.81 and 0.76, respectively.

Conclusion: The BAVElastPQ criteria correctly identified 99% of patients with high-risk varices. By applying such criteria we could have potentially avoided 40% surveillance endoscopies in our cohort. To our knowledge this is the first study that evaluated the potential role of a new s-PWE technique such as ElastPQ in the non-invasive assessment of clinically significant portal hyperten-
sion, similarly proposed Baveno VI criteria though using ElastPQ as an alternative to transient elastography.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1333 PROTON PUMP INHIBITORS INTAKE NOT ASSOCIATED WITH HEPATIC ENCEPHALOPATHY IN CIRRHOTIC PATIENTS

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Introduction: Proton pump inhibitors (PPI) are commonly prescribed and predis-
spose to small bowel bacterial overgrowth. Hepatic encephalopathy is a frequent complication of cirrhosis and is associated with intestinal dysbiosis.

Aims & Methods: This study aimed to identify a possible association between PPI intake and hepatic encephalopathy development in cirrhotic patients. Retrospective analysis of consecutive cirrhotic patients hospitalized in two Gastroenterology Departments over 3.5 years. Collection of clinical data, PPI intake, infection and hepatic encephalopathy at hospitalization. Statistical ana-
lyses: Pearson χ² and McNemar, HPS1.21, considering clinical significant definition of hepatic encephalopathy. Results: 386 patients, 321 males (83.2%), mean age 60.3 ± 12.1 years. Main etiol-
ologies of cirrhosis were alcohol (67.4%), alcohol plus hepatitis C (16.3%) and hepatitis B virus (5.2%). Hepatic encephalopathy was present in 222 (57.5%) of the patients and 26.9% had PPI intake. In univariate analysis hepatic encephalopa-
thapy was associated with infection (p < 0.001), gastrointestinal bleeding (p < 0.001) and Model for End-Stage Liver Disease (MELD) (p < 0.001). There was no association between hepatic encephalopathy and PPI intake (p = 0.057), gender (p = 0.228) or age (p = 0.352). In multivariate analysis, hepato-
ena cele fecal encephalopathy maintained association with infection (p < 0.001), gastroin-
testinal bleeding (p < 0.001) and MELD score (p = 0.001).

Conclusion: In our series, PPI intake was not associated with hepatic encepha-
lopahy development in cirrhotic patients.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

P1334 CLINICAL IMPACT OF MULTIDRUG-RESISTANT BACTERIAL INFECTIONS IN LIVER CIRRHOSIS

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Introduction: The incidence of bacterial infections in cirrhotic patients is signifi-
cantly higher than that observed in general population, being one of the most important causes of decompensation. In theory, the final result of an infectious disease depends of three major factors: the antibiotic resistance of the bacteria and the virulence of the organism, the immune status, age, diet and stress. There are conflicting results regarding the incidence of multidrug-resistant bacteria or MDR bacteria regarding the 30 (p = 0.801) and the 90-day (p = 0.761) mortality rate. In the multivariate analysis, elevated BUN and bilirubin, presence of bacterial infection and lower albumin, sodium and SP02 were independently associated with 30 and 90-day mortality. Higher INR and age were indepen-
dently associated with 90-day mortality.

Conclusion: The presence of bacterial infection, independently of the antibiotic treatment profile, was associated with a worse prognosis in cirrhosis. In patients with documented infections, no difference was noticed between non-MDI, non-MDR bacteria or MDR bacteria regarding the 30 (p = 0.801) and the 90-day (p = 0.525) mortality rate. In the multivariate analysis, elevated BUN and bilirubin, presence of bacterial infection and lower albumin, sodium and SP02 were independently associated with 30 and 90-day mortality. Higher INR and age were indepen-
dently associated with 90-day mortality.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
Finogold JA, Manisty CH, Goldacre B, Barron AJ, Francis DP. What proportion of symptomatic side effects in patients taking statins are genuinely caused by the drug? Systematic review of randomized placebo-controlled trials to aid indi-
In this study, we aimed to evaluate the applicability of the Baveno VI criteria in a cohort of known compensated HCV liver cirrhosis patients, to see how often we misclassify the presence of esophageal varices (EV). Material and method: We prospectively recruited 392 patients with cirrhosis from September 2015 to September 2016, who underwent all available non-invasive tests for liver cirrhosis. The EV presence was also confirmed in controls. The diagnostic performance of the Baveno VI criteria was evaluated using ROC analysis. The Baveno VI criteria correctly classified 80% of patients, with a sensitivity of 56.9%, specificity of 84.6%, positive predictive value (PPV) of 40.7%, negative predictive value (NPV) of 95.1%, and an area under the curve (AUC) of 0.831. Conclusion: The Baveno VI criteria are useful for predicting EV, with a good diagnostic performance in our cohort of HCV patients with cirrhosis. However, we should be cautious in the interpretation of the Baveno VI criteria as they may misclassify the presence of EV in a small proportion of patients.

Introduction:

The place of noninvasive techniques for the prediction of presence of portal hypertension in patients with liver cirrhosis is one of the current research activities.

Methods:
The aim of this study was to evaluate the applicability of the Baveno VI criteria in a cohort of known compensated HCV liver cirrhosis patients, to see how often we misclassify the presence of esophageal varices (EV). Material and method: We prospectively recruited 392 patients with cirrhosis from September 2015 to September 2016, who underwent all available non-invasive tests for liver cirrhosis. The EV presence was also confirmed in controls. The diagnostic performance of the Baveno VI criteria was evaluated using ROC analysis. The Baveno VI criteria correctly classified 80% of patients, with a sensitivity of 56.9%, specificity of 84.6%, positive predictive value (PPV) of 40.7%, negative predictive value (NPV) of 95.1%, and an area under the curve (AUC) of 0.831. Conclusion: The Baveno VI criteria are useful for predicting EV, with a good diagnostic performance in our cohort of HCV patients with cirrhosis. However, we should be cautious in the interpretation of the Baveno VI criteria as they may misclassify the presence of EV in a small proportion of patients.

Disclosure of Interest:

All authors have declared no conflicts of interest.

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P1335 IN HOW MANY PATIENTS WE WILL MISDIAGNOSE ESOPHAGEAL VARICES BY USING THE BAVENO VI CRITERIA? S.A. Popescu1, R. Lupsoraru2, R. Sirli1, M. Danila1, L. Ghereghe, A. Seicean1, A. Trifan1, M. Curescu1, A. Goldis1, L. D. Sundulescu3, C. Cijevschi Prelipcean1, C. Stanciu1, C. Brise1, S. Iacob1, L. S. Iacob2

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Introduction:

Non-invasive fibrosis scores (NIFs) are increasingly replacing liver biopsy (LB) for estimation of liver fibrosis. Only limited studies have evaluated the subgroup probably with EV, the Baveno VI criteria had PPV 40.7% and thrombocytes 150,000/mm3, was compound of 60 patients. Using these criteria we correctly classified 80% patients, with a Se 56.9%, PPV 44.7%, NPV 78.4%. Conclusion:

By using the Baveno VI criteria in patients with liver cirrhosis for the prediction of presence of esophageal varices, we can misclassify only 20% of patients.

Disclosure of Interest:

S.A. Popescu: I hereby confirm that I have received financial support (congress travel and speaker fee) from Philips, Siemens, General Electric, Abbvie, Zentiva, R. Sirli: I hereby confirm that I have received financial support (congress travel and speaker fee) from Philips, Siemens, General Electric, Abbvie, Zentiva, L. S. Iacob: I hereby confirm that I have received financial support (congress travel and speaker fee) from Philips, Siemens, General Electric, Abbvie, Zentiva.

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P1336 COMBINED RADIOLOGIC-BLOOD PARAMETERS AND NON-INVASIVE FIBROSIS SCORES IN PREDICTING OUTCOMES IN CHRONIC HEPATIS C T. Nuzum1, M. Hussey1, T. Khanna2, E. Macgregor2, J. Olanji2, C. Tersaruolo2, H. Bresil1, D. Menamer2, R. Lupusoru1, R. Sirli1, M. Danila1, L. Gheorghe2, A. Seicean3, C. Andree4, C. Brisc7, S. Iacob2, I. Sporea1

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Introduction:

CRBPs had higher accuracy for prediction of cirrhosis and EV, while NIFs had higher accuracy for predicting decompensation (Table 1). The highest AUROCs were seen for FIB-4 score for predicting cirrhosis (AUROC = 0.784) and EV (AUROC = 0.885) and with FIB-4 score for decompensation (AUROC = 0.854). At a cut of 1200 PSI had sensitivity of 87.2% and specificity of 73% for predicting cirrhosis and at a cut of 1100 PSI had sensitivity of 89% and specificity of 85% for predicting EV. At a cut of 2.5, FIB-4 had a sensitivity of 82.5% and specificity of 80.1% in predicting decompensation. Conclusion: CRBPs predict cirrhosis and development of esophageal varices with high accuracy. Some of the blood derived NIFs have high accuracy in predicting decompensation post antiviral treatment. Application of these simple scores may help in non-invasive screening of patients at high risk for development of esophageal varices and decompensation after antiviral treatment.

Disclosure of Interest:

All authors have declared no conflicts of interest.

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P1337 A SMART APPROACH TO THE DIAGNOSIS OF MINIMAL HEPATIC ENCEPHALOPATHY A. Trifan4, M. Curescu5, A. Goldis1, L. D. Sandulescu6, C. Cijevschi Prelipcean7, C. Stanciu4, C. Brisc7, S. Iacob2, I. Sporea1

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Introduction:

Minimal Hepatic Encephalopathy (MHE) is present in more than 30% of patients with chronic liver disease (CLD) and is associated with a worse prognosis including a higher incidence of falls, RTAs and overall mortality. Detection of MHE is often difficult due to time constraints associated with the current gold standard, the psychometric hepatic encephalopathy score (PHES), which includes five paper-based tests. A smartphone application (EncephalApp Stroop Test) has been suggested as a viable alternative.

Aims & Methods:

We aimed to validate the use of the EncephalApp Stroop Test as a screening tool for MHE in an Irish population. CLD patients and healthy controls were recruited from outpatients. CLD patients were identified based on clinical and radiological evidence. Written consent was obtained. Exclusion criteria: cognitive impairment from any other cause, colour-blindness or dyslexia. Baseline demographics, level of education and medical history were obtained, and a Child-Pugh score was calculated where relevant. Each patient performed the PHES test and the Stroop test. Outcomes included the time taken to perform each test as well as the total PHES, the Stroop on off time and time taken to complete 5 correct runs on the Stroop App. Results were analysed using the t-test and the Chi-square test to determine if there was a difference between the groups. Receiver Operating Characteristic (ROC) analysis was used to determine the best cut-off for each test. Results:

A total of 96 patients (51 males) were recruited. Overall, the mean age was 51.7 ± 16.6 years; mean years spent in education 13.8 ± 4.2. In all there were 35 CLD and 61 healthy controls. While there was no difference in age or years spent in education, there were more men in the CLD group compared to the controls, 23/35 (66%) vs. 28/61 (46%), p=0.06. Within the CLD cohort, 30 (86%) patients were Child-Pugh class A, 4 (11%) were class B and 1 (3%) was class C. As expected, more CLD patients had a positive PHES, 4/35 (11%) vs. 3/ 61 (5%). Overall, correlation between the two tests was poor, 7 (7%) participants had a positive PHES, while 47 (49%) had a positive Stroop test (k=0.1516). Among controls, 27 (44%) had a positive Stroop test, while 3 (5%) had a positive PHES (k=0.1223). Similarly, 20 (57%) CLD patients had a positive Stroop test and 4 (11%) had a positive PHES (k=0.1765). Regarding the Stroop test, the mean time taken to complete 5 correct runs was significantly higher in CLD patients, mean 117.9 s [58.5–217.8 s] vs. 101.2 s [55.3–218.6 s], p=0.02. However, mean Stroop on off times were similar, 198.4 s [102.6–307.7 s] in the CLD cohort versus 187.9 s [101.2–420.9 s] in the control group. Of note, CLD patients with a positive PHES had a significantly higher Stroop on off time compared to those with a negative PHES, mean 260 vs. 190 s, p=0.02. Among controls, 18/47 (38%) gave a Stroop on off time > 187.5 s as a positive cut-off for the test, sensitivity = 100%, specificity = 59%. In total, 39 patients had an on off time > 187.5, 18 (51%), 2 fewer false positives, in the CLD group, and a slightly better correlation (k=0.21). Among controls, PHES took 20 minutes to complete, while the Stroop test took 7 minutes. Older age and completed years of education correlated with a poorer performance on the Stroop test (r=-0.62, p<0.0001 and r=-0.322, p<0.0001, respectively). However, neither age nor years of education correlated with performance on the PHES (r=-0.087, r=0.12, respectively).
**Abstract: P1336. Table 1:** Predictive Accuracy of Different Combined Radiological and Blood Parameters and Non-invasive Fibrosis Scores for Predicting Cirrhosis, Development of Esophageal Varices and Decompensation

<table>
<thead>
<tr>
<th>Test</th>
<th>PHES+</th>
<th>PHES -</th>
<th>Stroop+</th>
<th>Stroop -</th>
<th>Kappa</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients</td>
<td>7</td>
<td>89</td>
<td>59</td>
<td>57</td>
<td>0.107</td>
</tr>
<tr>
<td>MLB</td>
<td>4</td>
<td>31</td>
<td>18</td>
<td>17</td>
<td>0.240</td>
</tr>
</tbody>
</table>

**Results:** A community of 37 operational taxonomic units (OTUs) was sufficient to pinpoint characteristic features of the microbiome before and after the intervention. Within this predictive community, three OTUs were found to be differentially abundant: *Lactobacillus brevis* and *Lactococcus lactis* increased significantly and *Enterococcus durans* decreased significantly in the probiotic group. Zonulin normalized in 20% of patients in the probiotic group. Predicted metagene functions (assessed by PICRUSt) and calprotectin did not show any differences during intervention.

**Conclusion:** In conclusion, a six months intervention with a multispecies probiotic enriched the microbiome of cirrhotic patients with probiotic bacteria. Additionally, the abundance of *Enterococcus durans* was reduced and the gut barrier was strengthened.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**P1338 MULTISPECIES PROBIOTIC ENRICHES THE MICROBIOME WITH LACTOBACILLUS AND LACTOCOCCUS AND REDUCES ENTEROCOCCUS ABUNDANCE IN PATIENTS WITH LIVER CIRRHOSIS: RESULTS OF A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL**

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**Introduction:** Cirrhosis is accompanied by significant changes of the intestinal microbiome including the overgrowth of the intestine with potential pathogens that can translocate through a weakened gut barrier and cause severe infections. We hypothesized that probiotic bacteria repress intestinal pathogen growth and for gut permeability and intestinal inflammation, respectively.

**Results:** Development of 37 operational taxonomic units (OTUs) was sufficient to pinpoint characteristic features of the microbiome before and after the intervention. Within this predictive community, three OTUs were found to be differentially abundant: *Lactobacillus brevis* and *Lactococcus lactis* increased significantly and *Enterococcus durans* decreased significantly in the probiotic group. Zonulin normalized in 20% of patients in the probiotic group. Predicted metagene functions (assessed by PICRUSt) and calprotectin did not show any differences during intervention.

**Conclusion:** In conclusion, a six months intervention with a multispecies probiotic enriched the microbiome of cirrhotic patients with probiotic bacteria. Additionally, the abundance of *Enterococcus durans* was reduced and the gut barrier was strengthened.

**Disclosure of Interest:** All authors have declared no conflicts of interest.
Rejection episodes (OR = 1.38; 95% CI: 0.47–4.1, P = 0.129) and acute kidney injury (OR = 0.96–1.84; P = 0.07) after liver transplantation were not statistically different in patients with and without DM. Using Kaplan-Meier method, mean post-liver transplant survival was 50.94 ± 0.67 months in cirrhotic patients without DM and 45.26 ± 1.46 months in cirrhotic patients with DM (P < 0.001). Post-liver transplant survivals at 6 months, 1 year and 4 years were outlined in Table. In patients with DM, presence of hepatocellular carcinoma (HCC) (OR = 4.81; 95% CI: 1.64–9.78, P = 0.002), acute kidney injury within 30 days after transplant (OR = 2.05; 95% CI: 1.02–4.10, P = 0.042) and pre-transplant PVT (OR = 2.51; 95% CI: 1.16–5.14, P = 0.019) were independent predictors of mortality after liver transplantation.

Table: Post-liver transplant survival at 6 months, 1 year and 4 years in patients with and without DM

<table>
<thead>
<tr>
<th>Survival Period</th>
<th>With Diabetes</th>
<th>Without Diabetes</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 months</td>
<td>81% ± 2.5%</td>
<td>90.6% ± 1.1%</td>
</tr>
<tr>
<td>1 year</td>
<td>79.1% ± 2.6%</td>
<td>87.8% ± 1.2%</td>
</tr>
<tr>
<td>4 year</td>
<td>75.9% ± 2.8%</td>
<td>85.4% ± 1.3%</td>
</tr>
</tbody>
</table>

Conclusion: Diabetes mellitus is prevalent in patients with liver cirrhosis especially among those with NASH. Patients with DM may have lower post-transplant survival and need more intense follow-up.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P3140 VALIDATION OF THE BAVENO VI CRITERIA ON A COHORT OF CIRRHOTIC PATIENTS

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Introduction: The Baveno VI guidelines propose that cirrhotic patients with a liver stiffness measurement (LS) < 20 kPa and a platelet count > 150,000/L can avoid screening endoscopy as their combination is highly specific for excluding clinically significant varices.

Aims & Methods: The aim of the study was to validate the Baveno VI criteria. We did a retrospective study, from 2009–2014. We took all the patients with transient elastography data. Inclusion criteria was a LS < 12 kPa and an upper gastrointestinal endoscopy within 12 months, with a diagnosis of chronic liver disease. Varies were graded as low risk (grade < 2) or high risk (grade ≥ 2).

Results: The study included 774 patients (hepatitis C virus 40.5%, hepatitis B disease: 59/774 (7.6%) met the Baveno VI criteria. The Baveno VI criteria gave a correct appoint 85.3% of patients who can avoid screening endoscopy as their combination is highly specific for excluding clinically significant varices.

Disclosure of Interest: All other authors have declared no conflicts of interest.

P3141 MORTALITY PREDICTING MODEL IN LIVER CIRRHOSIS PATIENTS

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Introduction: Cirrhotic patients very often need to be hospitalized and it is known that they have a higher mortality rate. We aimed to establish a mortality predicting model for cirrhosis patients.

Aims & Methods: The aim of the study was to assess the factors associated with mortality among cirrhotic patients and to create a new score for predicting mortality. The study was retrospective, and we included all hospitalized patients with a diagnosis of liver cirrhosis within a period of 7 years. We divided them in two cohorts, an initial group, which was analysed; and a control group, in which we validated the score. We performed univariate and multivariate analysis in order to determine a prediction model for mortality.

Results: A total of 1163 cirrhotic patients were included. In-hospital mortality rate was 10%. The initial cohort included 899 patients. Regarding cirrhosis etiology: 384/899 (42%) had hepatitis C, 158/899 (17.5%) had hepatitis B, 293/899 (32.5%) were alcoholic, 6/899 (0.6%) were autoimmune, 7/899 (0.8%) were cardiac, 13/899 (1.4%) were premalign liver cirrhosis and in 5% of cases the etiology was unknown. In univariate analysis, hypernatremia (p < 0.0001), hyperpotassemia (p < 0.0001), hypoalbuminemia (p < 0.0001), high values of bilirubin (p < 0.0001), high values of creatinine (p < 0.0001) were strongly associate with in hospital mortality. In multivariate analysis, the model including albumin, sodium, potassium, creatinine and bilirubin (all p-values < 0.05) had an AUROC = 0.78, CI (0.75–0.81), p < 0.001. Using this factors as predictors, by multiple regression analysis we obtained the following score: ABCPS score = 0.04 + 0.03*Albumin + 0.05 + 0.02*Creatinine + 0.04 + 0.04*Bilirubin + 0.05 + 0.28*Sodium. AUROC = 0.84, CI (0.79–0.9). Conclusion: Prevention and prompt treatment of kidney injury, hypernatremia, hyperpotassemia, can improve survival. ABCPS score can be an useful score to rule out patients with high mortality rate.

Disclosure of Interest: I. Sporea: I hereby confirm that I have received financial support (congress travel grant or speaker fee) from Philips, Siemens, General Electric, Abbvie, Zentiva, Bristol Meyers Squibb
S.A. Popescu: I hereby confirm that I have received financial support (congress travel grant, speaker fee) from Philips, General Electric, Abbvie, Astrazeneca, Zentiva
R. Siri: I hereby confirm that I have received financial support (congress travel grant or speaker fee) from Philips, Abbvie, Zentiva
All other authors have declared no conflicts of interest.

References

P3142 BARIATRIC SURGERY IS ASSOCIATED WITH INCREASED RISK OF DEVELOPING ACUTE LIVER INJURY: A NATIONWIDE ANALYSIS

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2New York University School of Medicine, New York/United States of America
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Introduction: Bariatric surgery provides a durable method of weight loss but is associated with serious adverse events. Some studies report an increase in drug-induced acute liver injury following bariatric surgery.

Aims & Methods: We aimed to assess if bariatric procedures increase the risk of acute liver failure in a large inpatient cohort. We retrospectively analyzed discharge data on patients who developed acute liver injury (ALI) using the New York State Inpatient Sample (NIS) database from 2010–2013. Discharges with an ICD-9 code indicating ALI were included. The primary outcome was ALI in patients with a history of bariatric surgery compared to all other patients with an inpatient diagnosis of liver injury. Secondary outcomes were mortality in the two cohorts and independent socio-demographic and medical risk factors for mortality in each cohort. Variables tested include age, gender, race, income, Charlson criteria, hospital factors and medical comorbidities including Malnutrition, HTN, Anemia, CKD, Diabetes, CHF, Coagulopathy, Alcoholism, HBV and HCV. Univariate and multivariate logistic regression analyses were performed to identify independent predictors.

Results: During the study period, a total of 437,390 patients were diagnosed with acute liver injury and were included in the study, of which 5,799 had previously undergone bariatric surgery. In the post-bariatric cohort, mean age was 58.7 years and 77% were women. The prevalence of acute liver injury in all inpatient admissions for that time period was higher in patients with history of bariatric surgery (0.88%) than in non-bariatric patients (0.75%), p = 0.01. Patients with history of bariatric surgery displayed odds ratio of 1.52 of developing ALI when compared to patients with no history of bariatric surgery (95%CI: 1.43–1.61, p < 0.01). The rate of overall inpatient mortality was higher in non-bariatric cohort (15.9% versus 9.3%). Post-bariatric patients admitted for ALI were more likely to be younger, female, Caucasian and residing in more affluent areas. Post-bariatric patients were also more likely to have higher rates of malnutrition, anemia, alcoholism, and significantly lower prevalence of hepatitis B and C; CHF, diabetes and kidney disease. In a multivariate regression model, the presence of CHF and coagulopathy increased mortality risk, and diagnosis of alcoholism was associated with lower mortality risk from ALI in patients with prior history of bariatric surgery (Table).
Conclusion: Bariatric surgery increases the risk of subsequent acute liver injury. Post-bariatric surgery patients admitted for ALI may therefore be more likely to have anemia, malnutrition, and alcoholism, supporting the hypothesis that baseline nutritional status may predispose to drug-induced ALI. Addressing these potentially modifiable risk factors may decrease the significant morbidity and mortality of ALI.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1344 LONGITUDINAL MONITORING OF LIVER STIFFNESS BY ACOUSTIC RADIATION FORCE IMPULSE IMAGING IN PATIENTS WITH CHRONIC HEPATITIS B RECEIVING ENTECAVIR
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Introduction: Acoustic radiation force impulse (ARFI) imaging measures liver stiffness (LS), which significantly correlates with the stage of liver fibrosis in treatment-naïve patients with chronic hepatitis B (CHB). So far, the use of ARFI elastography to monitor change in liver fibrosis has not been properly evaluated during antiviral therapy in CHB patients.

Aims & Methods: We aimed to prospectively assess the clinical usefulness of ARFI during long-term antiviral therapy in CHB patients. Seventy-one CHB patients were consecutively recruited and received antiviral therapy with entecavir. Paired liver biopsies were performed in 27 patients at baseline and week 78 of entecavir therapy. LS was assessed by ARFI at multiple follow-up sessions.

Results: LS significantly decreased with treatment and continued to decrease after normalization of alanine aminotransaminase. Overall, 97.2% patients achieved improvement of LS, whereas 19.7% patients had more than 30% reduction in LS values between baseline and week 104. Multivariate linear regression analysis showed that the degree of LS reduction significantly correlated with the baseline levels of LS value, platelet and cholinesterase. In the 27 patients who received paired liver biopsies, LS significantly correlated with stage of fibrosis and inflammatory grade at baseline. LS values decreased more significantly in patients with fibrosis regression than those with static histological fibrosis. Changes in LS value (change threshold = 15%) was significantly correlated with the changes in histological fibrosis staging (r = 0.63, P < 0.001).

Conclusion: In CHB patients, LS assessed by ARFI was significantly reduced during antiviral therapy. Longitudinal monitoring of LS might be a promising non-invasive assessment of fibrosis regression during long-term antiviral therapy in CHB. Further studies on large populations are warranted.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
N. Caporaso1, F. Morisco1
NUC antiviral therapy with stable viral suppression (HBV-DNA hepatitis the kinetics of HBsAg levels during the NUC therapy to evaluate the
Aims & Methods: We aimed to investigate in patients with chronic HBeAb side-analogues (NUC) responders, even if this event occurs rarely.
Introduction: Serum HBsAg loss is the recommended stopping rule in nucleo(t)-
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2
5
United European Gastroenterology Journal 5(5S)
Lamivudine. The median treatment duration was 111 months, range 25–183
enrolled. Precisely 56 patients underwent to Tenofovir, 22 Entecavir and 17
median age 50 yrs, 34% cirrhotic) with stable viral suppression by NUCs, were
Results: 
Conclusion: In summary, along with the clearance or remission of HBsAg, the gut bacterial communities of chronic hepatitis B patients were remarkably altered after fecal microbiota transplantation, with some taxa abundances changed accordingly, which suggested their potential application as targets for clinical diagnosis and treatments in future.
Disclosure of Interest: All authors have declared no conflicts of interest.
References
P1347 QUANTIFICATION OF SERUM HBsAG IS A HELPFUL MARKER TO OPTIMIZE THE MANAGEMENT OF ANTIVIRAL NUC THERAPY IN CHRONIC HBeAg-NEGATIVE HEPATITIS B
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Introduction: Serum HBsAg loss is the recommended stopping rule in nucleo(t)-side-analogues (NUC) responders, even if this event occurs rarely.
Aims & Methods: We aimed to investigate in patients with chronic HBsAg+ hepatitis the level of HBsAg levels during the NUC therapy to evaluate the predictive parameters of HBsAg seroclearance. Patients with CHB, receiving NUC antiviral therapy with stable viral suppression (HBV-DNA < 2010 IU/ml), were recruited at the Gastroenterology Unit of the University of Naples “Federico II”. serum samples from these patients were tested for HBsAg quantification with the ElecsysHBsAg II Quant immunassay (Roche Diagnostics, Indianapolis, USA). HBsAg levels were determined before starting NUC treatment and on-treatment every 12 months.
Results: 56 patients (57 ± 9.5 HBeAg-positive, HBsAg-negative patients (M/F: 73/22, median age 50 yrs, 34% cirrhotic) with stable viral suppression by NUCs, were enrolled. Precisely 56 patients underwent to Tenofovir, 22 Entecavir and 17 Lamivudine. The median treatment duration of NUC therapy was 111 months, range 25–183 months. There was a significant decrease of the HBsAg levels during NUC therapy from 3471 UI/ml at the baseline to 1758 IU/ml at the last determination (p < 0.001). The statistically significant HBsAg decrease was also maintained when the patients were clustered according to antiviral therapy, severity of liver disease and previous interferon treatment. HBsAg seroclearance occurred in 18/95 patients (19%). The multivariate analysis showed that the only predictive parameter statistically significant of HBsAg seroclearance is the HBsAg level at baseline. Moreover, HBsAg seroconversion to HBsAb occurred in 4/18 patients, in which undetectable HBsAg value was evidenced at least two years before the seroconversion, and NUC therapy was successfully stopped, without relapse after a mean follow-up period of 24 months.
Conclusion: The results of this study suggest a role of on-treatment HBsAg quantification in the management of NUC-treated patients. HBsAg measurement would be a useful parameter to optimize antiviral treatment schedule.
Disclosure of Interest: All authors have declared no conflicts of interest.
P1348 IMPROVEMENTS IN CHRONIC HEPATITIS B PATIENTS AND THE ALTERATION IN GUT MICROBIOTA AFTER FECAL MICROBIOTA TRANSPLANTATION
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Introduction: Chronic hepatitis B (CHB) is a common liver disease worldwide, and can be progressed to liver cirrhosis and hepatocellular carcinoma. Unfortunately, only a minority of CHB patients could achieve the clearance or seroconversion of hepatitis B virus e-antigen (HBsAg), the end point of treatment, even after multiple years of antiviral therapy. Therefore, it is urgent to develop new and effective strategy for treatment of CHB and examine the mechanisms.
Aims & Methods: In this study, we performed 60 times of fecal microbiota transplantation (FMT) by nosoantisternal tube for 20 CHB patients who continued interferon-based or previous antiviral treatment, and, accordingly, measured the HBsAg level four weeks after each FMT. Fecal samples of CHB patients before (Baseline) and after FMT as well as donors were collected for analyses of gut microbiota by sequencing 16S V3-V4 regions on Illumina MiSeq using PE 250 reagents.
Results: Results showed that HBsAg of 13 patients (65%) was cleared or reduced after one to seven times of FMT. Based on OTUs at cutoff of 3% dissimilarity, there were significant (PERMANOVA, P = 0.001) differences in overall gut bacteria communities among CHB-Baseline, CHB-FMT1, CHB-FMT2 and CHB-FMT3. Interestingly, the three major clusters in PCA ordination. Whereas, no significant differences (ANOVA, P > 0.05) were detected in α-diversity indexes among the three groups, including observed OTU numbers, Shannon index, Simpson index, and Pielou evenness. This implies that it is the taxonomic relative abundance, not taxon number, that contributed to the bacterial community differences. Overall, gut bacteria were mainly composed of Firmicutes (Lachnospiraceae, Ruminococcaceae, Veillonellaceae), Bacteroidetes (S24-7, bacteroidaceae, Prevotellaceae), and Proteobacteria (Alcaligenaceae, Enterobacteriaceae). More specifically, Actinomyces was significantly higher in CHB patients (CHB-Baseline) than FMT-treated patients (CHB-FMT) and donors, and was identified as the bio-marker of CHB using LEfSe analysis. Conversely, Prevotella and Euphorbiaceae were significantly decreased in CHB-Baseline after FMT to almost equal to the abundances in donors, and were also identified as biomarkers.
Conclusion: In summary, along with the clearance or remission of HBsAg, the gut bacterial communities of chronic hepatitis B patients were remarkably altered after fecal microbiota transplantation, with some taxa abundances changed accordingly, which suggested their potential application as targets for clinical diagnosis and treatments in future.
Disclosure of Interest: All authors have declared no conflicts of interest.
P1349 EFFICACY OF PEGLYLATED INTERFERON ALFA-2A ADD-ON THERAPY VERSUS NUCLEOSIDE ANALOGUE MONOTHERAPY IN TREATMENT-EXPERIENCED CHRONIC HEPATITIS B PATIENTS: A RANDOMISED, CONTROLLED, OPEN-LABEL TRIAL
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Introduction: Hepatitis B surface antigen (HBsAg) seroconversion is rarely achieved in chronic hepatitis B (CHB) patients during nucleoside analogue (NA) monotherapy. The efficacy of pegylated interferon alfa-2a (peg-IFNα-2a) add-on therapy in those CHB patients remains unclear.
Aims & Methods: We aimed to compare the efficacy of peg-IFNα-2a add-on therapy with serum sampletry in treatment-experienced CHB patients. We enrolled hepatitis B e antigen (HBsAg)-negative treatment-experienced CHB patients aged older than 16 from the First Affiliated Hospital of Sun Yat-sen University in China. All had received NA monotherapy for 3 years with sustained undetectable plasma HBV DNA. The exclusion criteria included: cirrhosis or other chronic liver diseases, previous immunological therapy, pregnancy and breastfeeding, contraindications for peg-IFNα-2a, or other serious diseases. The eligible patients were assigned to receive peg-IFNα-2a add-on therapy for 48/72 weeks to continue to receive NA monotherapy for 96 weeks. HBV DNA levels, HBV serologic indicators, liver function, renal function, thyroid function, blood cells count and imaging examination were assessed. The primary end point was HBsAg loss from baseline to week 96.
Results: 71 patients were enrolled (22 to peg-IFNα-2a add-on therapy group and 49 to NA monotherapy group), of whom 9 in peg-IFNα-2a add-on therapy group and 25 in NA monotherapy group completed more than 24 weeks of follow-up, the remaining patients have not yet reached 24 weeks of follow-up. There was no significant difference in age, gender, body mass index (BMI), HBsAg levels, alanine aminotransferase (ALT), or aspartate aminotransferase (AST) between the two groups at baseline. At week 24, HBsAg levels in peg-IFNα-2a add-on therapy group were significantly lower than the baseline (2.96 ± 0.14 vs 2.92 ± 0.82 Log10IU/ml, p = 0.009), but there was no obvious change in NA monotherapy group (3.43 ± 0.46 vs 3.44 ± 0.44 Log10IU/ml, p = 0.843). The HBsAg loss in peg-IFNα-2a add-on therapy group was significant higher than in NA monotherapy group at week 24 (0.76 ± 0.76 vs 0.01 ± 0.10 Log10IU/ml, p = 0.008). Among those patients who completed 96 weeks of follow-up, two patients in peg-IFNα-2a add-on therapy group (22.2%) achieved HBsAg serocconversion, but none in NA monotherapy group (0%). Conclusion: The peg-IFNα-2a add-on therapy increased loss of HBsAg in HBsAg negative treatment-experienced CHB patients as compared to NA monotherapy.
Disclosure of Interest: All authors have declared no conflicts of interest.
P1350  HEPATITIS C IN LEBANON: BURDEN OF THE DISEASE AND VALUE OF A COMPREHENSIVE SCREENING AND TREATMENT
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Introduction: As few reliable data on the burden of hepatitis C virus (HCV) are available from the Middle East, we analyzed HCV burden in the Lebanese population and the value of comprehensive screening and treatment at different age groups and fibrosis stages.

Aims & Methods: A multi-cohort, health-state-transition model was developed to project the number of HCV patients achieving a sustained virologic response 12 weeks after treatment (SVR12) or progressing to compensated cirrhosis (CC), decompensated cirrhosis (DCC), hepatocellular carcinoma (HCC), and liver-related death (LRd) from 2016 to 2036. Epidemiology and mortality data were extracted from the Ministry of Health bulletin while costs were collected from insurance claims. The proportion of patients screened for HCV was projected to increase to 60%–85% 99% (low/medium/high screening scenarios) in 2036, with a new cohort of patients being diagnosed each year. SVR12 rates were extracted from clinical trials. Separate models were used for 18–39 and 40–80 age groups to account for difference prevalence and screening rates.

Results: Low, medium and high HCV screening scenarios showed that 3838, 5656 and 7669 individuals would be diagnosed with HCV infection from 2016 to 2036, 40% aged 18–39 and 60% aged 40–80. In the absence of treatment, the projected numbers of patients with CC, DCC, HCC and LRd in 2036 was 899, 147, 131 and 147 respectively for the 18–39 age groups. In the 40–80 age groups, these projections were substantially greater: 2828 CC, 736 DCC, 668 HCC and 958 LRd. The overall economic burden of these liver complications would reach 150 million US$. Introducing direct-acting antiviral (DAAs) for F0-F4 patients would increase by 43% and 62% the proportion of remaining liver-years (LYs) spent in SVR12 compared to DAA-naive patients only. Although DAAs for F0-F4 increase the cost of HCV treatment, they also provide the greatest population health benefit and lowest cost per life year gained in SVR12. Compared to no treatment and screening, adopting the high screening variant and DAAs access to F0-F4 would cost an additional 1.957 €/LY gained in SVR12 for patients aged 18–39 and 188 €/LY for the 40–80 age group.

Conclusion: An enhanced screening policy coupled with broader access to DAAs will diminish the future clinical and economic burden of HCV in the Lebanese population and provide the greatest health benefits per amount invested, among middle-aged and elderly adults with a big difference in additional costs between the 2 groups.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

P1352  HEPATITIS C TREATMENT IN RENAL TRANSPLANTATION: THE EFFICACY AND SAFETY OF DIRECT-ACTING ANTIVIRALS IN THE REAL LIFE
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Introduction: Hepatitis C virus (HCV) infection in renal transplant patients pre-disposes to graft failure and progression of renal disease, increasing mortality. Due to immunosuppression and oscillating glomerular filtration rate (eGFR) in HCV infected patients, the evolution of virological response and clinical outcomes (kidney function, anemia and other adverse effects) is scarce. Additional studies are still necessary in order to evaluate the real impact of these agents in the daily clinical practice.

Aims & Methods: Our objective was to assess the efficacy and safety of DAA treatment for HCV-infected patients with renal transplantation, in the daily practice of a tertiary care centre, describing the HCV infection, treatment type, the evolution of virological response and clinical outcomes (kidney function, anemia and other adverse effects). HCV-infected and renal transplanted patients treated with DAA between April 2015 and February 2017 were analyzed.

Results: Including 19 patients, 10 males (55%) and 9 females (47%) with a mean age of 57 years (40–70 years). The majority of these patients (89%) were treatment-naive. Genotype distribution was the following: genotype 1–74% (14/19), genotype 3–16% (3/19) and genotype 4–10% (2/19). Distribution according to fibrosis stages was as follows: F0–2–63% (12/19), F1–21% (4/19) and F4–16% (3/19). Treatment response rates were monitored with a 24 weeks for others 2 (10%). One patient realized only 21 weeks of treatment, needing to suspend it due to severe anemia. Regarding treatment response rates, 74% (14/19) of patients had Rapid Virological Response (RVR) and 100% (19/19) of patients had End of Treatment Response (ETR).

Conclusion: An enhanced screening policy coupled with broader access to DAAs will diminish the future clinical and economic burden of HCV in the Lebanese population and provide the greatest health benefits per amount invested, among middle-aged and elderly adults with a big difference in additional costs between the 2 groups.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P1353  WHAT HAPPENED WITH LIVER STIFFNESS VALUES ASSESSED BY MEANS OF TRANSPARENT ELASTOGRAPHY IN PATIENTS WITH HCV LIVER CIRRHOSIS AFTER DAA TREATMENT
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Introduction: Liver stiffness (LS) measurements by Transparent Elastography (TE) has been widely accepted as a tool for fibrosis assessment.

Aims & Methods: The aim of this study was to assess LS dynamics in a group of patients with HCV liver cirrhosis after DAA treatment. This bicentric clinical study enrolled 18 patients: meta-analysis of clinical trials. Journal of viral hepatitis, 2011, 18, 7.

PLT

Baveno VI criteria suggest that cirrhotic patients with platelet count including variceal bleeding.

Results:

Out of 276 subjects, reliable measurements were obtained in 92.7%, so that the final analysis included 256 patients. The mean LS values decreased significantly after DAA: 25.4 ± 11.7 kPa vs. 22.5 ± 12.2 kPa (p = 0.009). Most patients (75% [152/205]) presented more than 10% in LS values. 23% [59/256] had stable LS values, while in 17.3% (45/256) cases, the LS values increased. In the subgroup of 180 patients where LSM were also performed 12 weeks after EOT (SVR 12), the mean LS values were significantly lower at EOT as compared to baseline: 20.3 ± 10.8 kPa vs. 25.5 ± 11.4 kPa (p < 0.001) and also as compared to EOT: 20.3 ± 10.8 kPa vs. 22.8 ± 12.2 kPa, (p = 0.04). In the subgroup of 55 patients when LSM were also performed 24 weeks after EOT (SVR 24), the mean LS values were significantly lower at SVR 12 and SVR 24 as compared to EOT: 18.7 ± 8.2 kPa vs. 21.6 ± 7.7 kPa, 0.01 and 18.3 ± 6.6 kPa vs. 21.6 ± 7.7 kPa, (p = 0.01).

Conclusion: In our group mean liver stiffness values evaluated by TE significantly decreased after antiviral treatment at SVR 12 and SVR 24, as compared to EOT. Overall, in our study almost 60% of patients had EOT liver stiffness values lower than at baseline, at SVR 12 almost 75% of patients had liver stiffness values lower than at baseline and at SVR 24 almost 77% of patients had liver stiffness values lower than baseline.

Disclosure of Interest: I. Sporea: I hereby confirm that I have received financial support (travel or speaker fee) from Philips, Siemens, General Electric, Abbott, AstraZeneca, Zentiva.

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References


P3154 ACHIEVING SVR AFTER DAA THERAPY FOR HCV CONCENTRATIONS IN SERUM DEPEND ON OVERWEIGHT IN CHRONIC HEPATITIS C PATIENTS AND INCREASE AFTER SUSTAINED Virologic RESPONSE.

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Introduction: Monocyte chemotactic protein-1 (MCP-1) is a chemokine mediating inflammation. It contributes to fibrogensis. The extent to which metabolic and immune factors are implicated in fatty liver of patients with CHC is still not clear.

Aims & Methods: The aim of the study was to explore the associations between serum MCP-1, liver fibrosis, fatty liver and metabolic factors in CHC patients before, and after antiviral treatment. We included 21 patients in the study (11 men, 10 women, age 42 ± 9.7) with chronic hepatitis C virus (HCV) infection – 17 with genotype 1 and 4 with genotype 3. Liver biopsy was done in 19 and histology showed fatty liver in 8 patients. Fatty liver was present in 17 of all patients on antiviral therapy. Serum probes were obtained before treatment and after response evaluation. Statistical analysis included Spearman’s rho, Mann-Whitney U test, Wilcoxon’s test and Student’s paired t-test.

Results: MCP-1 in serum correlated with BMI (r = 0.522, p = 0.015). MCP-1 correlated with overweight (r = 0.579, p = 0.020). In patients with BMI more than 30 overweight and obese patients were higher than in those with normal weight (p = 0.020). Patients with BMI score of 34 had higher BMI (p = 0.010) and HOME-IR (p = 0.042). An increase in serum MCP-1 was found in patients after SVR (p = 0.018), while no significant variation from baseline values was found in NVR patients. The result remained significant in subgroup analysis of SVR patients with F1-F2 (p = 0.028) and in those with fatty liver (p = 0.017). MCP-1 in serum did not show any association with assessment of liver fibrosis, fatty liver, insulin resistance and serum lipid levels.
Conclusion: MCP-1 concentrations in serum depend on overweight in patients with CHC. Overweight and insulin resistance are associated with progression of CHC. Serum levels of MCP-1 increase after HCV clearance. Fluctuation of the MCP-1 concentration in serum could reflect an antinflammatory activation of M1S and a gradient dependent dynamic replacement of the proinflamatory cell subsets in the liver, with a resolution ones after SVR. Fatty liver plays a role for inflammatory responses in CHC patients after SVR.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

P1356 HLA-A02, HLA-A03 AND HLA-B15: A NEW RISK FOR HEPATIC STEATOsis IN EGYPTIAN CHRONIC HEPATITIS C PATIENTS
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Introduction: HCV interferes with the host lipid metabolism leads to insulin resistance and hepatic steatosis. Although it is usually mild in genotype 4, markers of simple steatosis cannot reflect the potential toxic effects to fibrosis, cirrhosis and subsequent hepatocellular carcinoma. Many heritable host factors with observed inter-ethnic variation in the prevalence of steatosis are documented, and in many cases hepatic steatosis may be detected in absence of all these risk factors; so a role for genetic factors in development of hepatic steatosis in chronic HCV patients may be suggested.

Aims & Methods: In this study, we aim to evaluate the association of HLA class A-B alleles and presence of steatosis in chronic HCV genotype 4 infected patients. The study included two hundred unrelated non diabetic non obese chronic HCV patients with normal lipid profile, 98 of them had biopsy proven steatosis. Serological testing of HLA class I antigens (HLA-A, and HLA-B alleles) were performed with a standard complement dependent microlymphocytotoxicity

Results: The frequency of A02, A03, B15 and B17 alleles were significantly higher in chronic HCV patients with steatosis (OR = 1.77, 2.64, 4.44, 5.68) and 95% CI = 0.96–3.27, 1.02–7.04, 0.84–31.17, 1.12–36.85 with P = 0.034, 0.022, 0.044, 0.015 respectively. On the other hand, the frequency of A01 and B12 alleles were significantly higher in patients without steatosis (OR = 0.56, 0.41) and 95% CI were 0.30–1.05, 0.20–0.83 and P = 0.015 and 0.005. On logistic regression analysis, patients who carry HLA-A02, A03 and HLA-B15 alleles may have 2.2, 3.9 and 11.15 fold risk to have hepatic steatosis (B coefficient: 0.78, 1.37; 2.41) 95% CI = 1.09–4.42, 1.04–11.05, 2.15–58.13; P = 0.027, 0.009, 0.004) while carrying HLA-A01 alleles may be protected from having HCV associated hepatic steatosis; (OR = 0.34,95% CI = 0.16–0.72; P = 0.005) with constant 9.47 and overall accuracy of 69%. In addition, patients who have moderate activity index in liver histopathology have 5.9 risk to have hepatic steatosis (OR = 5.92, 95% CI = 2.92–11.99, P<0.001).

Conclusion: In chronic HCV genotype 4 patients, carrying HLA-A02, HLA-A03 and HLA-B15 alleles may have a risk for presence of hepatic steatosis while presence of HLA-A01 alleles may have a protective role.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

P1358 THE VALUE OF 2D-SWE.GE FOR THE EVALUATION OF LIVER FIBROSIS IN PATIENTS WITH HCV COMPENSATED CHRONIC HEPATOPATHIES
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Introduction: Chronic liver diseases are quite frequently encountered in daily practice and are due mostly to chronic viral infections (B or C viruses) and to other conditions such as alcoholic steatohepatitis - (ASH) and to non-alcoholic fatty liver disease (NAFLD). While liver biopsy remains the gold standard method for fibrosis assessment, stage classification and also for necro-inflammatory grading, in the last years, non-invasive assessment methods (biological tests and elastographic methods) were developed and they are being used more and more, to the detriment of liver biopsy.

Aims & Methods: The aim of this study was to evaluate the performance of the 2D shear wave elastography technique from General Electrics (2D-SWE.GE), for the evaluation of liver fibrosis in patients with HCV chronic hepatopathies, using Transient Elastography (TE) as the reference method. The study included 145 consecutive subjects with HCV compensated chronic hepatopathies, in whom liver stiffness was evaluated in the same session by means of 2 elastographic measurements: TE (FibroScan, EchoSens) and 2D-SWE.GE (LOGIQ E9, GE Healthcare). Reliable LS measurements were defined as follows: for TE–the median value of 10 measurements with a success rate of ≥60% and an interquartile range <30% and for 2D-SWE.GE - the median value of 10 measurements acquired in a homogeneous area and an interquartile range (IQR) <30%. To discriminate between various stages of fibrosis by TE we used the following cut-offs: F < 2: 7.1 kPa, F ≥ 2: 9.5 kPa, F = 4: 12.5 kPa [1].

Results: Reliable LS measurements were obtained in 138/145 (95.1%) subjects by 2D-SWE.GE and in 139/145 (95.8%) by TE (p = 0.408). The areas under the receiver operating characteristic curve (AUROC) were 0.909 for significant fibrosis (F ≥ 2), 0.954 for severe fibrosis (F ≥ 3) and 0.942 for cirrhosis (F = 4). The best cut-off values for F ≥ 2 was 7 kPa (Sensitivity 85.7, Specificity 80.5), for F ≥ 3 it was 9.2 kPa (Sensitivity 85.3, Specificity 91.5) and for F = 4 it was 10.7 kPa (Sensitivity 84.6, Specificity 91.4).

Conclusion: 2D-SWE.GE seems a reliable method for liver fibrosis staging in patients with HCV compensated chronic hepatopathies. The best 2D-SWE.GE cut-off values for F ≥ 2, F ≥ 3 and F = 4 in HCV chronic hepatopathies were 7, 9.2 and 10.7 kPa.

Disclosure of Interest: I Sporea: I hereby confirm that I have received financial support (congress travel grant or speaker fee) from Philips, Siemens, General Electric, Abbvie, Zentiva, Bristol Meyers Squibb S.A. Popescu: I hereby confirm that I have received financial support (congress travel grants, speaker fee) from: Philips, General Electric, Abbvie, AstraZeneca, Zentiva
R. Sirli: I hereby confirm that I have received financial support (congress travel grant or speaker fee) from Philips, Abbvie, Zentiva
All other authors have declared no conflicts of interest.

Reference

P1358 DE NOVO HEPATOCELLULAR CARCINOMA IN PATIENTS WITH CIRRHOSIS AFTER TREATMENT WITH DIRECT ANTIVIRAL AGENTS
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Introduction: The risk of developing novo hepatocellular carcinoma (HCC) persists after achieving sustained virological response (SVR) in patients infected with hepatitis virus C. It has been suggested that risk is increased in patients treated with the new direct antiviral agents (DAA). In this prospective study we present our results of incidence and prevalence of novo HCC in cirrhotic patients treated with DAA and SVR, and also, the risk factors involved in its development.

Aims & Methods: We included all cirrhotic patients due to HCV infection without previous HCC who reached SVR after DAA treatment in our hospital from February 2014 until December 2016 (n = 197, median of follow-up of 17 months). We evaluated chi square test the following qualitative variables: age, Child-Pugh stage, alcohol consumption pre-treatment, tobacco consumption pre-treatment, diabetes mellitus (DM) pre-treatment, genotype, radiological and endoscopic portal hypertension features pre-treatment. The quantitative variables were evaluated with student t test; age, no. of platelets pre-treatment, fibrosis stage pre-treatment.

Results: During follow-up 11 patients were diagnosed of HCC (5.6% prevalence, 3.9% annual incidence). Among all variables evaluated being in a Child- Pugh B stage vs. an A stage (p = 0.007), pre-treatment DM (p = 0.002) and presence of radiological portal hypertension (p = 0.001) were associated with developing novo HCC. Among the quantitative variables, we evidenced statistically significant differences in the mean value of platelets (p = 0.015).

Conclusion: In our group of patients, a worse hepatic function evaluated with Child-Pugh classification and indirect markers of portal hypertension (platelets and radiological features) and also DM are associated statistically significant with the development of novo HCC. The incidence (>1.5%) of novo HCC justifies the screening of HCC.

Disclosure of Interest: All authors have declared no conflicts of interest.
Aims & Methods: Aim of this study was to identify possible differences between patients with ALF and AOCLF regarding routine parameters and clinical course.

In this retrospective single-center study all patients were recruited, who were admitted to the University Hospital of Essen with the initial diagnosis of ALF between 2008 and 2015. Patients included in this study were fulfilling the criteria of the acute liver failure study group Germany. The diagnosis of AOCLF was established postoperatively examining the medical record. In total 17 patients were recruited (ALF: 13; AOCLF: 3). Clinical records, in particular demographic data, serum parameters and outcome were analyzed for differences between ALF and AOCLF.

Results: Patients with AOCLF were significantly older (50.3 ± 15.1 vs. 39.8 ± 16.2, p = 0.0008), had a higher BMI (27.5 ± 5.1 vs. 24.5 ± 6.2, p = 0.0014) and were more often male (65% in AOCLF vs. 34% in ALF p = 0.0008). In addition, the insults that caused the liver failure in AOCLF were significantly different from those patients with ALF. Significant differences were also found for liver enzymes, which were significantly lower in AOCLF patients (AST p = 0.01; ALT p = 0.001). Cell death markers and the MELD did not differ between ALF and AOCLF. Moreover, the outcome was not different between the two groups, neither survived or deceased nor suffered spontaneous remission or non-spontaneous remission (combined transplantation and deceased). Important, MELD and the modified MELD including the cell death marker M65 were similarly effective in predicting outcome for both ALF and AOCLF.

Conclusion: In the present study patients with ALF and AOCLF differed in age and BMI, but did not exhibit differences regarding disease severity (according to MELD) or clinical outcome. While the causes for an acute insult differed between ALF and AOCLF, which might imply a different clinical management, clinical outcome was predictable by common factors for ALF.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

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Introduction: Romania has the highest incidence of tuberculosis (TB) in the European Union, representing one quarter of the European TB burden. Additionally, bile duct lesions are frequent complications after liver transplantation (LT). The second level of screening for infections consists of screening for Mycobacterium tuberculosis, including history of TB, PPD, Interferon-gamma release assays. Aims & Methods: The aim was to assess the importance of QuantiFERON TB Gold test for evaluating patients included on the wait list for LT in Romanian setting.

The study was a single-center retrospective cohort study (the single center for LT)that included 264 patients admitted on the wait list for LT from January 1, 2014 to November 18, 2016. All patients underwent mandatory screening for Mycobacterium tuberculosis, either using QuantiFERON TB Gold test or skin testing using purified protein derivative (PPD). The variables analyzed using Minitab were age: gender, etiology of liver disease, biochemical test, MELD score. Results: From a total of 264 patients with liver diseases included on the wait list, 60.6% were males, the average age at diagnosis was 47.78 ± 9.92 years. The etiology of liver cirrhosis was HCV in 31.43%, HBV and HBV-HDV coinfection in 45.06%, and alcoholic liver cirrhosis in 18.93%; 24.62% of patients have been diagnosed with superimposed hepatocellular carcinoma. Eighty three patients (31.43%) had positive results for QuantiFERON test, 150 patients (56.81%) were negative and 17 patients (6.43%) had indeterminate results. Only 14 patients (5.3%) were skin tested using PPD, 2 (0.75%) of them with positive results.

Comparing the subgroups, positive QuantiFERON test was associated with HCV etiology (p value = 0.049) and lower lymphocyte counts, but did not achieve statistical significance (p = 0.187). Patients with indeterminate QuantiFERON associated with hyperbilirubinemia (p = 0.044), h/o tuberulosis (p = 0.032) and had a higher MELD score (p = 0.003). An assessment by a multidisciplinary team that included a pneumologist, 38.63% of patients were diagnosed with latent TB. Isoniazid chemoprophylaxis along with pyridoxine was postponed after LT, in order to prevent further hepatic dysfunction. 48.5% of patients underwent LT, followed by TB prophylaxis and no cases of TB reactivation have been reported during a follow-up period of 14 months.

Conclusion: Patients transplanted for HCV-related liver cirrhosis should benefit from a careful follow-up on the WL and prompt TB prophylaxis after LT in order to prevent liver damage from isoniazid chemoprophylaxis. Delays in TB prophylaxis after LT in order to avoid liver toxicity of anti-bacillary drugs was not associated with TB reactivation.

Disclosure of Interest: All authors have declared no conflicts of interest.

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Introduction: Romania has the highest incidence of tuberculosis (TB) in the European Union, representing one quarter of the European TB burden. Additionally, bile duct lesions are frequent complications after liver transplantation (LT). The second level of screening for infections consists of screening for Mycobacterium tuberculosis, including history of TB, PPD, Interferon-gamma release assays. Aims & Methods: The aim was to assess the importance of QuantiFERON TB Gold test for evaluating patients included on the wait list for LT in Romanian setting.

The study was a single-center retrospective cohort study (the single center for LT)that included 264 patients admitted on the wait list for LT from January 1, 2014 to November 18, 2016. All patients underwent mandatory screening for Mycobacterium tuberculosis, either using QuantiFERON TB Gold test or skin testing using purified protein derivative (PPD). The variables analyzed using Minitab were age: gender, etiology of liver disease, biochemical test, MELD score. Results: From a total of 264 patients with liver diseases included on the wait list, 60.6% were males, the average age at diagnosis was 47.78 ± 9.92 years. The etiology of liver cirrhosis was HCV in 31.43%, HBV and HBV-HDV coinfection in 45.06%, and alcoholic liver cirrhosis in 18.93%; 24.62% of patients have been diagnosed with superimposed hepatocellular carcinoma. Eighty three patients (31.43%) had positive results for QuantiFERON test, 150 patients (56.81%) were negative and 17 patients (6.43%) had indeterminate results. Only 14 patients (5.3%) were skin tested using PPD, 2 (0.75%) of them with positive results.

Comparing the subgroups, positive QuantiFERON test was associated with HCV etiology (p value = 0.049) and lower lymphocyte counts, but did not achieve statistical significance (p = 0.187). Patients with indeterminate QuantiFERON asso-
P1362 A NATIONAL STUDY OF CANCER DIAGNOSES IN IRISH LIVER TRANSPLANT RECIPIENTS WITH PRIMARY SCLEROSING CHOLANGITIS

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Introduction: Primary sclerosing cholangitis (PSC) is associated with an increased risk of cholangiocarcinoma, colorectal cancer (CRC) and gallbladder cancer. Orthotopic liver transplantation (OLT) patients are at increased risk of developing de novo malignancies, however limited and conflicting data exists regarding cancer risk post OLT for PSC.

Aims & Methods: To examine all recorded malignancies over 2 decades in OLT from PSC pts and compare to our non-transplanted PSC cohort. To analyse factors associated with development of malignancies post OLT. We retrospectively studied PSC patients attending the Irish National Liver Unit (INLU) and the Centre for Colorectal Disease (CCD) at St. Vincent’s University Hospital from 1/1/1994 to 30/6/2016. We integrated this database with the National Cancer Registry in Ireland. This enabled accurate determination of the no. of malignancies recorded in the PSC cohort. Analyzed data included age of recipient at OLT, gender, primary OLT indication, immunosuppressive regime, de novo malignancy post OLT, time from primary OLT to diagnosis of malignancy or death. Statistical analysis was primarily descriptive. Cox Proportional Hazard Model was used to analyse factors associated with mortality in the PSC OLT cohort.

Results: 107 of 173 patients had undergone transplant for PSC. 27/107 pts were transplanted for cholangiocarcinoma. 12 post-transplant de novo cancers and 12 BCC/SCC carcinomas were found in 107 patients during 737.8 person years of follow-up. Median time to cancer diagnosis post OLT was 5 years (IQR 2.8–5.9). Recurrence of PSC was observed in 21 patients (19.6%). Post-transplant lymphoproliferative disease (PTLD) remains a major complication after OLT. Previous studies have reported rates of 1–3% in adult OLT pts. 5 pts were diagnosed with lymphoma post OLT representing 4.7% of cohort. Median time to diagnosis was 5.3 yrs (IQR 2.8–10.2). Regarding CRC, 2 patients developed CRC post OLT. 4 patients had colorectal dysplasia/CRC post OLT had co-existing IBD. All those who developed colorectal dysplasia/CRC post OLT had co-existing IBD. All 5 colectomies for dysplasia/CRC showed significant co-existing inflammation. One patient post OLT underwent a completion proctectomy for rectal cancer. As expected, cholangiocarcinoma as a indication for OLT (p = 0.005, RR 2.573, 95%CI 1.3–4.95) and an older age at transplant (p = 0.05, RR 1.027, 95% CI 1.0–1.054) were associated with higher mortality.

Conclusion: These findings represent national cancer figures in our PSC OLT cohort. The rate of cancer is more than three times higher in this population than the general population. The rates of PTLD are >30 times higher than the non-liver transplant population, and slightly higher than previously reported in unselected liver transplant groups. We could not find any association between the development of PTLD and aggressive immunosuppressive regimes for co-existing IBD post OLT. The study highlights that IBD/PSC patients remain at significant risk of colonic neoplasia after OLT and require intensive surveillance.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1363 OUTCOME OF LIVER TRANSPLANTATION FOR PRIMARY SCLEROSING CHOLANGITIS IN CONTEXT OF HLA-DR MISMATCH: SINGLE CENTRE EXPERIENCE

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Introduction: Primary sclerosing cholangitis (PSC) is a chronic liver disorder of unknown etiology, characterized by inflammation, fibrosis and stenoses of both extra- and intrahepatic bile ducts. For those who develop end-stage liver disease, orthotopic liver transplantation (OLT) remains the only effective treatment currently available. PSC is accompanied with concomitant ulcerative colitis (UC) in a significant proportion of patients. Benefits of routine HLA typing in donor and recipient prior to OLT were proved in the past.

Aims & Methods: The aim of this study was to assess the impact of HLA-DR mismatch on acute cellular rejection (ACR), PSC recurrence (rPSC) and course of UC after OLT. After applying inclusion/exclusion criteria we retrospectively evaluated records of 57 patients transplanted at Institute for Clinical and Experimental Medicine (Prague, Czech Republic) between July 1994 and November 2011. Only patients with proper records ±5years from OLT were included. We evaluated likelihood for each variable (ACR, rPSC, course of UC) in patients with either single, double or no mismatch in HLA-DR. Recipient data were analysed with χ2 and Fisher’s exact test using MedCalc statistical software. A p-value < 0.05 was considered as statistically significant.

Results: Out of 57 patients, 27 (47.4%) had single mismatch (“M1” group) and 30 (52.6%) had double mismatches (“M2” group) in HLA-DR. No patient had full match. 33/57 (57.9%) patients had ACR: 15/27 (55.6%) of M1 and 18/30 (60%) of M2 (p = 0.94). 4/27 (14.8%) of M1 and 2/30 (6.3%) of M2 had corticosterone ACR (p = 0.57). Multiple-episodes of ACR occurred in 11/57 (19.3%) patients: 6/27 (22.2%) of M1 and 5/25 (20%) of M2 (p = 0.74). 12/57 (21.1%) had de-novo UC after OLT: 7/27 (25.9%) of M1 and 5/30 (16.7%) of M2 (p = 0.60). In 37 (68.5%) patients, UC was diagnosed prior to OLT. 9/16 (56.3%) patients with M1 and 6/21 (28.6%) patients with M2 had more severe course of UC as compared to course prior to OLT (p = 0.17). 38 patients were evaluated for rPSC, which was diagnosed in 17 (44.7%) individuals. 6/19 patients with M1 and 11/19 with M2 had rPSC (p = 0.19).

Conclusion: Patients with single mismatch in HLA-DR have slight tendency towards development of rPSC and worsening of UC after OLT as compared to patients with double mismatch. Analysis of combined mismatch in HLA-DR and HLA-DQ could demonstrate more substantial linkages in respective clinical variables. Therefore, these data have to be considered as preliminary as typing for HLA-DQ from frozen blood samples is currently underway. Supported by Ministry of Health of the Czech Republic, grant nr. 15-28064A. All rights reserved
P1367 OUTCOMES OF LIVER TRANSPLANTATION IN PATIENTS WITH HEPATOCELLULAR CARCINOMA
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Introduction: Hepatocellular carcinoma (HCC) is the second leading cause of cancer-related mortality worldwide. Patients with viral hepatitis and those without non-alcoholic fatty liver disease (NAFLD) are especially susceptible to HCC. Parallel to an increase in prevalence of NAFLD, the prevalence of HCC is estimated to be increased in next years. Liver transplantation is now considered as a modality of treatment for patients with HCC.

Aims & Methods: This study aimed to investigate outcomes of liver transplantation in patients with HCC compared to other causes of liver transplantation. In a cross-sectional study patients who had undergone liver transplantation between March 2012 and March 2015 at Shiraz Transplant Center, Shiraz, Iran were included. Patients’ characteristics including age, gender, model for end stage liver disease (MELD) score, number of allografts, length of hospital stay, presence of multiorgan failure, about mortality of patients were recorded. Characteristics of tumor including size, number and vascular invasion were recorded. Based on these findings HCC patients were divided to those within Milan criteria and those beyond Milan criteria. The impact of HCC on post-transplant outcomes was investigated using student t-test and chi-square tests. Multivariate logistic regression was used for analysis of independent risk factors of mortality after liver transplantation.

Results: Totally 1014 liver transplant patients were included. 94 patients with HCC underwent liver transplantation. In patients with HCC compared to other causes of liver transplantation. In a cross-sectional study patients who had undergone liver transplantation between March 2012 and March 2015 at Shiraz Transplant Center, Shiraz, Iran were included. Patients’ characteristics including age, gender, model for end stage liver disease (MELD) score, number of allografts, length of hospital stay, presence of multiorgan failure, about mortality of patients were recorded. Characteristics of tumor including size, number and vascular invasion were recorded. Based on these findings HCC patients were divided to those within Milan criteria and those beyond Milan criteria. The impact of HCC on post-transplant outcomes was investigated using student t-test and chi-square tests. Multivariate logistic regression was used for analysis of independent risk factors of mortality after liver transplantation.

Kaplan-Meier method was used for analysis of survival.

Disclosure of Interest: All authors have declared no conflicts of interest.

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References:

P1366 VITAMIN B12 AS A PROGNOSTIC MARKER IN PATIENTS WITH ACUTE CHRONIC LIVER FAILURE
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Introduction: Serum vitamin B12 levels are increased in myeloproliferative diseases by increased production of haptoglobin, a vitamin B12 transporter and in liver diseases by release of B12 by hepatocytes death.

Aims & Methods: The aim of this study was to evaluate vB12 as a prognostic marker in patients with cirrhosis and acute on chronic liver failure (ACLF) induced by infection. Retrospective assessment of 56 patients admitted to an intensive care unit with ACLF in the context of infection (group 1) and 53 patients with compensated hepatic cirrhosis followed as Hepatology outpatients (group 2). Evaluation of vB12 as a predictor of 30 days’ mortality.

Results: 111 patients, 68% male, age 58 ± 18 years. Group 1 had more acute liver disease (CPT 11.9 ± 0.3 vs. 6.5 ± 0.2 and MELD 27.0 ± 1.0 vs. 10.6 ± 0.5), higher vB12 (1413 ± 149 vs. 735 ± 69 pg/mL) and lower survival (1.6 ± 0.4 vs. 6.4 ± 2.7 years). VB12 positively correlated with hepatic function scores (CPT: R=0.411, MELD: R=0.534), and multigain failure (number of organ failures: R=0.536, SOFA: R=0.553). In group 1, survival was lower in patients with high vB12 (≥ 3 vs. 37 ± 11 months), and 1 month’ mortality was associated with vB12, CPT, MELD, number of organ failure, urea, lactates and fibrinogen, in univariate analysis (p < 0.001). In multivariate analysis only fibrinogen maintained statistical significance (p < 0.001).

Conclusion: There was a strong association between high levels of vB12 and clinical decompensation of liver cirrhosis. VB12 correlated with scores of liver function and multigain failure, as well as early mortality in patients with ACLF.

Disclosure of Interest: All authors have declared no conflicts of interest.

References:
P1368 THE ASSESSMENT OF THE ADC PREDICTIVE VALUE IN SURVIVAL OUTCOMES OF PATIENTS UNDERGOING RADIOFREQUENCY ABLATION FOR METASTATIC COLORECTAL CANCER LIVER TUMORS

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Introduction: Liver is one of the most common metastatic sites of colorectal cancer, nearly 50% patients develop hepatic metastases during the course of their disease. Metastatic spread influences survival rate of those patients. The diffusion weighted imaging (DWI) is MRI sequence designed to detect random movement of water protons in extracellular compartment. Biophysical parameter expressed for treatment is Brownian motion diffusion coefficient (ADC). ADC values for b parameter lower than 300 s/mm² are influenced by perfusion movement of water protons in extracellular compartment. Biophysical parameter to Chemotherapy in Hepatic Metastases.

Results: ADC values for b value of 6500 s/mm² was 1.43 mm²/s for b value of 0500 s/mm². The survival outcomes were assessed by Kaplan-Meier estimator. The p value lower than 0.05 was considered significant.

Conclusion: The statistical analysis included Kaplan-Meier estimator for 52 patients with 9 censored cases (17.3%). In ADC maps for b value of 0500 s/mm², the low ADC values correlate with presence of necrosis in highly malignant lesions influencing in lower survival rate.

Aims & Methods: This is a post hoc analysis of prospective study to assess the predictive value of the ADC in survival outcomes of patients undergoing radiofrequency ablation due to metastatic colorectal cancer lesions in the liver. We analyzed the MRI studies of 52 patients (18 F, 34 M, aged 4383) performed on 1.5 T scanner one day before the percutaneous RFA treatment. The total number of analyzed lesions was 110 (15 per patient), 83 of them were completely ablated 27 incompletely, what was assessed in follow-up CT studies. The standard protocol of the liver MRI was applied including DWI sequence in b values of 0, 15 and 300 s/mm², ADC maps were calculated for b values of 015 and 0500 s/mm². The final ADC value was obtained by threshold marking ROI covering the whole metastatic lesion. In cases of multiple foci only the lesion with the highest ADC value was included into analysis. On basis of ROC analysis the cut-off values of ADC were established: 2.49 mm²/s for b value of 015 s/mm² and 1.43 mm²/s for b value of 0500 s/mm². The survival outcomes were assessed by mean of Kaplan-Meier estimator. The p value lower than 0.05 was considered significant.

Results: The statistical analysis included Kaplan-Meier estimator for 52 patients with 9 censored cases (17.3%). In ADC maps for b value of 0500 s/mm², the value of 1.43 mm²/s correlated with longer survival time, whereas ADC value <1.43 mm²/s correlated with shorter survival time. Statistically significant differences were identified by log rank test (p = 0.007). Such a correlation was not observed for ADC values in ADC maps for b value of 015 s/mm² (p = 0.058).

Conclusion: The study showed significant differences in survival rate depending on diffusion influenced ADC values of metastatic lesions.

Disclosure of Interest: All authors declared no conflicts of interest.

References

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P1370 LEARNING CURVE EVALUATION USING ELASTPQ

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Introduction: Nowadays liver fibrosis can be assessed using non-invasive elastographic techniques. ElastPQ is a quite novel point share wave elastography integrated into an ultrasound system.

Aims & Methods: The aim of our study was to evaluate the learning curve of obtaining reliable liver stiffness measurements (LSM), using ElastPQ. LSM of a trainee were compared to LSM of an elastography expert (with an experience of more than 500 examinations). Our study group included 50 subjects (mean age 52.7 years, 66.6% men, mean BMI 25.6 kg/m²). Both the trainee and the expert obtained LSM for each subject, using ElastPQ (EPIQ 7, Philips Healthcare, Bothell, WA, USA). Reliable LSM were defined as the median difference measurements < 10% in a homogenous area avoiding large vessels and with an IQR/median < 30%. The learning curve was evaluated using the Receiver Operating Curve analysis using the expert’s results as reference.

Results: The trainee’s performance in obtaining reliable LSM was good (AUC: 0.735, 95% CI (0.557-0.913), p = 0.01). The trainee started to have similar results with the elastography expert after the 30th subject. When looking at the IQRs, they became significantly lower after the 30th subject (2.6 to 2.1 kPa vs 6.5 to 4.2 kPa, p = 0.03).

Conclusion: Obtaining reliable LSM using ElastPQ can be easily achieved after 30 LS examinations.

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All authors have declared no conflicts of interest.

References

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P1369 HOW OFTEN DO WE FIND STEATOSIS AND SEVERE FIBROSIS IN TYPE 2 DIABETES MELLITIUS PATIENTS

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References
Out of 354 diabetic screened we excluded those with associated viral hepatitis, those with an AUDIT-C score >8 and those with unreliable LSM. The final analysis included 239 subjects (39.4% women, 40.6% men, mean age 60.4±9.3; BMI = 31.8±6.1 kg/m²) with reliable LSM. According to BMI, 10.8% had normal weight, 26.4% were overweight and 62.8% were obese (35.6% obesity grade I, 17.2% obesity grade II and 10% obesity grade III). Moderate and severe steatosis by means of CAP was found in 18.4% and 69.5% cases respectively. Severe fibrosis was defined by means of TE (LSM > 8.2 kPa) in 29.3% (70/239) of subjects.

Conclusion: In our group, 87.9% of diabetic patients had moderate and severe steatosis by CAP and 29.3% of them had severe fibrosis (TE ≥ 8.2 kPa), suggesting the need for their systematical assessment.

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R. Sirili: I hereby confirm that I have received financial support (congress travel grant or speaker fee) from Philips, Abbvie, Zentiva.

S.A. Popescu: I hereby confirm that I have received financial support (congress travel grant or speaker fee) from Philips, General Electric, Abbvie, AstraZeneca, Zentiva

All other authors have declared no conflicts of interest.
**P1371 ENHANCEMENT PATTERN OF HEPATOCELLULAR CARCINOMA USING CONTRAST ENHANCED ULTRASOUND: A 10 YEARS EXPERIENCE IN PATIENTS WITH CHRONIC LIVER DISEASE**

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Introduction: In patients with liver cirrhosis, hepatocellular carcinoma (HCC) can be diagnosed by noninvasive imaging methods (contrast-enhanced ultrasound CEUS, contrast CT/MRI).

Aims & Methods: The aim of this study was to evaluate which is the most common enhancement pattern of HCC on CEUS in all three phases (portal, arterial and late phase). We performed a retrospective study that included patients with a final diagnosis of HCC established by an imaging method (contrast enhanced CT or MRI) or biopsy. A total of 249 patients with HCC were examined (180 men, 69 women, mean age 64.6 ± 10 years); 181 patients had liver cirrhosis and 68 patients chronic hepatopathy with severe fibrosis. All 249 HCCs were evaluated by CEUS using low mechanical index ultrasound, following an intravenous bolus of 2.4 ml SonoVue. CEUS was considered conclusive for HCC if a typical pattern was present following contrast examination (hyperenhancement in the arterial phase accompanied by portal and/or late phases washout).

The nodules were classified according to their size in <5 cm and >5 cm. We re-evaluated all 249 HCCs CEUS studies using the ACR CEUS LI-RADSv 2016 algorithm.

Results: After CEUS examination a conclusive diagnosis of HCC was obtained in 190/249 cases (76.3%). Arterial phase hyperenhancement pattern was present in 227/249 cases (91.2%). Common enhancement pattern of HCC in all three phases (arterial, portal, and late phase) was observed in 17/249 cases (6.8%) and hyperenhancement in 5/249 cases (2%). In the portal phase washout was observed in 111/249 cases (44.6%); in 121/249 (48.6%) patients the nodules were isoenhancing and in 17/249 (6.8%) the arterial hyperenhancing pattern was maintained. In the late phase washout was observed in 197/249 (79.1%) cases. The nodules <5 cm were diagnostic conclusive on CEUS in 63.7% (72/113), while nodules >5 cm had a conclusive result in 86% of cases (117/136), p < 0.0001. CEUS examination was conclusive for HCC in 76.3% of the cases (190/249), while using the ACR CEUS LI-RADSv 2016 algorithm in 72.2% of all HCCs (180/249), p = 0.35.

Conclusion: In our study, CEUS arterial hyperenhancement is the most common pattern observed in HCC (91.2% of cases), followed by washout in the late phase (79.1% of cases). The size of the nodule modifies CEUS sensitivity for the diagnosis of HCC: p < 0.0001.

Disclosure of Interest: I. Sporea: I hereby confirm that I have received financial support (grant or speaker fee) from Philips, Abbvie, AstraZeneca, Zentiva. M. Danila: I hereby confirm that I have received financial support (grant or speaker fee) from Philips, Abbvie, Zentiva. R. Sirli: I hereby confirm that I have received financial support (grant or speaker fee) from Philips, Abbvie, Zentiva, Bristol Meyers Squibb. All authors have declared no conflicts of interest.

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**P1373 DICKKOPF-1: AS A SERUM BIOMARKER FOR PREDICTION OF HEPATOCELLULAR CARCINOMA TREATMENT RESPONSE**

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Introduction: Hepatocellular carcinoma (HCC) is the 5th most common cancer worldwide and the 3rd leading cause of cancer-related mortality. In Egypt, HCC is the 2nd most common cancer in men and the 6th most common cancer in women. Egypt has the highest prevalence of HCV worldwide and has rising rates of HCC. HCC is a disease with fast infiltrating growth and poor prognosis. This bad prognosis is due to the lack of an effective method for early diagnosis. So, it is necessary to find a specific & sensitive marker for early diagnosis of HCC and for monitoring of treatment response.

Aims & Methods: The aim of this work is to assess prognostic value of serum DKK1 in predicting treatment response, complication and survival in HCC patients. This study included 60 Patients divided into two groups. Group A: 30 patients with liver cirrhosis. Group B: consisted of 30 patients with HCC. Group B patients underwent either radiofrequency ablation or ethanol injection. Clinical assessment, routine laboratory evaluation, CT studies and measurement of serum alpha-fetoprotein (AFP) and DKK1 were performed for all patients and repeated to group B patients 1 and 3 months after treatment.

Results: DKK1 significantly can be used for HCC diagnosis even in HCC with inconclusive AFP. The optimum cut off value of DKK1 for diagnosis of HCC was 4.3 ng/mL (AUC 0.89, sensitivity 66.7% and specificity 96.6%) (P < 0.001). Serum DKK1 level significantly decreases after HCC treatment with either radiofrequency ablation or ethanol injection (P < 0.001).

Conclusion: DKK1 has a promising prognostic value and can be used for follow-up of HCC patients before and after treatment.

Disclosure of Interest: All authors have declared no conflicts of interest.

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**P1374 EFFECT OF FIBROBLAST GROWTH FACTOR-2 AND ITS RECEPTOR GENE POLYMORPHISMS ON SURVIVAL IN PATIENTS WITH HEPATITIS B VIRUS–ASSOCIATED HEPATOCELLULAR CARCINOMA**

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Introduction: Fibroblast growth factor (FGF), vascular endothelial growth factor, and hepatocyte growth factor play a critical role in the pathogenesis of hepatocellular carcinoma (HCC). The FGF2 rs308447 A allele was significantly associated with small tumor size, early tumor stage, and less vascular invasion. The FGF2 rs4771249 C allele was associated with low alpha-fetoprotein levels. Kaplan-Meier analysis showed that the patients with the FGF2 rs308447 TT genotype had lower survival rates than the patients with the CC or CT genotype (P = 0.016) and that the FGF2 rs308579 A allele carriers had higher survival rates than those of patients with the TT genotype (P = 0.020). The FGF2 rs1219648 CC genotype was significantly associated with increased survival rates (P = 0.047). Multivariate Cox proportional analysis revealed that the FGF2 rs308579 A allele (hazard ratio = 1.663, P = 0.004) and advanced tumor stage (hazard ratio = 3.430, P = 0.001) were independent prognostic factors for overall survival rates in patients with HCC.

Disclosure of Interest: None of the SNPs was associated with the risk of HCC development in Egyptians. The FGF2 rs308579 A allele was significantly associated with small tumor size, early tumor stage, and less vascular invasion. The F1t-1 rs4771249 C allele was associated with low alpha-fetoprotein levels. Kaplan-Meier analysis showed that the patients with the FGF2 rs308447 TT genotype had lower survival rates than the patients with the CC or CT genotype (P = 0.016) and that the FGF2 rs308579 A allele carriers had higher survival rates than those of patients with the TT genotype (P = 0.020). The FGF2 rs1219648 CC genotype was significantly associated with increased survival rates (P = 0.047). Multivariate Cox proportional analysis revealed that the FGF2 rs308579 A allele (hazard ratio = 1.663, P = 0.004) and advanced tumor stage (hazard ratio = 3.430, P = 0.001) were independent prognostic factors for overall survival rates in patients with HCC.

Disclosure of Interest: None of the SNPs was associated with the risk of HCC development in Egyptians. The FGF2 rs308579 A allele was significantly associated with small tumor size, early tumor stage, and less vascular invasion. The F1t-1 rs4771249 C allele was associated with low alpha-fetoprotein levels. Kaplan-Meier analysis showed that the patients with the FGF2 rs308447 TT genotype had lower survival rates than the patients with the CC or CT genotype (P = 0.016) and that the FGF2 rs308579 A allele carriers had higher survival rates than those of patients with the TT genotype (P = 0.020). The FGF2 rs1219648 CC genotype was significantly associated with increased survival rates (P = 0.047). Multivariate Cox proportional analysis revealed that the FGF2 rs308579 A allele (hazard ratio = 1.663, P = 0.004) and advanced tumor stage (hazard ratio = 3.430, P = 0.001) were independent prognostic factors for overall survival rates in patients with HCC.
Conclusion: These observations suggest that the SNPs of the FGFR2 and FGFR3 genes can be potential prognostic indicators in patients with HBV-associated HCC.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P1375 EXTRAPANCREATIC HEPATOCELULAR CARCINOMA METASTASIS: IMPORTANCE OF AN EARLY DIAGNOSIS AND TAILOR-TREATED THERAPY
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Introduction: Extrapancreatic HCC metastasis are associated with a poor prognosis. Nevertheless there are some effective therapies available. Aim of the study was to assess the main sites of extrahepatic metastasis in hepatocellular carcinoma (HCC) patients and to evaluate the clinical evolution and treatment. This was a retrospective single-center study in which patients with HCC confirmed extrahepatic metastasis between January 2010 and December 2016 were evaluated.

Results: We evaluated 51 consecutive patients, 80% male, with a mean age of 64 ± 11 years at the time of metastasis. In 41% of the patients the metastases were present at the time of HCC diagnosis. In patients with subsequent metastasis, the median time until its development was 9 months (IQR 5–16). The diagnosis of metastasis was incidental in 51% of the patients. Computed tomography (CT) was the main diagnostic method (86%) and in 18% of the cases histological confirmation was obtained. Nineteen patients underwent thoracic CT and five performed bone scintigraphy prior to metastasis. A total of 70 metastatic sites were identified, the more frequent were lung (33%) and bone (14%). The MELD score at the time of metastasis was higher than the MELD score at the HCC diagnosis (p = 0.009). Metastasis detection implied changes in HCC therapy in all patients, 41% started sorafenib and 55% were referred for supportive therapy. Seven patients performed metastasis targeted treatment, namely 3 patients underwent radiotherapy. The median overall survival (OS) after metastasis was 4.0 months (95%CI 2.1–5.8 months) and the mortality rate was 81% at 12 months. Patients who underwent metastasis targeted treatment presented a longer OS than those who did not (median 18.5 vs 3.1 months; p = 0.002). In multivariate analysis, MELD score at the time of metastasis (p = 0.004) and metastasis treatment (p = 0.005) were independently associated with OS estimation.

Conclusion: A systematic HCC staging, with thoracic CT and bone scintigraphy, may provide an earlier metastasis detection and enable a targeted treatment with a consequent improvement in survival in this difficult-to-treat population.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P1376 MANAGEMENT OF INTERMEDIATE STAGE HEPATOCELLULAR CARCINOMA
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Introduction: According to the Barcelona Clinic Liver Cancer (BCLC) staging system, intermediate stage contains very heterogeneous hepatocellular carcinoma (HCC) patients. Recently, subclassification of intermediate stage on the basis of Milano criteria and up to 7 criteria is proposed. In this study, the effectiveness of determining bed-to-transarterial chemo-embolization (DEB-TACE) in intermediate stage was investigated.

Aims & Methods: 120 patients (M: F=90:30; median age = 76; Child A: B: C = 72:24:4; BCLC stage A: B: C: D = 6:85:23:6) with unresectable HCC who received DEB TACE in our hospital were studied. The objective radiological response was classified according to the modified Response Evaluation Criteria in Solid Tumors (mRECIST) v.1.1 by using dynamic CT at one or two months after therapy. Adverse events were evaluated using NCI CTCAE v. 4.03.

According to Bolondi’s subclassification, the patients of BCLC B stage were divided into four groups (B1: 31; B2: 19; B4: 10). The response rate and tumor factor associated response in these patients group were examined.

Results: The overall response rate and disease control rate in intermediate stage were 36% and 89%, respectively. Considering the subclassification, the response rate in B1 group (61%) was significantly higher than that of B2 + B3 group (29%). Although B2 + B3 group was constituted by the patients who did not satisfy the up to 7 criteria, only in the patients with less than 7 tumors, the response rate (60%) was similar to that of B1 group. Tumor factors associated response and found to be significant on univariate analysis were simple gross classification (single nodular type) and number of tumor. Tumor diameter was not associated with the response.

Conclusion: For the treatment of intermediate stage of HCC, although DEB-TACE is considered to be most effective in B1 group, it is suggested that DEB-TACE is also effective in the patients with less than 7 tumors in B2 + B3 group. In cases with more than 7 tumors, as the response rate is considered to be extremely low, sorafenib and arterial infusion therapy are recommended in B2 + B3 group.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P1377 HEPATOCELLULAR CARCINOMA RECURRENCE RATE IN HCV-INFECTED PATIENTS TREATED WITH DIRECT ANTIVIRAL AGENTS. A SINGLE-CENTER EXPERIENCE
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Introduction: In the last few years many HCV patients with previous diagnosis of hepatocellular carcinoma (HCC) have been treated with direct antiviral agents (DAAs) for HCV infection. However there are conflicting data on HCC recurrence rate after DAAs therapy.

Aims & Methods: Aim of this study was to prospectively evaluate the rate of HCC recurrence following sustained virological response (SVR) by DAAs. From April 2015 to September 2016 we consecutively enrolled HCV infected patients previously treated for HCC at Liver Unit of Cardarelli Hospital. All patients had a free-disease survival from HCC of at least 6 months before starting antiviral therapy. The efficacy of HCC therapy was evaluated according to mRecist criteria at CT or MRI. Radiological evaluation was carried out within 30 days from the start of therapy. All patients underwent DAAs therapy, selected on an individual basis according to the recommendation issued by the Italian association of the study of the liver.

Results: A total of 71 patients were enrolled. Among them, 42 patients had available data on SVR status and were considered for the analysis. There were 21 males (58.3%) and 15 females. The median age of the patients was 73 years (range: 45–85). The median time until the beginning of therapy (range: 6–18 months). Genotype distribution was as follows: 36 patients infected with genotype 1 (85.7%), 5 with genotype 2 and 1 patients with genotype 3. SVR was achieved in 38/42 patients (90.5%). HCC recurrence was observed in 11/38 patients with SVR (28.9%). The median time for recurrence was 9 months from the start of therapy with a range of 1–13 months; with 2 patients who showed recurrence during therapy. Among the patients who did not achieve SVR, 1/4 showed HCC recurrence after 10 months from end of treatment.

Conclusion: Treatment with DAAs are highly effective with a SVR of about 90% even in patients with advanced liver disease. Nonetheless, in patients with previous history of HCC, the eradication of HCC did not reduce the risk of short and medium-term recurrence.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P1378 PATTERN OF DISTANT EXTRAPANCREATIC METASTASES IN PRIMARY LIVER CANCER: A SEER-BASED STUDY
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Introduction: Primary liver cancer is the sixth most common cancer in the world, after cancers of the lung, breast, colorectal, prostate and gastrae[1]. However, the extremely poor prognosis for primary liver cancer makes it the second leading cause of cancer-related death globally (745,000 deaths, 9.1% of the total death)[2]. Histologically, the majority of primary liver cancer is either
P1381 INTERHEPATIC PORTAL HYPERTENSION WITHOUT CIRRHOSIS: EXPERIENCE OF A MORROCCAN UNIVERSITY CENTER (33 CASES)

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Introduction: Non-cirrhotic portal hypertension (PNH) is defined as a portal hypertension (PH) without cirrhosis in liver biopsy and without an obstruction of the portal and the hepatic veins.

Aims & Methods: This is a retrospective study conducted on the last 19 years in “Hospi Babat et al. district hospital in Rabat. 33 non-cirrhotic patients with interhepatic portal hypertension were analyzed. We medicalized all medical data of patients with hypertension portal without cirrhosis in liver biopsy and without an obstruction of the portal and the hepatic veins.

Results: 33 patients were included in this study. 22 were women. Mean age was 34 years old (18-70). The PNH has been revealed by a digestive bleeding in 10 cases (30%) and ascites in 7 cases (21.2%). Clinical examination found a splenomegaly in (75.7%). Abdominal ultrasonography combined with Doppler showed signs of PH in all patients and confirmed the absence of obstacle on or above the liver. Upper gastrointestinal endoscopy found esophageal varices in 29 cases (87.9%). Various etiologies were identified: in 21.2% (7 cases), extrahepatic PH was due to liver tumors and in 11.7% (n = 4), the etiology was hepatic tuberculosis. Etiological investigations retained: 3 cases (9%) of primary biliary cirrhosis in pre cirrhotic stage, 6 cases (18.18) of hepatic portal sclerosis, 4 cases (12.12%) of hepatic sarcoidosis, 2 cases (6%) of polycystic liver, one case (3%) of hepatic angiomatous liver, a case chronic hepatitis B, a case of Gaucher disease and one case secondary to hamartoma of the liver. Treatment was indicated according the etiology of PH and its severity (beta blockers, ligations).

Conclusion: Non-cirrhotic interhepatic portal hypertension is mostly asymptomatic and related to a heterogeneous association of diseases with a good prognosis excepted solid and hematological malignancies.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P1379 TIME-DEPENDENT EFFECT OF ALFA-FETOPROTEIN AND CONSIDERING STABLE FRACTIONS AS PROGNOSTIC FACTORS FOR SURVIVAL OF BCLC-C STAGE HEPATOCELULAR CARCINOMA

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Introduction: Surgical treatment is nowadays the only curative treatment of hydratic cyst of the liver. Surgical approach exposes to many complications especially biliary fistulas. All modalities are described for the treatment of these complications.

Aims & Methods: A retrospective study including 250 patients who underwent a surgical treatment for a hydratic cyst of the liver between 2007 and 2015. The aim of this study is to evaluate the place of conservative management and his benefits and his complications associated with fistulas.

Results: Conservative surgical treatment of hydratic cyst was done in 180 cases and radical surgery in 70 cases. A complication occurs in 66 cases. An external biliary fistula occurs in 45 cases (18%). Management of all this biliary fistulas was conservative or gastroenteric and was associated with fistula. In case of fistula, the treatment was primary endoscopic treatment necessary to heal fistulas. The median hospital stay was 15 days [range 12-60] when biliary fistulas occurred compared to 8 days [6-15] when there is no biliary complications.
P1383 THE EVOLUTION OF ESOPHAGEAL VARICES IN NON CIRRHOTIC PORTAL HYPERTENSION CAUSED BY PORTAL VEIN THROMBOSIS
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Introduction: Portal vein thrombosis (PVT) is defined as a partial or complete occlusion of portal vein and/or its tributaries by a thrombus. It exposes to portal hypertension (PHT) by infraportal occlusion and consequently to upper digestive hemorrhage, usually due to rupture of gastro esophageal varices.

Aims & Methods: The aim of this study is to specify the evolution of esophageal varices and thus risk of rebleeding in patients with PHT by PVT unrelated to cirrhosis. It is a retrospective study from January 2010 to February 2017, including 101 patients followed for PHT by PVT without liver disease in the depart-ment of hepatogastroenterology (medicine C) at Ibn Sina University hospital of Morocco. PVT was diagnosed by abdominal doppler ultrasonography in all patients.

Results: The mean age of patients was 36 ± 15 years with extremes ranging from 11 years to 70 years. The sex ratio M/F was 0.42. Five percent of patients had a splenectomy for undocumented reasons before the diagnosis of PHT. Concerning the etiology, 10.9% (n = 11) were hospitalized for melanoma and 60.4% (n = 61) for hematemesis and melena and 28.7% (n = 29) for non-specific abdominal pain. Clinical examination was normal in 10.9% (n = 11), showed an axasis in 11.9% (n = 12), and signs of PHT such as splenomegaly and collateral abdominal circulation in 95.1% (sludge in 27.7% cases), complete disappearance of the endoscope, and stones in 4 (15.4%) cases with subsequent endoscopic stones removal. In the remaining patients, PVT confirmed complete duct clearance. No adverse events occurred.

Conclusion: In case of CBD complete clearance confirmation using POC is a feasible, quick and safe procedure that can help on clinical decision making (for example obviat-ing the need for possible plastic stent or naso-biliary drainage placement) without substantial increase of time or costs. Our experience, however, is preliminary and mainly aimed to assess the feasibility of the procedure, which could represent the first step for the development of a possible new indication in the setting of difficult biliary stone management.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1384 EVALUATION OF COMMON BILE DUCT DUCT CLEARENCE AFTER ENDOSCOPIC MANAGEMENT OF DIFFICULT BILIARY STONES BY DIRECT PERORAL CHOLANGIOSCOPY: PRELIMINARY RESULTS OF A PILOT STUDY
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Introduction: Incomplete stones clearance after endoscopic management of diffi-cult biliary stones poses the risk of complications such as cholangitis. Confirmation of complete stones clearance is normally confirmed fluoroscopi-cally with obvious risk of false negative/false positive results, leading to possible ad-vanced stages or costs. Our experience, however, is preliminary and mainly aimed to assess the feasibility of the procedure, which could represent the first step for the development of a possible new indication in the setting of difficult biliary stone management.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1385 LONG-TERM OUTCOMES OF PATIENTS WITH ACUTE CALCULOUS CHOLECYSTITIS AFTER SUCCESSFUL REMOVAL OF GALLBLADDER STONES WITH PERCUTANEOUS TRANSEPHATIC CHOLANGIOSCOPY: A DECADE EXPERIENCE AT A SINGLE TERTIARY CENTER
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Introduction: Percutaneous cholecystostomy (PCT) has been an alternative treat-ment for acute calculous cholecystitis (ACC) for the patients unsuitable for early cholecystectomy. Lithotripsy with percutaneous transhepatic cholangioscopy (PTCS) after PCT track maturation is particularly considered for those patients with gallbladder (GB) stones who are poor surgical candidate. We examined the long-term outcomes of 171 patients with ACC treated by PTCS.

Aims & Methods: This study was a retrospective observational study of 171 consecutive patients who treated with PTCS for ACC in the period from 1 Jan 2005 to 31 Dec 2015. Outcome measures included the success rates, adverse events, recurrence rate and mortality. All data were collected from patients’ medical records.

Results: PTCS achieved complete clearance of GB stones in 157 patients (91.8%). The complication rate of PTCS was 3.5% (6/171). The adverse events included GB perforation (n = 3, 1.8%), hemorrhage (n = 2, 1.2%), disruption of the percutaneous transhepatic biliary drainage fistula (n = 1, 0.6%), and all of which resolved with conservative treatment. The overall recurrence rate of gallstone diseases was 11.5% during the follow up period. The incidence of recurrent gallstone diseases was significantly higher in those with completely removed GB stones than in those without complete clearance (10.2%, 16/157 vs 21.4%, 43/200). Portal contrast passage was used in 100% of patients to assess CBD clearance.

Conclusion: Gallbladder stone removal with PTCS would be recommended as an effective and safe treatment modality for the patients with acute cholecystitis who are unsuitable for surgery.

Disclosure of Interest: All authors have declared no conflicts of interest.
used for initial bile duct cannulation. Subsequently, sphincterotomy and stone extraction were performed using the combined catheter. The success rate of performing the combined procedure, procedure-related time, adverse events, and the cost of devices were compared with those in 10 patients with BDSs ≤10 mm in size who had undergone endoscopic stone clearance from April 2015 to December 2015 as historical control.

Results: The success rate of selective cannulation and stone clearance did not differ significantly (Stonetome group: 90.9% and 100% vs control group: 100% and 100%, respectively). The median time after bile duct cannulation to complete stone clearance and total procedure time in the Stonetome group were significantly shorter than those in the control group (401.5 s versus 982.5 s, 645.5 s versus 1350s, respectively). In the Stonetome group, delayed bleeding occurred in 1 patient. In the control group, bile duct injury caused by the guidewire occurred in 1 patient. The costs of the used devices did not differ significantly (Stonetome group: SEK78 versus control group: SEK69).

Conclusion: The combined catheter has the same selective cannulation ability as a conventional catheter and a similar capacity to remove BDSs as common retrieval. To therefore, the combined catheter can reduce the procedure time to remove BDSs.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1387 ACCURACY OF ASGE CRITERIA IN THE IDENTIFICATION OF PATIENTS WITH SUSPECTED CHOLEDOCHOLITHIASIS

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Introduction: Society for Gastrointestinal Endoscopy (ASGE) emitted, in 2010, guidelines for the clinical orientation of patients with suspected choledocholithiasis (CL), suggesting the direct referral to endoscopic retrograde cholangiography (ERC) in certain groups. However, the ERC is an invasive exam and some studies demonstrated that a significant amount of patients classified with very strong risk of CL did not have alterations in ERC.

Aims & Methods: The aim of this study was to assess the accuracy of the ASGE guidelines in portuguese population. This is a retrospective study that included 212 patients consecutively admitted to the hospital from 2014 to 2016.

Results: Of the 212 patients, 28 (13.2%) had intermediate risk of CL and 184 (86.8%) had high risk, according to the ASGE criteria. These patients were submitted to the following exams/interventions: ERC (154 patients); magnetic resonance cholangiography (50 patients) and endoscopic ultrasound (8 patients). In patients initially classified with high risk of CL, this was confirmed in 119 (64.7%). The same was seen in 10 (35.5%) of the patients with intermediate risk. The ASGE criteria, when applied to this population, demonstrated an accuracy of 64.3% (21.7% sensitivity; 92.3% specificity) in the high-risk group, and an accuracy of 35.5% (78.3% sensitivity; 7.8% specificity) in the intermediate-risk group. Of the patients with intermediate probability, 12 (42.8%) underwent ERC and CL was found only in 4 of these patients. The presence of cholangitis, a common bile duct > 6 mm, a common bile duct stone visualized on transabdominal US and a total bilirubin > 4 mg/dL were strong predictors of CL. The overall ERC complication rate was 13% (20 patients), of whom 8 had no change.

Conclusion: The ASGE guidelines showed a limited diagnostic accuracy in the identification of patients who actually require ERC, conditioning a significant number of unnecessary procedures with subsequent complications associated with it. It is the orientation of these patients, with greater use of less invasive diagnostic techniques such as magnetic resonance cholangiography and endoscopic ultrasound.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

The role of endoscopy in the evaluation of suspected choledocholithiasis by the American Society for Gastrointestinal Endoscopy, volume 71, No1: 2010 Gastrointestinal Endoscopy

P1388 DOES FIBRIN GLUE APPLIED ON THE CHOLANGIOTOMY DURING LAPAROSCOPY COMMON BILE DUCT EXPLORATION REDUCE THE RISK OF BILE LEAKAGE? A RANDOMIZED STUDY

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Introduction: Laparoscopic choledochotomy as a method of extracting common bile duct stones is a technique with many advantages. One problem, however, is bile leakage around the T-tube. To some extent the leakage may be reduced if the incision is sutured around the T-tube, but this technique has some disadvantages. The aim of this study was to investigate whether application of fibrin glue around the tube results in less leakage than suturing.

Aims & Methods: Between 2012 and 2016 a total of 1347 choledectomies were performed in Enköping Hospital. From this group, 42 patients were included in the study and randomized to suturing or fibrin glue for closing the cholangiotomy around the T-tube. Postoperative cholangiography was performed after 7–10 days after surgery. The amount of flow in the abdominal drain and the level of total bilirubin was measured daily. In case the flow ceased, the abdominal drain was extracted three days after surgery.

Results: No significant difference between the groups was seen regarding the flow of the abdominal drain or the T-drain for the first three days or operation time.

Conclusion: Fibrin glue may be an option to seal cholangiostomy around the T-tube, but studies with greater statistical power are needed to confirm this.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1389 THE IMPACT OF BARIATRIC SURGERY ON ACUTE CHOLANGITIS MORTALITY AND OTHER OUTCOMES: A NATIONWIDE ANALYSIS

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Introduction: Rapid weight loss after bariatric surgery (BS) has been associated with the formation of gallstones, and subsequent acute cholecystitis and cholangitis (AC). However, the complex post-surgical anatomy limits the possibility of performing an ERC as part of AC treatment. Therefore, the aim of this study was to assess the impact of bariatric surgery on mortality and resource utilization among patients with AC using a national database.

Aims & Methods: This was a case-control study using the National Inpatient Sample 2013, the largest publically available inpatient database in the United States. All patients with an ICD-9 CM code for a principal diagnosis of AC were included. There were no exclusion criteria. Patients with a past history of BS were identified using the appropriate ICD-9-SCM codes. The primary outcome was all cause mortality. The secondary outcome was resource utilization: use of ERCP, cholecystectomy, length of hospital stay (LOS), total hospitalization charges and costs. Multivariate regression analyses were used to adjust for the following confounders: Age, sex, race, income in patients’ zip code, Charlson Comorbidity Index, hospital region, location, size and teaching status.

Results: A total of 274,775 patients with AC were included in the study, of which 4,240 (1.7%) had undergone BS. The mean patient age was 51 years and 48% were female. After adjusting for confounders, patients with and without history of bariatric surgery had similar adjusted odds of mortality (adjusted Odds Ratio (aOR): 0.87, 95% CI: 0.51–1.49, p = 0.57). As far as resource utilization, patients with bariatric surgery had lower adjusted odds of ERC (aOR: 0.28, 95% CI: 0.09–0.83, p = 0.02), but higher odds of cholecystectomy (aOR: 3.18, 95% CI: 1.00–10.05, p = 0.04). Both patient groups had similar adjusted length of stay (adjusted mean difference: 1.19 days, 95% CI: 0.09–0.83, p = 0.16) total hospitalization charges and costs. Multivariate regression analyses were used to adjust for the following confounders: Age, sex, race, income in patients’ zip code, Charlson Comorbidity Index, hospital region, location, size and teaching status.

Conclusion: Bariatric surgery has no impact on inpatient all-cause mortality among patients who develop acute cholangitis, despite its association gallstone acute pancreatitis and limited ERC performance. In addition, bariatric surgery does not affect resource utilization in this patient population as measured by length of stay and total hospitalization charges.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1391 PATHOLOGICAL, CLINICAL AND RADIOLOGICAL CHARACTERISTICS OF NEOPLASTIC AND NONNEOPLASTIC GALLBLADDER POLYPS

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Introduction: Prevalence of gallbladder polyps in the Netherlands is 943 per 100,000 cholecystectomies. Histopathologically these gallbladder polyps can be divided into neoplastic polyps (with malignant potential) and nonneoplastic polyps (without malignant potential). Although cholecystectomy is only indicated for neoplastic polyps, 47% of polyps after cholecystectomy are nonneoplastic. Further information on the pathological characteristics and subsequent clinical and radiological features could be useful to predict neoplastic or nonneoplastic nature of the gallbladder polyp before surgery.

Aims & Methods: To assess pathological characteristics of neoplastic and nonneoplastic gallbladder polyps and identify preoperative clinical and radiological predictors for neoplastic and nonneoplastic polyps. Data of the Dutch Pathology Registry was used. In this search 2081 histopathologically proven gallbladder polyps (or focal wall thickening ≥5 mm) were identified in patients of ≥18 years undergoing primary cholecystectomy between 2003 and 2013. Of these
polyps 36.3% was neoplastic (adenoma, dysplasia, carcinoma or other malignancies) and 43.7% nonneoplastic (all other types of polyp). Age and sex of the patient, number of polyps, size of the polyp, coincidence with gallstones and presentation as protruding polyp or wall thickening were extracted from the excerpts. Additional clinical and radiological information was collected from patients. Clinical records at three hospitals in the Northeast India (n = 178). The following clinical and radiological predictors were considered: age, gender, ethnicity, BMI, medical history (PSG, Hepatitis, metabolic syndrome, gallbladder disease, Salmonella typhi or Helicobacter pylori infection), family history of gallbladder and cholangiocarcinoma and radiological features (size, number, shape, surface and echogenicity of the polyp). Associations between possible predictors and gallbladder polyps were assessed using univariate and multivariate logistic regression analysis.

Result: Patients with neoplastic polyps were found to be significantly older than patients with nonneoplastic polyps (mean age 65.0 vs 54.2 years, p < 0.001). Neoplastic polyps were significantly larger (mean size 18.1 mm (SD 17.9) vs 7.5 mm (SD 5.9), p < 0.001), more frequently presented as wall thickening (29.2% vs 15.6%, p < 0.001) as a single polyp (38.3% vs 68.0%, p < 0.001). Gallstones were more frequently found in gallbladders with neoplastic polyps (50.1% vs 40.4%, p > 0.001). No preoperative clinical features were predictive for neoplastic or nonneoplastic polyps. Presence of a single polyp on ultrasound was a predictor for neoplastic polyps (OR 6.00 (95%CI 1.32-27.31). Size and type of polyp were often not mentioned in ultrasound report, or different from histopathological confirmation.

Conclusion: Except for age, no clinical characteristics for neoplastic polyps were identified in this cohort. Although pathological characteristics of neoplastic and nonneoplastic polyps are confirmed, identification of these characteristics on preoperative radiological investigations is poor.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1392 METFORMIN INDUCES APOPTOSIS AND MODULATES PROLIFERATION IN THE BILE DUCT CANCER CELLS


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Introduction: Metformin has evidence of antineoplastic activity in some cancer cells.

Aims & Methods: This study was performed to demonstrate in the bile duct cancer cells whether metformin inhibits the proliferation of cancer cells by inducing apoptosis and affects the expression of gene-related proteins involved in cancer growth, and to identify how metformin affect molecular mechanisms involved in the inhibition of cancer cell growth. Human intrahepatic bile duct cancer cells were cultured. 3-(4,5-Dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assays were performed to determine the effect of metformin on cell proliferation. Apoptosis was measured by a cell death dye detection enzyme-linked immunosorbsent assay and caspase-3 activity assay. Various protein expressions with or without specific SiRNA transfection were measured by Western blot analysis. The migratory activity of the cancer cells was evaluated by wound healing assay.

Results: 1) Metformin suppressed cell proliferation in bile duct cancer cells by inducing apoptosis. 2) Metformin inhibited mammalian target of rapamycin (mTOR) by activation of AMPKThr172 - tuberous sclerosis complex 2 (TSC2) pathway, and hyperglycemia impaired metformin-induced activation and enhanced phosphorylation of AMPKThr172. 3) Metformin induced expression of key genes of the BER short and long patch pathway. The data also suggests which inturn is due to genetic, expression and epigenetic deregulations in the key genes of the BER short and long patch pathway. Conclusion: The data indicates an important role of oxidative stress in the pathogenesis of bile duct cancer, and the effect was impaired by hyperglycemia. The data are important to be important targets for future development of chemotherapeutic agents.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
2. Chaiteerakij R1, Yang JD, Harmsen WS, Slettedahl SW, Mettler TA, Fredericksen ZS, Kim WR, Gores GJ, Roberts RO, Olson JE, Therneau TM. The genetic alterations in hOGG1 and XRCC1 gene were highly prevalent in both controls and gallbladder disease cases in NEI population, and was associated with susceptibility and severity of gall bladder anomalies compared to controls, which is significantly lower for CRC in 280 polymorphism in GBC cases compared to controls [OR = 1.986, p = 0.047]. Differential mRNA expression profile clearly showed a sharp down-regulation in hOGG1, APE1, p53 and PARP1 expression in GBC, CL and CS cases compared to controls; and in GBC compared to CL and CS cases. The mRNA expression profile of both short and long patch pathway genes was analyzed as well as bile juice. Each sample was obtained prior to the treatment effect in future, so called “precision medicine” approach based on the biopsy results.
3. Chaiteerakij R1, Yang JD, Harmsen WS, Slettedahl SW, Mettler TA, Fredericksen ZS, Kim WR, Gores GJ, Roberts RO, Olson JE, Therneau TM. The development of non-invasive molecular diagnostics of gallbladder cancer by bile juice-liquid biopsy:

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Introduction: Gallbladder cancer (GBCa) is often diagnosed at advanced stage due to the lack of specific symptom,怎么办 diagnose in early stage, because patients with early GBCa has not showed any symptoms and the tissue cannot be obtained easily with anatomical reason. This resulting poor prognosis, because the patients with early GBCa has not showed any symptoms and the tissue cannot be obtained easily with anatomical reason. The genetic alterations in hOGG1 and XRCC1 in cases compared to controls; and in GBC cases compared to CS cases. The protein also showed down-regulation of hOGG1 and XRCC1 in cases compared to controls; and in GBC cases compared to CS cases. The protein also showed down-regulation of hOGG1 and XRCC1 in cases compared to controls; and in GBC cases compared to CS cases. The protein also showed down-regulation of hOGG1 and XRCC1 in cases compared to controls; and in GBC cases compared to CS cases. The protein also showed down-regulation of hOGG1 and XRCC1 in cases compared to controls; and in GBC cases compared to CS cases. The protein also showed down-regulation of hOGG1 and XRCC1 in cases compared to controls; and in GBC cases compared to CS cases. The protein also showed down-regulation of hOGG1 and XRCC1 in cases compared to controls; and in GBC cases compared to CS cases. The protein also showed down-regulation of hOGG1 and XRCC1 in cases compared to controls; and in GBC cases compared to CS cases. The protein also showed down-regulation of hOGG1 and XRCC1 in cases compared to controls; and in GBC cases compared to CS cases. The protein also showed down-regulation of hOGG1 and XRCC1 in cases compared to controls; and in GBC cases compared to CS cases. The protein also showed down-regulation of hOGG1 and XRCC1 in cases compared to controls; and in GBC cases compared to CS cases.

Conclusion: The data indicates an important role of oxidative stress in the pathogenesis of bile duct cancer, and hence holds clinical relevance.

Disclosure of Interest: All authors have declared no conflicts of interest.
treatment. As negative controls, 19 non-GBCa bile juice and 33 non-GBCa tissue samples were used. The mutations of oncogenes in the same way.

Results: The median (range) age was 77 (44–90) years and the male/female ratio was 0.43 (9:21). Six, six, and twelve patients were diagnosed as stage I, II, III, and stage IV, respectively. We set cut-off value at 5% for rare mutation rate based on the results of healthy samples to avoid false positive. Eleven of 20 (55%) tumor tissue samples were positive for mutation. TP53, MET, SMAD4, CTNNB1 and AR were detected in 7/20 (35.0%), 1/20 (5.0%), 1/20 (5.0%), 1/20 (5.0%) and 1/20 (5.0%) respectively. In this study, 14 of 30 (46.7%) patients had both tumor tissue samples and bile juice samples. Eight of 14 (57.1%) tumor tissue samples were positive for mutation. In these eight patients, 7 (87.5%) bile juice samples had the same mutation (TP53, ERBB2/3 were detected in 6/8 (75%), 1/8 (12.5%), respectively). On the other hand, bile juice samples of one of 6 tumor tissue mutation had no mutation. With regard to only bile juice, 14 of 24 (58.3%) bile juice samples with GBCa were positive for mutations. TP53 mutation, ERBB2/3, KRAS were detected in 11/24 (45.8%), 2/24 (8.3%), 1/24 (4.2%), respectively. Bile juice analysis for mutations indicated that bile juice has the ideal positive predictive value (PPV) and negative predictive value (NPV) were 58.3%, 100%, 100% and 65.5%, respectively. None of negative control samples had any mutations.

Conclusion: Mutations in tumor could be detected in bile juice using NGS. Liquid biopsy with bile juice may help us to diagnose GBCa because of high PPV (100%). It may allow us to make new genetic diagnosis of GBCa.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1395 EFFICACY OF INTRADUCTAL RADIOFREQUENCY ABLATION USING A NOVEL ENDOLUMINAL RADIOFREQUENCY ABLATION CATHETER IN A SWINE MODEL

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Introduction: Intraductal radiofrequency ablation (RFA) is a new endoscopic ablative technique with direct effect to local tumor has been developed to improve the course of self-expandable metal stents (SEMS) in the unresectable malignant biliary obstruction. However, there is the concern for the complication such as bile duct perforation or bleeding because the ideal power setting of RFA has not been clearly revealed still.

Aims & Methods: We aimed to investigate the effects of ablative injury after in vivo intraductal RFA according to the time variation using a novel RFA catheter (ELRA®, STARmed, Goyang, Korea). This novel catheter is a bipolar device and has a temperature sensor within the distal tip, therefore it has a characteristic of target temperature controlled mode. Nine female pigs were divided into three groups according to RFA time variation (60, 90 and 120 seconds) with the same power setting (10 watts) and RFA target temperature (80°C). All pigs underwent endoscopic retrograde cholangiography (ERC) and intraductal RFA. Additional cholangiogram was taken immediately after RFA and then a plastic stent was inserted. All the pigs were humanely sacrificed 24 hours after the intraductal RFA. Necropsy was performed and the common bile duct was examined for histologic analysis.

Results: The ERC and application of the intraductal RFA was successful in 100%, and post-RFA cholangiogram did not show the contrast leakage.

Conclusion: Intraductal RFA has not been clearly revealed still. The predictive model for the probability of neoplasia was fitted from the training set using the logistic regression method equipped with backward elimination with significance: level for removal of P > 0.05 for variable selection. The performance of a fitted prediction model was evaluated by the area under the curve (AUC) of a receiver operating characteristic (ROC) curve. A cutoff value of the fitted risk score was chosen by the Youden Index.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1397 COMPARISONS OUTCOMES FOR CONTROLLED PHOTODYNAMIC THERAPY IN HIGH GRADE UNRESECTABLE HILAR CHOLANGIOCARCINOMA

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Introduction: Photodynamic therapy (PDT) provide clinical benefit for patients with unresectable biliary malignancy. In this study, we evaluate the efficacies of controlled PDT for unresectable primary and secondary high-grade hilar cholangiocarcinoma (CC).

Aims & Methods: In cases of high-grade unresectable hilar CC (Bismuth type III or IV) and gallbladder (GB) cancer invasion to hilar portion (Group A), we performed controlled PDT. Controlled PDT means malignant stricture dilatation using balloon catheter up to 120 seconds in CC. We performed PDT with straight angled cylindrical diffuser using with gemcitabine-based chemotherapeutics in similar patients (Group B) in terms of clinical parameters and developing complications.

Results: Between July 2010 and June 2015, 26 cases(31) of high grade unresectable hilar CC (Bismuth type III or IV), 5 cases of GB cancer with hilar invasion were enrolled for Group A, 23 cases(26) of high-grade unresectable hilar CC (Bismuth type III or IV), 3 cases of GB cancer with hilar invasion were enrolled for Group B. On three months later, serum bilirubin levels decreased from 7.3 ± 5.2 to 2.4 ± 1.8 mg/dL in group A, 6.9 ± 5.5 to 5.2 ± 3.7 mg/dL in group B (P < 0.05). PDT-induced cholangitis is developed in Group A (3/1, 9.6%) and B (7/26, 26.9%) within seven days (p < 0.001), Progression free survival is superior Group A to Group B that of 14.8 months vs. 8.9 months (P < 0.05).

Conclusion: Controlled PDT with applying cylindrical diffuser promise efficacy for clinical parameters and progression free survival compared with transpyaipal PDT in unresectable high-grade hilar CC and GB cancer. Additionally, diminished post-PDT cholangitis within 7 days affect improving long term progression free survival.

Disclosure of Interest: All authors have declared no conflicts of interest.

References


Disclosure of Interest: While many studies have attempted to define the risk factors for neoplastic potential of gallbladder polyp, precise adaption of the risk factors individually in a real treatment strategy of gallbladder polyp remains elusive. Evaluating the probability for neoplastic potential of gallbladder polyp using a combination of several risk factors before surgical resection would be useful in patient consultation.

Aims & Methods: This study was designed to provide the statistical predictive model for neoplastic potential of gallbladder polyps. We collected data of patients confirmed as GBP through cholecystectomy at Samsung Medical Center between January 1997 and March 2015. Those with a definite evidence for malignancy, such as adjacent organ invasion, metastasis on preoperative imaging studies, polyp larger than 15 mm, and absence of proper preoperative ultrasonography imaging, were excluded. A total of 1976 patients were enrolled.

To make and validate the predictive model, we divided the cohort into the modeling group (n = 979) and validation group (n = 997). Clinical information, ultrasonographic findings, and blood tests were retrospectively analyzed. A prediction model for the probability of neoplasia was fitted from the training set using the logistic regression method equipped with backward elimination with significance: level for removal of P > 0.05 for variable selection. The performance of a fitted prediction model was evaluated by the area under the curve (AUC) of a receiver operating characteristic (ROC) curve. A cutoff value of the fitted risk score was chosen by the Youden Index.

Disclosure of Interest: All authors have declared no conflicts of interest.

References


P1398 IG4G-ASSOCIATED CHOLANGITIS MIMICKING PERIHILAR CHOLANGIOCARCINOMA: A PERSISTENT DILEMMA

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Introduction: Unexplained cholangitis (IAC) associated with IgG4-related disease (IgG4-RD), a multi-organ inflammatory disorder of unknown cause. IAC may present with jaundice, abdominal pain and weight loss; immunosuppression is the preferred treatment. Since the disease presentation may closely mimic that of malignancies of the pancreatobiliary tract and accurate diagnostic tests have only recently been evaluated, misdiagnosis and unnecessary surgery are common. The disease had been consistently reported in literature.

Aims & Methods: Our aim is to assess the incidence of Immunoglobulin G4-associated cholangitis (IAC) in patients resected for presumed perihilar cholangiocarcinoma (PHC).

Results: Between 1984 and 2015, 321 patients underwent liver and bile duct resections for presumed PHC. Of all patients 15% (47/321) were found to have benign disease with still alive were re-evaluated to assess IgG4 serum levels and IgG4/IgG RNA ratio to detect activity of IAC.

Conclusion: Benign hilar disorders mimicking PHC have led to considerable number of liver and bile duct resections during the last three decades. There was evidence of IAC in 45% of these patients. When left untreated, IgG4-RD can reduce misdiagnosis and unnecessary surgery. Novel accurate diagnostic tests for IAC might reduce misdiagnosis and unnecessary surgery.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1399 DIGITAL, SINGLE-OPERATOR CHOLANGIOPANCREATOSCOPY IN THE DIAGNOSIS AND MANAGEMENT OF PANCREATOBILIARY DISORDERS: RESULTS FROM THE MULTICENTER CZECH AND SLOVAK NATIONAL DATABASE

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Introduction: Digital cholangioscopy provides higher-resolution imaging of the pancreatobiliary tract compared to the 1st fiberoptic generation. The impact of a new single-operator digital cholangioscope (d-SOC) in diagnosis and treatment of pancreatobiliary diseases has not been intensely assessed.

Aims & Methods: The aim of this retrospective analysis of prospective case series is to evaluate the outcomes of patients from the Czech and Slovak (n = 321) first generation of d-SOC compared to the 1st fiberoptic generation. The primary outcome was achievement of a complete ductal clearance in patients with difficult biliary strictures (1) and diagnostic accuracy of d-SOC visual diagnosis and biopsies in patients with undetermined biliary strictures; (2) the efficacy of d-SOC directed treatment of difficult lithiasis and (3) to analyze procedure related adverse events (AEs). The diagnostic accuracies were (1) sensitivity (2) specificity for (1) without biopsies (2) achievement of a complete ductal clearance in patients with difficult lithiasis (3) procedure-related AEs.

Results: A total of 150 patients underwent 166 d-SOC procedures (165 cholangioscopies and 1 pancreatoscopy); 81 (48.8%) for diagnostic intents (with biopsy in 66/81 patients (81.5%), and 85 (51.2%) for therapeutic intents (1 patient had pancreaticolithiasis). The most frequent indication for diagnostic d-SOC was undetermined stenosis (n = 59). Reliable views of a target lesion were obtained in all patients. The sensitivity, specificity and diagnostic accuracy of d-SOC for visual diagnosis of malignant lesion was 88.9% (95%CI, 70.9–97.7), 81.2% (65.6–92.3) and 84.6% (73.5–92.4). The number of biopsies obtained per patient was 4 (range 1–13) and the specimen was adequate for histopathological review in 85.5% of patients. The sensitivity and diagnostic accuracy of d-SOC guided biopsies for malignancy were 78.3% (95%CI, 56.3–92.5), 96.4% (81.6–99.9) and 83.3% (70.7–92.1). The diagnostic accuracy of visual inspection was not statistically influenced by the presence of biliary stent (Yates’ χ²=0.9). Of 63 patients attended for d-SOC-guided stone therapy, a complete intraductal clearance was achieved in one session in 37 and in two sessions in further 10 patients, respectively and the overall success rate was 77%. A total of 11 patients (11/166; 6.6%) experienced an adverse event (cholangitis n = 6, pancreatitis n = 3, perforation n = 2), one patient with severe cholangitis died. The incidence of cholangitis was higher among patients who had received prophylactic antibiotics (n = 5) compared to those who had not received it (n = 1). The results of the second analysis were similar. The new generation of d-SOC shows that (1) It provides high diagnostic yield in patients with undetermined biliary stenosis; (2) The SOC directed biopsies have a high diagnostic accuracy; (3) d-SOC guided stone lithotripsy is effective in three quarters of patients and (4) Severe adverse events may occur and prophylactic antibiotics may not be effective in preventing post-d-SOC cholangitis.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1400 DISTINCT PROGNOSTIC VALUE AND BIOLOGICAL CHARACTERISTICS OF OSTEOPONTIN IN INTRAEPATHEPATIC CHOLANGIOCARCINOMA

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Introduction: Intrahepatic cholangiocarcinoma (ICC) is famous for its poor prognosis. Deepen the knowledge of the mechanism of ICC contributes to improving the treatment. Osteopontin (OPN) is believed to promote tumorigenesis and metastasis in many kinds of cancers, while its role in ICC is controversial.

Aims & Methods: This study aims to investigate the prognostic value and biological characteristics of OPN in ICC. The expression of OPN was evaluated by qRT-PCR to find the expression ratio to detect activity of ICC. Quantitative PCR was used to investigate the relationship between SPPI and overall survival (OS) in 85 patients. Immunohistochemistry was used for detecting the prognostic value of OPN, as well as the correlation between OPN and clinicopathological characteristics. Stably transfected ICC cell lines which express either higher or lower level of OPN were conducted for lenti virus. Cell-IQ, the live cell imaging and analysis system, was used for proliferation and migration assay. Wound healing assay and Transwell assay was taken to investigate the ability of migration and invasion among transfected cell lines. PCR array was taken to screen the potential oncogenes regulated by OPN.

Results: SPPI is the most highly expressed genes in ICC with fold change of 43.35 according to HTA 2.0. ICC cell lines express higher level of SPPI and OPN than normal live cell line (P < 0.01). SPPI is higher in tumor than adjacent tissues. Patients with higher expression of SPPI in ICC has better OS than those with low expression (P < 0.01). SPPI and OPN are independent prognostic factors. Higher expression of OPN correlates with better differentiation of ICC and less lymph node metastasis. Compared with negative controlled (NC) cells, ICC cell lines expressing more OPN showed accelerated proliferation rate, stronger ability of migration and invasion. Likewise, ICC cells lines expressing less OPN than NC cells proliferated slower, their capability of migration and invasion was inhibited as well. MMP1, MMP10 and CXCR4 were down regulated in ICC cell lines which express either higher or lower level of OPN were conducted for lenti virus. Cell-IQ, the live cell imaging and analysis system, was used for proliferation and migration assay. Wound healing assay and Transwell assay was taken to investigate the ability of migration and invasion among transfected cell lines. PCR array was taken to screen the potential oncogenes regulated by OPN.

Conclusion: High expression of OPN in ICC tumors indicates less aggressive behavior of ICC and better overall survival for patients after resection. OPN is an advantage prognostic factor in ICC. OPN might function as an inhibitory factor of MMP1, MMP10 and CXCR4 to weaken the capability of migration and invasion in ICC cell lines.

Disclosure of Interest: All authors have declared no conflicts of interest.

References


P1401  PANCREATIC STENT PLACEMENT AFTER ENDOSCOPIC RESECTION OF AMPULLARY TUMORS IS MANDATORY

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Introduction: Adenoma of the major duodenal papilla is clinically important because this lesion is premalignant and should be resected completely. Endoscopic papillectomy of ampullary adenomas is a promising alternative to surgical resection, however acute and delayed pancreatitis represent a major complication of this procedure.

Aims & Methods: We evaluated the clinical importance of pancreatic duct drainage after endoscopic papillectomy in order to prevent early (acute pancreatitis) and late (pancreatic duct orifice stenosis) complications of this procedure. Our single-center study with a minimal follow-up of 1 year, includes 19 patients who underwent endoscopic ampullectomy between 2012 and 2016. Careful preoperative evaluation was performed by EUS (100% of patients) and CT/MRI (94%). After a collective evaluation between the surgeon and the endoscopist, patients were candidate for endoscopic ampullectomy. Outcome parameters included ampulla morphology, biophysical accuracy as well as safety, efficacy, recurrence rate, and survival.

Results: Endoscopic resection was successful in 15 patients (79%). Histological resection margins revealed non-specific changes (10.5%), low-grade dysplasia (52.6%), high-grade dysplasia (18.5%) and carcinoma (21%). Biopraphic accuracy was 68.4%. In 4 cases histologic specimen revealed an invasive carcinoma: 2 patients underwent pancreaticoduodenectomy and two were treated conservatively with placement of biliary and pancreatic stents due to the high preoperative risk. After complete endoscopic resection (15 patients), pancreatic stents were placed in 10 cases (66%). In five cases the stents were treated by snare papillectomy and diathermal ablation (APC).

Conclusion: Pancreatic stent placement after endoscopic ampullectomy is mandatory to prevent acute and delayed pancreatitis complications. Preoperative strategy should be accurate by MRI, EUS and ERCP, in order to define the anatomy of the pancreatic duct aiming to improve the success rate of pancreatic stent placement after papillectomy.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

P1403  SELF-EXPANDABLE METAL STENT ARE SUPERIOR TO PLASTIC STENT FOR PREOPERATIVE BILIARY DRAINAGE IN RESECTABLE MALIGNANT DISTAL BILIARY STRicture: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: Early surgery is the standard treatment in patients with resectable periampullary or pancreatic head cancer with jaundice. However, early surgery is not always possible and PBD could be a necessary for patient with jaundice at diagnosis or for those undergoing neoadjuvant treatment. Most studies considered plastic stents for BPD, although SEMS are currently considered superior. A recent RCTS showed that fully covered SEMS are associated with better outcomes compared to plastic stents.

Aims & Methods: Aim compare the rate of endoscopic reintervention (Stent failure of PBD) before surgery and post operative outcome of metal vs plastic. We conducted a bibliographic search using PUBMED, EMBASE including random and non randomized trials. OR using the Manhfeld-Haenszel method was used for dichotomous variables. Weighted mean differences (WMD) were used as the summary statistic for quantitative analysis of continuous variables. Quantitative synthesis was performed using Review Manager version 5.0.

Cholangiocarcinoma & control Significance test

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<th>Cholangiocarcinoma</th>
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<th>Sex</th>
<th>Significance test</th>
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<td>Male</td>
<td>24 (48.9%)</td>
<td>23 (51.1%)</td>
<td>0.8, P &lt; 0.01</td>
<td>t=0.08, P = 0.4</td>
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<td>Female</td>
<td>22 (45.9%)</td>
<td>23 (51.1%)</td>
<td>0.8, P &lt; 0.01</td>
<td>t=0.08, P = 0.4</td>
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P1403  SERUM LEVELS OF HEAVY METALS IN CHOLANGIOCARCINOMA PATIENTS FROM THE NILE DELTA REGION OF EGYPT: A SINGLE-CENTRE STUDY

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Introduction: Cholangiocarcinoma is a neoplasm arising from the intra- or extrahepatic bile duct lining epithelium. Cholangiocarcinoma are presents less than 2% of human malignancies, however, it is the second common primary hepatic malignancy. Till date, many carcinogens have already been identified and the relevant information with regard to these agents is available. One example is the potentially harmful presence of heavy metals that can cause serious health problems. Mental retardation may be exposed to heavy metals as a consequence of their lifetime. The heavy metals in drinking-water pose the greatest threat to public health in this regard. Nile River water is seriously contaminated with heavy metals, pesticides, herbicides and hydrocarbons as a result of increasing discharge of untreated industrial wastes and agricultural irrigation wastewater. Several reports on Dakahlia Province show high levels of heavy metal and organochlorine pesticides in the soil and water in this region. High concentrations of heavy metals, including cadmium, are among the pollutants in the water. Plants and fish grown in this water are also contaminated with heavy metals, which can in turn accumulate in human tissues and animals that feed on these contaminated foods. The serum cadmium levels of residents of Dakahlia Province are almost 10-fold higher than those of residents from cadmium-polluted areas in Cairo and 32 times higher than reference levels for healthy populations in the United States.

Aims & Methods: We aimed to assess serum levels of Heavy metals namely Zink (Zn), lead (Pb), Cobalt (Co), Cadmium (Cd), Chromium (Cr) and Iron (Fe) as a markers of exposure in cholangiocarcinoma patients and healthy control subjects from the same region in Egypt and its correlation with differentiation of cholangiocarcinoma and tumour marker CA-19.9. This study included 45 patients with cholangiocarcinoma (diagnosed after radiological &histopathological examination) and 20 healthy control subject attending Mansoura Surgical Gastroenterology centre. All patients and control were permanent residents of North Delta region and the patients were recruited before receiving chemotherap- or radiotherapy. There were no restrictions based on age, sex, or tumor stage. The serum samples were analyzed for concentrations of zinc, lead, cobalt, cadmium, iron and chromium by the acid digestion method followed by using atomic absorption spectrometry.

Results: The serum levels of Zn, Pb, Co, Cd and Fe were significantly higher in patients having cholangiocarcinoma more than control subjects (P < 0.001). Pressive increase in the median values of serum levels of lead (Pb) was found in well differentiated to moderately differentiated to undifferentiated tumours. (P < 0.05). When correlation was made between the heavy metals and CA-19.9 and the survival of the patients, it was found that Cd only has a positive correlation with CA-19.9 and negative correlation with the survival of the patients (P < 0.5, (P < 0.01) respectively.

Conclusion: The results from this study suggest that cholangiocarcinoma in the Nile Delta region is significantly associated with high serum levels of heavy metals especially Cadmium and lead.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
Primary outcome was the rate of endoscopic reintervention before surgery. Secondary outcome was the rate of overall surgical complications, 30 days after surgery, post-operative complications, hospital readmission, overall pancreatic fistula, overall biliary anastomotic leak, overall postoperative mortality. Clinical heterogeneity was assessed by I² value, where a value exceeding 50% was indicative of heterogeneity. A random effect model was used in case of heterogeneity.

Results: Three RCTs and five non-RCTs were selected including 909 patients. Of these, 303 patients (33%) were treated with SEMS and 606 (67%) with plastic stents. The rate of endoscopic reinterventions after PBD was significantly lower in the metal stent group in the plastic stent group (p > 0.001). The rate of post operative pancreatic fistula was significantly lower in the metal stent group (OR 0.44 95% CI 0.20–0.96; p = 0.04). The rate of postoperative surgical complications, hospital readmission, overall biliary anastomotic fistula and postoperative mortality did not differ between the two groups.

Conclusion: Metal stents are more effective than plastic and should be preferred for the management of malignant and benign refractory peripancreatic or pancreatic head tumors when early surgery without PBD is not feasible. However, more RCTS are needed before a firm conclusion could be made.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1404 THE EFFICACY AND SAFETY OF PREOPERATIVE BILIARY DRAINAGE IN PATIENTS WITH OBSTRUCTIVE JAUNDICE: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: There is considerd controversy as to whether temporary relief of biliary obstruction prior to major definitive surgery (preoperative biliary drainage) is of any benefit to the patient. A Cochrane meta-analysis revealed a major morbidity with no difference in mortality in the group subjected to PBD. However, the clinical status of patients was heterogeneous between studies.

Aims & Methods: We aimed to investigate the benefits and harms of pre-operative biliary drainage versus no pre-operative biliary drainage (direct surgery) in patients with obstructive jaundice. A computerized medical literature search was performed by using MEDLINE, EMBASE, Cochrane Library, from 1980 to June 2016 aiming at identifying RCTS comparing PBD versus direct surgery. Data from RCTS related to safety and effectiveness of PBD versus no PBD were extracted. A meta-analysis was performed. Odds ratio or mean difference were calculated with 95% cent confidence intervals. Clinical heterogeneity was assessed by I² value, where a value exceeding 50% was indicative of heterogeneity. A random effect model was used in case of heterogeneity. Outcomes were mortality and morbidity.

Results: Nine trials including 734 patients with malignant or benign obstructive jaundice comparing PBD (375 patients) with no PBD (359) were included in this review. There was no significant difference in mortality (risk ratio 0.90, 95% CI 0.67 to 1.18; P = 0.42) and in the two groups. Complications were higher in the PBD group (RR 1.41; 95% CI 1.19–1.67; p = 0.008). Serious morbidity was higher in the PBD group than in the direct surgery group (RR 1.66 95% CI 1.04–2.65; p = 0.042). The rate of peritonitis in the PBD group as well (5.1% vs 11.8%, p = 0.041) was higher in the PBD group than in the direct surgery group (RR 1.66 95%CI 1.04–2.65; p = 0.04).

Conclusion: There is currently not sufficient evidence to support or refute the benefit of PBD stay between the two groups: mean difference 4.55 (95% CI 1.28–2.16 p = 0.001). In multivariate analysis, mortality did not differ between the two groups.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P1406 1-DEOXY-SPHINGOLIPIDS, NOVEL BIOMARKERS OF DIABETES, ARE CYTOTOXIC FOR EXOCRINE PANCREATIC CELLS

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Introduction: Exocrine pancreatic insufficiency and exocrine function alterations are characteristics of pancreatitis. They are frequent in diabetes mellitus (DM) patients with a prevalence up to 50%. Although reduced levels of insulin may explain some of the proposed mechanisms of exocrine pancreatitis in chronic DM, the same phenotype is also detected in insulin-independent DM. This highlights the concept that additional factors are likely to contribute to the pathophysiology of acinar cells. We recently discovered that 1-deoxy-sphingolipids (1-deoxy-SLs), the levels of which increase in DM and metabolic syndrome are cytotoxic for beta cells5. Our preliminary results showed that 1-deoxy-SLs are also cytotoxic for acinar cells in vitro. Furthermore, the high level of 1-deoxy-SLs in diabetic animal model aggravated acinar cell damage whereas lowering 1-deoxy-SLs improved cell deterioration.

Aims & Methods: In this research, we investigate molecular and cellular factors that contribute to compromise acinar cell functionality in the context of DM. Based on the endocrine and exocrine pancreas crosstalk, we hypothesize that elevated 1-deoxy-SLs levels affect directly the pancreatic exocrine compartment by compromising pancreatic acinar cells in DM, thus increasing its predisposition to develop exocrine pancreatic diseases. In vitro mouse models with STZ-induced diabetes and cerulein-induced pancreatitis were used in this study. Reduction of 1-deoxy-SLs synthesis was achieved by oral L-serine supplementation. Disease severity was assessed with biochemical and immunohistochemical methods. Molecular mechanisms of 1-deoxy-SL-dependent toxicity were evaluated in vitro on AR42J pancreatic acinar cells and primary acinar cells.
P1407 ROLE OF THROMBOPHILIA IN SPLANCHNIC VENOUS THROMBOSIS IN ACUTE PANCREATITIS

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Introduction: Splanchnic venous thrombosis (SVT) is a common vascular complication of acute pancreatitis (AP). There is paucity of data on its frequency, risk factors, outcome, and natural history. Coagulation abnormality has been implicated but not proven as a cause of SVT in AP.

Aims & Methods: We aimed to prospectively study the frequency, risk factors and extent of SVT in patients with AP as well as role of thrombophilia in causation of SVT. Patients with AP presenting to our centre between January 2015 and June 2016 were prospectively evaluated with contrast enhanced computerized tomography (CECT) abdomen for presence of SVT. These patients were subjected to Doppler study done in 7 patients with SVT, spontaneous venous thrombosis on follow-up.

Results: A total of 26 (27.1%) had SVT. Single vessel, two vessels and three vessels were involved in 19 (73.1%), 3(11.5%) and 4(15.4%) patients respectively. Splenic vein, portal vein and superior mesenteric vein involvement were seen in 23(88.5%), 14(53.8%) and 4(15.3%) patients respectively. Necrotizing pancreatitis, CTSI > 6 and Modified CTSI > 6 were found in significantly higher number of patients with SVT than those without SVT(96.2% vs 78.6%, 76.9% vs 47.1% and 67.1% vs 67.1%, respectively). Coagulation analysis was performed in all patients (18 with acute AP and 3 with pseudocyst). Protein C, protein S and AT III deficiency were found in 10(38.4%), 14 (53.8%) and 13(51.0%) patients respectively. β2GPI and lupus anticoagulant were positive in 2 (4.8%) and 1 (11.1%) patients respectively. Anticardiolipin antibody was negative in all the patients. Factor V Leiden mutation analysis was done in 33 patients (14 with SVT and 19 without SVT) of which 2 (6.1%) were positive. There was no correlation between abnormal coagulation results and outcome of AP. Coagulation abnormality did not differ significantly between the patients with and without SVT. Follow-up Doppler study done in 7 patients with SVT, spontaneous resoloution of SVT occurred in 5 (71.4%) within 1 year. None of the patients had varices on follow-up.

Conclusion: SVT in AP is more common in patient with necrotizing pancreatitis and higher CTSI and MCTSI indices suggesting that local inflammation plays a major role in its causation. Thrombophilia in some form is seen in one third of the patients with AP but does not increase the risk of AP.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

P1409 EUS-GUIDED PANCREATIC FLUID COLLECTION DRAINAGE WITH LUMEN-APPOSING METAL STENTS OR PLASTIC DOUBLE PIGTAIL STENTS: A MULTI-FACTORIAL ANALYSIS

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Introduction: We aimed to compare the efficiency of plastic and metal stents for symptomatic pancreatic fluid collection drainage and analyze other main associated factors that affect the outcome of drainage therapy.

Aims & Methods: Rates of technical and clinical success, procedure-related side effects (hemorrhage, stent migration, and cyst rupture), re-interventions, and duration of hospital stay.

Results: There were 52 patients, 40 who underwent plastic stent placement and 12 who underwent lumen-apposing metal stent placement. The total rate of technical success was 100%. The total rate of clinical success was 100%. The total rate of adverse events was 7.7% (4/52). On multiple logistic regression analysis, the use of plastic stents (P < 0.05, Exp B = 12.168) and presence of a large cyst (P < 0.05, Exp B = 1.036) were shown to significantly increase the risk of re-intervention. On multivariate linear regression analysis, etiology of pseudocyst (P < 0.05, B = -8.427; -9.785; -5.514) was associated with prolonged hospital stent, while stent type was not shown to be a factor (P > 0.05).

Conclusion: Both plastic and lumen-apposing metal stents are proven to be highly efficient in pancreatic fluid collection drainage. The lumen-apposing metal stent is superior in preventing complications such as migration and cyst leakage and reducing the rate of re-intervention. Large cyst size is associated with an increased risk of re-intervention and prolonged hospital stay.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference}

P1410 EARLY ACHIEVABLE SEVERITY (EASY) INDEX FOR SIMPLE AND ACCURATE EXPEDITE RISK STRATIFICATION IN ACUTE PANCREATITIS

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Introduction: The EASY index has been published a protocol of local infusion of antibiotics for the treatment of IPN (Panreatology; 2016;16:719–25).

Aims & Methods: We aim at analysing the efficacy of this step-up approach for the treatment of IPN in clinical practice. This was a retrospective single-centre study of patients admitted with acute pancreatitis (AP) between January 2015 and December 2016. The cases with the diagnosis of pancreatic necrosis (PN) and IPN (defined by positive culture of necrosis and clinical, analytical, and/or radiological data of infection) were identified and evaluated. IPN was treated following a step-up approach defined by 1. intravenous antibiotic therapy, 2. Endoscopic ultrasound (EUS)-guided transmural drainage plus local antibiotic therapy, 3. endoscopic necrosectomy. Number of patients responding to each therapeutic step was assessed.

Results: 694 cases of AP were included (mean age 79.5 ± 18.3, 555 male). CT scan was performed only if clinically indicated. 67 patients (9.6%) had acute necrotizing pancreatitis (APN), and 21 of them IPN (31% of APN). IPN patients were treated with intravenous antibiotics (imipenem [n = 15] and meropenem [n = 6], with good response in 8 (38% of IPN). The remaining 13 cases underwent a EUS guided transmural drainage plus local antibiotic therapy, 3 endoscopic necrosectomy. Number of patients responding to each therapeutic step was assessed.

Disclosure of Interest: All authors have declared no conflicts of interest.
**Results:**

Studies.

From multiple centers will be enrolled into this trial using the Registry. This is an wards) from patients diagnosed with AP will be performed to assess their poten-

**Aims & Methods:**

We aimed to create a new scoring system, which can predict the efficacy of local instillation of antibiotics into walled-off pancreatic necrosis. Between 2012 and 2016 we evaluated all patients treated with endoscopic transmural drainage and necrosectomy (EDTN) and concomitant local instillation of antibiotics. We added antibiotics (either gentamicin, vancomycin, or amphotericin B) to the irrigation fluid according to the microbiological findings. The anti-

**Disclosure of Interest:**

All authors have declared no conflicts of interest.

**Conclusion:** Our data suggest a better efficacy of local antibiotics in the treatment of infected WON compared to systemic antibiotics. The local instillation of antibiotics may be a promising alternative or supplement to systemic adminis-

**Disclosure of Interest:**

All authors have declared no conflicts of interest.

**Aims & Methods:**

The aim was to evaluate the efficacy of local instillation of antibiotics into walled-off pancreatic necrosis. Between 2012 and 2016 we evaluated all patients treated with endoscopic transmural drainage and necrosectomy (EDTN) and concomitant local instillation of antibiotics. We added antibiotics (either gentamicin, vancomycin, or amphotericin B) to the irrigation fluid according to the microbiological findings. The anti-

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All authors have declared no conflicts of interest.

**Disclosure of Interest:**

All authors have declared no conflicts of interest.

**Disclosure of Interest:**

All authors have declared no conflicts of interest.
P1413 WORSE OUTCOMES IN ACUTE PANCREATITIS IN PATIENTS WITH TYPE-2 DIABETES MELLITUS

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Introduction: Predicting severe pancreatitis is important for early aggressive management of patients with acute pancreatitis (AP). Despite the established role of type-2 diabetes mellitus (DM) in the risk of AP, the impact of DM on the clinical outcome in AP has not been fully elucidated.

Aims & Method: Retrospective study including hospital admissions between January 2003 and December 2016 in a single tertiary referral center. Clinical outcomes included organ failure of (OF), persistent OF (>48h) admission to intensive care unit (ICU) and mortality. Variables were analysed by logistic regression (SPSS v23.0). The objective of this study was to assess the risk of mortality and severity in AP among patients with type-2 DM.

Results: A total of 553 patients (58.4% male) with AP were included, median age 80 (18–98) years. Most common etiologies included gallstones (38.9%) and alcohol (27.5%). Twenty three percent developed OF (in 43% persistent) and 5.6% died. There were 127 AP patients (23.0%) with type-2 DM. Type-2 DM were not associated with higher Ranson’s score. There was an association between DM and development of OF (OR 3.17, CI95% 18.8–53.7, p < 0.001), persistent OF (OR 45.1, CI95% 18.7–108.9, p < 0.001), ICU admission (OR 12.3, CI95% 2.8–4.1, p < 0.001) and AP severity (OR 17.1, CI95% 6.8–42.8, p < 0.001). At multivariate analysis DM was an independent predictor of OF development and ICU admission.

Conclusion: In our population, Type-2 DM was associated with severity and increased mortality in patients with AP. Our findings provide evidence of the potential role of DM in the management of severe AP.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P1414 ACUTE Pancreatitis IN LIVER TRANSPLANT RECIPIENTS: INCIDENCE AND OUTCOME

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Introduction: Acute pancreatitis (AP) is an uncommon but potentially devastating condition that may occur in patients with organ transplantation. Reported incidence ranges from 1.5 to 8% in patients undergoing liver transplantation with significant mortality.

Aims & Methods: The aim of our study was to assess the incidence, potential risk factors and outcome of AP following liver transplantation in our center. We performed a retrospective medical analysis of medical records of all adult patients who underwent liver transplantation in our center between September 1996 and November 2014. The diagnosis of AP was defined by combination of clinical manifestation, finding on imaging methods (CT, USG) and elevation of serum amylnase and lipase. AP was confirmed if it occurred within 1 month after liver transplantation and late (>1 month).

Results: Nine hundred and sixty-seven orthotopic liver transplantations were performed in 578 males and 389 females (mean age 51 years, range 18–74). AP occurred in 18 patients (1.9%, 16 males, 2 females) and resulted in death in 5 patients (28%). According to timing of AP we recognized two clinical presentation—early AP (<1 month after liver transplantation) and late (>1 month). Four patients (22%) developed early AP, which was severe necrotizing with MODS in all cases and resulted in death in 3 of them (75%). Two of them were transplanted for fulminant hepatic failure, one for end-stage liver disease due to chronic hepatitis B infection and one for polycystic liver disease. Two patients were treated by surgical necroctomy and died, the third deceased patient was treated conservatively. In the only surviving patient, a successful EUS-guided drainage of walled of pancreatic necrosis and repeated endoscopic retrograde cholangiopancreatography were performed, and the patient was discharged. The patient was discharged and in good condition within 3 months after the admission and was discharged. However, there were 2 patients who died from acute pancreatitis. One patient developed a pseudocyst. Two patients with late acute pancreatitis had a severe necrotizing form and both died. One patient with cirrhosis of the liver graft, the second patient a chronic rejection of liver graft. AP diagnosed by necrotic pancreatitis which was complicated by retroperitoneal hemorrhage and graft failure. The other patient with necrotizing pancreatitis of unknown etiology developed MODS and eventually died. Male patients (p = 0.01) and patients transplanted for liver cirrhosis resulting from chronic hepatitis B were at a significantly higher risk of AP development (p = 0.03).

Conclusion: The incidence of AP after liver transplant in our center is low. In it necrotizing form which is more frequent early after liver transplant, it carries a significant risk of mortality exceeding 60%. Male patients and those transplanted for end stage liver disease resulting from chronic hepatitis B are more likely to develop post-liver transplantation pancreatitis.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
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Introduction: Biliary sludge (BS) may be one of the factors, related to development of chronic pancreatitis (CP) via sphincter of Oddi dysfunction. As it was demonstrated by Okazaki K et al. in 1988, patients with biliary sludge have higher sphincter of Oddi (SO) pressure and contraction frequency vs. controls.

Aims & Methods: To assess the frequency of CP signs in patients with BS and to investigate the state of major duodenal papilla (MDP) in patients with idiopathic CP with BS by endoscopic ultrasound (EUS), to evaluate whether antispasmodics can be effective in pain relief at CP, that developed on the background of gallbladder sludge. Protocols of computer tomography, endoscopic and transendoscopical ultrasound studies of over 6000 patients of gastroenterological tertiary clinic were examined. Those who had signs of BS were selected to evaluate the present study. Among at least “mild CP” we found a significant correlation with BS. A total of 30 patients were included. Exclusion criteria were: established etiology of CP and signs of pancreatic neoplasm. Patients, who received ursodeoxycholic acid and drugs that affect smooth muscle contractility for less than 3 month prior to the study were excluded. Thirty consecutive patients (15 m, 15 f, mean age ±SD: 52.8 ± 15.3), who had both BS and CP were summoned for physical examination, quality of life assessment, US-cholecystography and endoscopic pancreatobiliary ultrasound with elastography, calculation of MDP area: SMDP = (MSx + MSp)/(2*2.72) and state of MDP before and after 3 weeks of hyoscymine monotherapy 400 mg tid.

Results: Signs of CP were revealed in 6.3% of BS cases. CP was most common in those who had outpatient-like bile (33.3%) vs. patients with heterogeneous bile with clots -7.7% and hypocholic particles-1.7% (chi-square 38.21, p < 0.0001). Mean SMDP was 14.9 ± 5.2 mm2 (95%CI 10.9–18.9). SMDP was below the normal range (20–25 mm2) in 78% of patients. SMDP had positive correlation to the value of the “bodily pain” according to US-cholecystography (r = 0.042, p = 0.007) and gallbladder contractility coefficient (r = 0.0817, p = 0.007). All patients with higher density of MDP at US- elastography had SMDP lower than the normal range and were attributed to “fibrosis” group. Only 38% of patients with CP and BS had normal MDP at EUS. Perianpillary diverticula were found in 13% of the cases, papillary edema — in 38%, fibrosis — in 13%. MDP changes were associated with higher AP level and larger MPD diameter. Hyoscymine monotherapy resulted in significant improvement in abdominal pain (r = −3.79, p = 0.001) and mean “bodily pain” score of SF-36 questionnaire (r = −3.79, p = 0.001). Dynamics of “bodily pain” score by SF-36 demonstrated significant negative correlation to the post-treatment level of abdominal pain (r = −0.395, p = 0.037) Post-treatment pain level had significant negative correlation with MDP size (r = −0.687, p = 0.002), though no correlation of pre-treatment pain level to MDP features was found, i.e. patients with less MDP size (most of them had decreased elasticity of papilla of Vater, that was considered as indirect marker of fibrosis) had lower hyoscymine efficacy.

Disclosure of Interest: BS may cause MDP changes, resulting in development of obstructive CP. Intensity of pain in biliary CP may be related to sphincter of Oddi dysfunction. Efficacy of antispasmodic therapy in these patients can be predicted by the features of MDP at pancreatobiliary EUS.
Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

P1416 RETROSPECTIVE ANALYSIS OF EXOCRINE PANCREATIC FUNCTIONALITY IN PATIENTS WITH CHRONIC PANCREATITIS

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Introduction: Pancreatic exocrine insufficiency is a late complication of chronic pancreatitis; its clinical onset is characterized by steatorrhea and weight loss, borborygmi, flatulence, abdominal pain and malnutrition. Exocrine and endocrine pancreatic function decreases differently in various diseases (autoimmune, paraudenal, genetic, idiopathic). It has been observed that there has been a recovery of exocrine pancreatic function in autoimmune pancreatitis. In the literature, there are no studies analysing the pancreatic exocrine function over time. The fecal elastase test is a good test procedure to evaluate the exocrine pancreatic function

Aims & Methods: The objective of the retrospective study was to re-evaluate a series of patients with chronic pancreatitis with the aim to evaluate the pancreatic exocrine function over time, in particular, by comparing the exocrine pancreatic function in subgroups of patients with different types chronic pancreatitis. Pancreatic exocrine function was estimated through fecal elastase in 143 patients with at least 2 values each (classified into normal, mild and severe exocrine pancreatic insufficiency), the first one taken at the diagnosis of chronic pancreatitis. Patients undergoing surgical pancreatic resection before the second value of fecal elastase were excluded. Etiology was classified in: biliary pancreatitis/sequale of necrotizing pancreatitis (15), autoimmune (69), paraudenal (15), genetic (17) and idiopathic (27).

Results: The results show a high frequency of severe exocrine pancreatic insufficiency in the moment of diagnosis of chronic pancreatitis (38%) and it appears stable over the years. Autoimmune and paraudenal chronic pancreatitis are correlated with severe exocrine pancreatic insufficiency at diagnosis in a high percentage of cases (51% and 40%), biliary/outcomes of necrotizing pancreatitis and idiopathic pancreatitis in an intermediate (33% and 26%), while genetic in a low percentage (12%).

Conclusion: The exocrine pancreatic function in patients with autoimmune chronic pancreatitis improved in the first five years of the disease, probably due to the efficacy of steroid/immunosuppressive therapy. Pancreatic endocrine function was less compromised at diagnosis, but showed a progressive deterioration in the first five years. Endocrine and exocrine insufficiency were strictly correlated.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1417 "PAINLESS" CHRONIC PANCREATITIS: EPIDEMIOLOGICAL, CLINICAL AND RADIOLOGICAL CHARACTERIZATION

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Introduction: The "painless" chronic pancreatitis (P-CP) represents a specific subset of CP characterized by the lack of pancreatic pain. So far, scarcity of data has been reported in the literature about this matter and what differentiates this group of patients from those with chronic pancreatitis associated with pancreatic pain.

Aims & Methods: The aim of the present study is to characterize "painless" CP from the epidemiological, clinical, radiological, functional, and follow-up standpoint, through a comparison with other forms of chronic pancreatitis presenting with pancreatic pain. The Institutional Database of the Gastroenterology Unit of the Verona University was queried, and all chronic pancreatitis cases were retrieved. Patients were clustered based on the presence of “pancreatic-specific pain” into “painless” and “pain-associated” CP. A retrospective case-control analysis was carried out.

Results: Of 678 patients included from March 2006 to March 2016, 436 were considered eligible for the present study. Of these, 368 (84%) were affected by pain-associated CP, while 68 (16%) had “painless” CP. “Painless” patients were older (median age of 38.5±10.8 y/o vs. 42.5±15.3 y/o; p<0.001), less frequently presenting with a history of alcohol consumption (35% vs. 55%; p<0.001), more frequently diabetics (18% vs. 1%; p<0.001), presenting with steatorrhea (16% vs. 2%; p<0.001), and asymptomatic (63% vs. 2%; p<0.001) compared to pain-associated controls. From the radiological standpoint, these cases were more often presenting with calcifications than controls (90% vs. 68%; p<0.001). Moreover, in most of painless cases, the CP cause remained unknown (56%). After a median follow-up of 2.6±2.3 years, the incidence of diabetes was higher in the painless cases than in controls (48% vs. 30%; p<0.006).

Conclusion: The present study represents the first definition of "painless" CP so far reported in the literature. The "painless" CP is a distinct entity from the epidemiologic, clinical, and radiological standpoint when compared to other forms of CP characterized by pancreatic pain.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P1418 LONG-TERM OUTCOMES OF A FULLY COVERED SELF-EXPANDABLE METAL STENT WITH ANTIMIGRATION PROPERTIES FOR EU-S-GUIDED PANCREATIC DUCT DRAINAGE


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Introduction: Recently, EU-S-guided pancreatic duct drainage with transmural stenting (EU-S-PD) has been used for patients with painful obstructive pancreatitis in whom endoscopic retrograde pancreatography (ERP) has failed. Although the feasibility and safety of EU-S-PD with a fully covered self-expandable metal stent (FCSEMS) has been assessed, little is known about the long-term outcomes of EU-S-PD with a fully covered self-expandable metal stent (FCSEMS). Removability of an FCSEMS in long-term use and higher cost are the main concerns of EU-S-PD with an FCSEMS compared with EU-PD with a plastic stent.

Aims & Methods: The aim of this study is to evaluate the procedural and long-term outcomes of EU-S-PD with an FCSEMS for patients with painful obstructive pancreatitis who failed ERP. Forty-one consecutive patients with painful obstructive pancreatitis underwent EU-S-PD with an FCSEMS after failed ERP. All patients underwent without sufficient exchange of a previously considered in malignant MPD strictures or complete MPD obstruction in benign pancreatic stricture. Technical and clinical success, adverse events, and stent patency were assessed. An endoscopic examination and CT scan was performed every 6 months to assess stent patency in benign stricture.

Results: 15 patients had malignant MPD obstruction and 26 patients had benign stricture. EU-S-PD was successful in all 41 patients (technical success rate, 100%), and symptoms improved in all patients (clinical success rate, 100%). EU-S-guided pancreaticojejunostomy (n = 39) and pancreatocutaneous (n = 2) were successfully performed. Pain scores improved significantly after FCSEMS placement (P = .01). Early mild-grade adverse events occurred in 5 patients (12.2%), including distal stent fracture (n = 6), stent occlusion (n = 2). These patients were successfully treated endoscopically. No other adverse events related to FCSEMS, including stent migration, pancreatic sepsis, and stent-induced ductal stricture were observed during follow-up periods.
Overall mean stent patency duration was 412 days (range 14–1081) during mean follow-up period of 243.5 days. Median stent patency in all malignant strictures was 95 days (range 14–297). Mean stent patency in benign stricture was 525 days (range 121–1081). No patients with malignant strictures required FCSEMS revision or exchange during follow-up periods. FCSEMS removal and exchange was successful in patients with benign strictures until 3-year placement of an FCSEMS. Prospective randomized trial comparing EUS-PD with FCSEMSs and plastic stents may be warranted for painful obstructive pancreatitis after failed ERP.

Disclosure of Interest: All authors have declared no conflicts of interest.

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Disclosure of Interest: All authors have declared no conflicts of interest.
ML 228 and inhibited using Echinomycin. PTK and STK analysis of cell lysates displays correlation between phosphorylation and O-glycosylation in hypoxic samples.

Results: Mechanistically we could show, that hypoxia-induced decreased levels of C1GALT1C1 results in reduced T-Synthase activity with subsequent expression of truncated O-glycosylated (Tn antigen). Differential O-GalNAc glyclosylation is inducible using HIF pathway activator ML228 under normoxia and the effect is reversed using 5μM Echinomycin under hypoxia underscoring the role of HIF1α regulated transcription. Interestingly, the pattern of Tn antigen modified proteins are altered from hypoxic samples differing significantly from engineered COSMC-deficient cells, displaying O-GalNAc moieties in addition to O-GlcNAc in cytosolic protein fractions. Further, we could show PTK/AKT/ MAPK signalling is depending on the state of cellular O-glycosylation providing a new rationale for the correlation of PDAC Tn antigen glyctype and cancer cell proliferation.

Conclusion: Our findings point to a novel crosstalk of O-GalNAc and O-GlcNAcylation under hypoxia extending the knowledge base of differential O-GalNAc glyclosylation in pancreatic cancer.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P1424 THE EXPRESSION AND FUNCTION OF MIR-195 IN PANCREATIC CANCER: THE EXPRESSION AND FUNCTION OF MIR-195 IN PANCREATIC CANCER
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Introduction: Pancreatic cancer is one of the most common malignant tumors in digestive system. The overall survival rate is less than about 6% of pancreatic cancer. Pancreatic cancer with poor prognosis and survival rate is low, due to the early clinical symptoms is not easy to find, have a high transfer possible, and the operation difficulty, radiotherapy and chemotherapy is not sensitive. Radical surgical resection is the only opportunity to pancreatic cancer patients get longer survival. Therefore, a deeper understanding of the molecular mechanism of pancreatic cancer occurs, explore new effective treatment is imminent.

Aims & Methods: Pancreatic cancer is a highly malignant tumor and fourth leading cause of cancer-related death in the world. The median survival after diagnosis is 2-8 months, and approximately 3-6% of all patients with pancreatic cancer survive 5 years after diagnosis. This is mostly due to the fact that it is diagnosed at a stage when it is either locally advanced or has already metastasized to other organs. Hence, there is a paramount need to understand the molecular mechanisms underlying its initiation, progression and therapy.

The recent discovery of microRNAs (miRNAs) has revealed a novel mechanism of gene regulation and provided new ways for cancer research. MicroRNAs are small non-coding RNA molecules, which regulate the gene expression at post-transcriptional level. It is widely reported that miRNAs can act as oncogene or tumor suppressor genes.

Conclusion: The research on pancreatic cancer is still in its infancy. Further research is needed to understand the detailed mechanism of the role of microRNAs in pancreatic cancer. Therefore, this study investigated the expression of miR-195 in pancreatic cancer and potential mechanisms of its role in tumor progression.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P1423 TRYPTOPHAN DEGRADATION AS AN ALTERNATIVE ENERGY SOURCE IN PANCREATIC CANCER
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Introduction: Pancreatic cancer (PDAC) is one of the most lethal diseases worldwide, due to its aggressive nature and about 90% of patients die within 5 years of diagnosis, because of early metastasis. The 5-year survival rate of PDAC patients is less than 10%, putting it as the fourth most lethal cancer. Pancreatic cancer presents a challenge for current therapeutic interventions of this disease.

Aims & Methods: We defined the identification of new biomarkers for chemoresistant pancreatic cancer. A secretory survey of chemoresistant PDAC cell lines was performed using SILAC-based mass-spectrometric analyses. Relative differences in protein concentrations among samples were investigated and led to the identification of previously unknown proteins. The impact of RNAi-mediated knockdown of selected genes in proliferating PDAC cells were analyzed using MTT-viability assays. Global protein-expression analyses were performed using Real-Time-PCR and immunohistochemistry using patient-derived PDAC samples.

Results: SILAC-based identification of the Tryptophan degrading enzyme KYNU (KYN), expressed in chemoresistant PDAC cells revealed an overexpressed and secreted form of the KYNU protein, compared to the chemosensitive counterpart. We further identified various stress-related external stimuli (Glicatalbine, IFNg, Hypoxia) as inducers of KYNU expression/secretion. A knockdown approach was linked to substantially lower proliferation of chemoresistant and aggressive PDAC cells. Global expression analyses using a tissue-microarray of PDAC patient samples (n = 368) revealed that high KYNU expression is significantly correlated with a worse outcome in PDAC patients.

Conclusion: The trypotphan degradation pathway member KYNU is overexpressed in a subset of PDAC patients and is linked to substantially increased cancer cell proliferation. Abundant KYNU expression in PDAC patients is linked to a worse clinical outcome. We found that KYNU is a new secreted biomarker of chemoresistant PDAC cells.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P1424 INTEGRIN ALPHAS IS SPECIFICALLY EXPRESSED IN Pancreatic Tumor Stroma and a Key Target in Regulation of Pancreatic Tumor Stroma Myofibroblasts
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Introduction: The progression of pancreatic ductal adenocarcinoma (PDAC) is promoted by its highly abundant tumor stroma. As one of the main components of the tumor stroma human pancreatic stellate cells (hPSCs), precursor cells of pancreatic tumor stromal myofibroblasts (CAF), support PDAC progression by enhancing tumor cell growth, invasion and metastasis [1]. The collagen binding transmembrane receptor integrin α11 (ITGA11) is known to be overexpressed by myofibroblasts [2].

Aims & Methods: The aim of the presented study was to investigate the expression of ITGA11 in human PDAC and to study the role of ITGA11 inCAF regulation. ITGA11 expression was evaluated using immunostaining on human PDAC sections and various other organs. The relationship between ITGA11 expression and cancer markers and tumor marker was evaluated in a stroma rich co-injection model in mice. The biological role of ITGA11 in CAF differentiation was studied in hPSCs and hPSCs activated with TGF-β or conditioned medium from Pan1-c endothelial tumor cells using qRT-PCR, immunostaining, western blot, wound healing, collagen contraction and cell growth assays.

Results: In this study we have for the first time stained ITGA11 in human PDAC specimens. We found that ITGA11 was highly expressed in stromal myofibroblasts of PDAC patients, as shown by co-localization with the myofibroblasts marker alpha smooth muscle actin (α-SMA). Interestingly, there was no expression in healthy human pancreas and various other tissues from human organs. Furthermore, we induced subcutaneous tumors in mice by injecting Pan1-c or Pan1-c+hPSCs and found that ITGA11 was significantly over-expressed in stroma-rich Pan1-c+hPSCs tumors. The quantitative gene and protein expression of ITGA11 in subcutaneous tumors, positively correlated with the expression of the CAF markers α-SMA, Col1a1 and PDGFr. Activation of hPSCs with TGF-β or conditioned medium from Pan1-c resulted in the significant upregulation of ITGA11 and α-SMA. Stable ITGA11 knockdown, mediated by shRNA, significantly inhibited hPSC differentiation, migration potential, contractility and cell growth.

References
P1425 EFFECT OF ACOUSTIC CAVITATION ON A THREE-DIMENSIONAL CULTURE MODEL OF PANCREATIC ADENOCARCINOMA


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Introduction: The dismal prognosis of pancreatic ductal adenocarcinoma (PDAC) is mainly due to chemoresistance linked to the tumor microenvironment. Recent developments in therapeutic ultrasound (US), particularly US-induced cavitation, could help overcome chemoresistance by breaking microenvironmental barriers and increase cytotoxic drug availability. Three-dimensional (3D) culture in the form of spheroids is a useful model for reproducing multicellular resistance and analyzing the effects of cavitation.

Aims & Methods: The objective of this work was to study the effects of acoustic cavitation on a model of PDAC spheroids and to investigate possible potentialities of chemotherapy by US. CAPAN-2 PDAC cell line-derived spheroids were cultured as previously described by Ivascu et al. Four conditions, i.e. control, chemotherapy by US, control + chemotherapy by US, and US alone were studied. Experiments were carried out to optimize US settings, in order to observe the occurrence of controlled cavitation. Experiments were carried out to optimize US settings, in order to observe the occurrence of controlled cavitation. Comparisons between groups were based on proliferation and growth. Proliferation was evaluated 24 hours after treatment(s) by MTS assay. Growth was assessed by diameter measurement on light microscopy at day 7 and day 10.

Results: Compared to the control group, cell proliferation was decreased in spheroids treated with CT (p < 0.0001), but not with US alone. Proliferation was also further impaired in spheroids treated with CT-US combination compared to those treated with CT alone (p < 0.0001), but this synergistic effect of US and CT did not exceed growth of spheroid, meaning that spheroid diameter did not decrease after US-CT compared to CT alone.

Conclusion: This study shows the feasibility of applying an ultrasonic treatment (acoustic cavitation) in a three-dimensional culture model of PDAC. The combination of US and CT or US ultrasound synergistically reduced cell proliferation. Further analysis of the cytotoxic effects of acoustic cavitation on PDAC spheroids is in progress.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1427 EVALUATION OF LONG TERM SURVIVAL OF CHEMORADIOThERAPy WITH GEMCiTABiNE AND S-1 COMPARED WITH CHEMOTHERAPY ALONE IN THE CASES WITH LOCALLy ADVANCED PANCREATIC CANCER

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Introduction: Because of the progression of systemic chemotherapy (CT) for locally-advanced pancreatic cancer (LA-PC), chemoradiotherapy (CRT) was selected for limited case. However, very long survival rates were reported in CRT and detection of prognostic factors were warranted. In this analysis, we analyzed the LA-PC cases received CRT compared with CT.

Aims & Methods: Gemcitabine (GEM) and S-1 combination chemoradiotherapy was performed to our previous trial 1 (trial of Japan Pancreas Society 2010). Till March 2016, 30 LA-PC cases received GS-CRT, and the selection criteria were LA-PC with 1) pathological diagnosis, 2) large vessels (CA, SMA, CVA, PV, SV) invasion, 3) allocorphic and concurrency without multiple primary cancer, 4) unexecuted antitumor therapy. The chemotherapy in CRT administration of GEM (200 mg/m²) once a week for 6 weeks, administration of S-1 (80 mg/m²) for 2 weeks a month for 5 days per week for 5.5 weeks, and total dose was 50.4 Gy (Total 28 times). As after treatment, GEM 1000 mg/m² was continued until PD. The patients of CT group were also recruited by the same criteria. One of the regimens among GEM alone, S-1 alone and GEM+S-1 was selected for the primary treatment, and total 26 cases were implemented in more than 2 courses.

Results: Baseline characteristics in CRT and CT group were median age (62, 72.5: p = 0.004), male (20, 12: ns) and tumor location Ph/Pb (17/13, 16/10; ns), respectively. Efficacy was disease control rate (DCR) in 3 months after treatment (90%, 57.7%: p = 0.01), response rate (RR) (26.7%, 0%: p = 0.005) and conversion surgery (10%, 0%: ns). There were significant differences in progression free survival (PFS) (6 months, 5 months: p = 0.002) and overall survival (OS) (13M, 9M: p = 0.0165), respectively. The cases who survived for 18 months and longer were significantly (p = 0.0495) more in CRT (43.3%) than CT group (19.2%). Grade 3/4 adverse events in CRT group were 13 cases of neutropenia (G4-3 cases) and one case of gastrointestinal symptom, and those in CT group, neutropenia was 11 cases (G4-case), interstitial pneumonia (IP) aggravation was one case.

Conclusion: For LA-PC, GS-CRT showed better local tumor control and longer survival, and was considered as good candidate of neo-adjuvant therapy. More than 18 months survivors in LA-PC cases was other benefit of GS-CRT. We should think about good selection criteria of CRT and improve the survival of LA-PC.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

Reference

P1428 HIGH-INTENSITY FOCUSED ULTRASOUND (HIFU) THERAPY FOR UNRESECTABLE PANCREATIC CANCER
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Introduction: High-intensity focused ultrasound (HIFU) is expected as a new advanced therapy for unresectable pancreatic cancer (PC). The aim of this study was to detect the limitation of HIFU therapy combined with chemotherapy and to clarify the role of HIFU therapy in the treatment of pancreatic cancer.

Aims & Methods: We have evaluated the therapeutic effect of HIFU therapy in locally advanced and metastatic PC. We treated PC patients by HIFU as optional therapy, as well as systemic chemotherapy, in combination with chemotherapy, and then analyzed survival in the long term.

Results: The therapeutic effect of HIFU therapy was as follows: the rate of complete tumor ablation was 87.9%, the rate of symptom relief effect was 69.4%, and the effectiveness of primary lesion was CR or PR for more than 60% of cases. The treatment of HIFU therapy was very effective in resectable pancreatic tumors, with a response rate of 75.7%.

Conclusion: This study suggested that HIFU therapy has the potential of new method of combination therapy for PC.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1429 EUS AND CT SCAN ACCURACY IN ESTABLISHING THE T STAGE IN Pancreatic CANCER BASED ON THE UPCOMING TNM 8th EDITION
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Introduction: Pancreatic ductal adenocarcinoma (PDAC) has a dismal prognosis with an overall 5-year survival rate <6%. Surgically resected patients, although undergoing adjuvant therapy, have nevertheless a 5-year survival of <5%. In fact, it has been recently suggested that patients with a tumor of more than 2 cm might harbor micrometastases at diagnosis. In this view, the availability of new highly effective chemotherapy regimens that might be employed in the neoadjuvant setting, the correct evaluation of the T stage of pancreatic cancer plays a key role. The new proposed AJCC Staging System for Pancreatic Adenocarcinoma TNM (8th edition), in fact, differs from the 7th edition mostly for the evaluation of the T, giving high importance to the diameter of the tumor. The new TNM staging system has already been shown to predict survival differences more efficiently compared to previous editions. In this context, an efficient preoperative evaluation of the T is of high importance as it might shift the therapeutic decision from upfront surgery to neoadjuvant chemotherapy, that could improve survival in selected cases. This study aims at evaluating the accuracy of CT scan and EUS in evaluating the T stage of the tumor. We performed a retrospective study in a cohort of surgically resected histopathologically-confirmed PDAC patients at a pancreatic cancer referral center between 2015-2017, who were prospectively included in a dedicated database. Inclusion criteria: a) having both preoperative EUS and CT scan with pancreatic phase evaluation at the centre; b) CT and EUS were performed, at the latest, 30 days apart from each other and from surgical resection; c) no neoadjuvant chemo or radiotherapy was performed. The evaluation of the T by both imaging modalities was compared to the final pathology T re-established based on the new TNM 8th edition, in order to calculate specificity and sensitivity. T-test was used for comparison of categorical variables.

Results: Among the 184 PDAC patients surgically resected between 2015 and 2017 at our center, 30 met inclusion criteria. Of these, 19 (63.3%) were males, with a mean age at resection being 67.8 ± 9.5 years. The tumor was located in the head in 23/30 (76.7%) patients. Mean diameter of the tumor at pathology was 24.9 ± 10.8 mm, mean diameter at EUS was 24.0 ± 8.6 mm (p = 0.74), and mean diameter at CT was 25.9 ± 10.9 mm (p = 0.73). In 4/30 (13.3%) cases CT scan was classified as T1, in 17 cases (56.6%) T2, in 6 cases (20%) T3, and in 3 cases (10%) T4 (p = 0.001). The effectiveness of primary lesions was classified: CR: 8 (26.6%), PR: 8 (26.6%), SD: 8 (26.6%), PD: 6 (20%). The sensitivity and specificity of CT scan versus EUS and CT scan was 86.7% and 76.7%, respectively.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1430 RISK FACTORS AND SURVIVAL IN PancreATIC ADENOCARCINOMA
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Introduction: Pancreatic adenocarcinoma is associated with a 5-6% survival at 5 years and a poor quality of life. In Romania there are few information about the prognostic influence of known risk factors for pancreatic cancer. The purpose of this study was to analyze the possible association with survival.

Aims & Methods: The aim of this study is to evaluate the association between risk factors and the occurrence of pancreatic adenocarcinoma and patients’ survival, which may constitute a theoretical basis for screening. We performed a prospective, multicentric study of patients with suspected pancreatic tumors detected in abdominal ultrasound or CT examination, during January 2015-December 2016, in which were analyzed risk factors and the occurrence of pancreatic adenocarcinoma and patients’ survival.

Results: There were 279 patients with pancreatic adenocarcinoma included in the study. Male patients were 58% from all patients, and the mean age was 63.5 years. Smoking, new-onset diabetes and history of chronic pancreatitis are risk factors for pancreatic adenocarcinoma (p < 0.05). At 5 years more than one-third of patients with pancreatic adenocarcinoma died (median survival = 5 months). It was demonstrated a statistically significant association adjusted for tumor stage between the presence of new-onset diabetes and survival: 5 months vs 3 months with a HR = 3. Other risk factors (alcohol, obesity, sex, genetics, coffee intake, some infections and abdominal surgery, history of chronic pancreatitis) had no prognostic role.

Conclusion: In our study, the risk factors for pancreatic cancer were smoking, having history of chronic pancreatitis and new-onset diabetes, but the only prognostic factor was smoking. The role of sex and alcohol consumption was not confirmed.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
P1431. PREVALENCE STRATIFICATION OF MALIGNANCY IN RESECTED INTRADUCTAL PAPILLARY MUCINOUS NEOPLASMS INVOLVING MAIN DUCT: IS THE 10 MM WIRSUNG DIAMETER AN ADEQUATE CUTOFF?

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Introduction: According to the 2012 International guidelines on the management of intraductal papillary mucinous neoplasms (IPMN), main-duct IPMN patients with main pancreatic duct (MPD) diameter of ≥10 mm should have surgical resection, whereas surgery is not always mandatory in those with MPD diameter between 5 and 9 mm.

Aims & Methods: The aim of the study was to analyse the prevalence of malignancy (high grade dysplasia or invasive carcinoma) in 20 resected IPMN with MPD diameter between 5 and 9 mm and to identify predictive factors of malignancy. Retrospective analysis of patients with surgically resected IPMN between 2001 and 2016. Demographics, clinical presentation, imaging and histological features were compared between patients with preoperative evidence of MPD diameter between 5–9 mm (Group A) and ≥10 mm (Group B). Malignancy was defined as high-grade dysplasia or invasive carcinoma.

Results: From 122 patients with IPMN submitted to surgery, 66 with MD- or mixed-IPMN entered the final analysis. Mean age was 66 ± 12 years and 48 (72.7%) patients were men. Group A comprised 47 patients and Group B 19. Abdominal pain was present in 23 (34.3%) patients, jaundice in 19 (28.8%), diabetes in 18 (27.3%), pancreatitis in 15 (22.7%) and weight loss in 12 (17.4%). Group A was older (P = 0.043), had a higher incidence of diabetes (P = 0.003), and a lower incidence of weight loss (P = 0.001) than Group B. Overall, malignancy was found in 10 (40%) patients; 8 of them (80%) were in Group A and 2 (10%) in Group B (P = 0.002). The median survival time of the patients who were receiving chemotherapies was 197.0 days in group A and 291.0 days in group B. No significant differences were also found between the two groups. The median survival time of the patients who underwent chemotherapy in group A (332.0 days) was significantly longer than that of patients who underwent BSC (71.0 days).

Conclusion: Chemotherapy could be safe and effective for patients older than 75 years who have unresectable pancreatic cancer.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1432. CLINICAL SIGNIFICANCE OF CHEMOTHERAPY FOR ELDERLY UNRESECTABLE PANCREATIC CANCER PATIENTS

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Introduction: Pancreatic cancer has poor prognosis despite of improvements in multimodal treatments. As aging of the population advances, it is expected that elderly pancreatic cancer patients increase.

Aims & Methods: The aim of this study was to investigate the clinical significance of chemotherapy for patients with unresectable pancreatic cancer. At our hospital, 96 patients were diagnosed as having unresectable pancreatic cancer between January 2010 and December 2016. In this study, we defined elderly patients as those older than 75 years. We retrospectively examined the safety and efficacy of chemotherapy in patients with unresectable pancreatic cancer. We analyzed and compared the survival periods according to chemotherapies.

Results: Twenty-seven patients were older than 75 years (group A), and 59 were younger than 74 years (group B). We treated 6/10/2/5/4 patients in group A with GEM/S-1-modified FOLFIRINOX (mFOLFIRINOX)/GEM + nabPTX/first line supportive care (BSC)/others, respectively. On the other hand, we treated 12/14/11/13 patients in group B with GEM/S-1/mFOLFIRINOX/ GEM + nabPTX/BSC/others, respectively. Severe adverse events (more severe than grade 3 according to CTCAE v4.0) occurred in 18.2% of the patients in group A and in 33.3% of the patients in group B. No significant difference was found between the two groups. The median survival time of the patients who were receiving chemotherapies was 197.0 days in group A and 291.0 days in group B. No significant differences were also found between the two groups. The median survival time of the patients who underwent chemotherapy in group A (332.0 days) was significantly longer than that of patients who underwent BSC (71.0 days).

Conclusion: Chemotherapy could be safe and effective for patients older than 75 years who have unresectable pancreatic cancer.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1433. THE USE OF A NEW CORE NEEDLE IN THE ENDOSCOPIC ULTRASOUND ASSISTED TISSUE SAMPLING FOR Pancreatic SOLID MASSES: A MULTICENTRE PROSPECTIVE STUDY

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Introduction: Endoscopic ultrasound-guided biopsy (EUS-biopsy) is considered a reliable, safe, and effective technique for obtaining samples from pancreatic masses with a very high sensitivity and specificity (ranged to 85%–92% and 96–98%, respectively)[1–3]. A new EUS needle (SharkCore FNB needle, Medtronic, Dublin, Ireland) was introduced in order to improve the tissue acquisition.

Aims & Methods: The aim of the present study was to evaluate the presence of a histological sample using Shark Core Needles. This study was an observational multicenter prospective non-randomized clinical trial (NCT02946840). All consecutive patients referred for EUS examination and sampling of solid pancreatic masses underwent EUS-guided biopsy with 25 G Shark Core needles. This needle is an innovative tip geometry with a cutting surface designed to acquire cohesive tissue through both tissue fracturing and tissue snaring. Three needle passes were performed in every mass. At all attempts, a macroscopic on-site quality evaluation (MOSE) was done by endoscopist. If a “worm-like” material was observed at gross visual assessment, it was placed into formalin. If only liquid material was visible, it was smeared between 2 glass slides, fixed with ethanol, and stained with a Papanicolaou-stain for cytological analysis. Endoscopists recorded macroscopic features of the specimens. Pathologists described macroscopic, microscopic, and immunohistochemical features. The primary outcome was the treatment of masses with a diameter of at least 5 mm in greatest axis. All the other specimens (< 5 mm) were defined as micro-fragments. The final diagnosis was based on surgical resection, and clinical/radiological follow up. The secondary outcomes were diagnostic accuracy and procedure-related adverse events.

Results: Study population included 82 patients, enrolled in three centres, between 1st and 3rd quarter 2015 and 2016, with a mean age of 64.0 (SD 13.7, range 21–84) and 57.3% female gender. The mean size of the lesions was 27.6 mm (SD 12.2) and the location was the body and tail in 27 patients (32.9%), neck in 11 (13.4%), head and uncinated process in 44 (53.7%). Three needle passages were performed in all 3 patients who experienced mild bleeding precluding more than one needle passage. At MOSE, endoscopists described presence of “worm-like” material in 192 biopsy samples over 242 (79.3%). In 8 patients only cytological specimens were obtained after 3 needle passes (9.8%). Six cases of mild self-limited bleeding were observed (7.3%). The pathologists described the presence of a core in 80 samples (41.7%), in the other cases, after the specimen preparation, a micro-fragmentation was observed, that didn’t affect the histological evaluation. A final histological diagnosis was reached in 73 patients (90%): 50 pancreatic adenocarcinoma, 16 NET, 5 chronic pancreatitis, 2 pancreatic metastasis from other organs.

Conclusion: The new biopsy needle showed a good overall adequacy and a good rate of histological specimens (both core and micro-fragments) during EUS-guided tissue acquisition of pancreatic masses, with a minimum number of needle passes and no major complications. This ability could allow to avoid the use of rapid on-site evaluation and to perform immunohistochemical, molecular and genetic studies on histological samples.

Disclosure of Interest: All authors have declared no conflicts of interest.
In 399 (86.9%) cases on-site cytopathology support was available, while insufficient information.

Introduction: EUS FNA is accepted as the primary modality for tissue diagnosis of solid pancreatic lesions. The presence of on-site cytopathology for immediate evaluation of aspirated material and need for further evaluation.

Results: In 399 (86.9%) cases on-site cytopathology support was available, while the remaining was unsupported. There were 228 males (57.1%) in the supported group and in 38% (23%, 10%, 3%, 2%) of the unsupported (P = 11.9) respectively. The mean number of passes in the two groups were 2.8 (SD: 1.12) and 1.9 (SD: 1.0) (P < 0.001). The diagnostic yield of the presence of on-site cytopathologist significantly increases the diagnostic yield.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
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PREOPERATIVE EUS-FNA (THE SPN G.R.A.P.H.E SERIES)
ABOUT A RETROSPECTIVE SERIES OF FIFTY PATIENTS WITH A MASS IN THE HEAD OF PANCREAS?
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Introduction: Self-expanding metal stents (SEMS) are increasingly preferred to plastic stents (PS) for preoperative drainage and palliation of biliary obstruction secondary to a stricture in the head of pancreas (HOP). Their use has increased over the last 5–6 years. Endoscopic ultrasound (EUS) with fine needle aspiration or biopsy (FNA or FNB) is commonly utilised to make a tissue diagnosis and to aid in staging in those with borderline resectable tumours. Stents may reduce diagnostic performance of FNA/FNB by reducing the visible mass to puncture. There have been two studies that assessed the impact of stenting on EUS-FNA performance, one found no difference in yield and sensitivity among patients with or without stents and between SEMS and plastic. Whilst a more recent study found accuracy was significantly reduced by the presence of a stent.

Aims & Methods: The aim was to assess whether stents (SEMS or PS) impair diagnostic performance of EUS tissue acquisition, in a retrospective study of all patients with HOP mass undergoing EUS biopsy between January 2010 and June 2016. Stenting information was obtained from the EUS report and images. Biopsies reported as malignant were considered as such, all other reports were considered benign. A definitive diagnosis of cancer was based on positive pathology or imaging signs of progression. A benign diagnosis required negative pathology, stable imaging and symptoms for a year or more. Patients with cystic lesions were excluded.

Results: A total of 1861 patients had EUS-FNA/FNB of which 731 were for HOP lesions, mean age 65 years (410 F), with tissue sensitivity of 72% for all types of needles used. Tissue accuracy was significantly different between the 3 groups (p=0.0001); SEMS 67%, PS 71% and 83% in the unstented group. The difference in accuracy was significant between the unstented group versus SEMS (p=0.0002) and PS (p=0.033) and not significant between PS and SEMS. Stepwise multi-variable analysis revealed significant difference for accurate tissue diagnosis favouring size needle 25G (OR 1.7 [95% CI 1.1–2.7] and tumour size (OR 1.04 [1.02–1.07]) and not affected by presence of stent. SEMS (OR 0.3 [0.2–0.6]) or PS (OR 0.5 [0.3–0.8]). Other needle sizes (19G or 22G), number of passes or types of needle did not significantly affect tissue accuracy.

Conclusion: Our results show a significant adverse impact of both SEMS and PS on tissue accuracy via EUS FNA/FNB. The effect is greatest with SEMS. These lesions, mean age 65 yrs (410 F), with tissue sensitivity of 72% for all types of needles used. Tissue accuracy was significantly different between the 3 groups (p=0.0001); SEMS 67%, PS 71% and 83% in the unstented group. The difference in accuracy was significant between the unstented group versus SEMS (p=0.0002) and PS (p=0.033) and not significant between PS and SEMS. Stepwise multi-variable analysis revealed significant difference for accurate tissue diagnosis favouring size needle 25G (OR 1.7 [95% CI 1.1–2.7] and tumour size (OR 1.04 [1.02–1.07]) and not affected by presence of stent. SEMS (OR 0.3 [0.2–0.6]) or PS (OR 0.5 [0.3–0.8]). Other needle sizes (19G or 22G), number of passes or types of needle did not significantly affect tissue accuracy.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

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Introduction: Solid-pseudopapillary neoplasm (SPN) is a rare condition, first described by Frantz in 1959. It occurs mostly in young women, and surgical resection is recommended. Its local recurrence rate is less than 10% and usually occurs within 4 years after surgery. Before such a surgery, especially in young people, EUS-FNA (Endoscopic ultrasonography with fine needle aspiration) is discussed to confirm diagnosis but rarely performed due to suspected needle tract contamination by neoplastic cells. The aim of our large multicenter study was to assess the short- and long-term safety of preoperative EUS-FNA in SPN.

Aims & Methods: This study is a multicenter retrospective register of all SPN diagnosed in the last decade in 14 European expert centers (GRAPHE task force). Inclusion criterion was realization of preoperative EUS-FNA followed by surgical resection. Patient and tumor characteristics were collected, as the EUS-FNA technique (number of passes, needle size, trans-gastric or trans-duodenal access). Immediate or late complications of EUS-FNA and recurrence of SPN were then recorded.

Results: During the period study, 49 patients (41 women/8 men) with preoperative EUS-FNA for SPN were recorded. Mean age of patients was 37 ±13y; 14 patients (28%) had resection within 1 year (9/36), caudal in 11% (4/36) and in uncus in 5% (2/36). Mean tumor size measured on EUS was 40 ±22 mm. Needle used was a 25G in 3% (1/37), 22G in 76% (28/37), 20G in 8% (3/37) and 19G in 13.5% (5/37). Transgastric EUS-FNA was performed in 56% (24/43) and trans-gastric in 44% (19/43). Mean number of needle passes was 2.2 ±0.7. EUS-FNA allowed certain preoperative diagnosis of SPN in 74% of cases (35/47), probable diagnosis in 6% (3/47), negative in 4% (2/47) and wrong in 6% (3/47). No acute complication of EUS-FNA was reported. With a mean follow-up of 36 ±12 months, only one local recurrence was noted. In this year 4 old man case, a 19G needle was used (2 trans-gastric passes), and recurrence occurred after 84 months.

Conclusion: In this large multicenter retrospective series, a systematic preoperative EUS-FNA did not seem to modify the SPN recurrence rate. Therefore this study allows to validate this attitude as a possible alternative. The data for the series are incomplete at the date of submission of the abstract. The final data will be completed on the day of presentation.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
**PI440** EFFECTS OF IGF2BPS ON GROWTH AND PROLIFERATION OF NEUROENDOCRINE TUMOR CELL LINES

**Aims & Methods:** We aimed to characterize the role of IGF2BPs in neuroendocrine tumor progression and their potential expression pattern in various solid tumors including pancreatic neuroendocrine tumors.

**Results:** The pan-neuroendocrine tumor cell line BON1, knock-down of IGF2BPs resulted in a significant reduction of cell viability. Cell cycle analysis by FACS showed a decreased S phase proportion paralleled by a reduction in the number of phosphorylated mitotic cells. Moreover, knock-down of IGF2BP1 significantly reduced clonogenic growth as assessed by colony formation analyses and led to decreased cell migration as determined by scratch assays. Interestingly, knock-down of IGF2BP1 was insufficient to induce apoptosis, as assessed by PARP and caspase-3 cleavage as well as annexin-V FACS. Rather, si-IGF2BP1 increased the expression of both the anti-apoptotic and pro-survival factors BCL-2 and the cell cycle inhibitor CDKN1B. In contrast, si-IGF2BP1 knock-down of IGF2BP3 rather induced cell viability, whereas si-IGF2BP2 modulation had no impact on cell viability and cell cycle progression indicating opposing effects on the three IGF2BPs on PNEN progression. These in vitro findings were parallelized by distinct expression patterns of IGF2BPs in human and murine PNEN tissues. Elucidation of IGF2BP-modulated RNAs in PNEN cells is ongoing.

**Conclusion:** In summary, our data suggest that IGF2BP1 promotes tumor progression by enhancing cell cycle progression and clonogenic growth, whereas IGF2BP2 and -3 exert no tumor-promoting role in PNEN.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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**PI442** EFFECTS OF LOW-DOSES ASPIRIN ON CLINICAL OUTCOME AND DISEASE PROGRESSION IN PATIENTS WITH GASTRO-ENTERO-PANCREATIC NEUROENDOCRINE TUMORS: RESULTS OF A MULTICENTRIC RETROSPECTIVE STUDY

**Aims & Methods:** Aim of the study was to retrospectively evaluate the clinical outcome of GEP NEN patients treated with ASA at three different European referral centres for NENs. All the GEP NEN patients followed up in three European Centres (Fondazione IRCCS Cà Granda Ospedale Policlinico Milano, Italy; Fondazione IRCCS Istituto Tumori Milano, Italy; Mater Misericordiae University Hospital, Dublin, Ireland), from January 2005 and September 2016, were retrospectively enrolled. The possible association between ASA use and disease grading, staging, primary site, overall OS and PFS were evaluated.

**Results:** In the 99 patients included (121 M, median age 64 yrs), the primary neuroendocrine tumor was located at the stomach (35%), pancreas (82%), small bowel (8%), appendix (27%), colon (49) or unknown (6%). Grading was G1 in 51 patients, G2 in 64, G3 in 5 and not available in 28. TNM staging was I in 99 patients, II in 16, III in 32 and IV in 86. No clear impact on OS or PFS was observed in patients taking ASA compared to those not taking it. Interestingly, in small bowel NEN an inverse relation was observed with lower Ki-67 values and less node involvement. Further studies are needed to confirm this observation.

**Conclusion:** According to present data, ASA therapy seems not to have a direct clinical impact on disease progression or survival of NENs, even if it is associated with lower Ki-67 values and less node involvement. Further studies are needed to confirm this observation.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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**Disclosure of Interest:** All authors have declared no conflicts of interest.
References

P1443 PANCREATIC LESIONS IN VON HIPPEL-LINDAU SYNDROME: CLINICAL AND EPIDEMIOLOGICAL DATA FROM A SINGLE CENTER
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Introduction: Von Hippel-Lindau disease (VHL) is a rare heritable genetic syn- drome that may affect different systems and organs: pancreatic manifestations of the disease are frequent during lifetime of the patients. The key feature is the presence of simple cysts, but serous cystadenomas (SCAs) or neuroendocrine tumors (NETs) can be frequently found as well. The aim of this study is to describe pancreatic manifestations in patients with VHL, considering the peculiarity and rarity of this disease.

Aims & Methods: All patients who referred to the established multi-disciplinary team in our center (Molinette Hospital - Turin) for management and follow-up of VHL disease in the period 2000-2013 were considered. In the study we considered the ones with pancreatic involvement (simple cysts, SCAs or pNETs). We collected data about the patients (demographics and medical history), about the lesions (imaging features, histological and cytological analysis) and about the management.

Results: A total of 5424 patients were identified. There were 1226 patients (22.6%) with tumour size of 2 cm or less. The probability of metastasis increased in a non-linear fashion with increasing tumour size. Univariate analysis showed that tumour size was significantly correlated with survival (P<0.001), no matter surgery was performed or not. However, subgroup analysis suggested this asso- ciation to be linear for patients with localized and regional tumours (P<0.001), but stochastic in patients with distant stages (P=0.703). On multivariate analy- sis, tumour size was an indicator for metastasis (HR=1.010, 95% CI: 1.008-1.012, P=0.001 and size <20 mm was an independent prognostic factor for good survival (HR=1.211, 95% CI: 1.048-1.399, P=0.009 for size of 21-40 mm; HR=1.282, 95% CI: 1.161-1.474, P<0.001 for size >40 mm). For tumours ≤20mm, surgical treatment was associated with significantly improved survival compared with those patients who did not undergo operation (P<0.001).

Conclusion: Tumour size affects the probability of metastasis. Its prognostic impact on survival is restricted to patients with localized and regional disease. For tumours with tumour size ≤20mm, surgical treatment should be considered preferably.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
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P1445 THE LARGEST FAMILY IN TURKEY WITH MULTIPLE ENDOCRINE NEOPLASIA-TYPE 1 AND A NOVEL MUTATION
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Introduction: Multiple Endocrine Neoplasia type-1 (MEN-1) occurs usually sporadically but because it is an autosomal dominant disorder it may affect other family members too. The combination of parathyroid and pituitary tumors, and anterior pituitary tumors is characteristic of MEN-1 although it may be accompanied by a substantial number of non-endocrine tumors. The muta- tions in MEN-1 gene result in aberrant expression of MENIN promoter and associated with the transcription of the ACTR1G protein encoded by this gene and is responsible for tumor-suppression under normal circumstances. Herein we present the largest MEN-1 family in Turkey to the best of our knowledge and a newly discovered mutation in MEN-1 that effects this family.

Aims & Methods: The family inherited the specific MEN-1 mutation is originally \( 5 \) einkarhaisar, Giresun and most of the members have moved to Istanbul and Yalova. Consanguineous marriages have been practiced within the family. Familial mapping was constructed and contained fifty-five members. Among them, eleven patients underwent biochemical, radiological and if necessary endosonography and histological testing along with the genetic testing. Additionally, we learnt that 2 members of the family had died of pancreatic malignancy. Diagnostic criteria of familial MEN-1 in-clude: 1 - the presence of at least one MEN-1 associated tumor that are from parathyroid, pituitary, or GEP tract origins, 2 - at least one first-degree relative with one or more of these endocrine tumors and/or 3 - positive genetic testing for abnormal MEN-1 mutation. For our index case, DNA sequencing of the MEN-1 gene performed using Sanger sequen- cing technique at ABI 3500 sytem. For the other family members only the tar- geted mutation analysis is performed.

Results: Among the family members we had peripheral blood DNA from 9 and within these patients tumour tissue DNA from 1 patient. MEND1 gene was used for Sanger sequencing. Our index case was ZK who had hypophys adenoma, parathyroid and pancreas neuroendocrine tumour and the surgery performed. A three nucleotide deletion p.ser560argfs*3(c.1680_1683 del TGAG) was identified. Sevem out of ten members who were analysed tested positive for the mutation. Genetic counseling and information about pre-implantation genetic diagnosis (PGD) was given to all patients who are tested positive for the mutation. All 7 patients had p.ser560argfs*3(c.1680_1683 del TGAG) three nucleotide deletion same with that of index case. Out of 15 patients, MEN-1 diagnosis was confirmed in 11. Tumours detected at patients with MEN-1 diagnosis were: nonfunctional pancreatic neuroendocrine tumour at three, parathyroid adenoma/hyperplasia at 6 patients and hypophysis adenoma
at 4 patients. The mean age of our MEN-1 patients was 51 and the age at diagnosis was 41.8. The mean plasma calcium level was 11.46 ng/dl and there was no history of renal calculi at any of them.

**Conclusion:** The family presented here is the one which had the largest number of affected individuals with genetic and clinical properties of MEN-1 at Turkey. Because the patient presented here is the first with autosomal dominant mutation causing loss of function that is described for the first time. Also at MEN-1 families, counseling to prevent the neoplasia development and to prevent the new family member to be effected with PGD has a pivotal importance. We could point out that awareness is the most important caution for prevention.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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**P1446 PROGNOSTIC VALUE OF THE DIFFERENT PRETREATMENT BIOMARKERS FOR PATIENTS WITH NEUROENDOCRINE TUMORS**

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**Introduction:** Several inflammatory response materials could be used for predictive purposes to assess survival in patients with NETs and to determine their potential use in clinical practice. In this work, we studied the expression of selected proteins in the plasma of NET patients in order to develop a new marker. Aiming to improve the survival of patients with NETs, we analyzed the expression of Plac8 (Placenta-specific 8) in various NETs types. Plac8 introduces a new biomarker for the diagnosis and treatment of NETs. We attempted to develop a novel, non-invasive blood test for the early diagnosis of NETs.

**Aims and Methods:** The object of this study was to determine whether the Plac8, PLR, or thrombocytosis could predict the clinical outcomes in G1-G2 neuroendocrine tumors. We performed a retrospective review of 31 patients with neuroendocrine tumors with ki 67 below 20% diagnosed in Fundeni Clinical Institute between 2011-2017. Data about site of the primary tumor, presence of metastasis, PLR, PLR, thrombocytosis (platelet count > 400) and survival were collected and analyzed.

**Results:** The patients characteristics were: primary tumor location was: 61.29% pancreas, 22.58% gastrointestinal tract, 16.13% unknown, 61.29% had hepatic metastasis, 6.45% had locally advanced tumor. The primary tumor was resected in 35.48% of patients. The overall 2-year survival rate was 77.42%. The Ki-67 index (p < 0.04), PLR (cut off > 300) p < 0.01 have statistical significant impact on survival. Univariate analysis and on multivariate analysis (P < 0.05). Other factors like ki 67 index, metastatic disease, thrombocytosis and NLR have an impact on survival statistical significant on multivariate analysis.

**Conclusion:** This study demonstrates the prognostic role of different variables like Ki-67, PLR and PLT value, thrombocytosis and metastasis. This factors may be integrated in different scoring systems for prognostic that could guide clinicians for a better management in patients with neuroendocrine tumors.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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**P1447 FUNCTIONAL RELEVANCE OF THE OVEREXPRESSION OF PLAC8 IN NEUROENDOCRINE PANCREATIC TUMORS**

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**Introduction:** Neuroendocrine pancreatic tumors represent the second prevalent entity of malignant tumors of the pancreas and show an overall mortality of about 60%. At the moment surgical resection is the only option of potentially curative therapy, as with the currently available chemotherapeutic and radiotherapeutic approaches an inhibition of tumor growth but no regression of the tumor can be achieved. Therefore for about 80% of pNET patients there is no curative treatment available. To obtain the identification of novel potential target genes for the development of new therapeutic strategies, primary issues from pNET patients were analyzed. Amongst others Plac8 (Placenta-specific 8) was identified, which is a small protein of unknown function, showing different forms of cellular localization depending on the cell type analyzed, indicating at its ability to fulfill a variety of physiological functions.

**Aims & Methods:** In the course of this study, the function of Plac8 in neuroendocrine pancreatic tumors is to be unveiled to evaluate its value as a potential target for pNET therapy. Therefore primary tumor tissue of about 100 pNET patients were analyzed for Plac8 expression by quantitative realtime PCR and immunohistochemistry. Furthermore established pNET cell lines from human origin where transfected with siRNAs against Plac8 and there proliferative activity and localization were analyzed by chemiluminescent and MTT assay. Changes in these important characteristics of tumor cells were further examined by western blot analysis of key regulators of apoptosis and cell growth.

**Results:** Plac8 is highly expressed in primary human pNET tissue on RNA- as well as on protein level. Functional in vitro analyses show that the siRNA-mediated knockdown of Plac8 not only in human but also in rat cell lines leads to significantly reduced proliferative activity and reduced cell growth. These effects come along with indicative changes in the expression of central regulators of cell cycle while cell cycle pathways seem not to be affected.

**Conclusion:** Overexpression of Plac8 in neuroendocrine tumors of the pancreas promotes the proliferative phenotype of the tumor cells while the inhibition of Plac8 inhibits cell growth and metabolism. Therefore in the future Plac8 could represent a very interesting target for the treatment of pNETs.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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**WEDNESDAY, NOVEMBER 01, 2017 ENDOSCOPY AND IMAGING III - HALL 7**

**P1448 CLINICAL OUTCOMES OF SUPERFICIAL LARYNGOPHARYNGEAL CANCER WITH LYMPHO-VASCULAR INVASION AFTER ENDOSCOPIC LARYNGOPHARYNGEAL RESECTION**

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**Introduction:** Since the majority of laryngopharyngeal carcinomas are detected at an advanced stage, most cases are treated with concurrent chemoradiation therapy and radiation therapy. The key to improving the prognosis and quality of life is early detection of the primary cancer and treatment using minimally invasive surgery. We previously reported the good oncologic outcomes with ELPS (Endoscopic laryngopharyngeal superficial laryngectomy) for all cases. However there is no clinical evidence for an additional treatment nor prognosis about the cases conducted endoscopic resection which were diagnosed to be superficial carcinoma with lympho-vascular invasion histopathologically.

**Aims & Methods:** This study aimed to investigate the optimal additional treatment and clinical course for the surferal laryngo-pharyngeal carcinoma with lympho-vascular invasion. We analyzed clinicoopathological data in 9 patients showed Lympho-vascular invasion receiving ELPS between 2007 and 2014.

**Results:** Positive lympho-vascular invasion was found in 9 cases. Detected the tumor depth was SEP in 7 lesions and MP in 2 lesions. Mean alcohol consumption is 9.9 abv packs. Years 5 cases are low activity ALDH2 heterozygotes and have alcohol flushing reaction. Immunohistological findings of 7 cases with lympho-vascular invasion (n=0, v1), 2 cases with vascular invasion(l0, v1), and 2 cases with lympho-vascular invasion,(l1, v1). Two patients underwent an additional chemoradiotherapy without recurrence. Four patients had a cervical lymph node or local recurrence, two of them were salvage ELPS cases after chemoradiotherapy. One other two cases also had distant metastasis and was given palliative treatment, and finally died. The other one underwent surgical salvage and remained alive. One case with lymphatic and vascular invasion had no adjuvant therapy and remained without recurrence. And the other 2 cases had no recurrence but died of other causes. Finally Conclusion: Lympho-vascular invasion is a risk factor for cervical lymph node metastasis, which has a possibility to a very aggressive disease. In those cases, chemoradiotherapy as an additional treatment is recommended as far as possible.If patients already had prior radiotherapy, close follow-up is essential to detect recurrence early. In those cases, chemoradiation or additional surgical resection are also considerable if the general conditions are satisfactory.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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**P1449 LONG-TERM OUTCOMES OF EARLY GASTRIC CANCER WITH LATERAL MARGIN POSITIVE AFTER ENDOSCOPIC RESECTION**

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**Introduction:** The positive lateral margin after endoscopic resection(ER) of early gastric cancer(EGC), additional surgery or endoscopic submucosal dissection(ESD) are recommended. However, the additional surgery often difficult due to advanced age or patient’s comorbid conditions.

**Aims & Methods:** The aims of this study is to investigate of appropriate management in patients with positive lateral margin after ER. We analyzed...
retrospectively 103 patients with positive lateral margin after ER from January 2009 to December 2015, in single tertiary center. Clinicopathological data were retrieved to assess the local recurrence rate, survival rate, procedure related adverse events.

Results: Of the 103 patients, 27 patients (26.4%) underwent early re-treatment within 3 months after initial ER,17 patients in re-do ESD, 10 patients in additional surgery. And 76 patients (73.6%) were observed under close surveillance. Median duration of follow-up period was 45.7 (6-132) months. Recurrence rates of early re-treatment patients (3.7%, n = 27) was lower than surveillance group (18.4%, n = 10, p = 0.05). Five-year survival rates were not significantly different between the two groups, at 100%, 97.4% respectively. In close surveillance periods, 12 patients were confirmed to local recurrence by follow-up biopsy, then delayed re-treatment was performed (7 patients in re-do ESD, 5 patients in surveillance mode). Median duration after initial ER was 27 (27-29) months). Finally, a total of 24 patients were treated with re-ESD, and 17 patients were treated with additional surgery. Among these two groups, there were no significant difference in recurrence rates (8.3% vs. 0%) and five-year survival rates (both 100%). However, adverse events that related to re-treatment was more frequent in additional surgical group (2 ileus, 1 umbilical hernia).

Conclusion: The additional treatment should be recommended for patients with positive lateral margin after initial ER for EGCs. In addition, re-ESD which have a similar efficacy and a better quality of life, compared to additional surgery is a favorable option for control of recurrence or residual EGCs.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference
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scopic precogulation technique for blood vessels during endoscopic submu-

P1451 EXPOSURE TO ENDOTHERAPY FOR UPPER GASTROINTESTINAL BLEEDING AT THE POINT OF GASTROSCOPY CERTIFICATION- IS IT SUFFICIENT?
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Introduction: Although certification in diagnostic gastroscopy has been established in the UK, there is no formal process for quality assurance (QA) in endotherapy for upper gastrointestinal bleeding (UGIB). Training opportunities are variable, with 11% of final year UK gastroenterologists citing inadequate exposure, despite an expectation to independently manage UGIB upon achieving specialist status. Data on endotherapy exposure during endoscopy training is limited. We aim to assess whether trainees are receiving adequate exposure to endotherapy at the time of gastroscopy certification.

Aims & Methods: Trainees awarded certification in gastroscopy between September 2009–2016 were identified from the national trainee electronic portfolio (JETS). Trainee inputs and formative assessments (direct observation of procedural skills - DOPS) for UGIB therapy, up to their certification date, were analysed. Only trainees with >200 procedures were included, which is the minimum number to allow certification within the UK, thereby excluding those who had submitted baseline information which may have contained therapeutic data. Exposure rates from medical endoscopists (physician and surgical trainees) were compared with non-medical endoscopists (NME).

Results: 885 trainee portfolios were analysed (765 medical and 120 NMEs), with a median procedural count of 276 (IQR 124). The median number of therapeutic entries and DOPS were 4 (IQR 11), and 1 (IQR 3) respectively. Overall rates for endotherapy and DOPS were 2.9% and 0.8% per procedure. When stratified by therapy, the median exposure to each therapy was either 0 or 1, with means displayed in Table 1. 25.2% of trainees had no exposure to any type of endother-

apy (67.5% of NME and 18.6% of medical endoscopists, p < 0.0001). Of medical endoscopists awarded certification, 37.1% had not performed band ligation, 50.7% had not placed a clip, and 54% had not used heater probe. NME had significantly less exposure to each modality of endotherapy considered (overall odds ratio 0.10, p < 0.0001).

Conclusion: Training on endotherapy prior to certification is limited. The current UGIB certification process does not guarantee adequate exposure to endotherapy for UGIB.

Table 1: Mean procedural counts at the point of UGI certification

<table>
<thead>
<tr>
<th>UGIB</th>
<th>Total</th>
<th>Therapy</th>
<th>DOPS</th>
<th>Argon</th>
<th>Banding</th>
<th>Clipping</th>
<th>Injection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical</td>
<td>346</td>
<td>10.7</td>
<td>2.6</td>
<td>2.1</td>
<td>4.4</td>
<td>1.6</td>
<td>1.6</td>
</tr>
<tr>
<td>Non-medical</td>
<td>323</td>
<td>1.1</td>
<td>0.29</td>
<td>0.3</td>
<td>0.4</td>
<td>0.1</td>
<td>0.1</td>
</tr>
</tbody>
</table>

p-value 0.143 < 0.0001

Conclusion: Training on endotherapy prior to certification is limited. The current UGIB certification process does not guarantee adequate exposure to endotherapy for UGIB.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference
1. GMC National Training Survey Results 2016, Gastroenterology.

P1452 ELECTRONIC CHROMOENDOSCOPY WITH MAGNIFICATION IN THE DETECTION OF DYSPLASIA IN BARRETT’S ESOPHAGUS
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Introduction: Barrett’s esophagus (BE) is a known premalignant condition with risk for progression to esophageal adenocarcinoma. Electronic chromendo-
scopy with magnification (ECM) is an evolving imaging technology being inves-
tigated as a novel imaging tool to identify dysplasia in BE to assist with higher yield BE surveillance and improve the diagnostic yield of esophageal biopsies for BE.

Aims & Methods: This is a single-center study to evaluate the efficacy of ECM (Scan by Pentax) in the detection of BE and dysplastic BE in a screening, average risk population with BE in Northeast Mexico. We conducted a retrospective study of 100 consecutive patients (41 males) with known BE (confirmed by pathology) during surveillance upper endoscopy for dysplastic BE between

Disclosure of Interest: T. Toyonaga: Dr. Takashi Toyonaga invented the FlushKnife-BT in conjunction with Fujifilm and received royalties from its sale. All other authors have declared no conflicts of interest.

Reference
1. Tanaka S, Toyonaga T, Morita Y. Endoscopic vessel sealing: a novel endo-
scopic precogulation technique for blood vessels during endoscopic submu-
March and September of 2016. All patients underwent EC with iScan. The esophagus was inspected with a ECM capable endoscope (EG-2900-Z) and deliberate biopsies were taken from tissue identified by ECM that suggested BE. All biopsies were confirmed by a GI pathologist. Primary endpoint was the correlation between visual inspection diagnosis of dysplasic BE by ECM versus pathologic diagnosis of BE as the gold standard.

Table 1: Patient characteristics and outcomes

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>100</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean)</td>
<td>47.7</td>
</tr>
<tr>
<td>Male</td>
<td>41/100</td>
</tr>
<tr>
<td>Endoscopic diagnosis: nondysplastic BE</td>
<td>96/100</td>
</tr>
<tr>
<td>Endoscopic diagnosis: BE with LGD</td>
<td>4/100</td>
</tr>
<tr>
<td>Pathologic diagnosis: nondysplastic BE</td>
<td>94/100</td>
</tr>
<tr>
<td>Pathologic diagnosis: BE with LGD</td>
<td>4/100</td>
</tr>
<tr>
<td>Pathologic diagnosis: benign gastric mucosa</td>
<td>1/100</td>
</tr>
<tr>
<td>Pathologic diagnosis: esophageal ulcer</td>
<td>1/100</td>
</tr>
<tr>
<td>Accuracy</td>
<td>98%</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>100% [95% CI (96%–100%)]</td>
</tr>
<tr>
<td>Specificity</td>
<td>0% [95% CI (0%–84%)]</td>
</tr>
<tr>
<td>Positive predictive value</td>
<td>98% [95% CI (93%–99.7%)]</td>
</tr>
<tr>
<td>Negative predictive value</td>
<td>NA</td>
</tr>
</tbody>
</table>

Results: In our cohort 41% were male, with mean age of 47.7 years. Endoscopic diagnoses by ECM were divided into nondysplastic BE (96/100) and suspected dysplastic BE (4/100). On pathology nondysplastic BE was found in 94/100 patients, BE with low-grade dysplasia was found in 4/100 patients. Benign gastric mucosa with no alterations (1/100), and ulcerated esophagitis (1/100). The overall accuracy of endoscopic diagnoses using ECM against pathologic diagnosis was of 98%, with sensitivity of 100% [95% CI (96%–100%)] and positive predictive value of 98% [95% CI (93%–99.7%)].

Conclusion: Endoscopic diagnosis of BE by directed biopsies of esophageal tissue with use of ECM is highly accurate. Future prospective studies are needed to validate our preliminary findings and assess inter-observer variability.

Disclosure of Interest: All authors have declared no conflicts of interest.

References:

P1454 SAFETY, EFFICACY AND CLOSURE TECHNIQUES OF ENDOSCOPIC FULL THICKNESS RESECTION-INITIAL CLINICAL EXPERIENCE

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Introduction: Endoscopic full-thickness resection (EFTR) for sub-epithelial lesions (SfELs) of GI tract is less frequently described; possibly due to technical challenges involved in dissection and need for resultant defect closure. Current study describes single-center experience of EFTR for treatment of SETs.

Aims & Methods: Prospective database of patients undergoing EFTR for SETs over 6-years (2011–2017) was abstracted. Patient selection for EFTR-endoscopy, endoscopic ultrasound (EUS) and CT and/or MRI. Inclusion criteria—submucosal lesions, predominantly endophytic component and absence of features of invasive malignancy. Exclusion criteria—patients unfit for general anesthesia or major invasive procedure, unacceptable coagulopathy or high risk features for malignancy. All procedures performed under general anesthesia with endotracheal intubation.

Results: Total N = 18(M:F = 11:7), mean age 53.6(Range 28–78). Presentation—GI bleed (38%), abdominal pain (42%), asymptomatic, incidentally diagnosed (63%). Layer of origin—MP layer (61%), SM (17%), DE (9%), muscularis propria (13%). Size of SET—3.3 cm (range 1–7). Mean procedure time—182 mins (30–545), and mean hospital stay was 4 days. Adverse events—two (11%)—esophageal laceration during specimen retrieval—1 (closed using endoclips), failure—1 (due to undetected large exophytic component—surgical resection). Histopathology with
Aims & Methods: We aimed to evaluate the efficacy of EVL therapy in both primary prophylaxis of variceal bleeding in cirrhosis and to establish the patient’s clinical outcome. This was a retrospective observational cohort study of a total of 444 EVL procedures performed in 250 cirrhotic patients, who were admitted in a gastroenterology department of a tertiary centre, between 2004–2016, to receive EVL as prophylaxis of variceal bleeding. Sessions of ligation were repeated every 2 to 3 weeks in order to reach variceal eradication. The clinical outcome included the recurrence of bleeding (primary endpoint), the eradication success rate of oesophageal varices, EVL-related complications and overall and bleeding-related mortality.

Results: The mean follow-up period for all 250 cirrhotic patients enrolled in the study was 73.2±40.0months, with mean age of 63.9±10.8years and a predominance of male gender (80.4%;n=201). At initial endoscopy, 237 (90%) patients had active or previous symptomatic variceal bleeding severe in 168 (67.2%) cases. EVL was performed as primary prophylaxis in 50.9%(n=226) and secondary prophylaxis in 49.1%(n=218). Varices were obliterated in 209 (83.6%) patients with mean number of EVL procedures necessary to eradicate varices of 1.8±0.95 and a maximum of procedures of 6. Recurrent bleeding occurred in 11.2%(n=28) of cases with a mean time to re-bleeding occurrence of 8.1±14.2months. Major and significant complications were verified in 8.1%(n=36) of patients. The main complications were bleeding related to post-banding ulceration (75.0%(n=27)) and infection (22.2%(n=8)), with mean time between EVL and complication occurrence of 11.1±11.8days (minimum:0;maximum:43). Intra-procedure complications occurred in 11(2.5%) patients with no death, despite of two cases of Sengstaken-Blakemore-Halligan therapy. The overall mortality was 3.4%(n=24), being 0.4%(n=2) related to variceal bleeding. EVL seems to be an efficient, safe and relatively simple therapeutic modality for primary and secondary prophylaxis and serial bleeding in cirrhotic patients. Since the main complications occurs over 1 week after EVL procedure, the majority of patients can be safely treated in an ambulatory setting.

Discussion of Interest: All authors have declared no conflicts of interest.

Disclosure of Interest: All authors have declared no conflicts of interest.

**Conclusion:** EVL without laparoscopic assistance is minimally invasive, safe, and effective for treating gastric and duodenal SMTs, which originate from the MP layer and adhere tightly to the serosa. High en blos resection rate could be achieved. However, a larger number of the cases and long-term outcome deserve further research.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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**P1456 THE VALUE OF ENDOSCOPIC FULL-THICKNESS RESECTION FOR GASTRIC AND DUODENAL SUBMUCOSAL TUMORS ORIGINATING FROM THE MUSCULARIS PROPRIA LAYER**

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**Introduction:** Given diminishment of quality of life caused by surgery in the stomach and duodenum, a minimally invasive treatment is desirable for gastric and duodenal submucosal tumors (SMTs).

**Aims & Methods:** We aimed to assess the value of endoscopic full-thickness resection (EFTR) technique for gastric and duodenal submucosal tumors (SMTs) originating from the muscularis propria (MP) layer. A total of 276 patients with single gastric SMTs originating from the MP layer were performed EFTR between January, 2010 and February, 2014. The tight adhesion of the tumor to gastric or duodenal serosal layer could be seen in every case from endoscopic ultrasound (EUS) before the procedure. The SMTs oriented endoscopically were performed EFTR using a standard ESD technique without laparoscopic assistance under direct endoscopic view. The defect of gastric and duodenal wall was closed after resection.

**Results:** A total of 276 patients included 94 males and 182 females. Their median age was 57.8 years (range, 30–81 years). Among all the 276 SMTs in our study, 165 located in gastric fundus, 96 located in gastric body, 8 located in the antrum, 1 located in the pylorus, 1 located in duodenal bulb and 1 in duodenal bulb + antrum. The mean size was 1.7 cm (range 0.7-6.0 cm). The success rate of EFTR was 98.9% (273/276). EFTR failed in 3 cases: one case was out of control because of bleeding into enteroceola, two cases required conversion into laparoscopic surgery because of torrential lobulations of the tumor outside the cavity. The median operation time was 65 min (range, 14-210 min). En bloc resection rate was 98.1% (268/273), piecemeal resection rate was 1.9% (5/273). The median length of hospital stays was 4.4 days (range, 1–23 days). Pathological outcomes revealed that the SMTs were classified 137 (47.8%) fibrous tumors, 57 (21.3%) leiomyomas, 13 (4.7%) schwannomas, 8 (2.9%) calcifying fibrous tumors, 7 (2.5%) glomus tumors, 5 (1.8%) displaced pancreas, and 3 (1.1%) fibromatosas. The procedure-related complications were as follows. Different degrees of postoperative gastric or duodenal ulcer occurred in 168 (60.9%) cases, among which 24 (8.7%) cases showed cases required analgesics. Pneumoperitoneum occurred in all the patients and was treated successfully with peritoneoscopic decompression. Seroperitoneum occurred in 15 (5.4%) cases, localized peritonitis occurred in 3 (1.1%) cases, and digestive tract leakage occurred in 1 (0.4%) case. All the cases with above complications recovered spontaneously or after conservative treatments. No massive bleeding or abdominal abscess was found after EFTR. None of the 273 cases developed procedure-related death. No tumor residual or recurrence was found during the follow-up period ranging 5–55 months.

**Conclusion:** EVL without laparoscopic assistance is minimally invasive, safe, and effective for treating gastric and duodenal SMTs, which originate from the MP layer and adhere tightly to the serosa. High en blos resection rate could be achieved. However, a larger number of the cases and long-term outcome deserve further research.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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**P1457 BLUE LIGHT IMAGING AND LINKED COLOR IMAGING FOR DETECTION AND CHARACTERIZATION OF CHRONIC GASTRITIS**

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**Introduction:** Current standard in the characterization of gastric mucosal changes is the use of virtual chromoendoscopy with magnification to visualize the pit pattern and vascular changes. The most recent development in light emitting technology is the so called Multi Light Illumination, that composes light out of 4 coloured LED. Blue Light Imaging (BLI) is composed of a continuous spectrum with peaks at 410 and 430 nm to enhance surface and vascular structures. Linked Color Imaging (LCI) uses BLI light together with post processing that realocates colour tones resulting in a high contrast of different red tones. Until now only few data exist about the use of BLI and LCI in chronic gastritis (CG).

**Aims & Methods:** We aimed to analyse the use of LCI and BLI in detecting and characterizing of chronic gastritis and premalignant conditions of the stomach. In total 217 consecutive patients (149 male; mean age 65 years) were enrolled. All patients had undergone standard upper GI endoscopy under conscious sedation. In all cases an endoscope equipped with zoom (Fujifilm EG-760Z) was used. Endoscopic classification was based on the following parameters: normal gastric mucosa was defined as mucosa with visible superficial capillary network (SCN) without any focal lesions; atrophy (AG) was defined by whitening of the mucosa with visible deeper vascular architecture in white light, BLI and LCI; intestinal metaplasia (IM) was diagnosed if mucosa had visibilised indented surface with whitening in LCI or white light or light blue crest sign in BLI; CG was diagnosed in case of loss of SCN or focal lesions not matching the definition of other focal lesions or cancer. Biopsies were sampled according to the updated Sydney classification system and in addition of every visible focal lesion. After endoscopy a prediction of histology was made by the endoscopist.

**Results:** We investigated 24 patients (15 female, 9 male, age 65 yrs (25-87yrs)). H. pylori was detected by histology or urease test in 7 patients. 3 patients showed normal gastric mucosa, 13 patients presented IM or AG either in the antrum or the corpus. According to MAPS criteria 7 patients had extensive disease with premalignant conditions in both, antrum and corpus. The concordance of endoscopic classification and histology was 79.1% (19/24) in the antrum and corpus each. Despite the inconcordance of histology and endoscopic diagnosis in 5 cases the intervals for surveillance according to MAPS guidelines would have been correctly respected with the use of endoscopic assessment in all cases.

**Conclusion:** LCI and BLI are accurate in detection and characterization of changes in gastric mucosa with an acceptable concordance to histology. These new imaging modalities are a step towards precise endoscopic diagnosis of gastric mucosal changes and have the potential to reduce the number of unnecessary histologic investigations and offer the possibility for more appropriate endoscopic diagnosis.

**Disclosure of Interest:** J. Weigt: Research and presenter for Fujifilm. All other authors have declared no conflicts of interest.
P1458 LONG-TERM OUTCOMES OF ENDOSCOPIC SUBMUCOSAL DISSECTION (ESD) FOR RELATIVE INDICATION GROUP OF EARLY ESOPHAGEAL SQUAMOUS CARCINOMA (ESESC) IN AGED PATIENTS
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Introduction: According to the Japanese Esophageal Society Guidelines, Early Esophageal Squamous Cell Carcinoma (ESESC) involving the muscularis mucosae or <200 μm invasion of the submucosa, and circumferential extent of >2/3 were relative indications (RI) for ESD. Additional treatment (AT, including esophagectomy or chemoradiotherapy) may be needed for ESESC. But in aged RI patients, most will refuse AT due to higher rates of debilitating symptom in China.

Aims & Methods: The aim of this study was conducted to evaluate the long-term outcomes of aged RI patients without AT after ESD.

Results: Between January 2008 and December 2013, a total of 158 aged ESESC patients were included in the present retrospective study. Prognosis outcomes were analyzed.

Results: 89 patients included in absolute indication (AI) group and 69 in RI group. The baseline characteristics were balanced between the two groups. During the follow-up time (median 56 (1-108) months), short-term adverse events (4.3% vs. 1.1%, p = 0.319) and postoperative stricture rate (31.8% vs. 21.3%, p = 0.134) were higher in RI group than in AI group. 5-year recurrence-free survival rate (85.8% vs. 87.2%, p = 0.561), metastasis-free survival rate (100% vs. 98.6%, p = 0.437), overall survival rate (96.6% vs. 90.0%, p = 0.613) and cause-specific survival rate (98.9% vs. 98.5%, p = 0.264) for AI group and RI group were comparable.

Conclusion: Aged RI ESESC patients without AT (esophagectomy or chemoradiotherapy) showed comparable prognosis outcomes with AI group after ESD. So follow up may be recommended, substituted for AT in aged RI group.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1459 RETROSPECTIVE ANALYSIS ON SUSPICION OF FOREIGN BODY INGESTION AND FOOD IMPACTION ON GASTROENTEROLOGY EMERGENCIES
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Introduction: Suspicion of foreign body (FB) and food impaction (FI) are one of the most common motives for endoscopic emergency. This retrospective study reviewed 288 cases of suspicion on FB/FI, by the frequency of endoscopic alterations, predictive factors to presence, types of FB found, and therapeutic approach.

Aims & Methods: Unicentric retrospective cohort study of endoscopies performed during one year of gastroenterology emergency setting.

Results: In 2015, 288 endoscopies were performed on suspicion of FB/FI (22% of total endoscopies), n = 1309, of them 69.1% (n = 199) were performed during the night. Patients’ median age was 58 years, and 52.8% were women. The presence of FB/FI was confirmed in 71.2% (n = 205); of them 61.5% (n = 126) were complete FB/FI. The most frequently found foreign bodies were meat bones 18% (n = 37) and fish bones 14.6% (n = 30). Most FB/FI were found on the proximal esophagus (56.1%, n = 115). Endoscopic removal was performed on 129 cases (63.4%), endoscopic mobilization in 54 (26.3%), and in 22 endoscopic removal wasn’t achieved (10, where referred of otolaryngology; 2 for surgery and 10 were deferred to endoscopy with sedation, in operating room). Endoscopy under sedation was performed in 20 cases (9.7%). About ¼ had associated comorbidities, the most common were esophageal ring in 22 (10.7%) and benign stenosis in 17 (8.3%) patients. Major complications were rare: 1 perforation (0.3%) and 3 deep esophageal lacerations (1.5%). Age (≥55years), presence of comorbidities, and previous episodes were associated with presence of FB/FI on Endoscopy (Odds Ratio 2.01, 3.39 and 4.63 respectively).

Conclusion: Endoscopy is frequently preformed for suspicion of FB/FI in our emergency setting. Presence is confirmed in the majority of the cases. Predictive factors for presence were identified. Most FB/FI were removed with success low complication rates. This data favor the endoscopic approach on suspicion of FB/FI.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1460 LEARNING CURVE FOR ENDOSCOPIC SUBMUCOSAL DISSECTION OF GASTRIC NEOPLASMS; LOW-VOLUME SINGLE-CENTER EXPERIENCE
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Introduction: Endoscopic submucosal dissection (ESD) has become a standard therapy for early gastric neoplasia. There is no consensus yet about the number of experiences required for performing ESD alone.

Aims & Methods: We aimed to investigate the learning curve of ESD performed by a single beginner endoscopist focusing on developing the performance of dissection, shortening the procedure time, and preventing complications.

Methods: Records of 120 consecutive ESD procedures performed by a single beginner endoscopist with an ESD knife from March 2012 to February 2016 were collected. For analysis of the learning curve, total procedures were divided into four periods, each comprising 30 sequential ESD. The parameters assessed were the en-bloc resection rate, complete resection rate, procedure time, and related complications.

Results: In the procedure time according to the number of experiences, the procedure time decreased from 30 experience. However, there was no statistical difference from the first (63.5±54.0) to the second quarter (44.7±31.4, p = 0.19), to the third quarter (40.7±27.8, p = 0.08), and to the fourth quarter (40.8±23.1, p = 0.09). There was no procedure that exceeded 100 minutes from the first quarter. There were a total of seven perforations, four of which were in the first quarter, two in the second, and one in the third. In the procedure time according to the location of the lesions, upper third lesion (92.0±43.7) showed longer procedure time than middle (46.6±40.2, p < 0.01) and lower third (39.5±27.5, p < 0.01) with statistically significant difference. In addition, the fibrotic lesions, regardless of size and location, all took a very long time, more than 100 minutes.

Conclusion: It needs accumulate experience with the help of a professional expert up to 30 cases, and to the more advanced level, about 90 procedures are needed. And, the location of the lesion is the important factor in determining the difficulty of the procedure. Therefore, it is best to avoid the upper third lesion as far as possible until experience 90 cases or at least 30 procedures.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P1461 COMPARATIVE STUDY OF ESD AND SURGICAL RESECTION FOR GASTRIC SETS ORIGINATED FROM MUSCARISPORIPA
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Introduction: Endoscopic resection for gastric subepithelial tumors (SETs) originated from the muscarisporiopsis (GSET-PM) has offered less invasive alternatives to surgical resection. The aims of this study were to compare endoscopic submucosal dissection (ESD) with surgical resection for the removal of GSET-PM.

Aims & Methods: This study involved 17 patients with GSET-PM removed by ESD and 76 patients who underwent curative surgical resection. ESD was attempted in GSET-PM with well marginated tumors which was below 5 cm and showed an endoluminal growth pattern according to endoscopic ultrasound (EUS) finding.

Results: ESD group were more likely to have upper portion (10/17, 58.8%) and surgery group were more likely to have mid portion (41/76, 53.8%) (p = 0.039). ESD group were smaller median tumor size (25.6 mm vs 35.9 mm, p = 0.037) and higher endoluminal ratio (58.5 ± 9.1% vs 45.8 ± 15.4%, p = 0.002). ESD group were mostly to have Yamada type III (10/17, 58.8%) and surgery group were mostly Yamada type I (52/76, 68.4%) (p < 0.001). Complete resection by ESD was lower than by surgical resection (82.4% vs 100%, p < 0.001). In ESD group, 3 performed surgical resection after ESD (1 incompletely resection and 2 uncontrolled bleeding) and 1 showed perforation was completely resected with endoscopic closure. In surgery group, complications occurred in 6 patients (1 leakage, 1 stricture, 1 hernia and bowel obstruction, 1 wound infection and 2 worsened general condition after surgery). Although surgery group were lower in complication rate than ESD group (p = 0.006), severity of complications were higher in the surgery group and there were no mortalities in the ESD group compared with 2 in the surgery group. There was no statistical difference of recurrence and the follow-up period between two groups.

Conclusion: ESD can be one of good options for the resection of endoluminal GSET-PM and could be replace treatment by surgical resection in Yamada type III with a high endoluminal ratio.

Disclosure of Interest: All authors have declared no conflicts of interest.
Aims & Methods: The aim of this study was to compare CA-EGD to SVE for complete examination of the MDP. CA-EGD allowed a better overview of the papilla and overall satisfaction of the evaluators. For secondary outcomes, measures were image quality of mucosal pattern, ability to obtain an overview after image processing, by three blinded multicenter-experts. Our primary outcome was complete examination of the papilla and overall satisfaction of the evaluators. For secondary outcomes, a score was given from 1 to 10 (1=poor, 10=excellent).

Results: A total of 62 patients were randomized and completed the study. Complete examination of MDP was achieved in 59 patients using CA-EGD compared to 60 patients using SVE (95 vs. 97%, p = 1.0). CA-EGD had mean scores of 8.7±1.3, 7.1±0.86 and 7.9±1 regarding mucosal pattern, overview and overall satisfaction, respectively, versus 5.3±1.6 (p < 0.001), 8.3±0.9 (p < 0.001) and 7.6±0.6 with SVE (p = 0.01).

Conclusion: CA-EGD is non-inferior to SVE for complete examination of MDP. CA-EGD had significantly higher scores than SVE regarding the image quality and overall satisfaction, while SVE had a better overview. CA-EGD is a safe and effective method for examination of MDP and can replace the SVE for diagnostic indications.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

Hereditary Diffuse Gastric Cancer: Early Diagnosis and Endoscopic Therapy

Disclosure of Interest: All authors have declared no conflicts of interest.
Results: 19 patients underwent EA, with a mean age of 63.5 ± 17.7 years and a successful resection in the tumor of 17.4 ± 7.8 mm. The male to female ratio was 0.7. "En bloc" resection was done in most cases 15/19 (78.9%). Bleeding occurred in 6 cases (31.6%) and two patients (10.5%) developed acute pancreatitis. One patient died due to severe bleeding. The average days of hospitalization after endoscopic ampullectomy were 5.7 with a range from 2 to 25 days. Adenocarcinoma was described in the final histopathological result in 4/19 cases (21.1%). One year follow-up noted a recurrence rate of 15.8% (3/19 cases).

Conclusion: In conclusion, endoscopic ampullectomy is a difficult procedure with an increased risk of complications but performed by experienced endoscopists is safe and surgical interventions can be avoided.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

Table 1 Continued

<table>
<thead>
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<th>Patient Demographics</th>
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<tr>
<td>Prior POEM (n) (%)</td>
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<td>Prior Heller Myotomy</td>
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<td>LHM (n)</td>
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<td>ASA Physical Status Classification</td>
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<tr>
<td>ASA grade I (n) (%)</td>
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<td>ASA grade II (n) (%)</td>
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<td>ASA grade III (n) (%)</td>
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Conclusion: This is the largest UK case series of POEM for achalasia including the first successful UK POEM procedure for DES. At our institute, POEM was performed successfully in a potentially more challenging cohort where 52.9% had prior endoscopic/surgical treatment with substantial morbidity. Our results are in line with international consortia and ASGE findings that POEM is a safe and efficacious procedure for the treatment of achalasia and oesophageal spastic disorders for both short term and sustained symptomatic benefit.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference
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Table 1: Baseline characteristics

<table>
<thead>
<tr>
<th>Patient Demographics</th>
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<tr>
<td>Age (mean, SD, range) (years)</td>
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<tr>
<td>Male (n) (%)</td>
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<tr>
<td>Female (n) (%)</td>
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<tr>
<td>Clinical Data</td>
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<tr>
<td>Duration of disease (mean, SD, range) (years)</td>
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<tr>
<td>Eckardt Score (median, range)</td>
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<tr>
<td>Chicago Subcategorisation</td>
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<tr>
<td>Achalasia Type I (n) (%)</td>
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<td>Achalasia Type II (n) (%)</td>
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<td>Achalasia Type III (n) (%)</td>
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<tr>
<td>DES</td>
</tr>
<tr>
<td>Uncategorised (EndoFLIP used)</td>
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<tr>
<td>Non-Sigmoid Oesophagus (n) (%)</td>
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<tr>
<td>Sigmoid Oesophagus (n) (%)</td>
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<tr>
<td>Treatment History</td>
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<tr>
<td>Prior Achalasia Treatment</td>
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<tr>
<td>Prior Botulinum Toxin Injection; BTX (n) (%)</td>
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<tr>
<td>Prior Pneumatic Dilatation; PD (n) (%)</td>
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<tr>
<td>Prior Heller Myotomy; LHM (n) (%)</td>
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(continued)

Conclusion: The purpose of this study was to evaluate the feasibility of L-ESD and the quality of the resected specimen obtained by L-ESD in living porcine compared with C-ESD. We performed ESD for a total of 144 sessional lesions in three porcine stomachs (C-ESD: 7 lesions; C-ESD: 7 lesions) under general anesthesia. En-bloc resection rate, procedure time, adverse events, and the quality of the resected specimen were evaluated. To evaluate the smoothness of the cutting surface in the resected specimens, we compared the length of the resected side of the submucosa (LRS) with the length of the muscularis mucosa (LMM). Results: The en-bloc resection rate was 100% in both groups. Although the mean L-ESD procedure time was 23.3 ± 10.8 minutes, and was significantly longer than that of the C-ESD group (9.4 ± 6.6 minutes; p < 0.005), there was no uncontrollable bleeding or perforation in either group. The mean ratio of LRS to LMM was 107 ± 33% in the L-ESD group, and was significantly lower than that of the C-ESD group (138 ± 28%)(p < 0.005).

Conclusion: ESD using CO2 laser might be a feasible and effective method for the treatment of early gastrointestinal cancers.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference
1. S. Gulati, A. Emmanuel, H. Inoue, A. Haji, B. Hawe1

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Introduction: Probe-based confocal laser endomicroscopy (pCLE) provides real-time microscopic visualization with 100-fold magnification, allowing endoscopic access to the histological evaluation of gastrointestinal lesions. pCLE may thereby be helpful in guidance of endoscopic therapy. However, histopathological assessment still remains a gold standard for histological diagnosis so far, while pCLE-based diagnosis has not been generally accepted yet. Therefore, more studies assessing diagnostic accuracy of pCLE are warranted.

Aims & Methods: The aim of this study was to compare diagnostic accuracy of pCLE with standard biopsies in the diagnosis of macroscopically visible esophageal and gastric lesions.

Results: We examined 45 lesions (38 esophageal, 7 gastric) in 41 patients. Definitive diagnoses revealed 28 malignant lesions (21x adenocarcinoma (AC), 7x squamous carcinoma (SCC) and 1 benign lesion. In summary, pCLE diagnosis was definitive in 34 (75.5%) and incorrect in 11 (24.5%) (11/45) while diagnosis based on biopsy was correct in 75% (33/44) and incorrect in 25% (11/45) when diagnosis was based on biopsy. The sensitivity of pCLE for the correct histological diagnosis was 82% (62/76), specificity (Sp) 65% (17/26), positive predictive value (PPV) 90% (22/24) and negative predictive value (NPV) 72% (53/74).

Conclusion: pCLE provides satisfactory diagnostic accuracy comparable with standard biopsies in malignant esophageal and gastric lesions in particular.

Disclosure of Interest: All authors have declared no conflicts of interest.
(12.5%) had esophageal cancer, 207 patients (78.1%) had stage IV disease. At the time of inclusion, 138 patients (52%) had grade 3 dysphagia and the mean body mass index (BMI) was 20.9 Kg/m². All the patients underwent anti-biotic prophylaxis previous to the procedure. There was an increase on BMI to 23.8 Kg/m² at 6 months follow up. Eight patients (3.8%) had immediate complications after the procedure (bleeding from the PEG tract; 6; anesthetic complications - 2). The overall complication rate at the first month of follow up was 14.4%, at the third month 20.5% and at the sixth month 11.7%. The overall peri-PEG infection rate was 14%, and was the main complication at the first month of follow up. The development of hyper-granulation tissue was the most frequent complication at the third month of follow-up. Buried bumper syndrome occurred in 10 patients (3.7%). None of the patients had tumor seeding at the gastrostomy site. Overall mortality was 26.4%, none of the deaths attributable to PEG tube insertion.

Conclusion: PEG placement is a safe and effective technique in cancer patients. The rate of major complications and tube site infection were similar to the results found in literature for non-cancer patients.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P1472 A PROSPECTIVE, SINGLE-CENTER, CROSS-OVER CONTROLLED TRIAL OF CONFOCAL LASER ENDOMICROSCOPY ASSESSMENT OF PERSISTENT OR RECURRENT INTESTINAL METAPLASIA AND RECURRENT OF NEOPLASIA AFTER ENDOSCOPIC TREATMENT OF BARRETT’S ESOPHAGUS-RELATED NEOPLASIA (BORN)

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Introduction: Probe-based confocal laser endomicroscopy (pCLE) has been developed to overcome limitations of the current endoscopic sampling techniques. pCLE allows detailed examination of cellular structures and may examine larger areas compared to standard biopsy. Patients after endoscopic treatment of Barrett’s esophagus (BE)-related neoplasia (BORN) should undergo endoscopic surveillance with biopsies to detect persistence or recurrence of intestinal metaplasia (IM) or neoplasia (N).

Aims & Methods: The aim of this prospective study was to evaluate the efficacy of pCLE (vs. standard biopsies) in detection of persistent/recurrent IM/neoplasia in patients after endoscopic treatment of BORN. A single-center, prospective, controlled and pathologist-blinded (still ongoing) study in patients undergoing surveillance after endoscopic treatment of BORN. pCLE images were obtained from the neo-Z-line (a few cases including macroscopically visible tongues), the cardia and the esophagus. Thereafter, standard biopsies were taken and sent for histopathological analysis (4 biopsies from macroscopically normal neo-Z-line, 2 biopsies from the cardia and the esophagus and targeted biopsies from visible abnormalities, if present). BE was defined in pCLE as columnar-lined epithelium with dark mucin in goblet cells, a villiform pattern, and regular-shaped capillaries in the mucosa. The dysplastic BE was characterized by black cells with irregular borders and shapes, high dark contrast to the surrounding tissue, and irregular leaking capillaries in the mucosa.

Results: We examined 29 patients, from these 14 patients (48%) had the initial diagnosis of low-grade intraepithelial neoplasia (LGIN), 7 patients (24%) had high-grade intraepithelial neoplasia (HGIN) and 8 patients (28%) had an early adenocarcinoma (EAC). Persistent/recurrent IM was detected at the level of neo-Z-line in 10 patients (34.5%) by both standard biopsies and pCLE. pCLE but not biopsies detected persistent/recurrent IM in 2 patients (6.7%), another 2 patients had IM present in biopsies but not in pCLE. pCLE diagnosed one patient with recurrent LGIN in a macroscopic visible tongue arising from neo-Z-line, which was not confirmed in biopsies. Sensitivity and specificity of pCLE detection of persistent/recurrent IM was 83.3% (95% CI 51.6-97.9) and 80.4% (95% CI 66.9-98.7), respectively, with positive predictive value 83.3% (95% CI 51.6-95.0) and negative predictive value 89.5% (95% CI 70.4-96.8). Agreement of pCLE and histopathological findings was 86%.

Conclusion: pCLE seems to be comparable with standard biopsies in detection of persistent/recurrent IM after endoscopic treatment of BORN. Nevertheless, these results need to be confirmed in a larger cohort of patients. Supported by a grant from Ministry of Health of the Czech Republic, No. 16-27548A.

ClinTrials Registry: NCT02220049

Disclosure of Interest: All authors have declared no conflicts of interest.
**Conclusion:** In FI patients, the location of the symptoms has a better correlation with the endoscopic findings compared with FII patients. The esophagohioido-
inscopy is safe and effective in patients with FI and FII.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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**Aims & Methods:** 33 patients (13 male; mean age 45, range 17–80) underwent a total of 294 endoscopic procedures over 2 years. Treatments were either 100 IU units of Botox injected into 4 quadrants of the pylorus or pneumatic dilation (PD) incrementally up to 16–20 mm (Hercules; Cook Medical). Patients with gastric malignancy, previous pyloric surgery or no documented follow-up were excluded. High-dose-therapeutic responses were assessed at first follow-up post-proce-
dure and graded as ‘good’, ‘partial’ or ‘none/poor’. Patients were grouped according to type of therapy and indication.

**Results:** There were no immediate or late complications observed. 31 procedures were performed for gastroparesis with a mean post-procedure follow-up of 11 weeks. Overall, a partial or good response was observed in 81% (25/31). Specific treatment with Botox alone (18 procedures) or as part of combination therapy (10 procedures) led to a good or partial response in 86% (24/28) compared to 33% (1/3) who had PD alone (p = 0.03). 14 procedures were performed in the post-surgical group with a mean post-procedure follow-up of 10 weeks. Overall, a partial or good response was observed in 93% (13/14); treatment with Botox alone or as part of combination therapy led to a good or partial response in 100% (10/10) compared to 75% (3/4) who had dilation alone (p = 0.1). 6 therapies were performed without a defined indication, 2 patients (33%) had a partial or good response, both of which had combination therapy.

**Conclusion:** Pyloric intervention with Botos, PD or combination therapy are safe and effective treatment options for patients with gastroparesis or delayed gastric emptying following gastrosopic transposition. Subjective treatment without a clear indication shows little improvement.

**Disclosure of Interest:** All authors have declared no conflicts of interest.
factor for delayed bleeding. Given that the majority of delayed complications occurred than 5 post-procedure, a standardised 5 day inpatient stay would prove futile in our cohort.

Disclosure of Interest: P. Bhandari: Educational grants from Fujifilm, Olympus and Pentax
All other authors have declared no conflicts of interest.

P1487 PREDICTIVE FACTORS AND MANAGEMENT OF REFRACTORY BENIGN OESOPHAGEAL STRICTURES
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Introduction: The management and the predictive factors of response to endoscopic dilation of refractory benign oesophageal strictures remains controversial.

Aims & Methods: To evaluate the prevalence and factors predicting response to treatment of benign refractory oesophageal strictures with scheduled endoscopic dilatations

Retrospective analysis of 75 patients submitted to scheduled endoscopic dilatation of benign oesophageal strictures between October 2010 and November 2016. Strictures were classified as refractory when ≥5 endoscopic dilations were needed with at least one dilation achieving ≥15 mm of diameter during the course of management of the oesophageal strictures.

Results: The study sample included 42 (56%) male patients and the mean age was 55 ± 18 years. Dysphagia scale at baseline was: solids (1)–17 (22.7%), semi-solids (2)–23 (30.7%), liquids (3)–23 (30.7%) and complete (4)–12 (16%). Body mass index (BMI) at baseline was 22 ± 5 Kg/m². The aetiology of the benign strictures was: surgical–31 (41.3%), peptic–15 (20%), caustic–10 (13.3%), radiotherapy–10 (13.3%) and others–9 (12%). The location of the oesophageal stricture was as follows: proximal third–34 (43.5%), middle third–12 (16%), distal third–27 (36%) and multiple locations–2 (2.7%). The type of stricture: simple–44 (58.7%), complex–31 (41.3%). Patients underwent a median of 4 (1–26) endoscopic dilation over a median period of 19 weeks (1–229). Dilations were done with Savary-Gilliard dilators–35 (46.7%), TTS-balloons–24 (32%) or both–16 (21.3%). The mean diameter of dilation achieved was 15.7 ± 2.2 and a dilation diameter of ≥15 mm was achieved in 36 (74.6%) patients. Local injection of corticosteroids have been shown to improve outcome. Local corticosteroids were associated with improved clinical outcomes in patients undergoing endoscopic dilation of benign oesophageal strictures. In our study sample with multiple aetiologies of benign oesophageal strictures, only the maximum dilation diameter and local injection of corticosteroids (OR: 7.22, 95%CI: 0.021–0.55, p = 0.007) were strongly associated with improved dysphagia scores.

Conclusion: In our study sample with multiple aetiologies of benign oesophageal strictures, only the maximum dilation diameter and local injection of corticosteroids were associated with improved clinical outcomes in patients undergoing endoscopic dilation of benign oesophageal strictures.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1489 LOCAL CORTICOSTEROIDS IMPROVE EARLY CLINICAL OUTCOMES IN PATIENTS UNDERGOING ENDOSCOPIC DILATION OF BENIGN OESOPHAGEAL STRICTURES
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Introduction: Localised corticosteroids have been shown to improve outcomes in patients undergoing endoscopic dilation of peptic strictures.

Aims & Methods: To evaluate factors predicting early clinical response to endoscopic dilation of benign oesophageal strictures. Retrospective analysis of 75 cases submitted to scheduled endoscopic dilatations between October 2010 and November 2016. Clinical improvement was defined as dysphagia score ≤1, IBM SPSS®/21 was used for statistical analysis.

Results: The study sample involved 42 (56%) male patients and the mean age was 54 ± 18 years. Dysphagia scale at baseline was: solids (1)–17 (22.7%), semi-solids (2)–23 (30.7%), liquids (3)–23 (30.7%) and complete (4)–12 (16%). Body mass index at baseline was 22 ± 5 Kg/m². Stricture aetiology: surgical–31 (41.3%), peptic–15 (20%), caustic–10 (13.3%), radiotherapy–10 (13.3%) and others–9 (12%). The location of the oesophageal stricture was as follows: proximal third–34 (43.5%), middle third–12 (16%), distal third–27 (36%) and multiple locations–2 (2.7%). The type of stricture: simple–44 (58.7%), complex–31 (41.3%). Patients underwent a median of 4 (1–26) endoscopic dilations achieved a median period of 19 weeks (1–229). Dilations were performed with Savary-Gilliard dilators–35 (46.7%), TTS-balloons–24 (32%) or both–16 (21.3%). The mean dilation diameter of achieved was 15.7 ± 2.2 and a dilation diameter of ≥15 mm was achieved in 36 (74.6%) patients. Local corticosteroids were associated with the need for local corticoid injection (p = 0.001) and higher dilatation diameter (p < 0.001). Refractory strictures were significantly associated with the need for local corticoid injection (OR 9.76, 95%CI 0.035–0.46, p = 0.02) by binary logistic regression analysis. However, none of the other factors were found to be independent predictors of response to therapy.

Conclusion: Surgical aetiology was significantly associated with refractory benign oesophageal strictures and these patients were significantly more likely to require local corticosteroids during scheduled endoscopic dilations.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1488 EFFICIENCY AND SAFETY OF ENDOCUTSCOPIC PAPILLECTOMY FOR TREATMENT OF DUODENAL PAPILLA TUMORS
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Introduction: A duodenal papilla tumor is an uncommon neoplasm in the upper gastrointestinal tract. In the early stage, patients often have no complaints and the tumors are usually occasional found during gastroduodenoscopy examination. Endoscopic papillotomy can be achieved with curative resection for benign adenoma and some early papillary carcinoma. However, some complications are accompanied with the procedure, like pancreatitis and bleeding. This retrospective study is to evaluate therapeutic effect and safety of endoscopic papillotomy on duodenal papilla tumors.

Aims & Methods: From June 2009 to November 2016, the information of patients who received endoscopic papillotomy was recorded, which included basic characteristics and clinical outcomes, such as recurrence rate, bleeding, pancreatitis. Clinical outcomes (totally 40 cases) received endoscopic papillotomy. The procedure was completed with gastroscopy in 32 cases and duodenoscopy in 8 case. Endoscopic mucosal resection (EMR), endoscopic piecemeal mucosal resection (EPMR) and endoscopic submucosal dissection (ESD) was performed in 21, 17 and 2 cases respectively. None of the lesions invaded the submucosal layer.

bbling (n = 1). Surgery was performed in 10 patients (13.3%) (refractory strictures) and post dilation perforation (n = 3). Improvement of dysphagia symptoms was only associated with the maximum dilation diameter (p = 0.026) and local injection of corticoids (p < 0.001) as confirmed by binary logistic regression wherein both maximum dilation diameter (OR: 4.92, 95%CI 1.05–20.4, p = 0.027) and topical injection of corticosteroids (OR: 7.22, 95%CI: 0.021–0.55, p = 0.007) were strongly associated with improved dysphagia scores.

Conclusion: We aimed to analyse trends in endoscopic e-certification, and assess for differences between trainees in gastroenterology (GI), surgical (GS) and non-medical endoscopy experts (NME).
PANCREATIC STENTS AND BILIARY STENTS WERE INSERTED IN 9 AND 12 PATIENTS RESPECTIVELY. IN GENERAL, 5% (2/40) AND 12.5% (5/40) CASES HAD INTRAOPERATIVE AND POSTOPERATIVE BLEEDING RESPECTIVELY. 20% (8/40) CASES suffered from pancreatitis, of which mild, moderate and severe happened in 3, 4 and 1 cases. Six patients had tumor recurrence. AND 3 patients received repeat endoscopic papillotomy, two received pancreatic-codonemectomy and one received no other treatments with close follow-up. Two patients died from failures of treatment for papillary tumors and one patient died due to other unrelated cause.

**Characteristics and adverse events of endoscopic papillary in cases**

**Sex**
- Male Female: 29 8

**Age (years, mean ± SD)**
- 55.1 ± 10.0

**Endoscope type**
- Gastroscope: 32 8

**Gastroscopy Endoscopy**
- Duodenoscope: 32 8

**Resection method**
- EMR EPMR ESD: 21 17 2

**Pathological results**
- LGD, HGSD, Tis, Tim, Tsm, Non-tumor: 12, 24, 0, 2, 0, 2

**Tumor sizes (cm)**
- Longer diameter: 2.02 ± 0.88, 1.50 ± 0.69

**Biliary Stent**
- Yes, No: 12, 28

**Pancreatic stent**
- Yes, No: 9, 31

**Hospital stays (days, mean ± SD)**
- 6.7 ± 13.4

**Follow-up time (months, mean ± SD)**
- 36.6 ± 28

**Adverse events**
- Intraoperative bleeding: 5% (2)

**Postoperative bleeding**
- 12.5% (5)

**Perforation**
- 2.5% (1)

**Cholangitis**
- 0

**Pancreatitis, Mild, Moderate, Severe**
- 20% (8), 7.5% (3), 10% (4), 2.5% (1)

**Recurrence**
- 16.2% (6)

**Surgery**
- 7.9% (3)

**Mortality**
- 7.9% (3)

**Conclusion:** Endoscopic papillotomy is proved to be efficient in treating papilla tumors without submucosal invasion. However, adverse events like pancreatitis and bleeding should be taken seriously and managed properly.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**Reference**

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**P1482** CHANGES IN SCORING OF DIRECT OBSERVATION OF PROCEDURAL SKILLS (DOPS) FORMS IN ENDOSCOPY TRAINING AND THEIR IMPACT ON COMPETENCE ASSESSMENT

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**Introduction:** DOPS are validated tools for assessing competence in endoscopy. Previously, DOPS were scored on a 4-point competence-based scale, with scores of 3 and 4 signifying competence. In July 2016, the DOPS rating scale changed to a supervision-based scale that has been shown to be more reliable,1,2 with 4 ratings from maximal supervision, up to competent without supervision. We aimed to assess whether changes to the rating scale have affected distribution of scores and hence demonstrate validity.

**Aims & Methods:** We used the UK trainee endoscopy database (JETS) to collect DOPS scores for gastroscopy (n = 1934), sigmoidoscopy (n = 517), colonoscopy (n = 2296) and polypectomy (n = 370) in the 6-months before July 2016 (old DOPS) and in the 6-months after (new DOPS) for trainees at early stages of training. All trainees were included for analysis. To allow the new DOPS rating scale to be aligned to a 4-point scale, DOPS scores of 3 or 4 on old DOPS, and scores on the new and old DOPS were considered using the Mann-Whitney U-test.

**Overall, there were variations in distributions of all scores (p < 0.001) between forms (Figure 1). Compared to new DOPS, scores of 1 were underutilised on old DOPS (6.6% vs. 3.0%, p < 0.001). Frequencies of low scores (pooled scores of 1-2) were similar for gastroscopy (p = 0.33) and sigmoidoscopy (p = 0.34), but not for colonoscopy (new 11.9% vs. old 13.9%, p < 0.001) and polypectomy (new 6.8% vs. 19.9%, p < 0.001). Trainees on old DOPS were more likely to be rated as competent (score 3 or 4) compared to new DOPS (86.4% vs. 55.8%, p < 0.001). On subgroup analysis, this was evident for gastroscopy (86.3% vs. 49.1%, p < 0.001), colonoscopy (86.1% vs. 58.2%, p < 0.001), sigmoidoscopy (90.6% vs. 62.0%, p < 0.001), but not polypectomy (80.1% vs. 67.9%, p = 0.12).

**Conclusion:** Endoscopists are assessing a greater range of scores using a new DOPS rating scale based on degree of supervision, in two cohorts of trainees matched for experience. This indicates better construct validity with the new rating scale. Further work is underway to determine the reliability of the new DOPS to inform summative assessment and certification for UK endoscopy trainees.

Disclosure of Interest: All authors have declared no conflicts of interest.
References

P1485 ENDOSCOPIC CLOSURE OF ACUTE PERFORATIONS OF THE GASTROINTESTINAL TRACT IN ANIMAL MODELS: A SYSTEMATIC REVIEW AND META-ANALYSIS
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Introduction: Acute perforations are one of the recognized complications of both diagnostic and therapeutic gastrointestinal endoscopy. For decades, surgical treatment has been the standard of care, but endoscopic closure has become a more popular approach, due to feasibility and the reduction of the burden of surgery, combined with the availability of various endoscopic closure devices.

Aims & Methods: We aimed to assess the technical and clinical success and safety of endoscopic closure, in total, and for each endoscopic device used in closing acute perforations in animal models. Medical literature (Cochrane library, EMBASE, MEDLINE) from 1966 till September 2016 was searched. A systematic review and meta-analysis were performed on studies reporting technical and clinical success of endoscopic closure of acute perforations, according to PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analyses) guidelines.

Results: 46 studies on animal models were identified. 15 studies, including 4 randomized controlled trials, met our inclusion criteria (acute, less than 2 hours, iatrogenic, no fistulas or leaks, clear documentation of the method of closure, and technical and clinical success and 5 cases or more of endoscopic closure per study), were analysed. A total of 214 endoscopic closures were attempted in these studies. The overall technical success rate was 94.8% (n = 201/214, 95% CI: 92%-97.6%), clinical success was 92.3% (n = 195/214, 95% CI: 88.5%-95.8%), and complication rate was 4.2% (n = 6/214, 95% CI: 1.6%-6.8%). Technical success for endoclamp closure was 84.9% (95% CI: 71.4%-93.6%), and clinical success was 83.2% (95% CI: 69.5%-92.5%), and complication rate was 4.2% (95% CI: 1.9%-6.9%). Technical success for endoclip closure was 84.9% (95% CI: 71.4%-93.6%), and clinical success was 83.2% (95% CI: 69.5%-92.5%), and complication rate was 4.2% (95% CI: 1.9%-6.9%). Technical success for endosuturing (endoscopic suturing device) was 97% (95% CI: 98%-99.9%), clinical success was 97% (95% CI: 88%-99.7%), and complication rate was 1.7% (95% CI: 0.6%-8.3%). Technical success for endosponge was 97% (95% CI: 90%-99%), and complication rate was 1.6% (95% CI: 0.1%-2.8%). Technical success for endoclip perforation closure was 97% (95% CI: 98%-99.7%), clinical success was 94.8% (95% CI: 89.9%-99.3%), and complication rate was 1.9% (95% CI: 0.6%-7.1%).

Conclusion: Our study suggests that endoscopic closure is a suitable treatment has been the standard of care, but endoscopic closure has become a more popular approach, due to feasibility and the reduction of the burden of surgery, combined with the availability of various endoscopic closure devices.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P1487 COMPARISON BETWEEN AN ASYMMETRIC (SMALL DOSE IN THE MORNING) AND A SYMMETRIC SPLIT-DOSE REGIMEN OF POLYETHYLENE GLYCOL PLUS BISACODYL FOR BOWEL PREPARATION FOR SCREENING COLONOSCOPY: A RANDOMIZED CONTROLLED CLINICAL TRIAL
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Introduction: Bowel cleaning has a critical role to increase the quality and effectiveness of colonoscopy. International guidelines recommend the use of split-dose regimens of PEG solutions. However, the adoption of split-dose regimens in clinical practice remains sub-optimal, in particular in early morning.

Aims & Methods: We aimed to compare the efficacy of bowel preparation using an asymmetric split-dose regimen (approximately 25% of the dose is given on the day of the procedure and 75% of the dose is given on the day before) with the standard split-dose regimen in patients undergoing screening colonoscopy. We prospectively enrolled consecutive outpatients undergoing screening colonoscopy. All subjects received a split-dose preparation with a 2L PEG-citrate-simethicone plus Bisacodyl. Patients were randomly assigned to: group A, asymmetric split dose regimen (1.5 L of PEG + bisacodyl the day before and 0.5 L 3 hours before colonoscopy); group B, symmetric split dose regimen (1 L of PEG + bisacodyl the day before and 1 L 4 hours before colonoscopy). Bowel preparation was evaluated using the Boston Bowel Preparation Scale (BBPS) score. The primary endpoints were the proportion of adequate bowel cleaning (BBPS = 2) in both groups. Moreover, all patients filled in a nurse-administered questionnaire assessing compliance, tolerability and safety of bowel preparation. The threshold for statistical significance in this study was p < 0.05 and a 10% margin was used to demonstrate non-inferiority of asymmetric vs. symmetric split-dose regimen.

Results: 179 patients were enrolled (mean age 60 ± 8 years, males 56%), 88 in group A and 91 in group B. Split-dose was taken by 76/88 and by 77/91 patients in group A and B, respectively (85.2% vs 88.5%, p = 0.831). Failure of ceased preparation occurred in 2 patients for each group. In the ITT analysis, adenoma detection rate [32/76 (42.1%) vs 35/77 (45.4%); p = 0.745] and scores of each colon segment. The full amount of product and adjunctive fluids were taken by 68/76 (89.4) and 71/77 (92.2%) (p = 0.158) in group A and B, respectively. Tolerability and occurrence of adverse events were similar in the two groups.

Conclusion: An asymmetric (morning-dose) split-dose preparation with a low volume formulation with additional Bisacodyl is not inferior to the standard split-dose regimen in achieving an adequate bowel cleansing in patients undergoing screening colonoscopy. A lower amount of preparation in the morning allow to the patients to wake up later; this regimen could be thus preferred by patients undergoing colonoscopy early in the morning. Further study are needed to determine the efficacy and tolerability of the asymmetric preparation for colonoscopy scheduled in early morning.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P1488 SINGLE BALLOON OVERTUBE-GUIDED COLORECTAL ENDOSCOPIC SUBMUCOSAL DISSECTION: A NEW APPROACH TO MANAGEMENT OF COLORECTAL ENDOSCOPIC SUBMUCOSAL DISSECTION
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Introduction: Colorectal endoscopic submucosal dissection (ESD) is a technique with remarkably greater difficulty than upper gastrointestinal ESD because of unstable maneuvers and inherited anatomic variability in the colon. Thus, aiming at reducing these restrictions, we have used single balloon (SB) overtube to assist colorectal ESD in cases considered to have difficult operability. In this study, we evaluate the usefulness of a single balloon overtube to assist colorectal ESD.
Aims & Methods: The study included 35 patients with 39 colorectal lesions who underwent ESD (group SB) or endoscopy nurse alone in (1) 5.5% and a second physician in (1) 5.5% of the institutions, with either nurse anaesthesiologist or an anaesthesiologist in (5) 27.8%, a designated anaesthesiologist was in charge of sedation in (7) 38.9% of the institutions. General anaesthesia was used in (4) 22.2%, while conscious sedation was used in (3) 16.7%. In (3) 16.7% of institutions deep sedation, conscious sedation or general anaesthesia was used according to the cases and clinician decision. A third physician was independently for eligibility by two reviewers (S.B. and M.S.). Any Disagreements were resolved by consulting a third reviewer (A.P.).

Disclosure of Interest: All authors have declared no conflicts of interest.

Disclosure of Interest: 18 eligible original articles, of which (5/18) 27.8% agreed for eligibility by two reviewers (S.B. and M.S.). Any Disagreements were resolved by consulting a third reviewer (A.P.). All articles were examined independently for eligibility by two reviewers (S.B. and M.S.). Any Disagreements were resolved by consulting a third reviewer (A.P.).

Results: This review resulted in 18 eligible original articles, of which (5/18) 27.8% agreed for eligibility by two reviewers (S.B. and M.S.). Any Disagreements were resolved by consulting a third reviewer (A.P.). All articles were examined independently for eligibility by two reviewers (S.B. and M.S.). Any Disagreements were resolved by consulting a third reviewer (A.P.).

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1. The Munich Polypectomy Study (MUPS): Prospective randomised controlled trial of overtubing for polyps of >10 mm, 5-10 mm and <5 mm respectively.


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100. Neil Hawkes, F. Kokwara, B. Davies, J. Cornish
domains—Communication (COMM), Situational Awareness (SITA), Leadership (LEAD), and Teamwork and Decision-making (T&DM). Each MARS domains was represented by 10 items and is assessed on a 7-point scoring scale - endoscopists should score > 90 in each domain (80-90 = need for improvement, < 80 = suboptimal performance). CIR and PDR measures are routinely calculated for all endoscopists using the HICCS Electronic Reporting System with manual validation of this data. Feedback is presented on a quarterly basis to practitioners—endoscopists are expected to achieve 90% CIR and 20% PDR. Correlation of these factors with practitioners ENTS scores were measured using the Pearson test.

**Results:** 9 endoscopists with known variability in standard colonoscopy KPIs consented to an assessment of ENTS using the MARS tool. Their ENTS scores were correlated with existing KPIs for each colonoscopy (Oct 2016-May 2017). A positive correlation was found between ENTS domains and CIR (COMM 0.58, SITA 0.66, LEAD 0.66; JDM 0.75) and PDR (COMM 0.49; SITA 0.55; LEAD 0.50; JDM 0.60). Three endoscopists were identified as having sub-optimal scores in all of the ENTS domains (operators 5, 7, 9). Taking into account important KPI thresholds 2 out of 3 (33%) of these endoscopists identified were not meeting CIR targets (c.f. 66% of ENTS competent group) and one (33%) did not meet PDR targets (c.f. 0% in ENTS competent group).

Colonoscopy as a screening tool is a practical way to measure of ENTS performance designed as a 360 degree feedback and identifies areas for development within independently practitioners that are not currently highlighted by standard colonoscopy KPI measures. There is some correlation with current KPI feedback panels but using a specific validated ENTS assessment tool augments current assessment panels. Both CIR and PDR primarily depend on the colonoscopists' individual skills rather than the team elements required for polypectomy or EMR and these more complex tasks may show stronger correlation with MARS ENTS evaluation.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

P1492 EARLY ECONOMIC MODELLING OF EMI-137 TO IMPROVE THE DETECTION RATE OF POLYPS IN PATIENTS IN THE UK NATIONAL BOWEL CANCER SCREENING PROGRAMME

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**Introduction and Rationale:**

Colorectal cancer (CRC) is the third most common cancer diagnosed in men and second most common cancer in women, affecting 1,361,000 people worldwide each year. CRC is a slow growing tumour that most commonly develops from polyps which form in the inner lining of the colon or rectum. The identification and removal of polyps whilst still in a pre-cancerous state has been shown to be effective in reducing mortality from CRC. Current clinical practice relies on white light (WL) colonoscopy for detecting colorectal polyps, but this is associated with a detection "miss-rate" of up to 26% for small (<10 mm) polyps and 2% for large polyps (van Rijn et al., 2006). Missed lesions (false negative results) puts patients at an unnecessary risk of late stage detection, when management has higher costs and worse clinical outcomes. Recent technological developments have resulted in more accurate technologies for polyp detection and this will be used to inform the design of future clinical studies. EMI-137 has the potential to be cost-effective for patients participating in the UK National Bowel Cancer Screening Programme. The value of information analyses have highlighted the key parameters for which further evidence is required, and this will be used to inform the design of future clinical studies.

**Disclosure of Interest:** A. Davies: I am the CMO at Edinburgh Molecular Imaging. I. Wilson: I am the CEO at Edinburgh Molecular Imaging. All other authors have declared no conflicts of interest.

Reference

The use of a visual educational booklet for the preparation of colonoscopy. An optimized preparation should be considered for colonoscopies does not provide a significant improvement in hospitalized patients in the impact of patient education on the quality of inpatient bowel preparation for colonoscopy. Booklet Increases the Quality of colonoscopy Bowel Preparation.

References

All authors have declared no conflicts of interest.

Aims & Methods: We identified all DOPS submitted between July 2016 and Feb 2017 from the UK endoscopy trainee database (JETS) and acquired data on trainees, procedures and scores. We collated scores for each of the 4 assessable domains (pro-procedural, procedural, post-procedural and ENTS) into overall ENTS competency (defined as all items scoring competent) varied across procedures (p < 0.001): ERCP 39.8%, EUS 44.1%, gastroscopy 59.6%, colonoscopy 62.3%, Polypectomy 71.1%, gastrointestinal bleed (71.5%), sigmoidoscopy 72.4% and polypectomy 73.2%. Scores by individual ENTS components are displayed in Table 1. Of DOPS awarded overall competency, 5.9% (240/4077) lacked full competence in ENTS (p < 0.10 across modalities). Across trainee specialties and endoscopic modalities, competence was greatest for ‘communication and teamwork’ (77.1% overall), but least with ‘judgement and decision making’ (68.3%). Statistical analysis was performed using chi2 and regression modelling.

Results: 3601 DOPS were prospectively collected, with ENTS assessed in 99.3%. Competency rates of individual ENTS items are summarised in Table 1. Rates of overall ENTS competency (defined as all items scoring competent) varied across procedures (p < 0.001): ERCP 39.8%, EUS 44.1%, gastroscopy 59.6%, colonoscopy 62.3%, Polypectomy 71.1%, gastrointestinal bleed (71.5%), sigmoidoscopy 72.4% and polypectomy 73.2%. Scores by individual ENTS components are displayed in Table 1. Of DOPS awarded overall competency, 5.9% (240/4077) lacked full competence in ENTS (p < 0.10 across modalities). Across trainee specialties and endoscopic modalities, competence was greatest for ‘communication and teamwork’ (77.1% overall), but least with ‘judgement and decision making’ (68.3%). Statistical analysis was performed using chi2 and regression modelling.

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Conclusion: The use of a visual educational booklet for the preparation of colonoscopies does not provide a significant improvement in hospitalized patients in the impact of patient education on the quality of inpatient bowel preparation for colonoscopy. Booklet Increases the Quality of colonoscopy Bowel Preparation. Clinical Gastroenterology and Hepatology 2016;14:858-864.

PI1494 STUDY OF ULCERATIVE COLITIS COMPLICATED BY PRIMARY SCLEROSING CHOLANGITIS

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Introduction: Primary sclerosing cholangitis (PSC) is often associated with autoimmune diseases, and approximately 70% of PSC patients in Europe/United States and 32% in Japan also have ulcerative colitis (UC). The complication of PSC is confirmed in about 5% of UC patients, the clinical features of UC associated with PSC differ from those of UC without PSC.

Aims & Methods: We investigated the clinical and colonoscopic features of colitis associated with PSC. We retrospectively examined the clinical features, including the clinical course and colonoscopic findings, of 25 colitis patients with PSC attending our hospital between 2000 and 2017.

Results: The male-female ratio was 12:13 and the age at diagnosis of PSC was 49 ± 15 years. PSC was the initial diagnosis in 12 patients (48%), while colitis was the first to be diagnosed in 4 patients (16%), and both diseases were found concurrently in 9 patients (36%). Among the 21 patients with the diagnosis of PSC, 7 patients (33%) had the symptoms of PSC and the latter was recognized by screening. There were 12 patients with UC (52%) and 11 patients with nonspecific colitis (48%). Among the 24 patients in whom the disease extent was assessed, 22 had pancolitis, 1 had left-sided colitis, and 1 had proctitis. Inflammation predominantly affected the right colon in 20/22 patients with pancolitis and also involved the terminal ileum in 9 patients (45%). The Mayo score for colonoscopic evaluation of UC was 1 in 16 patients (64%), 2 in 8 patients (32%), and 3 in 1 patient (4%). There were no rectal lesions in 10 patients (40%). Liver biopsy was performed in 17 patients, and Ludwig’s stage was Stage I in 1 patient (6%), Stage II in 12 patients (71%), Stage III in 3 patients (18%), Stage IV in 1 patient (6%). Ludwig’s stage did not correlate with the Mayo score. All patients with PSC and enterocolitis received oral ursodeoxycholic acid (UDCA), including 13 patients with UDCA only (52%), 2 patients with combination of salazosulfapyridine (SASP) (8%) in combination with 5-aminosalicylic acid (5-ASA) (20%), 2 patients in combination with prednisolone (PSL) (8%), 1 patient with the combination of SASP + PSL (4%), and 2 patients with 5-ASA + PSL (8%). The UDCA dose was 400 mg in 2 patients (8%), 600 mg in 15 patients (60%), and 900 mg in 9 (32%).

Conclusion: In colitis patients with PSC, there was no clear association between colonoscopic disease activity and the severity of PSC. There was no sex difference and the age at diagnosis of PSC showed a bimodal distribution (30s and 60s). Prednisolone was very frequent and predominantly affected the right colon, but disease activity was low. Rectal lesions were mild or absent. About half of the patients had inflammation of the terminal ileum.

Disclosure of Interest: All authors have declared no conflicts of interest.

Table 1: Unadjusted ENTS scores by endoscopic modality.
Introduction: The development of Endoscopic Non-Technical Skills (ENTS) is associated with improved performance and high quality endoscopic outcomes. Whilst ENTS domains have been incorporated into Joint Advisory Group (JAG) Direct Observation of Procedural Skills (DOPS) forms, used as training tools, knowledge of ENTS domains amongst independent practitioners varies. To improve performance in this area of practice requires validated measurement tools and specific feedback against which improvement can be measured. We have previously developed a validated 360-degree multi-assessor rating scale (MARS tool) based on experienced endoscopy assistant ratings for ENTS providing data on 4 main domains of ENTS—each comprising 10 related but independent practice points. Providing an optimised feedback format for this data is likely to maximise the potential benefits of measuring ENTS performance.

Aims & Methods: We aimed to provide an optimised format for performance enhancing feedback in the ENTS domains and basis for specific auditable outcomes and performance indicators. Local colonoscopists gave consent to application of the ENTS questionnaire. The validated MARS tool assesses 4 ENTS domains—Communication (COMM), Situational Awareness (SITA), Leadership (LEAD) and Judgement & Decision-making (J&DM). Each MARS domain in the administered questionnaire was represented by 10 items and is assessed on a 7-point scoring scale. We sought to develop 1) a format to illustrate an individual’s overall performance in each of the 4 main ENTS domains in comparison to other operators and 2) a detailed domain breakdown highlighting areas of underperformance 3) Collate feedback on the presentation formats.

Results: 9 endoscopists consented to an assessment of ENTS using the MARS tool. The MARS questionnaires were administered during January 2017–relating to the prior 3 months clinical practice. Acceptable performance thresholds were set as >90% good-excellent ratings in each domain. Need for improvement was defined as 80–90% good-excellent ratings (i.e. 10–20% average or poor ratings) and sub-optimal performance as 80% or less good-excellent ratings (i.e. >20% average-poor ratings). Good intra- and inter-rater reliability was demonstrated defined as 80–90% good-excellent ratings (i.e. 10–20% average or poor ratings).

Conclusion: Failed prior attempts at resection or heavy manipulation of lesions reduces the chance of achieving en bloc resection and increases the risk of complications and recurrence. Nevertheless, specialist management in a dedicated setting improves results in safe and successful organ preserving endoscopic treatment of these extremely challenging lesions in over 95% of cases with few significant complications.

Disclosure of Interest: All authors have declared no conflicts of interest.
and O2 have relatively dark xenon light sources and maximum optical magnifi-
cation at 110 times, respectively. Therefore, the differences in visualization of mucosal blood flow in the small and large bowel among the groups were considered to be attributable to differences in instrument efficiency.

**Conclusion:** Our results show that magnifying observation with BILI is superior to that with endo-illumination. However, the more invasive tumor is, the more presence of submucosal fibrosis, the percentage of adenoma, intramucosal cancer, SM-1(>30 mm), and SM-2(>100 mm) cancer with fibrosis were 32.31%, 66.67%, 87.5%, and 90% (P < 0.00). Additionally, the fibrosis rate for tumors ≤3 cm and >3 cm were 44.12% and 58.97% (P < 0.002). When biopsies were performed two or more times on a same lesion, it showed significant difference comparing to patients who only underwent biopsy just once. (OR 4.98, 1.20–20.51, 95% CI, P = 0.026)

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**References**


**P5101 ADVANCED NEOPLASIA YIELD IN NEOPHILATES UNDERGOING COLONSCOPY AFTER SCREENING FLEXIBLE SIGMOIDOSCOPY: DOES THE DISTAL COLON PATHOLOGY PREDICTS THE YIELD IN PROXIMAL COLON?**


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**Introduction:** Current patients undergoing a screening flexible sigmoidoscopy (Bowel Scope examination) at the age of 35 are referred for colonoscopy if the following polyp criteria are met: polyp >1 cm, villous histology, high grade dysplasia, 3 or more adenomas or ≥20 hyperplastic polyps (HP).

**Aims & Methods:** Objective is to assess the proportion of patients who had an advanced adenoma (size >1 cm, villous or high grade dysplasia on histology) in the proximal colon when referred for a colonoscopy after a screening flexible sigmoidoscopy. A retrospective cross-sectional study of patients who underwent Bowel Scope screening between July 2013 - July 2016 at St Mark’s Bowel Cancer Screening (BCS) Centre was performed. Epidemiological, procedural and polyp data were retrieved from the on endoscopy and Bowel Cancer Screening database.

**Results:** 960 patients had a screening flexible sigmoidoscopy in the time period. Descending colon was reached in 82% of patients. Advanced adenomas were detected in 351 (35.2%) patients. 520 (52.5%) patients had a colonoscopy following screening flexible sigmoidoscopy as per the BCS protocol. Median age was 55 years (male: female ratio 2:1). Caecal intubation was achieved in 98% (510/520) of cases. At least one adenoma or a sessile serrated adenoma/polyp (SSA/P) was detected, proximal to the extent of flexible sigmoidoscopy examination, in 45% (236/520) of patients (Table 1). The incidence of advanced adenoma in the distal colon was an indication for colonoscopy in 351/520 patients (68%). Of these, 52 (14.8%) had a synchronous proximal colonic advanced adenoma and 20 (5.7%) had a synchronous SSA/P. Only 5 (1.4%) patients had an advanced lesion. A pattern of only SSA/P in the proximal colon. Presence of distal advanced adenoma was associated with proximal advanced adenoma (p = 0.0006). However, there was no association between presence of distal advanced adenoma and proximal SSA/P (P = 0.47) or advanced SSA/P (P = 0.4).

**Table 1:** Proximal colorectal pathology during colonoscopy (continued)
**Table 1 Continued**

<table>
<thead>
<tr>
<th>Indication</th>
<th>Number of patients</th>
<th>Proximal advanced adenoma</th>
<th>Proximal SSA/P</th>
<th>Proximal advanced SSA/P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adenoma &gt; 1 cm</td>
<td>153</td>
<td>14.4%</td>
<td>8.5%</td>
<td>2.6%</td>
</tr>
<tr>
<td>Villous features</td>
<td>189</td>
<td>14.3%</td>
<td>3.2%</td>
<td>0.5%</td>
</tr>
<tr>
<td>High-grade dysplasia</td>
<td>36.4%</td>
<td>8.3%</td>
<td>0.9%</td>
<td></td>
</tr>
<tr>
<td>Others (&gt;1 cm non adenomatous polyp, &gt; 20 hyperplastic polyps, &gt; 3 adenomas)</td>
<td>169</td>
<td>5.3%</td>
<td>5.8%</td>
<td>1.6%</td>
</tr>
</tbody>
</table>

**Conclusion:** Distal colonic advanced adenomas are a marker of synchronous proximal colonic adenomas and sessile serrated polyps. When colonoscopies were performed for other indications (non-adenomatous polyp > 1 cm, multiple distal HP polyps) the yield in the proximal colon was significantly smaller. These “soft” indications for colonscopy accounted for a significant additional workload that appears unjustified.

**Disclosure of Interest:** B.P. Saunders: Advisory board member of Olympus UK All other authors have declared no conflicts of interest.

**P1502 LEARNING CURVE FOR OPTICAL DIAGNOSIS OF COLORECTAL POLYPS USING CUMULATIVE SUM ANALYSIS**

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**Introduction:** Optical diagnosis for diminutive and small colorectal polyps is an attractive option to reduce costs and streamline patient care. The American Society of Gastrointestinal Endoscopy Preservation and Incorporation of Valuable Endoscopic Innovations (PIVI) established a 90% diagnostic threshold for real time endoscopic assessment of the histology of diminutive colorectal polyps. For adoption of optical diagnosis in clinical practice, colonoscopists must be trained and show on-going competence. The learning curve for trainees to achieve the competency has not been fully explored.

**Aims & Methods:** Aim is to evaluate the minimum number of polyps to achieve and maintain the optical diagnostic thresholds per PIVI standards using an upward CUSUM plot. Four trainees without previous experience in optical diagnosis at our institution participated in this prospective study.

**Results:** A total of 708 polyp observations were performed by trainees during the study period. Total number of adenomas, hyperplastic polyps and sessile serrated adenomas/polyps (SSA/P) were 364, 214 and 52 respectively. Trainees OD performance was plotted on a upward CUSUM plot. Four trainees without previous experience in optical diagnosis were carried out, including a consecutive cohort of 56 patients who underwent EFTR for colorectal SMTs originating from the MP layer. A prospective study was carried out, including a consecutive cohort of 56 patients who underwent EFTR for colorectal SMTs originating from the MP layer between January 2008 and September 2014 in our center. Among these, 21 lesions were located in the colon, 9 located in the intraperitoneal rectum and 26 located in the extraperitoneal rectum. The tight adhesion of the lesion to the serosal layer was identified before EFTR in all cases. EFTR was performed using a standard ESD technique under direct endoscopic view. The defect of colorectal wall was closed after resection in all cases. Complete resection rate, complications and lesion recurrence were evaluated.

**Results:** Successful EFTR was performed in 54 (96.4%) patients. The other 2 patients were transferred to suffer laparoscopic right hemicolectomy and EFTR combining laparoscopic operation respectively, because the lesions involved the external organs and were too difficult to get en bloc resection endoscopically. The endoscopic resection rate and complete resection rate were both 96.4% (54/56). Among 54 cases, 52 of these lesions were performed with EFTR without laparoscopic assistance, while 2 needed laparoscopic assistance to get the defect closed after resection. The median operation time was 45 min (range, 20–130 min). The median maximum diameter of resected tumors was 1.5 cm (range, 0.5–5.0 cm). Accurate histopathologic results were acquired from all the resected lesions, including 18 leiomyomas, 11 gastrointestinal stromal tumors (GISTs), 8 fibrous tumors, 5 schwannomas, 11 granulomas, 2 displaced endometrium, and 1 hamartoma. Three patients had local peritumors and two patients developed postoperative bleeding. All of them recovered after receiving conservative treatments. No single case developed diffuse peritumors. No lesion residual or recurrence was found during the follow-up period ranging 2–54 months.

**Conclusion:** EFTR appears to be a safe, feasible, and effective procedure for providing accurate histopathologic evaluations, as well as a curative treatment for colorectal SMTs originating from the MP layer. However, it should be performed by the very experienced endoscopists.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**P1503 THE CLINICAL VALUE OF ENDOSCOPIC FULL-THICKNESS RESECTION FOR COLORECTAL SUBMUCOSAL TUMORS ORIGINATING FROM THE MUSCULARIS PROPRIA: A PROSPECTIVE SINGLE-CENTER STUDY**

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**Introduction:** Given diminishing quality of life caused by colectomy and resection, a minimally invasive treatment is desirable for colorectal submucosal tumors (SMTs).

**Aims & Methods:** The aim of the current study was to evaluate the clinical efficacy, safety and feasibility of endoscopic full-thickness resection (EFTR) for colorectal SMTs originating from the MP layer. A prospective study was carried out, including a consecutive cohort of 56 patients who underwent EFTR for colorectal SMTs originating from the MP layer between January 2008 and September 2014 in our center. Among these, 21 lesions were located in the colon, 9 located in the intraperitoneal rectum and 26 located in the extraperitoneal rectum. The tight adhesion of the lesion to the serosal layer was identified before EFTR in all cases. EFTR was performed using a standard ESD technique under direct endoscopic view. The defect of colorectal wall was closed after resection in all cases. Complete resection rate, complications and lesion recurrence were evaluated.

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**Disclosure of Interest:** All authors have declared no conflicts of interest.

**P1504 COLONIC ESD BY UTILIZING SHORT DOUBLE BALLOON ENDOSCOPE—HOW TO TREAT DIFFICULT CASES IN COLONIC ESD**

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**Introduction:** Colon ESD has been becoming a standard treatment in the world. However, sometimes it is hard to remove the colon tumor during ESD. When we found it is difficult to detach the colorectal neoplasm in ESD, we should consider the following three points: if we don’t have enough experience and skill, we should take the training more. If there are lots of vessels and fibrosis in the submucosal layer, it is necessary to choose adequate tools. And if patients have complicated colon, suitable endoscope need to be selected. In such cases we always use DBE.

**Aims & Methods:** We evaluated the outcomes of colonic ESD by using DBE (DBE-ESD). Short DBE we used were EC450B1, EN530BI and ES60BT (Fujifilm Co., Tokyo, Japan). We've performed DBE-ESD on 211 lesions in 184 patients. We analyzed the lesions located in the proximal colon, and the following items were examined: arrival time, procedure time, rate of negative margin, perforation rate, length of hospital stay and recurrence rate in the 5th-year after the ESD.

**Results:** There were 159 lesions located in the proximal colons. The median arrival time to the lesion was 7.9 min, operation time 51.1 min, negative rate of horizontal margin 99.4%, vertical margin 99.4%, perforation rate 0%, median length of hospital stay 3.1 days, and recurrence rate in patients with more than 5 year follow-up 0%.

**Conclusion:** Because the balloons and the overtube retained the scope at stable position, we were able to get good working space. Therefore, DBE should be one option for difficult cases in ESD.

**Disclosure of Interest:** All authors have declared no conflicts of interest.
P1505 WITHDRAWAL TIME MONITORING AND FULL-SPECTRUM ENDOSCOPY IMPROVE ADENOMA DETECTION RATE

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Introduction: Adenoma detection rate (ADR) is a quality indicator of screening colonoscopy. Monitoring withdrawal time (WT) and use of full-spectrum endoscopy (FUSE) have been suggested to increase the ADR since allow an accurate evaluation of the hidden areas of the colon.

Aims & Methods: We aimed to evaluate whether monitoring of WT alone or in combination with the use of FUSE would be able to increase the ADR. In a prospective non-randomized observational study, consecutive outpatients, aged 18-85 yr, undergoing colonoscopy with different indications were enrolled. In phase 1, endoscopists performed 660 colonoscopies either with standard forward-viewing endoscope (SFVE) (n = 330) or with FUSE (n = 330) without a dedicated WT protocol. In this phase, colonoscopy WT were measured without the endoscopists' knowledge of being monitored. In phase 2, endoscopists were informed of being monitored and performed further 660 colonoscopies either with SFVE (n = 330) or with FUSE (n = 330).

Results: No differences were observed among the four arms in terms of demographic, clinical features, and dedications to colonic WT. Colonoscopy WT was lower in phase 1 arms compared to phase 2 arms (SFVE: 267 ± 96 vs. 387 ± 65, p = 0.001; FUSE: 293 ± 112 vs. 430 ± 93, p = 0.001). When endoscopists were aware of being monitored and used full-spectrum endoscope we observed a higher ADR [phase 1 SFVE: 27.3% (90) phase 1 FUSE: 33.0% (109) phase 2 SFVE: 33.6% (111) phase 2 FUSE: 41.8% (138); p = 0.001] and adenoma per colonoscopy (APC) [phase 1 SFVE 0.43 ± 0.85 phase 1 FUSE 0.58 ± 1.08 phase 2 SFVE 0.64 ± 1.24 phase 2 FUSE 0.71 ± 1.08; p = 0.004]. The detection rate of adenoma located proximally to the splenic flexure was higher in phase 2 arms (phase 1 SFVE 11.2% vs. phase SFVE 16.4%; p = 0.056; phase 1 FUSE 12.7% vs. phase 2 FUSE 18.9%; p = 0.033), whereas adenoma located distally to the splenic flexure was higher in the FUSE arms compared to SFVE arms, but these differences were not significant (Phase 1 SFVE 20.0% vs. Phase 1 FUSE 24.8%, p = 0.081; Phase 2 SFVE 21.8% vs. Phase 2 FUSE 27.0%, p = 0.147).

Conclusion: Unmonitored endoscopists have a sub-optimal WT, which increases when they are aware of being monitored and used full-spectrum endoscope combined with WT monitoring results in increase of adenoma detection rate. In particular, monitoring WT increases the detection of adenoma in proximal colon, whereas the use of FUSE seems to increase the detection of adenomas in distal colon.

Disclosure of Interest: All authors have declared no conflicts of interest.

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P1506 HIGH LEVELS OF ‘PRESUMED POLYP MISS RATE’ AT 1 AND 3 YEARS FOLLOWING INDEX SCREENING COLONOSCOPY: NO ROOM FOR IMPROVEMENT

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Introduction: Polypectomy with polypectomy is considered the optimal method of bowel cancer prevention. Despite improvements in colonoscopy training and technology, it remains as an imperfect tool and the adenoma miss rates vary when they are aware to be monitored. Use of full spectrum scopes combined with WT technology, it remains as an imperfect tool and the adenoma miss rates vary.

Aims & Methods: Data from 25,407 patients undergoing healthy check up assessing periodontal disease according to periodontosis-risk classes (PRC 0-healthy gingiva, PRC 1 - tarter or plaque, PRC 2 - redness or swelling) and screening colonoscopy between 2009 and 2012 in Austria were included. Colonoscopy outcomes were compared between patients with and without signs of periodontal disease using multivariate models adjusting for age, sex, smoking, alcohol consumption, diabetes and BMI.

Results: In multivariate adjusted models, patients with periodontal disease had similar odds for the detection of colorectal polyps as those without signs of periodontal disease [adjOR 1.070; 95% CI: 0.918; 1.247]. Regarding the prevalence of adenomas, patients with periodontal disease, likewise, had similar odds as those with healthy periodontal tissue [adjOR 1.010; 95% CI: 0.840; 1.213]. Similarly, those with periodontal disease had comparable odds for colorectal adenomas as those without signs of periodontal disease [1.055 (0.785; 1.418)].

Disclosure of Interest: All authors have declared no conflicts of interest.

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P1507 IMPACT OF PERIODONTAL DISEASE ON PREVALENCE OF COLORECTAL NEOPLASIA IN PATIENTS UNDERGOING ROUTINE SCREENING COLONOSCOPY

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Introduction: Systemic diseases including several types of cancer have been associated with periodontitis, potentially owing to the constant systemic inflammatory state in those patients. Data on a potential association of periodontal disease and colorectal neoplasia is scarce and conflicting.

Aims & Methods: All authors have declared no conflicts of interest.

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Disclosure of Interest: All authors have declared no conflicts of interest.

Table 1: Missed polyps at different colonic segments

<table>
<thead>
<tr>
<th>Location</th>
<th>Adenoma miss rate (%)</th>
<th>Sessile serrated adenoma miss rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rectum</td>
<td>9</td>
<td>33</td>
</tr>
<tr>
<td>Rectosigmoidium</td>
<td>19</td>
<td>0</td>
</tr>
<tr>
<td>Sigmoid colon</td>
<td>23</td>
<td>50</td>
</tr>
<tr>
<td>Descending colon</td>
<td>10</td>
<td>0</td>
</tr>
<tr>
<td>Splenic flexure</td>
<td>26</td>
<td>0</td>
</tr>
<tr>
<td>Transverse colon</td>
<td>27</td>
<td>30</td>
</tr>
<tr>
<td>Hépatic flexure</td>
<td>30</td>
<td>57</td>
</tr>
<tr>
<td>Ascending colon</td>
<td>26</td>
<td>50</td>
</tr>
<tr>
<td>Caecum</td>
<td>26</td>
<td>0</td>
</tr>
</tbody>
</table>

Conclusion: Our study highlights that there is likely to be a significant miss rate for adenomas and SSA/Ps even after careful index colonoscopy. Miss rate was higher when multiple polyps are seen at the index examination. This finding appears to justify the current BSG (British Society of Gastroenterology) guidelines for an early, 1 year colonoscopy when multiple polyps are seen. The presumed polyp miss rate at 1 & 3 years may be justified as a new quality metric within screening programmes.

Disclosure of Interest: B.P. Saunders: Advisory board member of Olympus UK All other authors have declared no conflicts of interest.

Contact E-mail Address: angelika.dokladanska@meduniwien.ac.at

Introduction: Systemic diseases including several types of cancer have been associated with periodontitis, potentially owing to the constant systemic inflammatory state in those patients. Data on a potential association of periodontal disease and colorectal neoplasia is scarce and conflicting.

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In the table below the adenoma detection rate (ADR) and advanced adenoma detection rate (AADR) divided into the periodontosis-risk classes.

Table 1: ADR (adenoma detection rate) and AADR (advanced adenoma detection rate) according to the periodontosis-risk classes

<table>
<thead>
<tr>
<th>PRC 0</th>
<th>PRC 1</th>
<th>PRC 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adenoma (ADR)</td>
<td>19.34%</td>
<td>19.56%</td>
</tr>
<tr>
<td>Advanced adenoma (AADR)</td>
<td>5.42%</td>
<td>6.1%</td>
</tr>
</tbody>
</table>

Conclusion: Periodontal disease has no impact on the adenoma and advanced adenoma detection rates in a large screening colonoscopy cohort.

Disclosure of Interest: All authors have declared no conflicts of interest.
NON-POLYPOID LESIONS IN INFLAMMATORY BOWEL DISEASE: The King’s Institute of Therapeutic Endoscopy (KITE) is a tertiary centre for endoscopic assessment and resection of large challenging colorectal polyps. Here we present the largest single-centre case series of large non-polypoid resections associated with colitis.

Aims & Methods: Adults with confirmed colitis (ulcerative colitis extending beyond the rectosigmoid junction and crohn’s colitis affecting at least the left colon) with lesions at least 20 mm in size within the colitis segment were included. Data including demographics, clinical history, lesion characteristics, method of resection and post-resection surveillance were collected prospectively in patients from January 2011 to November 2016. Resection techniques included endoscopic mucosal resection (EMR), endoscopic submucosal dissection (ESD) and hybrid ESD. Surveillance of resection site with magnification chromoendoscopy (mCE) was performed at 3 months with pan colonic mCE at 1-year post resection and annually thereafter.

Results: Thirty-lesions satisfied the inclusion criteria in 13 patients. Patient demographics and clinical data are provided in table 1. Mean lesion size was 47.3 +/- 22.4 (20-90) mm. All lesions were non-polypoid with distinct margins and no ulceration. High-frequency mini-probe ultrasound confirmed intramural lesions in 5 cases where pit/vascular pattern was distorted due to inflammation. En bloc resection was achieved in 6 cases. 69% lesions were deeply scarred of which 66% had experienced prior instrumentation. Resection of a single lesion was segmentally extended due to intense fibrosis. Macroscopic evidence of complete resection was confirmed histopathologically in 6/6 of resected lesions. Complete excision was confirmed in all en bloc resections. A single case of small perforation and another with delayed minor bleeding were both managed endoscopically. Mortality/hospital admission within 30 days post resection was 0%. Median follow up was 28 months (12-35) with no recurrence. Alternative site dysplasia was detected in 2 patients. All lesions were sub 20 mm and resected endoscopically. Two patients were referred for colectomy due to a concomitant diagnosis of neuroendocrine tumour and the second with alternate site advanced dysplasia.

Table 1: Baseline characteristics.

<table>
<thead>
<tr>
<th>Patient Demographics</th>
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| Age at time of resection (mean, SD, range) (years) | 57.31 +/- 12.7, 30-81  
| Male (n) (%) | 10 (77)  
| Female (n) (%) | 3 (23)  
| Clinical Data |  
| Duration of disease (mean, SD, range) (years) | 19.9, 14.2, 1 - 50  
| Disease extent |  
| Splenic Flexure (n) (%) | 3 (23)  
| Pan-colonic/Extensive (n) (%) | 10 (77)  
| Primary Serosing Cholangitis | 1 (7)  
| IBD Medication |  
| 5-ASA* (n) (%) | 11 (84)  
| Azathioprine (n) (%) | 2 (15)  
| Biologics (n) (%) |  
| ASA Physical Status Classification |  

(continued)

Table 1 Continued

<table>
<thead>
<tr>
<th>Patient Demographics</th>
</tr>
</thead>
</table>
| ASA grade II (n) (%) | 7 (54)  
| ASA grade III (n) (%) | 4 (31)  
| ASA grade IV (n) (%) | 2 (15)  

Conclusion: This cohort series demonstrates that endoscopic resection of large non-polypoid lesions in association with colitis is feasible using an array of resection methods, safe and has good long term outcomes in a western tertiary endoscopic centre.

Disclosure of Interest: All authors have declared no conflicts of interest.

References


P1509 RESEARCH ON APPLICATION OF TRANSDURAL TUBE DECOMPRESSION FOR PREVENTION OF COMPLICATIONS IN COLORECTAL MUCOSAL LESIONS AFTER ESD

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Introduction: Endoscopic submucosal dissection (ESD) has been widely used in the miniminally invasive treatment of early colorectal mucosa and submucosal lesions. This technique has made it possible to resect even large mucosal or submucosal lesions en bloc, and the recurrence rate is lower. However, due to the thinner colorectal wall and more abundant blood vessels, postoperative complications after ESD is higher in this site. As a result, how to prevent complications related to ESD for colorectal lesions has raised widespread concern. In recent years, more and more researchers placed transanal tube for patients with colorectal cancer resection or intestinal obstruction to promote the early discharge of the gas and liquid in the intestine. The efficacy of this method to reduce incidence of complications and to promote recovery of intestinal function have been verified by a number of studies. Based on this, we applied transanal tube to some patients with colorectal ESD, hoping to provide new ideas for the prevention and treatment of complications.

Aims & Methods: We aimed to evaluate transanal tube for prevention of complications in colorectal mucosal lesions after endoscopic submucosal dissection (ESD). Data of 61 patients with colorectal mucosal lesions undergoing ESD from January to December 2016 were reviewed. All patients were followed up and we analyzed the incidence rate of complications after ESD within one month.

Results: The median age of 61 patients was 61(32 - 83) years. 21 of all lesions were located at right-half colon, 9 at left-half colon and 31 at rectum. The mean diameter of the lesions was 3.26 ± 2.27 (0.8-12) cm. There were not intraoperative complications including serious bleeding and perforation. Delayed bleeding on the eighth post-ESD day was detected in 1 (1.6%) patient who was cured by transfusion. 3(4.9%) patients suffered post-ESD electrocoagulation syndrome and perforation did not present in all cases. In this group with transanal tube for decompression, the rates of perforation, delayed bleeding and post-ESD electrocoagulation syndrome were all lower than others which was 1.4% ~ 8.5%, 0.5% ~ 9.5% and 12.1% ~ 40.2% respectively in literature reports.

Conclusion: The application of transanal tube in colorectal mucosal lesions after ESD could effectively reduce the incidences of complications. However, we should do more research to know whether transanal tube need to be placed routinely after ESD or not.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P1510 OUTCOMES FOLLOWING UNDERWATER ENDOCOPIC MUCOSAL RESECTION OF > 10MM COLONIC POLYPS: A PROSPECTIVE DUAL-CENTRE STUDY
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Introduction: Underwater endoscopic mucosal resection (UEMR) is an alternative to traditional EMR for the resection of colonic polyps. With this technique, water insufflation is used in place of air or CO2, and submucosal lifting is usually not required, as water-immersed submucosa cushions itself from the muscularis propria.2,3 Theoretically, this reduces the risk of diathermy-induced injury,4 and allows for more complete resection margins.3,4

Aims & Methods: In this prospective dual-centre study, we aim to evaluate the safety and efficacy of UEMR for clinically significant (> 10 mm) colonic polyps. Studies of outcomes included: 1) completeness of UEMR, 2) intraprocedural and 30-day complication rates, 3) percentage requiring submucosal lift, and 4) rates and predictors of polyp recurrence. Procedures were performed by two screening endoscopists accepting tertiary referrals at St. Mark’s Hospital, London, and Russell’s Hall Hospital, Dudley, UK. Recurrence was defined as the presence of any polyp tissue at the resection site. Endoscopy records were examined and correlated with history. Univariate analyses were performed using Pearson’s chi2 to identify predictors of measured outcomes.

Results: Between June 2014 and March 2017, and A total of 85 patients (median age 69.5 years, interquartile range [IQR] 11, 50.6%) underwent UEMR of 97 colonic polyps (median size 25 mm, IQR 25 mm, range 10–160 mm). 13 (13.4%) were recurrences following previous conventional EMR. Polyps were predominantly left sided (66%) with flat (63.5%) or sessile (35.4%) morphology. 43.8% of polyps were removed en bloc, whilst argon plasma coagulation (APC) was used in 13.7%. Histology comprised of: low-grade dysplasia (80.2%), high-grade dysplasia (12.5%), adenocarcinoma (3.1%) and non-adenomatous sessile serrated polyp (4.2%). Overall, resection at index UEMR was deemed endoscopically complete in 97.9%. Submucosal lift was required in 27.8% and positively correlated with polyp size >30 mm (OR 3.58, 95% CI 1.37–9.38, p=0.01), but not morphology (flat vs. sessile, p=0.099). The 30-day complication rate was 4.1% (n=4), consisting of 2% requiring submucosal lift, and 4% delayed rebleeding (n=2; average diameters: 35 mm) and delayed rebleeding (n=2; average diameter: 57.5 mm), with haemostasis achieved for all cases. No cases of perforation or mortality were identified. Of the 60.8% (n=59) who attended for repeat endoscopy post-UEMR, the rate of recurrence or residual polyp was 14.8% (9/62) at 4 months and 13.59 (22.0%) within 1 year. Significant predictors of post-UEMR recurrence included: piecemeal vs. en bloc resection (OR 5.50, 95% CI 1.10–27.6, p=0.03) and recurrent polyp (OR 4.17, 95% CI 1.02–17.05, p=0.04), but not polyp size, site, morphology or dysplasia status, use of submucosal lift, APC, patient age, or study centre.

Conclusion: UEMR is a safe alternative to conventional EMR for the management of clinically significant colonic polyps. However, our post-UEMR recurrence rate of 22.0% appears higher than other studies,2,3 but may be skewed by the tertiary referral nature of our institution. Although randomized trials are awaited, we suggest that those performing UEMR should attempt en bloc resection where possible, and consider wider resection margins for recurrent polyps.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
3. All authors have declared no conflicts of interest.

P1511 WATER-AIDED COLONOSCOPY - RESEARCH FOCUS IN THE PAST DECADE AND CURRENT CLINICAL PRACTICE
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Introduction: Water-aided techniques have forged a paradigm shift in endoscopic diagnosis and therapy. The inauguration (10/22/2014) of the International WATERS with memberships worldwide attested to participants’ commitment to advance clinical, educational and research missions. To aid planning of future work in each of these areas, a descriptive study of water-aided colonoscopy was performed.

Aims & Methods: The aims of this study were two-folds. Study 1: To assess the frequency and trends of water-aided colonoscopy in the past decade. Study 2: To obtain a cross-sectional snapshot of current clinical practice. Study 1: Studies registered at Clinicaltrials.gov were searched for using the search term "water colonoscopy". Study 2: Members of International WATERS voluntarily participated in a survey to assess the proportion of patients with different modes of sedation, respondents selected yes (1) or no (0) responses to each of 16 questions related to their practice of water-aided colonoscopy.

Results: Study 1: In the past decade, 48 trials of water-aided colonoscopy were registered at Clinicaltrials.gov. They aimed at evaluation of insertion pain in unsedated, minimally sedated, or on demand sedation patients; assessment of efficacy in difficult colonoscopy; study of the impact on adenoma detection; and underwater mucosal resection or polypectomy. Study 2: Questionnaire responses are summarized in Table 1. Respondents: n = 23. Water-aided colonoscopy is used in patients sedated with propofol, minimal sedation on demand sedation (3–16%); but more commonly in patients with moderate or no sedation (30–34%). During insertion 95.5% use infusion of water and only 36.4% leave the air/CO2 pump on. 42.9% and 33.3% record volumes infused and suctioned upon arrival to the cecum. 52.4% remove almost all infused water during insertion. 71.4% and 59.1% performed polypectomy (<20 mm and >20 mm, respectively) underwater during withdrawal.

Table 1A: % of respondent’s patients

<table>
<thead>
<tr>
<th>Sedated with propofol</th>
<th>Receiving minimal sedation</th>
<th>Are unsedated</th>
<th>Receiving on demand sedation</th>
<th>Receive moderate sedation</th>
</tr>
</thead>
<tbody>
<tr>
<td>36</td>
<td>15</td>
<td>55</td>
<td>55</td>
<td>55</td>
</tr>
</tbody>
</table>

Table 1B: Proportion of respondents using the following approaches (%)

<table>
<thead>
<tr>
<th>Infuse water during withdrawal</th>
<th>Leave air/CO2 pump during withdrawal</th>
<th>Keep track of volume of water infused at different insertion locations</th>
<th>Keep track of volume of water infused when colonoscopy is finished</th>
</tr>
</thead>
<tbody>
<tr>
<td>58</td>
<td>82</td>
<td>77</td>
<td>77</td>
</tr>
</tbody>
</table>

Conclusion: The variable modes of application amongst respondents who profess to use water-aided colonoscopy reflect the versatility and strength of the paradigm-changing approach, which is easily adaptable to meet the diverse needs of individual colonoscopists. Standardization based on results of randomized controlled trials appears to be prudent to permit further assessment of water-aided colonoscopy in clinical, educational and research settings.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
3. All authors have declared no conflicts of interest.

P1512 ENDOCOPIC SUBMUCOSAL DISSECTION: RESULTS AND LEARNING CURVE OF A LARGE PROSPECTIVE SERIE OF 183 CASES IN THREE CENTERS
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Introduction: Endoscopic submucosal dissection (ESD) is a suitable technique used for the endoscopic management of selected early gastrointestinal neoplasms (EGN).

Aims & Methods: This is a prospective study of patients with EGN eligible for ESD in three tertiary hospitals. The main goal was to evaluate initial therapeutic results and learning curve of ESD. Initial Technical success rates, procedure speed, en-bloc & ROX resection, RO, speed and complications rates were prospectively evaluated. The results of the learning curve were analyzed by chronological order of blos of cases. Perforation was established as any disruption of the muscular layer, regardless of size or identification of peritoneal fat. Time of procedure was considered from initial submucosal injection to final detachment of the specimen.

Results: ESD was attempted in 183 lesions from January 2012 to April 2017. Majority of procedures were performed at Puerta de Hierro University Hospital (160/87.4%). Mean age was 67 (SD 10.6) years, with male proportion 55.23%. Most common location was colorectal (77.6%), followed by gastric (12.8%) and esophageal (9.4%). Success was observed in 96.2% of patients with en-bloc and R0 resection of 93.9% and 92.3%, respectively. Mean lesion size was 46.5 mm (range 8–130) with a mean speed of 9.01 min/cm2 (range 1–209). Perforation was
The main complication (48 (26.2%) events), requiring surgery in 5 (10.4%) cases. Perforation was statistically less frequent than other complications (p = 0.05) and LST morphology (p = 0.05). Most frequent location of perforation was transverse colon (OR 88.3; SE 137), followed by descending colon (OR 13.5; SE 19.4) and splenic flexure (OR 6.3; SE 11.8). Perforation was more common in LST-NG lesions vs LST-G (OR 19.3; SE = 15.6). Perforation rates were not statistically associated with the presence of severe submucosal fibrosis compared to absence of fibrosis (0.8 SE 0.6 vs 1 SE 1.0; p = 0.9). Post-ESD complications were observed in 15 (8.2%) patients (delayed perforation(7), bleeding(4), esophagus rupture syndrome(1), severe esophageal stricture(1), haemopteritus(1) and splenic rupture(1)). Six cases (40%) were managed with surgery. Results from the learning curve progression according to consequent chronological blocks of 50 cases (33 last bloc) are summarized in table 1. Initial success increased from 94% to 100%; speed of ESD decreased after the first 50 cases (15.5 cm²/min), up to 6.7 and 6.5 cm²/min in the last 2 blocs. A high perforation rate in the first period (32%) was reduced to 18-30.3% in the following periods. Endoscopic treatment was successful in most cases of perforation (86%). Surgery was required for severe complications, incomplete ESD and/or perforation (n, %) (16 cases, 8.7%).

Conclusion: On clinical ESD, high rates of success and en-bloc and R0 resection can be achieved along the learning curve. Perforation is the most common complication and is still a challenge for Western countries. However, increasing experience reflects a high success in endoscopic management of perforation.

Disclosure of Interest: All authors have declared no conflicts of interest.

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Endoscopic submucosal dissection: European Society of Gastrointestinal Endoscopy (ESGE) Guideline

Abstract
N = 183
101–150
151–183
Total (n, %)

Colorectal location (n, %) 40/50 (80%) 42/50(84%) 34/50(68%) 25/35(71.4%) 141/183(77%)
Succees(n, %) 47/49 (94%) 46/50(92%) 50/50(100%) 33/33(100%) 176/183(96.2%)
En bloc(n, %) 47/49 (94%) 46/50(92%) 50/50(100%) 33/33(100%) 172/183(93.9%)
R0(n, %) 45/49 (90%) 45/50(90%) 48/50(96%) 31/33 (94%) 169/183(92.3%)
Speed (cm/2/min) Mean (SD) 7.68 (5.02) 15.5(37.8) 6.7(5.5) 6.5(5.1) 9.01 (19.1)
Perforation(n, %) 16/50 (32%) 13/50(26%) 9/50(18%) 10/33(30.3%) 48/183(26.2%)
Surgery due to perforation (n, %) 2/16 (12.5%) 1/13(7.7%) 0(0%) 2/10(20%) 5/48(10.4%)

P1514 RISK OF STENOSIS AND OUTCOMES FOLLOWING ENDOSCOPIC RESECTION OF LARGE COLORECTAL LESIONS INVOLVING MORE THAN 75% OF THE LUMINAL CIRCUMFERENCE
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Introduction: Little is known about the risk of stenosis and outcomes following endoscopic resection of lesions in the colorectum which leave extensive mucosal defects. A limited number of studies suggest significant stenosis rates, although reports on outcomes and suggested management are conflicting. We determined the risk of stenosis and outcomes of endoscopic resection of colorectal lesions leaving mucosal defects ≥75% of the circumference.

Aims & Methods: Consecutive patients who underwent endoscopic resection of colorectal lesions ≥2 cm were included. Resection technique included EMR, ESD and hybrid techniques involving ESD. Patients were grouped according to circumferential extent of the mucosal defect after resection. Surveillance colonoscopy was performed at 3 and 12 months. Clinicopathological characteristics and outcomes were compared between groups.

Results: 435 colorectal lesions ≥2 cm were resected using EMR (n = 342), ESD (n = 45) or hybrid techniques (n = 48). Circumferential extent of the resulting mucosal defect was ≥75% in 41 patients. 8 lesions were fully circumferential: 1 caecal lesion and the rest in the recto-sigmoid and rectum. 3 of these circumferential lesions contained deeply invasive adenocarcinoma and 1 benign lesion ultimately required surgery. The 41 lesions with a mucosal defect ≥75% of the circumference had a mean size of 100.5 mm vs 49.0 mm for other lesions (p < 0.001). These patients had significantly more complications (16.7% vs 4.7%, p < 0.001), including a higher rate of perforation (8.3% vs 2.3%, p = 0.02), although none required surgery, and a significantly higher rate of recurrence (44.8% vs 9.2%, p < 0.001). 79% of patients without cancer were free from recurrence and had avoided surgery at last follow-up compared to 97% of patients with mucosal defects <75% (p < 0.001). Stenosis occurred in 7 patients: 4 lesions extensively involving the rectum and recto-sigmoid and 2 lesions involving the sigmoid colon extending to the rectosigmoid. Of these involved a mucosal defect of only 50% of the circumference and 3 were fully circumferential. 1 patient had a symptomatic anorectal stenosis requiring dilatation under anaesthesia, 1 patient was asymptomatic but underwent early dilatation after the first surveillance endoscopy at 3 months. The remaining patient was asymptomatic and managed expectantly. In all these latter cases spontaneous improvement in the stricture was noted at the subsequent surveillance colonoscopy.

Conclusion: The majority of patients with these extensive complex lesions can successfully be treated with endoscopic resection and avoid surgery. However, these patients have a significantly greater risk of complications and recurrence and should be managed in a tertiary institution. Although there is a significant risk of stenosis, it appears that most cases are asymptomatic and spontaneously improve with expectant management.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1515 RISK OF HIGH-GRADE DYSPLASIA AND SUBMUCOSAL INVASION IN DIFFERENT MORPHOLOGICAL SUB-TYPES OF LARGE COLORECTAL NEOPLASTIC LESIONS RESEDCTED AT A UK TERTIARY REFERRAL UNIT
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Introduction: The majority of patients with colorectal neoplasia will require endoscopic resection. Risk stratification and selection in western practice should be improved to reduce the incidence of prior heavy manipulation and guide appropriate referral.

Disclosure of Interest: All authors have declared no conflicts of interest.
Introduction: Although it is well recognised that the risk of invasive carcinoma in apparent benign colorectal lesions differs according to morphology, the incidence of invasive cancer varies between studies and there is limited data from large western series to inform practice. The importance of appropriate resection techniques, including the use of ESD, is increasingly recognised in western practice. It is therefore imperative that the risk of submucosal invasion is assessed as accurately as possible to prevent inappropriate attempts at resection. We determined the risk of submucosal invasion and high-grade dysplasia (HGDi) in different morphological sub-types of large colorectal lesions subjected to endoscopic resection.

Aims & Methods: Colorectal lesions ≥2 cm subjected to endoscopic resection were included. Lesions were assessed with magnification chromoendoscopy. Clinicopathological data recorded included morphological type according to Paris classification, sub-types of laterally spreading tumours (LST), degree of dysplasia, presence of submucosal invasion and outcomes following resection.

Results: 435 colorectal lesions ≥2 cm were resected. Mean lesion size was 55.2 mm (range 20 mm–160 mm). The frequency of and the incidence of high-grade dysplasia (HGD) in different morphological sub-types are shown in Table 1. The incidence of high-grade dysplasia (8.6%) and invasive adenocarcinoma (1.2%) was very low in LST granular homogenous lesions.

Conclusion: In our study, a withdrawal time exceeding seven minutes was significantly associated with the number of polyps detected in colonscope. Further studies may be helpful to confirm these results ideally by comparing these parameters in the same patients.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1517 OUTCOMES OF ENDOSCOPIC RESECTION OF RECURRENT COLORECTAL LESIONS TREATED AT A UK TERTIARY REFERRAL CENTRE

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Introduction: Endoscopic resection of large colorectal lesions, especially by piecemeal EMR, carries a significant risk of recurrence. Although several series examine the outcomes and risk of recurrence following endoscopic resection, few focus on the outcomes of patients being treated for recurrence after initial expert resection, and these mostly focus on one technique to deal with recurrence. We evaluated the outcomes after recurrence of colorectal lesions after apparent successful endoscopic resection in a specialised UK tertiary institution employing a range of resection techniques.

Aims & Methods: Consecutive patients who underwent endoscopic resection of colorectal lesions ≥2 cm were included. All lesions were assessed with magnification chromoendoscopy supplemented by colonoscopy ultrasound in selected cases. A lesion specific approach was used to decide on resection technique. Outcomes were evaluated for patients treated for recurrent lesions.

Results: Of 396 colorectal lesions ≥2 cm initially resected, recurrence occurred in 48 patients. 36% of these patients had already had a mean of 1.6 previous failed attempts at resection prior to referral to our institution, and 66% had had either a failed attempt at resection or extensive sampling involving ≥6 biopsies or tattoo placed under the lesion. 69% of patients were successfully treated with further endoscopic resection and avoided surgery. 27 recurrent lesions larger than 20 mm were treated with endoscopic resection, with a mean lesion size of 48.3 mm (± 19.3). Techniques used were EMR (n = 16), ESD (n = 2), Hybrid ESD and EMR (n = 9). The remaining lesions < 2 cm were resected using EMR. A mean of 1.4 ± 0.75 procedures were required to achieve successful endoscopic treat- ment of recurrence. 23 patients who were ultimately successfully treated with endoscopic resection, 1 required a single further endoscopic resection after recurrence, 8 patients required 2 or more further resections. 8 patients required surgery, 3 as a result of developing invasive adenocarcinoma with the recurrence. There were no perforations as a result of endoscopic resection of recurrent lesions managed conservatively.

Conclusion: These data demonstrate the challenges of an advanced endoscopic resection service in much of western practice where patients with recurrent lesions represent a particularly complex cohort, most of whom have already had extensive prior manipulation or attempts at resection. Familiarity with a range of resection techniques and appropriate equipment is essential to successfully treat recurrent lesions in this group with endoscopic resection, which can be achieved in the majority of patients without significant morbidity.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1518 THE EFFECTIVENESS OF NEW TECHNIQUE WITH SELF-EXPANDABLE METALLIC STENT INSERTION IN TREATING RIGHT-SIDED COLORECTAL OBSTRUCTION

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Introduction: Self-expandable metallic stent (SEMS) is widely used to treat malignant colorectal obstruction. However, most reports about SEMS insertion have concentrated on right colon, and very tough to insert SEMS on the left colon, especially distal ascending colon.

Aims & Methods: This study aimed to (1) investigate the effectiveness of new insertion technique with SEMS for right-sided colonic obstruction and (2) compare safety and technical success of SEMS insertion. The data from ten patients who underwent SEMS with a new technique for malignant obstruction of ascending colon in our hospital were analyzed retrospectively. Initially, we tried to insert with the straight type guiding tube and wire for obstructed area of ascending colon under CO2 insufflation. It was difficult to start cannulation more than 20 minutes manipulation. For difficult cannulation, we change to curved type guiding tube (CleverCut2V/CleverCut3V Double and Triple Lumen sphincterotomes). All cases were difficult cannulation and change to curved type. The mean time of SEMS insertion was 11.6 minutes (range 3–21 minutes). Only 2 patients required pre-cannulation with distal colonoscopy. All patients were extubated and discharged with stent inserted in colon. The clinical success, complications, and technical difficulties were analyzed. We compared the results between SEMS insertion and decompression tube placement in right and left-sided colorectal obstructions.

Results: Cannulation time with a curved type guiding tube decreased of all cases (20 min vs 8.5 min). For ascending colon, the technical and clinical success rate of SEMS insertion with new technique significantly 100% (10/10). There was no
compilation (0.10). Concerning SEMS insertion, the technical difficulty and safety of SEMS insertion were similar between right- and left-sided colorectal obstructions. Conclusion: A new technique of curved type guiding tube with SEMS insertion for right-sided colon, especially distal ascending colon is significantly more effective than straight type guiding tube, and this procedure was safer and less technically challenging than expected. SEMS insertion should be considered for treating right-sided malignant colonic obstruction.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P1519 ENDOSCOPIC FULL-THICKNESS RESECTION FOR COLONIC LESIONS. INITIAL EXPERIENCE IN 3 CENTERS OF CATALONIA
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Introduction: Endoscopic full-thickness resection (EFTR) in the colon using the FTRD kit is a recent technique that allows en-bloc resection of colonic lesions that are poor candidates for resection by endoscopic mucosal resection (EMR). It does not require the injection of a solution into the submucosa and allows an en-bloc resection of colonic lesions up to approximately 30 mm. We present results of the initial experience in 3 centers of Catalonia.

Aims & Methods: We retrospectively analyzed the clinical, endoscopic and anatomic features of all cases of EFTR performed in 3 centers in Catalonia using the FTRD kit (Ovesco Endoscopy, Tübingen, Germany) during the period between June 2015 and January 2017. All patients underwent the procedure under deep sedation with propofol, all patients were duly informed of the technique and potential complications derived from the procedure, obtaining written informed consent prior to the procedure. All EFTR resections in the colon were performed using the FTRD kit (Ovesco Endoscopy, Tübingen, Germany), grasping and pulling the lesion inside the cap, deploying the OTSC and resecting the tip over the OTSC with the preloaded snare. Clinical assessment was performed before and after procedures with a complete blood test before procedure. Blood test was not routinely used after procedures. Demographic, clinical, endoscopic and histologic data were collected from each patient, and analyzed with Stata 14.2.

Results: 16 endoscopic full-thickness resections of the colon were performed. The mean age of the patients was 69 years (53–79), with men being 88%. The indications were recurrent/residual lesions with non lifting sign (75%) and untreated lesions with non lifting sign (25%). The locations were juxtavalvular (n = 2), ileocecval (n = 3), sigmoid, stump or anastomosis (n = 2). The mean diameter of the resected samples was 20.8 mm (13–33 mm). The histology of the lesions was adenoma with low grade dysplasia (50%), adenoma with high grade dysplasia (25%), sessile serrated polyp without dysplasia (6%) and three lesions were adenocarcinoma with deep submucosal invasion (19%). There were no clinically relevant complications or emergency surgery. 1 patient had mild self-limited hemorrhage, 6 patients had mild abdominopelvic pain (38%) and 3 patients developed postpolypectomy syndrome (19%).

Conclusion: Endoscopic full-thickness resection is a safe and feasible technique for selected cases in colon.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P1520 A META-ANALYSIS: CHROMOENDOSCOPY OR WHITE LIGHT ENDOSCOPY FOR NEOPLASIA DETECTION IN LYNCH SYNDROME
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Introduction: Lynch syndrome (LS) is an autosomal-dominant disease, with increased risk of colorectal cancer (CRC), hence annual surveillance colonoscopy is recommended. do not recommend one over the other.

Aims & Methods: We aimed to compare the diagnostic yield (DY) of different endoscopic modalities for detection of colorectal neoplasia in patients with LS by performing a meta-analysis of existing literature. We searched PubMed for prospective studies. For each modality, we performed comparative total per-adeno-noma analysis and sub-analyses for flat lesions and location (right/left colon).

Results: Meta-analysis was performed using pooled rate ratios (RR) with fixed effects model within each subgroup. The low heterogeneity within each subgroup was confirmed. Conclusion: A new technique of curved type guiding tube with SEMS insertion for right-sided colon, especially distal ascending colon is significantly more effective than straight type guiding tube, and this procedure was safer and less technically challenging than expected. SEMS insertion should be considered for treating right-sided malignant colonic obstruction.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P1512 HOT AVULSION TECHNIQUE - A FIRST-LINE APPROACH FOR TREATMENT OF VISIBLE RESIDUAL NEOPLASIA DURING ENDOSCOPIC MUCOSAL RESECTION OF COLORECTAL POLYPS?
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Introduction: Endoscopic mucosal resection (EMR) has been shown to be useful in the removal of large colorectal adenomas. These lesions are often resected by using a piecemeal technique, which is a risk of recurrence in 10% to 30% of cases. Recently, hot avulsion technique (HA) has shown promising results in the resection of residual fragments of large colorectal adenomas, with lower recurrence rate.

Aims & Methods: The aim of this study was to evaluate the efficacy and safety of HA at index EMR and at EMR local recurrence. We did a retrospective study based on all the HA performed between June 2015 and February 2017. The endoscopic characteristics, complications and recurrence rate after the initial HA were evaluated.

Results: 33 HA were performed among 29 patients (16 men and 13 women) with an average age of 69 years. The average follow up time was 11 months. HA was used to remove residual adenomatous tissue at 17 index EMR (mean size of the lesion 30 mm) and to remove recurrent fibrotic adenomatous tissue at EMR scar in 12 cases (mean size of recurrence tissue 14 mm). HA was successful in removing residual/recurrent adenomatous tissue in all patients. There were no immediate or long term adverse events. Comparing the two groups, local recurrence after initial HA recurred in one case at the index EMR group (1/17) and in 2 cases at the local EMR group recurrence (2/12). The overall recurrence rate in patients with a minimum 6 months follow up was 15% (3/20). Conclusion: HA is a safe and effective technique to eradicate both residual tissue in large colorectal adenomas and recurrent fibrotic adenomatous tissue at EMR site, with low recurrence rate.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

Introduction: Quality of bowel preparation and adenoma detection rate (ADR) are routinely assessed in screening colonoscopy. However, data on patient experience are scarce.

Aims & Methods: This prospective non-interventional study compared bowel preparation quality according to the Harefield Scale, performance quality measures and patients satisfaction in screening colonoscopies performed within an Austrian quality assurance program.

Results: Colonoscopies performed by 20 endoscopists were included in this study. 53.0% of screened individuals were women. Because of the unequal patient count using Citoflex® (CF, n = 261), Prepcore® (PP, n = 2678), Klean-Prep® (KP, n = 804) and Moviprep® (MP, n = 1252), PC and CF were grouped into a joint group (LV). Age and gender adjusted success rates and ADR per purgative were 97.0% and 23.3% for LV, 97.5% and 32.5% for KP and 93.5% and 26.0% for MP. Women had higher success rates than men (p = 0.073) and success rate decreased with patients' age (p = 0.008). The compliance regarding consumption of the entire volume was best with LV (89.2%, KP 87.6%, MP 87.3%), which had a significant effect on success rate (p = 0.027). 93.5% of patients in the LV group would use the same purgative again compared to 68.4% in the KP and 73.2% in the MP group.

Conclusion: All investigated purgatives met the required quality standards of ≥90% rate of adequate bowel preparation according to the current ESGE guidelines. Success rates were higher in women and younger patients. Although only <90% of patients consumed the whole volume, the majority of patients would use the same purgative again.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference: 107.614 examinations from 288 endoscopists were analysed between 2012 and 2017 within the Austrian certificate of screening colonoscopy. For comparison two different categories were included: excellent, good, fair, unsatisfactory, poor only in the right colon. Data are shown as Mean and SD.

Results: 8578 surveillance colonoscopies (43.88% female, mean age 66.67) and 9927 screening colonoscopies (51.04% female, mean age 62.31) were included. Within screening colonoscopy 37.59% (SD = 31.50) were excellent prepared vs. 34.60% (SD = 33.98) within surveillance colonoscopy, good 47.43% (SD = 27.28) vs. 45.61% (SD = 31.28), fair 11.39% (SD = 11.58) vs. 14.39% (SD = 21.69), poor 2.38% (SD = 3.06) vs. 3.68% (SD = 9.75), unsatisfactory 0.77% (SD = 1.20) vs. 0.89% (SD = 3.69), poor only in the right colon 0.69% (SD = 1.81) vs. 0.39% (SD = 1.22). Calculations revealed no significant differences among screening and surveillance colonoscopies relating the following categories: excellent (p = 0.4357), good (p = 0.5911), unsatisfactory (p = 0.6262) and poor (p = 0.4357) and poor only in the right colon (p = 0.4357). Bowel preparation varies significantly between screening and surveillance in groups of fair (p = 0.0454) and poor (p = 0.0497).

Bowel preparation influences the adenoma detection rate (ADR). Mean ADR in excellent preparation was 22.16% (SD = 16.36%), in good 25.41% (SD = 17.30%), in fair 24.63% (SD = 19.44), in poor 19.94% (SD = 25.57), in unsatisfactory 12.08% (SD = 22.77) and in poor only in the right colon 24.22% (SD = 30.89%). Adequate rate in screening colonoscopy was 96.22% (SD = 3.98%) vs. 95.07% (SD = 10.45%) in surveillance colonoscopy. Rates correspond to ESGE guidelines and do not differ significantly from other work (p = 0.1265).

Conclusion: Data showed distinct differences between fair and poor, whereas there were more fair and more poor prepared patients at the surveillance colonoscopy, than at the screening colonoscopy. Age of patients at surveillance colonoscopy was higher, hence D-H, Fredrik improved enlightenment. ADR in excellent, good and fair bowel preparation was adequate. In poor, unsatisfactory was low and ADR at poor only in the right colon is high due to low count (N = 374).

Disclosure of Interest: All authors have declared no conflicts of interest.
A total of 4949 patients were included in the study, of whom 2103 had (PEG-ES) bowel preparation (n = 20.13%) patients were excluded from further analysis for the following reasons:

**Contrast:**
- Evaluation for this procedure has consistently been debated1,2,3.
- The optimum bowel preparation for this procedure has consistently been debated1,2,3.

**Aims & Methods:** The aim of this study was to determine the impact of endoscopic surveillance on CRC prevention in patients after surgery. We did a retrospective single center study on findings of follow up endoscopies and determination of the cumulative risk of adenomas and prevalence of high risk adenomas (HRA) (villose histology, high-grade dysplasia and ≥10 mm) and CRC.

**Results:**
- 30 patients submitted to IRA were included (50% women), with a mean age of 43 years, 2 patients with attenuated phenotype. Nine patients had adenocarcinoma in the resected colon. Six patients started chemoprophylaxis after surgery (sulindac-4; celecoxib -1). The median time to adenoma appearance was 5 years (95% CI 3.4-6.6) and to HRA/CRR 12 years (95% CI 5.2-18.8), with a decreased median time to both adenomas and HRA/CRR in patients under chemoprophylaxis. The cumulative risk of adenomas was 20% at 1 year after surgery, 34.1% at 3 years and 57.4% at 5 years. During the follow up period, 1284 patients had CRC developed in 17 patients (56.7%) HRA–12 patients (40%); intramuscosal carcinoma–2 patients (6.7%); invasive adenocarcinoma–3 patients (10%). None of the patients died with CRC. The cumulative risk of HRA/CRR was 21.8% at 5 years, 46.1% at 10 years and 66.3% at 15 years. All the patients with HRA/CRR had rectal involvement prior to surgery (p = 0.008) and a higher number of adenomas resect in the rectal remnant (p = 0.017).

**Conclusion:** The FAP endoscopic surveillance program allowed detection of HRA/CRR in a high percentage of patients. Based on these results, an intensive endoscopic surveillance program should be suggested but endoscopic surveillance intervals widen in the first 5 years after surgery.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**References**

**P5127 BOWEL PREPARATION FOR FLEXIBLE SIGMOIDOSCOPY: COMPARISON OF POLYETHYLENE GLYCOL ELECTROLYTE SOLUTION (PEG-ES) AND PHOSPHATE ENEMA IN 4949 PATIENTS AT 16 UK HOSPITALS**

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**Introduction:** Flexible sigmoidoscopy is increasingly used to examine the left side of the bowel for diagnostic and surveillance purposes, and is now part of the UK bowel cancer screening programme. It is crucial to achieve adequate bowel cleansing in order to optimise the diagnostic yield of the test, and also to minimise the number of repeat procedures. However, the optimum bowel preparation for this procedure has consistently been debated1,2,3.

**Aims & Methods:** Both phosphate enema and (PEG-ES) are commonly used for bowel preparation in flexible sigmoidoscopy at both hospitals participating in this study. We therefore wanted to compare the outcomes for these two methods. We retrospectively reviewed all the patients who underwent flexible sigmoidoscopy from January 2014 to December 2016 using each hospital's electronic endoscopy reporting system. We analysed their demographics, type of bowel preparation used in each case, and the quality of their individually achieved bowel preparation, subjectively graded as “Excellent, Adequate or Inadequate” by the endoscopist performing the procedure. A chi-squared test was used to calculate p-values.

**Results:**
- In total 6196 patients underwent flexible sigmoidoscopy during the study period (males 2885 (46.5%), mean age 62.80 years, range 16–101 years). 1247 (20.13%) patients were excluded from further analysis for the following reasons: No bowel preparation (n = 451), non-compliance of the quality of the bowel preparation (n = 657), and non-PEG-ES oral preparation used (n = 139).
- A total of 4949 patients were included in the study, of whom 2103 had (PEG-ES) bowel preparation (n = 657), and non-PEG-ES oral preparation used (n = 139).
- A total of 4949 patients were included in the study, of whom 2103 had (PEG-ES) oral preparation used (n = 139).
- A total of 4949 patients were included in the study, of whom 2103 had (PEG-ES) oral preparation used (n = 139).

**Conclusion:** Our large retrospective study showed that oral preparation with (PEG-ES) gave significantly better results than phosphate enema, which gave acceptable results in only 67.5% of the patients. As a result of this study, PEG-ES is now the preferred option at our hospitals, if there is no contraindication for this. Disclosure of Interest: All authors have declared no conflicts of interest.

**References**
P1529 ENDOSCOPIC REMOVAL OF HIGH-RISK COLORECTAL ADENOMAS: SAFE AND EFFECTIVE?

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Introduction: The incidence and mortality of colorectal cancer (CRC) can be decreased through the removal of precancerous adenomas. Endoscopic removal of polyps over 2 cm is considered a high-risk procedure both for complications and malignant transformation.

Aims & Methods: The aim of this study was to evaluate the outcome and complication rate after endoscopic removal of polyps over 2 cm. In this retrospective study clinical and demographic data of patients undergoing polypectomy due to colorectal adenomas over 2 cm between 2012 and 2017 were collected. Data on endoscopic procedures, complications of polypectomy and histological assessments of the removed polyp were obtained.

Results: Data of 100 patients (male/female: 58/42) was analyzed in the study. Full removal of the 106 removed polyps proved to be pedunculated, 21 were sessile and 34 flat. Six patients had more than one large polyp (>2 cm). The locations of the removed polyps were rectum in 33, sigmoid colon in 38, coecum in 12 and other parts of the colon in 23 patients. In 65 cases, polyps were excised with endoscopic mucosa resection (EMR) or hybrid endoscopic submucosal dissection (ESD). In 41 cases snare was used to remove the polyps in one or more pieces. Based on histological findings 54 (50.9%) polyps were shown to be low-grade adenomas, 34 (32.07%) high-grade adenomas, 1 (0.9%) polyp was hyperplastic, and 17 (16.03%) proved to be malignant among which complete endoscopic removal was achieved in 9 patients (52.9%). Additional smaller polyps were found in 39 patients and a synchronous cancer in 7. During polypectomies 91 hemoclips were deployed to close suspected perforation (8 cases) to cease bleeding within a mean of 4 days after the first examination. Hemoclip insertion was needed in 5 cases and epinephrine injection in 1 case. The bleeding stopped spontaneously in 2 cases. Second-look colonoscopy was required in 8 cases due to bleeding within a mean of 4 days after the first examination. Hemoclip insertion was needed in 5 cases and epinephrine injection in 1 case. The bleeding stopped spontaneously in 2 cases. Surgical intervention was not needed in any case.

Conclusion: Malignant transformation was revealed in 16% of the polyps over the size of 2 cm. Complete endoscopic removal of these polyps was successfully performed in half of the patients. Endoscopic removal of high-risk polyps is safe in experienced hand.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference


P1530 WHAT IMPROVED AND WHAT REMAINS TO BE ACHIEVED IN ORDER TO COMPLY WITH THE NEW RECOMMENDATIONS OF POLYPECTOMY BY THE EUROPEAN SOCIETY OF GASTROINTESTINAL ENDOSCOPY

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Introduction: The choice of polypectomy technique differs according to regional preferences and availability. This year, in order to standardize the approach to this techniques, the European Society of Gastrointestinal Endoscopy (ESGE) published recommendations for colorectal polypectomy and endoscopic mucosal resection (EMR).1

Aims & Methods: We aimed to evaluate the recent years evolution of the adherence to the recommendations of colorectal polypectomy and EMR at a tertiary center. We conducted a univariate analysis of polypectomy and mucosectomy techniques performed consecutively between January and June of 2011 and 2016 at a tertiary center. According to the recommendations, the excision of sessile and flat polyps is considered adequate when performed with cold biopsy forceps or cold snare for polyps ≤3 mm, cold snare if 4-9 mm, or hot snare if 10-19 mm and EMR if ≥20 mm. Polypectomy of pedunculated polyps is considered adequate when performed with a diathermic loop in polyps <20 mm, always in association with any prophylactic therapy when polyp size ≥20 mm.

Results: We included 1721 endoscopic procedures of polypectomy and EMR, considering 796 patients (64.5% male; mean age: 64.2 ± 11.0 years). 1381 (80.2%) sessile polyps, 153 (8.9%) flat lesions and 187 (20.9%) pedunculated polyps were identified, with a mean size of 7.9 ± 7.0 mm. Regarding sessile and flat polyps, one of the recommended excision techniques was performed in: 84.6% (n=270) of ≤3 mm polyps (75.7% in 2011 vs. 95.8% in 2016; p < 0.001); 22.2% (n=109) of 4–5 mm polyps (12.5% vs. 36.5%; p < 0.001); 13.4% (n=59) of 6–9 mm polyps (5.4% vs. 23.8%; p < 0.001); 100% (n=206) of 10–19 mm polyps; and 100% (n=88) of ≥20 mm lesions. For pedunculated polyps, the excision technique was adequate in: 99.3% (n=134) of polyps of size <20 mm (100% vs. 97.6%; p > 0.05) and in 84.6% (n=44) of those ≥20 mm (82.6% vs. 86.2%; p > 0.05). Overall, 52.3% (n=900) of endoscopic procedures of polypectomy or EMR were performed as recommended; 42.7% (n=410) in 2011 vs. 64.5% (n=490) in 2016; p < 0.001.

Conclusion: Even before publication of the European recommendations, there has already been an increase in the proportion of polypectomies performed adequately in the different groups of lesions. There is still a need to adjust clinical practice in some subgroups, especially in polyps of size 4–9 mm, in order to strictly comply with the recommendations.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference


P1531 ENDOSCOPIC SUBMUCOSAL DISSECTION (ESD) OF SUPERFICIAL COLORECTAL NEOPLASMS AT THE ANAL CANAL AND ILEOCECAL VALVE

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Introduction: Endoscopic resection of superficial neoplasms at the perineal rectum is difficult due to pain sensitivity, narrowness of the anal canal, presence of internal rectal plexus, whereas that of at the ileocecal valve (ICV) due to the variable morphology of the ICV itself and ileal involvement.

Aims & Methods: Aim was to assess the feasibility and outcomes of ESD in these locations. Prospectively collected database in a single nonacademic center. From 2010 to 11.2016, all consecutive patients scheduled to ESD for a superficial neoplasm in the perineal rectum (distal margin <30 mm from the dentate line) and at the ICV were compared to those in the pelvic rectum and in the cecum and ascending colon, respectively. ESD was performed with the standard technique. Follow-up was scheduled at 3 and 6 months within the first year and then yearly. Biopsies were taken from the scar of the resection site if a residual tissue was detected.

Results: A total 16 neoplasms at IVC were compared to 110 neoplasms in the cecum and ascending colon; 30 neoplasms in the perineal rectum were compared to 58 cases in the pelvic rectum (Table). Features of neoplasms in the perineal and pelvic rectum were no different as well as neoplasms at the IVC and cecum and ascending colon. ESD en bloc rates were lower in the perineal rectum and at the IVC, but no significant differences were found with the respective control groups (P = 0.490 and 0.404, respectively). ESD R0 rate was significantly lower at the IVC (P = 0.021). Adverse events were not different, although 3 perforations occurred in the cecum and ascending colon. During follow-up (median 16 months; range 24-84): residual tissue was diagnosed at the IVC in 2 (13%) cases, in the cecum and ascending colon in 2 (2%) cases (P = 0.078); in the perineal rectum in 4 (13%) cases and pelvic rectum in 2 (3%).

Conclusion: The ESD of neoplasms at the IVC and perineal rectum is feasible and effective. The complete resection rate is low due to the challenging anatomy of
that precludes conducting a mucosal incision far from tumor margins. A careful endoscopic follow-up is mandatory to detect residual neoplasms.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1532 SELF-EXPANDABLE METAL STENT IN THE OCCLUSIVE COLORECTAL CANCER AS PALLIATIVE TREATMENT
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Introduction: Colorectal cancer (CRC) is one of the most common malignancies in the industrialized world, with associated oncologic disease being relatively common. Endoscopic placement of self-expandable metallic stent (SEMS) is the first-line palliative treatment for malignant bowel obstruction.

Aims & Methods: Evaluate the outcome of endoscopic SEMS placement in CRC obstruction. Retrospective analysis of patients CRC submitted to endoscopic placement of SEMS from 2009 to 2016 in the Gastroenterology Department of Centro Hospitalar do Algarve. Statistical analysis was performed with SPSS version 22.

Results: The study included 23 patients with CRC obstruction, who were submitted to endoscopic SEMS placement, with a mean age of 75.2±13.47 years. The stents were placed with a palliative purpose in 69.6% of cases (n=16) and a transitory procedure before surgery in 30.4% of cases (n=7). Technical and clinical success was found in 91.3% of the patients, without any recorded death during the procedure. In patients whose goal was palliative treatment (75% men and 25% women) they had a mean age of 81.6±9.28 years. In 43.8% of the patients the tumor was located in the rectum, 31.6% in the sigmoid region and 25% in the recto-sigmoid transition. Being the majority (75%) well differentiated. There was a need for dilatation in 31.3%, most of the stents were uncovered (56.3%), 25% of the patients had complications. After stent placement about 25% of the patients did chemotheraphy. There was a 75% mortality rate (37.5% died by 6 months and 37.5% died by 12 months of follow-up). The use of chemotheraphy after SEMS placement influenced the complications associated with the procedure (p<0.05) but none of the other variables had a statistically significant influence on early death (up to 6 months).

Conclusion: SMES is an effective and safe palliative option for unresectable tumors, although the use of chemotheraphy after the placement of prosthess may have an influence on the appearance of complications. Malignant colon obstruction of the colon can be treated effectively with the use of endoscopic techiniques.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P1533 RISK FACTORS FOR ADENOMA RECURRENCE AFTER ENDOCOPIC MUCOSAL RESECTION OF LARGE COLORECTAL POLYPS
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Introduction: Endoscopic mucosal resection (EMR) has been shown to be a safe and effective technique for removal of large colorectal adenomas. However, local adenoma recurrence remains a significant limitation, with prior published data describing recurrence rates of 10% to 30% post EMR.

Aims & Methods: This study aimed to evaluate the outcomes of EMR for large colorectal adenomas and identify the risk factors for adenoma recurrence. We did a retrospective analysis of the cancer registry in the management between June and December 2016. Resected lesions larger than 20 mm in diameter with at least 3 months follow up were included. Patients referred for surgery were excluded.

Results: During the study period, 201 colorectal lesions ≥20 mm in size were resected using EMR with associated adenoma sizes ≥10 mm. Mean lesion size was 35 mm and 137 (68.2%) were located in the rectum and left colon. 66 lesions (32.8%) were larger than 40 mm in diameter. Piecemeal resection was performed in 171 lesions (85.1%). Local adenoma recurrence occurred in 44 cases (21.9%) after a mean time of follow up of 7.6 months, and the majority was managed with polypectomy or new EMR. The cumulative risk of adenoma recurrence was 7.5% at 3 months, 15.5% at 6 months and 17.1% at 12 months. In the multivariate analysis, the variables associated with a high risk of recurrence were lesions ≥40 mm in size (p<0.0001) and intra-procedural bleeding (p=0.020). The recurrence rate was higher in the patients treated with argon plasma coagulation (p=0.046).

Conclusion: After EMR of large colorectal adenomas, local recurrence rate was 21.9%. The risk factors for adenoma recurrence include lesions ≥40 mm and intra-procedural bleeding. Argon plasma coagulation was not associated with lower recurrence rate.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P1534 THE INFLUENCE OF THE REAL FOLLOW-UP TIMES DURING A COLORECTAL CANCER SCREENING PROGRAM IN DAILY PRACTICE
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Introduction: European colorectal screening guidelines have modified the follow-up interval times based on baseline colonoscopy findings in recent years. In addition, the waiting list and individual conditions may modify the real follow-up times and this could impact in advanced adenoma detection rate in follow-up and patients outcome.

Aims & Methods: The aim of the present study was to comparatively analyse the risk of advanced lesions (advanced adenoma, invasive cancer) in high-risk patients included in a colorectal cancer screening program with different real follow-up times. One-thousand one-hundred and sixty-six patients (mean age 60.66±5.86 years, 69.1% men) who underwent a baseline colonoscopy with ≥3 adenomas and/or ≥10 mm between 2007–2012 were included. A Kaplan-Meier regression and a comparative subgroup analysis by Long-Rank test were carried out to determine the impact of early and late examinations. An adjustment for baseline covariates (high-grade dysplasia, villous component) by Cox analysis was also performed.

Results: The real follow-up times in ≥3 adenomas (n=853, 73.18%) and ≥lade- noma ≥10 mm (n=779, 66.81%) were 38.54±11.57 and 38.66±11.68 months respectively. The risk of advanced lesions were 0.26%, 1.46%, 2.83%, 9.09% and 10.38% (p=121 advanced lesions) in 12, 24, 36, 48 and ≥60months respectively. The most important increase was at 3–4 years (0.52%/month). The proportion of advanced lesions within 1–2 adenomas subgroups at 48 months was 5.43% and 10.43% (p<0.001), with no differences in small adenomas ≤<10 mm (p=0.478).

Conclusion: The risk of advanced lesions in high-risk patients increased significantly at 36–60 months after baseline colonoscopy, being more important in ≥3 adenomas subgroup. There were no differences for 1–3 years interval.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1535 CLINICAL OUTCOME OF ENDOCOPIC SUBMUCOSAL DISSECTION OF MALIGNANT NON-PEDUNCULATED COLORECTAL LESIONS
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Introduction: Conventional endoscopic resection, such as snare polypectomy and endoscopic mucosa resection (EMR) of benign polyps in colon and rectum reduces colorectal cancer (CRC) incidence and mortality but the role of endoscopic resection of colorectal Egregement of patients with early CRC (i.e. submucosa and invasion) remain elusive. Large sessile and flat lesions are difficult to remove en bloc with EMR, resulting in a high level of tumor recurrence. Thus, endoscopic resection of large (>2 cm) sessile and flat malignant lesion with snare or EMR is not recommended in men and topical submucosal dissection (ESD) results in high en bloc resection rates of large (≥2 cm) benign lesions resulting in low numbers of recurrences. However, there is limited data in the literature on the potential role of ESD in the treatment of patients with early CRC. In the present study, we present our results on performing ESD in patients with large sessile and flat malignant lesion in the colon and rectum in a large European center.

Aims & Methods: Our aim was to investigate the potential role of ESD in treatment of early colorectal cancer. We retrospectively reviewed medical records of
254 patients that underwent colorectal ESD at the endoscopy unit at Skane University Hospital, Sweden between 2012 and 2016. Indications for ESD were flat and sessile lesions larger than 20 mm in diameter with low or high grade dysplasia (251 cases). Moreover, three patients with known colorectal adenocarcinoma underwent ESD due to significant comorbidity excluding surgery. In all, we identified and included 29 cases of histologically verified submucosal invasive CRC in this study.

Results: This study included 29 patients with median age of 69 years (range 44-89 years). Median tumour size was 40 mm, ranging from 20 - 70 mm. Tumours were either flat (Paris classification Ha, 6 cases), sessile (Paris classification 1s, 19 cases) or a combination of flat and sessile (4 cases). Half of the lesions were located in the rectum and half in the colon. En bloc resection was achieved in 24 cases (83%), piecemeal resection in 4 cases (14%) and ESD was incomplete in one case (3.4%). Median time to complete the procedure was 89 min (Range 594 min). Macroscopic complete resection was obtained in 26 cases (90%). R0 resection was found in 20 specimen (69%), R1 in 3 cases (10%) and R1 was found in 5 cases (17%). Lymphovascular involvement was seen in 6 cases (21%) whereas lymph node involvement was seen in 2 cases (7%). In total four patients were diagnosed with cancer in the resected sigmoid segment revealed T3N0. No acute significant bleeding occurred during the procedure. One patient sought emergency care 12 days after the procedure with rectal bleeding, no colonoscopy was performed to determine the site of bleeding. Five patients underwent additional surgery since the pathological report stated that the resection was R1. Tumour residue was only found in one of the five resected specimens. 18 patients have undergone endoscopic follow up, to this date without any sign of recurrence. Two patients await surgery and therefore no follow up could be performed.

Conclusion: We herein present our findings on performing ESD on 29 patients with early CRC. Our results indicate that colorectal ESD is a safe and effective treatment in meticulously chosen patients even with malignant lesions. Further studies with a larger number of cases are needed.

Disclosure of Interest: All authors have declared no conflict of interest.

P1536 ENDOCOSPIC SUBMUCOSAL DISSECTION (ESD) VS HYBRID DISSECTION TO WHICH TECHNIQUE TO FAVOR IN LARGE COLORECTAL LESIONS?

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Introduction: Large colorectal lesions (>20 mm) can be removed endoscopically by endoscopic mucosal resection (EMR), often in a piecemeal fashion resulting in low en bloc and radical (R0)-resection rates. In this indication, submucosal dissection (ESD) allows en bloc resection whatever the size, but still remains technically difficult and time consuming. A hybrid endoscopic technique has been developed, called simplified or hybrid dissection. The aim of our study was to evaluate the outcomes of complications of endoscopic resection performed by hybrid technique compared to classical endoscopic submucosal dissection.

Aims & Methods: Our study was carried out from January 2013 to June 2016 from a prospective database. The 40 lesions removed by hybrid technique were compared to the 103 lesions of the hybrid dissection group, which were performed as follow: submucosal injection around the lesion of macromolecules, circumferential mucosal incision and submucosal dissection using the tip of a single-strand snare by endoscopist mode, central submucosal injection of the lesion and final resection with the single-strand snare, if possible in en-bloc. Patient characteristics, tumor location and size, dissection characteristics, "block" resection rate, R0 resection rate (healthy margins), procedure and hospitalization time, and complications were identified and compared with the so-called "classical" ESD technique.

Results: Lesions were more frequently located in the colon (vs rectum) in the hybrid dissection group compared to the ESD group (72.5% versus 28.5%, p < 0.001). Lesion size were type Ac according to Paris classification in 10% of the hybrid dissection group and 13.1% in the ESD group (p = 0.8). The mean size of the lesions was lower in the hybrid dissection group than in the ESD group (32.4 mm ± 13 mm compared to 54.4 mm ± 26.7 mm, p = 0.001). An en bloc resection was performed in 52.5% and 84.4% in the hybrid dissection and ESD group, respectively (p < 0.001). The procedure time (including general anesthesia time) was lower in the hybrid dissection group compared to the ESD group (105 min ± 62 min vs 191 min ± 73 min, p < 0.001, respectively). The hospitalization time was lower in the hybrid dissection group than in the ESD group (1.1 days ± 1.13 days vs 2.5 days ± 1.8 days, p = 0.001). R0 resection rates were lower in the hybrid dissection group than in the ESD group (47.5% and 61% respectively, p = 0.001). Hybrid dissection was performed for adenocarcinoma, adenoma with high grade dysplasia and patient with low grade dysplasia in 12.5%, 42.5% and 40%, respectively. The rate of adenocarcinoma was lower compared to the ESD group (12.5% versus 30.8%, p = 0.009). In the hybrid dissection group, the rate of perforation was lower than the ESD group (5%). There was no significant difference in the rate of bleeding (1.8% in the hybrid dissection group and 2.5% in the ESD group). In case of complication, there was no need of surgical treatment in the hybrid dissection group, but was needed in one patient in the ESD group.

Conclusion: Hybrid dissection is less effective in terms of en bloc resection of large colorectal tumors. Classical endoscopic submucosal resection should be preferred, especially in case of suspected adenocarcinoma despite longer procedure and hospitalisation time.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1537 TRENDS IN STATISTICS REGARDING EFFECTIVE ELECTRIC ERCP PROCEDURES IN THE VENETO REGION: A RETROSPECTIVE STUDY BASED ON ADMINISTRATIVE DATABASES

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Introduction: Since its introduction in 1968, Endoscopic retrograde cholangiopancreato-gramy (ERCP) has become a routine endoscopic procedure used to diagnose and to treat conditions associated to the pancreatobiliary system. It is nevertheless associated to the highest risk of complications of all routine endoscopic procedures. It is important to have a thorough understanding of the potential complications and the adverse events that may be associated to ERCP procedures so that these may be managed appropriately should they occur. The aim of this study was to examine the trends in ERCP usage here in the Veneto Region (Northeastern Italian area) and, in particular, the complications and mortality rate associated to it.

Aims & Methods: Utilizing an anonymous database of hospital discharge records referring to the period between 2007 and 2015, a retrospective study was carried out to examine the complications associated to ERCP. All of the elective hospitalizations for gallstones in the bile duct during which the procedure was carried out within two days of being hospitalized were examined. Hospitalizations for neoplasms were not considered. The study considered the onset of complications or death as outcome indicators as well as the patients status at the time of hospitalization. All hospitalizations were divided and no differences linked to their characteristics. The stratification of complications according to the type of hospital (rural vs urban) did not show any significant differences.

Conclusion: Study findings uncovered that pancreatitis was the most common post-procedural ERCP complication in the patients studied; the total complication rate was in line with that reported in the literature. That result and the fact that no correlation was found between the type and percent of complications and the type of hospital can be attributed to the effective regional hospital organization characterized by a capillary network of specialists capable of performing complex endoscopic procedures throughout the region limiting the need of transfer patients from one hospital to another.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1538 EFFECT OF OBESITY, DYSLIPIDEMIA AND DIABETES MELLITUS ON THE RISK OF POST-ERCPC PANCREATITIS

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Introduction: Risk factors for post-endoscopic retrograde cholangiopancreato-gramy pancreatitis (PEP) have been widely investigated. Nevertheless, studies focusing in metabolic conditions especially obesity, dyslipidemia and diabetes mellitus (DM) are still limited in number.

Aims & Methods: The aim of our study was to evaluate the effect of these factors on the frequency of PEP. We retrospectively analyzed all ERCP performed over a 12 months period [January 2015 - December 2015] and carried out at the gastroenterology unit of our hospital. All patients were evaluated prospectively for the frequency of PEP based on the consensus criteria.

The patients with obesity (Body mass index BMI ≥ 30 kg/m²), dyslipidemia (triglyceride > 2 g/L or LDL-cholesterol ≥ 1.6 g/L) and DM (history of DM or fasting glucose level
**P1539** PLACE OF ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY (ERCP) IN THE MANAGEMENT OF HEPATIC HYDATID DISEASE


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**Introduction:** Hepatic hydatid disease (HHD) is a major endemic health problem in certain areas of the world such as Tunisia. Intrabiliary rupture of a hepatic hydatid cyst is a common complication ranging between 3 and 17%. Furthermore, biliary stenage is the most frequent postoperative complication following surgery for hydatid cysts of liver. Both conditions require percutaneous biliary drainage. One patient presented post ERCP pancreatitis (1.5%).

**Aims & Methods:** The aim of this study was to assess the results of ERCP in patients presenting with HHD. We retrospectively analyzed the results and complications of all ERCP performed for HHD whether before or after surgical treatment over a 10 years period (January 2007 - December 2016) and carried out at the gastroenterology unit of our hospital.

**Results:** Sixty seven procedures were included (mean age 40.4 years [15-82] and sex ratio male/female [31:36]). Of the 67 procedures, 58 (86.6%) were performed in patients who had undergone previous surgery. The indications of the ERCP were persistent external biliary fistula in 77.6%, obstructive obstruction or cholangitis due to residual materials within bile duct in 20.7% and secondary biliary strictures in 1.7%. In patients who had not undergone previous surgery (13.4%), the indications of the ERCP were cholangitis due to intra-biliary rupture of hydatid cyst in 44.4% associated with acute pancreatitis in 55.6%. The cannulation of the papilla was impossible in 6 cases (8.9%) and the endoscopic sphincterotomy (ES) could not be performed. When papilla cannulation was obtained, per endoscopic cholangiographic findings were: dilation of the biliary tract (21.3%) with filling defects of varying size and shapes (52.3%), leakage of contrast medium into the cavity (41%) and juxta ductal stenoses (3.3%). ES was then performed in all cases with satisfactory results. Thus, hydatid membranes (36%) or daughter cysts (1.6%) encountered in bile ducts have been emptied out in 93.4% by biliary occlusion balloon and/or Dormia basket. Nevertheless, two patients required biliary stenting due to the bile duct stricture, and two others required nasobiliary drainage. One patient presented post ERCP pancreatitis (1.5%).

**Conclusion:** ERCP is a safe and effective way to manage biliary complications of HHD. In most patients, ES is the most efficient treatment of postoperative external biliary fistulas, jaundice and accompanying cholangitis. In some cases, biliary stenting or nasobiliary drainage may be required.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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**P1540** QUALITY INDICATORS AND POST OPERATIVE OUTCOME OF ERCP PERFORMED IN A LOW RESOURCE SETTING; CAN QUALITY INDICATORS FROM DEVELOPED SETTIMGES BE ADOPTED?

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**Introduction:** Endoscopic Retrograde Cholangiopancreatography (ERCP) is a complex and invasive procedure. Quality control and monitoring for complications is an important part of ensuring patient safety. Gastroenterology and Hepatology unit of the National Hospital of Sri Lanka performs the most number and variety of ERCP procedures in Sri Lanka. Although facilities are limited, detailed patient records and logs were maintained since commencement of ERCP procedures in this unit.

**Aims & Methods:** A retrospective analysis was carried out on quality indicators and complications of the ERCP procedures performed in this unit since 2006. Data from written records were entered into an electronic database and analysis was done using STATA version 13. Quality indicators and standards published by the American Society of Gastrointestinal Endoscopy and American College of Gastroenterology in 2015 were used.

**Results:** A total of 3780 ERCP procedures were performed. Females consisted of 54% of the patients (n = 2041). Mean age in years was 57.6 (SD = 8.4). Male patients were older with a mean age of 61.2 years whereas the mean age of females was 54.6 years (p < 0.05). Cholelithiasis was the commonest indication (85%) and 68% out of these patients had active cholangitis at the time of the procedure. Chronic pancreatitis, benign and malignant strictures requiring stenting, postoperative bile duct damage the other common indications. Data were not made available on 19 out of the 24 quality indicators. A total of 15 quality standards were met (7/9 pre procedure, 4/5 intra procedure and 4/10 post procedure).

Major prevalent major complications were Post ERCP Pancreatitis (PEP) and post ERCP Cholangitis (PCE) complicating 2.22% and 4.78% procedures respectively. Mortality was less than 0.1% (n = 3). Cardiovascular complications and complications of anesthesia were seen in 16 patients (0.41%) resulting in one mortality. These were significantly associated with older age and the total number of medical comorbidities the patients had (p < 0.05). Deficiency practices were noted mostly in the role of these conditions in larger prospective studies since the expanded prevalence of metabolic syndrome in general population.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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**P1541** USE OF MICROCATHETERS IN ECHOENDOSCOPY-GUIDED BILIOPANCREATIC RENDEZ-VOUS–INITIAL EXPERIENCE


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**Introduction:** EUS-guided biliary or pancreatic rendezvous is a technically demanding procedure, and the intraduodenal manipulation of the guidewire remains the most challenging step. Passing the guidewire through the needle may cause its fragmentation on the sharp metallic bevel. We have described the method of using a microcatheter for EUS-guided rendezvous, which allows easier handling and exchange of the guidewire, while avoiding both the risk of fragmentation and the need of injection of contrast to achieve a complete ductogram. 

**Aims & Methods:** We aimed to evaluate the early experience of the microcatheter method in EUS-guided rendezvous procedures in the biliary and pancreatic ducts. During EUS-guided biliary or pancreatic rendezvous, initial puncture of the duct of interest was attempted with a 19G needle without stilet to...
Previously flushed with contrast. A 0.025” guidewire was then inserted through the needle, followed by duodenal advancement antegrade to the papilla. If further manipulation was necessary to enter the duodenum, movements were performed with caution in order to avoid fragmentation of the guidewire. Whenever the passage through the papilla was not achieved or the guidewire movements were hazardous, we performed a microcatheter technique. After removing the needle, leaving the guidewire in situ, a 3F, 150 cm long microcath- eter was inserted over the guidewire into the duct. Then, manipulation of the guidewire, guidewire exchange and contrast injection were performed according to the discretion of the endoscopist. We reviewed the cases of EUS-guided pancreatic or biliary rendezvous performed in our unit using microcatheters from September 2015 to March 2017. Technical success was considered when the rendezvous could be completed.

Results: Nine patients presented with previous unsuccessful manipulation of the guidewire with the needle during EUS-guided biliary or pancreatic rendezvous underwent a microcatheter-guided attempt on the same procedure. Pancreatic rendezvous was attempted in 3 cases (2 chronic pancreatitis, 2 pancreas divisum and 1 pancreatic cancer) and biliary rendezvous in the other 4 (3 biliary stenosis and 1 ampul- loma). Technical success was achieved in 7 patients (78%) with the microcatheter technique. Technical failure occurred in 1 patient with biliary stenosis in whom a EUS-guided hepatico-gastrostomy was performed in the same procedure and in 1 patient with chronic pancreatitis with symptomatic pancreatic duct stent insertion. There were no adverse events after the procedure, irrespective of technical success.

Conclusion: In our series, using a microcatheter for the indractural manipulation of the guidewire increases the EUS-guided rendezvous technical success without increasing the complication rate, irrespective of technical success.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

P1543 RESULTS OF THE FRENCH NATIONAL OBSERVATIONAL STUDY CONCERNING THE PRACTICE OF GUIDANCE-BASED CONFOCAL ENDOMICROSCOPY (CELLVIZIO®)
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Introduction: Confocal endomicroscopy is an endoscopic imaging technique permitting the microscopic analysis of the digestive mucosa in real time (oesophagus, stomach, duodenum, colon, biliary tract and pancreas) due to injection of fluorescein which is an intravenous contrast. The aim of this national observational study under the guard of SFED is to evaluate the practice of confocal endomicroscopy in France, specifically its indication, histologic correlation, therapeutic benefits depending on the operator and complications.

Aims & Methods: We executed a multicentric observational prospective study from September 2013 to February 2015. Collection of data was based on a structured data collection sheet. All patients were treated on performing confocal endomicroscopy. The intravenous injection of fluorescein was given either in bolus or in a perfusion method at a dilution of 1 or 10%. Demographic, clinical, endoscopic and endomicroscopic data were collected. For each act the correlation between the confocal endomicroscopy and histology and the outcome of the ECM depending on the operator was reported.

Results: In total 399 procedures of confocal endomicroscopy were done on 399 patients (median age was 39 +/- 14.5, males were 52%) and these were performed in 12 centers. The main indications were: diagnosis and monitoring of Barrett esophagus 28% (111/399), surveillance of gastritis 4% (16/399), characterization of polyp and searching for dysplasia in IBD patients 17% (68/399), undefined biliary stenosis 11% (42/399), pancreatic cysts 30% (123/ 399), undefined rare cases (lymphodes characterization, pancreas polyp, cholestasis with inflammation, GIST, celiac disease, control post mucosectomy of gastric and duodenal polyp) 10% (39/399). The quality of imaging was good in 83% of cases (331/ 399), average in 16% (64/399) and poor in 1% (6/399). The correlation with histology was measured by using Cohen’s kappao coefficient. The results were respectively k = 0.9, 0.78, 0.82, 0.7, 0.94, 0.93 for Barrett’s esophagus, gastritis, IBD, colorectal polyps, undefined biliary stenosis and pancreatic cysts. The outcome of the procedure according to the operator was beneficial for three main indications: Barrett’s esophagus, small intestinal polyp and uncertain pancreatic cysts (100% of cases), and undefined biliary stenosis (90% of cases and especially for real time therapeutic decision). One major side effect was seen during the study, which was an anaphylactic choc after a bolus injection of 2.5cc of fluorescein in a 69y old patient who didn’t have any previous history of allergies. This patient was hospitalized for surveillance for three days.

Conclusion: In conclusion, confocal endomicroscopy is an in vivo microscopic examination that is easily performed throughout the digestive tube with a good histologic correlation especially for Barrett’s esophagus, undefined biliary stenosis and pancreatic cysts. Its importance in the management of patients remains to be evaluated with the advent of new endoscopic magnification techniques.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1542 ERCP AND PTCD IN BILIARY TRACT COMPLICATIONS AFTER LIVER TRANSPLANTATION: PREDICTORS OF LONG-TERM OUTCOME
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Introduction: Biliary tract complications (BTC) are the leading problem in patients after orthotopic liver transplantation (LT). The present study analysed the results and predictors of treatment outcomes in patients with biliary stenoses undergoing endoscopic retrograde cholangiopancreatography (ERCP) and/or percutaneous cholangiodrainage (PTCD) at the University Medical Centre Hamburg-Eppendorf.

Aims & Methods: All adult patients who received ERCP or PTCD for BTC after LT between 2009 and 2015 were retrospectively analysed. Remission of BTC was defined as no need of intervention for at least 12 months. To identify predictors of endoscopic treatment outcome in patients with biliary stenoses, a multivariate logistic regression analysis was performed after univariate variable selection. Laboratory parameters that were significant in the multivariate analysis, were dichotomised stepwise according to the most informative cut-off predicting outcome. Furthermore, endoscopic techniques were analysed in both the ERCP- and PTCD-subgroup.

Results: Of 144 patients with BTC after LT, 116 were diagnosed with biliary stenoses. Among these, 86 received ERCP, 17 PTCD and 13 both techniques. Long-term remission was achieved in 55 patients (47% overall; 53% in ERCP alone and 30% when PTCD was applied). Patients with non-anastomotic strictures (NAS) (odds ratio [OR] 0.25, 95% confidence interval [CI] 0.1-0.57; p = 0.001), requirement of PTCD (OR 0.30, 95% CI 0.10-0.79; p = 0.018) and higher pre-interventional serum-bilirubin levels (OR 0.88, 95% CI 0.76-0.98; p = 0.037) were less likely to achieve remission. The most informative bilirubin cut-off to predict the outcome was 5 mg/dl. This cut-off maintained a significant association with outcome in the multivariable model (OR 0.30, 95% CI 0.08-0.95; p = 0.049). In the ERCP-subgroup, dilatation with a higher maximal balloon-dia- meter was associated with a favourable outcome (p = 0.043).

Conclusion: Both ERCP and PTCD can provide long-term benefit in patients with BTC after LT. However, patients with NAS and requirement of PTCD had less favourable outcomes. The pre-interventional bilirubin level could be a valuable parameter to identify patients at risk of treatment failure. Larger ERCP balloon dilatation techniques.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1541 ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY IN PATIENTS WITH SURGICALLY MODIFIED GASTRO-ENTERIC-BILIARY ANATOMY: RESULTS FROM A TERTIARY CENTER
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Introduction: Endoscopic retrograde cholangiopancreatography (ERCP) represents a crucial procedure in the management of biliopancreatic pathology. However, its performance in patients with surgically modified gastro-enteric-biliary anatomy (SMGA) is a challenging issue.

Aims & Methods: We aimed to evaluate the efficacy of this advanced endoscopic technique in patients with SMGA. This was a retrospective observational cohort study of all patients with surgical modification of biliopancreatic access undergone ERCP, between 01/2002 and 02/2017. Demographic variables, indications, the breakdown of surgical procedures and technical success rate were evaluated as well as potential predictive factors of therapeutic efficacy rate. Compared patients with successful technique(G1) and therapeutic failure by ERCP...
P1548 ASSOCIATION BETWEEN PREDICTIVE FACTORS AND RADIATION EXPOSURE DURING ENDOSCOPIC RETROGRADE CHOLANGIPANCREATOGRAPHY
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Introduction: Endoscopic retrograde cholangiopancreatography (ERCP) relies on the use of ionizing radiation in the form of fluoroscopy. Because use of fluoroscopy has positive relationship with radiation exposure, it makes a risk of the development of cancer and other radiation toxicity. The increasing exposure of patients and endoscopists to radiation is concerning.

Aims & Methods: The aim of our study was to evaluate of predictive factors of radiation exposure to the patients and endoscopists during ERCP. We measured the radiation exposure of patients and endoscopists during procedure as determined by radiation dose in dose area product (DAP), absorbed dose (AD) and fluoroscopy time. And we correlated them with age, sex, body mass index, diagnosis, duration of procedure, procedure name and procedure complexity.

Results: As a result of analysis of the 892 ERCPs performed during 4 years, the mean duration of fluoroscopy time was 5.52 mins (95% CI, 5.15–5.93). Mean radiation duration were as follows: CBD stones (n= 511, 5.76 mins); malignant stenosis of bile duct (n = 189, 5.78 mins); pancreatic disease (n = 95, 5.28 mins); benign stenosis of bile duct (n = 51, 5.52 mins); and peripapillary stenosis (n = 138, 5.26 mins). Multivariate analysis revealed that prolonged duration of fluoroscopy time was related with specific factors of patient included age, BMI, diagnosis and procedure complexity (all p < 0.05). Among the parameters, procedure complexity was the most significant relation with radiation dose. In addition, we compared the following three procedure by procedure duration; two more procedures performed during ERCP and mechanical lithotripsy (all p < 0.05).

Conclusion: ERCPs are associated with significantly higher radiation exposure to patients and endoscopists to the specific procedure type. Increased radiation exposure is the aware of increased dose of radiation required when performing ERCP in patients with increased BMI, old age, and who need two more ERCP procedure.

Disclosure of Interest: All authors have declared no conflicts of interest.

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Introduction: Double-balloon enteroscopy-assisted endoscopic retrograde cholangiopancreatography or DBE-ERCP allows access to the biliary ducts of patients with surgically altered upper gastrointestinal anatomy. We studied the feasibility and efficacy of DBE-ERCP at our institution.

Aims & Methods: This is a retrospective study of all patients with surgically altered GI anatomy who underwent DBE-ERCP at our institution between February 2011 and March 2017. The primary endpoint was the global success rate of DBE-ERCP. The secondary endpoints were (1) the success rate of enteroscopy defined as reaching the desired postsurgical anatomic target, (2) the diagnostic success rate defined as successful cannulation of the native papilla or
anastomosis, and (3) the therapeutic success rate. We used a 2.2 m DBE with a 2.1 cm 2.2 mm of operating channel (EN-450 75, or EN580TU Fujinon inc Saitama Japan).

Results: A total of 12 patients (sex ratio 1/1) with a mean age of 65 [47–82] underwent 14 DBE-ERCP. 7 patients had Roux-en-Y gastro-jejunostomy with a bile-jejunostomy, 4 patients had Roux-en-Y with a native papilla, and 1 patient had a Billroth II gastric bypass. Enteroscopy success rate was 93% (13/ 14 procedures). The diagnostic success rate was 85% (11/13 procedures) with 4/5 of native papillae. Therapeutic interventions including sphincterotomy (n = 4), biliary stone extraction (n = 4) and biliary dilation (n = 2) were needed in 8/11 procedures and their success rate was 100%. The global success rate of DBE- ERCP was 78% (11/14 procedures). Our results were comparable to those of the literature (global success rate of 82%). The only complication was one case of superficial intestinal lacerations without perforation (complication rate 7%).

Conclusion: DBE-ERCP in patients with surgically altered upper GI anatomy is a safe and efficient procedure with a global success rate of 78%. Using shorter enteroscopes with wider operating channel in the future might improve the success rate of the technique.

Disclosure of Interest: All authors have declared no conflicts of interest.

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P1550 TRANSPANCREATIC SPHINCTEROTOMY: A VALUABLE TECHNIQUE FOR GAINING CBD ACCESS

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Introduction: Transpancreatic Sphincterotomy (TPS) involves wire-guided can-
nulation of the main pancreatic duct (MPD) followed by standard pull-type
spingertome cutting towards the main channel. Typically a MPD stent inser-
tion should follow TPS to prevent post-ERCP pancreatitis (PEP). ESGE [1] recommends that in patients with a small papilla that is difficult to cannulate, TPS should be considered if additional wire-guided MPD cannulation succeeds. A previous study had suggested that TPS might be as effective as double guide wire (DGW) technique in achieving biliary cannulation in difficult cases and has a lower risk of pancreatitis [1].

Aims & Methods: The main objective of this study was to review the practice, complications and outcomes of TPS in University of North Tees hospital (district general hospital in the north-east of UK). All ERCP procedures between January 2014 and October 2016 were reviewed. Endoscopy reports, blood results and discharge letters were used for data collection.

Results: 1365 ERCP procedures were performed in the study period. Overall CBD cannulation rate was 91.3%, 105/1365 (7.7%) wire guided TPS procedures were required. Mean age in the TPS group was 67 years (range 18-91) 65/105 (61%) male and 41/105 (39%) females. 3 senior consultants and a senior endo-
copic fellow performed TPS. TPS was used as the initial strategy in the event of MPD cannulation and without using alternative methods such as DGW.

Choledocholithiasis was the most common ERCP indication in TPS group (58/ 105). Other indications include pancreatic cancer, biliary stricture, choIanocarcinoma and bile leak post cholecystectomy. CBD cannulation was achieved in 96/ 105 (90.5%) of cases - 81/105 (77.1%) during the first ERCP and 15/105 (14.2%) at second ERCP [where CBD cannulation was achieved at second attempt, TPS had been done at the first ERCP]. In 9/105 patients CBD cannulation was not achieved. 8/105 (7.6%) had a complication. 6/105 (5.7%) patients had PEP - 5/6 had a prophylactic MPD stent. 1/105 had a post sphincterotomy bleed which was controlled with endoscopic therapy. 1/105 had a perforation and a subsequent long hospital stay. There were no procedure-related deaths.

Conclusion: This study demonstrates that TPS is a safe and effective way of gaining CBD access. Our data suggests that experienced operators in a DGH setting can safely carry out TPS. Our study is the second largest cohort in the literature and the largest cohort in the UK. We would suggest early adoption of TPS if wire access to the pancreatic duct is achieved, this will likely reduce complication rate as a result of less engagement with the papilla and overall reduced time at CBD cannulation.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference
was performed using SPSS version 20.0. A P-value of less than 0.05 was considered statistically significant.

**Results:** We included 1976 patients who presented choledocholithiasis and underwent different endoscopic extraction techniques. Mean diameter of stones (extracted using only the basket (Group A) was 6.8 mm with a mean CBD diameter of 14.3 mm (mean CBD diameter) for patients treated eventually by surgery (P < 0.001). Only 3.2% of cases had to be referred to surgery. Stones removed using only a retrieval balloon (Group B) was for a mean stone diameter of 7.6 mm with a mean CBD diameter of 13.3 mm. By associating the basket with a retrieval balloon (Group 4) we obtained a 100% success rate of endoscopic removal for a mean stone diameter of 9.6 mm with a mean CBD diameter of 12.9 mm. We also analyzed the parameters of patients who underwent endoscopic extraction by using a retrieval balloon combined with balloon dilator (Group 5). The success rate in this group was 90% for a mean stone diameter of 14.8 mm with a mean CBD diameter of 12.4 mm. In Group 6 we included cases which required combined techniques (n = 3). We observed a mean stone diameter of 9.4 mm with a mean CBD diameter of 13.8 mm in patients solved endoscopically, compared to those referred to surgery who had a mean stone diameter of 14.2 mm with a mean CBD diameter of 14.3 mm (P < 0.001). In this group the success rate was 67.2%. Overall, we had a success rate of 91.3% for endoscopic removal of choledocholithiasis with a mean stone diameter of 7.1 mm and a mean CBD diameter of 12.1 mm, compared to 3.8% of cases referred to surgery with a mean stone diameter of 13.6 mm and a mean CBD diameter of 14.3 mm (P < 0.001).

**Conclusion:** The most successful endoscopic method to remove large stones >15 mm was balloon dilator combined with retrieval balloon. Intermediate sized stones (<7 mm) were successfully removed by using retrieval balloon or lithotriptor or a combination of basket with retrieval balloon ± balloon dilator. Most CBD stones <7 mm were successfully removed by using basket. In conclusion, any diameter >7 mm will most probably require more elaborate techniques.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**References**


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**P1552 DICLOFENAC AND INDOMETHACIN IN THE PREVENTION OF POST-ERCP PANCREATITIS: A SYSTEMATIC REVIEW AND META-ANALYSIS OF PROSPECTIVE CONTROLLED TRIALS**

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**Introduction:** Diclofenac and indomethacin are the most studied drugs for preventing post-ERCP pancreatitis (PEP), but their use is controversial.

**Aims & Methods:** Our aim was to evaluate all trials published in full text and studied efficacy of diclofenac or indomethacin prospective controlled with placebo or non-treatment for the prevention of PEP in adult patients undergoing ERCP. Systematic search of databases (PubMed, Scopus, Web of Science, Cochrane Database) was performed. Relevant data were published from inception to 30 June 2016.

**Results:** Our meta-analysis of 4741 patients from 17 trials showed that diclofenac or indomethacin significantly decreased the risk ratio (RR) of PEP to 0.60 (95% CI 0.46–0.78, P < 0.001). Only 3.2% of cases had to be referred to surgery. Stones removed using only a retrieval balloon (Group B) was for a mean stone diameter of 7.6 mm with a mean CBD diameter of 13.3 mm. By associating the basket with a retrieval balloon (Group 4) we obtained a 100% success rate of endoscopic removal for a mean stone diameter of 9.6 mm with a mean CBD diameter of 12.9 mm. We also analyzed the parameters of patients who underwent endoscopic extraction by using a retrieval balloon combined with balloon dilator (Group 5). The success rate in this group was 90% for a mean stone diameter of 14.8 mm with a mean CBD diameter of 12.4 mm. In Group 6 we included cases which required combined techniques (n = 3). We observed a mean stone diameter of 9.4 mm with a mean CBD diameter of 13.8 mm in patients solved endoscopically, compared to those referred to surgery who had a mean stone diameter of 14.2 mm with a mean CBD diameter of 14.3 mm (P < 0.001). In this group the success rate was 67.2%. Overall, we had a success rate of 91.3% for endoscopic removal of choledocholithiasis with a mean stone diameter of 7.1 mm and a mean CBD diameter of 12.1 mm, compared to 3.8% of cases referred to surgery with a mean stone diameter of 13.6 mm and a mean CBD diameter of 14.3 mm (P < 0.001).

**Conclusion:** The most successful endoscopic method to remove large stones >15 mm was balloon dilator combined with retrieval balloon. Intermediate sized stones (<7 mm) were successfully removed by using retrieval balloon or lithotriptor or a combination of basket with retrieval balloon ± balloon dilator. Most CBD stones <7 mm were successfully removed by using basket. In conclusion, any diameter >7 mm will most probably require more elaborate techniques.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**References**


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**P1555 RECTAL DICLOFENAC AND PANCREATITIS AFTER ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY**

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**Introduction:** Rectal diclofenac or indomethacin reduces the risk of pancreatitis after endoscopic retrograde cholangiopancreatography (ERCP). Most studies of its efficacy included high-risk cohorts and excluded low-risk patients. We investigated the potential of rectal diclofenac to prevent post-ERCP pancreatitis (PEP) in a variety of patients.

**Aims & Methods:** A cohort of 1534 ERCPs performed at the Hospital Clínico de Valladolid between 2009 and July 2016 was collected. The median age of the patients was 75 years old (between 12 and 102 years). 54% were male and 45.9% female. There were 93 procedures in which cannulation of the desired pathway was not achieved but the papilla had been manipulated so they are patients who were not included in the study. A total of 25 ERCPs (1.64%) were successfully performed but not treated with diclofenac or indomethacin. The endoscopic retrograde cholangiopancreatography pancreatitis depends on difficulties of cannulation. Results from a randomized study with sequential binary intubation. *J Clin Gastroenterol* 2015


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**Results:** Two groups were similar in age, sex, suspicion of Oddi sphincter dysfunction, recurrent acute pancreatitis, chronic pancreatitis, cannulation time, use of cut-off, previous PEP, dilation without sphincterotomy. There were differences in the number of sphincterotomies in which it was greater in the Diclofenac group (p=0.004). There was also a greater number of Wirsung cannula in the group treated with Diclofenac (p=0.004). There were a total of 47 PEP (3.1%), being 78.3% mild and 21.7% moderate pancreatitis. Taken as a whole the patients had no difference in the number of PEP between the two groups, since in those treated with Diclofenac there was 3.4% and in the non-treated patients 2.8%. Taking into account only patients with de novo sphincterotomy, there was no difference between the number of PEP between the two groups being 4.4% in those treated with Diclofenac versus 4% in the untreated patients. In those patients who were cannulated Wirsung, an incidence of PEP of 8.2% was observed in the group treated with Diclofenac, compared to 0% in the placebo group (p=0.006). There were no differences between those treated with Wirsung’s prosthesis and those not treated in both groups. There was no PEP in patients treated with pancreatic prosthesis.

There was a higher incidence of PEP in women in both groups and a trend towards greater number of PEP among those treated with Diclofenac, although without statistical significance. There was also a greater number of PEP in patients under 40 years of age treated with Diclofenac compared to those not treated with 14.3% versus 7.1% (p=0.024). No differences were found between the groups treated and not treated with Diclofenac when crossing with sphincter dysfunction of Oddi, previous PEP, number and sizes of choledocholithiasis and sizes with the appearance of PEP.
Conclusion: In this retrospective cohort study of patients undergoing ERCP that included low-risk patients, rectal diclofenac was not associated with a significant decrease in the absolute rate of pancreatitis. In our study, diclofenac decreases the impact of PEP in those patients who are cannulated the pancreas.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1555 A PILOT STUDY OF PROBE-BASED CONFOCAL LASER ENDOMICROSCOPY FOR COMPUTER-AIDED DIAGNOSIS OF BILE DUCT CANCER USING THE DEEP LEARNING TECHNOLOGY

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Introduction: The confocal laser endomicroscopy (CLE) is of two types, an endoscope-based CLE (eCLE), which is integrated in the tip of the endoscope, and a probe-based CLE (pCLE), which goes through the accessory channel of the endoscope. The biliary tract, which cannot be reached by using eCLE, is observable with pCLE by using cholangiopercopy. pCLE has the advantage of obtaining a magnification image that is like taking a biopsy tissue specimen but noninvasively, without the interference of bleeding and mucous secretion. However, it is sometimes difficult because only few gastroenterologists can achieve the required level of diagnostic accuracy.

Aims & Methods: We developed a computer-aided diagnosis (CAD) system based on pCLE imaging using deep learning technology. The purpose of this study was to determine the usefulness of this CAD system for the diagnosis of bile duct cancer. We prepared the classifier of the extracted features of the bile duct cancer pCLE images by using the deep learning framework presented by Kyocera communication system Co. Ltd. Japan. The pCLE images by Cellvisio (Mauna Kea Technologies, France) were obtained through the SpyGlass DS (Boston Scientific Corporation, USA) imaging system. pCLE images were compared with histological examination results from the surgical specimen and biopsy using SpyBiTE (Boston Scientific Corporation, USA). Learning sets were constructed by using 49 images of normal area and 23 images of cancer lesion. The test sets of the pCLE images were constructed using 6 images of normal area and 14 images of cancer lesion separately from the learning set.

Results: The accuracy, sensitivity for cancer diagnosis, specificity, negative-predictive value, positive-predictive value of our CAD system by test set were 72.0%, 93.0%, 98.6%, and 100%, respectively. The false-negative diagnostic errors reduced the sensitivity and negative-predictive value. The images of 6 false-negative diagnoses, indicating a 1.0 probability, did not show signs of cancer at all. A constant diagnosis was possible while being extremely small lesions. The specificity and positive-predictive value were good, and the pCLE image was thought to have a characteristic suitable for CAD by using deep learning technology. However, many false-negative diagnoses with a probability 1.0 may have occurred owing to deflection and the lack of learning sets. To improve the accuracy, the learning set of set of adenocarcinoma was expanded.

Conclusion: Automation diagnosis of bile duct cancer can be achieved by using the deep learning technology of pCLE imaging. Our CAD system will be improved with the appropriate learning sets.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1556 COMPARISON OF EUS-GUIDED FINE NEEDLE BIOPSY TECHNIQUES FOR CORE TISSUE ACQUISITION AND DIAGNOSTIC PERFORMANCES IN PANCREATIC SOLID LESIONS

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Introduction: Acquisition of core tissue in endoscopic ultrasound-guided tissue sampling (EUS-TS) is necessary for histologic diagnosis and immunohistochemical staining in the diagnosis of some solid mass lesions. Although recent studies revealed the superiority of core biopsy needle in the specimen adequacy, core recovery still remains that which EUS-TS technique would result in better acquisition of core tissue and diagnostic accuracy.

Aims & Methods: The aim of our study was to evaluate EUS-TS techniques with a ProCore needle using suction and slow pull suction for solid pancreatic lesions with the intention of obviating any unnecessary cytoreductive potential. Patients who referred to EUS-TS for pancreatic mass were enrolled. We performed EUS-guided fine needle biopsy (EUS-FNB) using a ProCore needle (Cook Medical, Limerick, Ireland) with two needle passes and applied each pass of different techniques (suction or slow pull suction) which were randomly allocated. EUS-TS specimens were evaluated by one experienced cytopathologist who was blinded to applied techniques. The acquisition of core tissue and diagnostic performances were compared between two techniques.

Results: From Aug. 2014 to Dec. 2016, 94 patients with pancreatic mass were enrolled and 12 patients were excluded due to no final diagnosis (n = 5), cystic lesion (n = 5) and loss of follow up after EUS-TS (n = 2). Finally, 82 patients (48 males; median age, 63 years) with 164 needle passes were included without technical failure and procedure-related adverse events. The median size of the lesions was 37 mm (range, 11 to 144 mm). There were 61 pancreatic and 14 benign lesions. Overall core tissue acquisition and diagnostic accuracy was 84.8% (139/164) and 73.2% (120/164), respectively. There was no significant difference between suction and slow pull suction in the acquisition of core tissue (85.4% vs. 84.1%, p = 1.000) and diagnostic accuracy (72.0% vs. 74.4%, p = 0.860).

Conclusion: Although our study revealed no differences between EUS-TS techniques in the core tissue acquisition and diagnostic accuracy for pancreatic solid lesions, further prospective study including variable lesions and sizes of needle is needed to validate for optimal application and sequences of EUS-FNB techniques.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1560 EUS-GUIDED GALLBLADDER DRAINAGE FOR ACUTE CHOLECYSTITIS WITH A SILICONE-COVERED NITINOL SHORT FLARED ENDS STENT: A CASE SERIES

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Introduction: Gallbladder drainage, performed by EUS-guided positioning of specially designed fully covered metal stents, may be considered a valid option in patients with cholecystitis unfit for surgery. We describe the first case series of patients with diagnosis of acute cholecystitis treated conservatively using a silicone-covered nitinol stent with bilateral anchor flanges (NAGI-stent).

Aims & Methods: Our aim was to evaluate the feasibility and clinical impact of EUS-guided drainage with NAGI-stent in patients with acute cholecystitis unfit for surgery. Sixteen consecutive patients (9 males; mean age: 84 years; with diagnosis acute cholecystitis according to Tokyo guidelines criteria, not suitable for surgical approach, were conservative treated and drained with EUS-guided short flared stents positioning. The procedure was performed in 2 tertiary endoscopy units by 4 experienced endoscopists (≥ 500 EUS-FNB performed yearly), by using the NAGI-stent. Each attempt to access the gallbladder was firstly performed from the transduodenal position and resulted successful in 13 (81%) patients, whilst a transgastric approach was preferred in the remaining 3 patients. Two different approaches were performed for the EUS-guided gallbladder puncture: a) a 0.035-inch wire was advanced through a 19G-needle into the gallbladder and dilation of the access was achieved with a 1 Fr cystoenterostome; b) a 0.035-inch wire was advanced through a 10 Fr cystoenterostome directly into the gallbladder after access. At the end of the procedure, a fully covered metallic stent, 12-16 mm of diameter and 20-30 mm of length with bilateral anchor flanges (NAGI-stent) was advanced on the wire by using the fluoroscopy guide. Technical success, clinical success, adverse events, and long-term outcome were assessed.

Results: Technical success was achieved in all cases, clinical success was observed in 15 (95%) patients, whilst in 1 case the procedure failed due to stones impaction into the stent but it resolved with a new stent positioning. Symptomatic relief occurred in all patients, 1 day after the procedure in 12 (75%) cases and 2 days later in remaining 4 (25%) patients. A bleeding episode occurred in 2 (12.5%) patients, in one case such complication was intra-procedural and it was successfully stopped during the same endoscopic session, in the other case it was a delayed adverse events requiring arterial embolization but the patient died 10 days later. At follow-up, two patients died due to myocardial infarction at 2 and 6 months, one for acute renal failure after 6 months, two for pancreatic cancer at 7 months and one for cholangiocarcinoma after 5 months. In the remaining patients no cholecystitis recurrence or biliary obstruction were observed at median follow-up of 112 days (range 49–180 days).

Conclusion: Our data showed that EUS-guided gallbladder drainage with NAGI-stent is a feasible and successful option in patients with cholecystitis unfit for surgery. We describe the first case series of patients with diagnosis of acute cholecystitis treated conservatively using a silicone-covered nitinol stent with bilateral anchor flanges (NAGI-stent).

Disclosure of Interest: All authors have declared no conflicts of interest.

P1561 EFFICIENCY COMPARISON BETWEEN 22 G VERSUS 25G NEEDLES DURING ENDOCOPIC ULTRASOUND FINE NEEDLE ASPIRATION FOR SOLID PANCREATIC Masses: A SYSTEMATIC REVIEW AND META-ANALYSIS BASED ON RCTS


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P1562 OUTCOMES AND LEARNING CURVES OF EUS-GUIDED GALLBLADDER DRAINAGE WITH LUMEN APPOSING STENTS

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Introduction: Endoscopic ultrasound-guided fine needle aspiration (EUS-FNA) is considered the gold standard method for assessment solid pancreatic masses. The needles for aspiration currently available are 19G, 22G and 25G and there is no concrete evidence to prove the benefit of one against another.

Aims & Methods: We aimed to compare the efficiency in the diagnosis of solid pancreatic lesions through the EUS-FNA with 25G and 22G needles. Studies were analyzed from five databases (Medline, Scopus, Cochrane, LILACS and CINAHL), without year or language restriction, using an extensive search strategy. Only randomized trials comparing 22G and 25G needles were included. Two independent reviewers went through the literature search and the results were analyzed by fixed and random effects. The diagnostic characteristics were calculated for a 95% confidence interval.

Results: 504 studies were found in the search, of which 21 were read and then finally 10 randomized controlled studies were selected to be included in the analysis. Thus, a total of 462 patients were evaluated (233: 25G needle; 222: 22G needle). The sensitivity of the 25G needle was 93% (CI: 89–96%; 22G: 90%), and for the 22G needle was 91% (CI: 85–94%; 22G: 92%). The specificity of the 25G needle was 96% (CI: 84–99%; 22G: 94%). The positive likelihood ratio of the 25G needle was 4.57 (CI: 2.08–10.03, 22G: 4.26 (CI: 0.43–41.88, 22G: 94%). The post-test probability of the 25G needle in the study population was 96% and for the 22G needle was 91.30%. The area under the sROC curve of the 25G needle was 0.9705 and for the 22G needle 0.9795, also showing no statistically significant correlation between them (p = 0.497).

Conclusion: Based on randomized studies, this systematic review and meta-analysis did not demonstrate a significant statistical difference between the 22G and 25G needles used during EUS-FNA in the diagnosis of solid pancreatic lesions.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

Results: All 3 cadavers underwent successful EUS-guided injection of the hydrogel. Cadaver 1 received a total injection volume of 9.5cc with creation of peri-pancreatic space for the course of the tumor. Cadaver 2 received a total injection volume of 27cc with creation of peri-pancreatic space along the head and uncinate of the pancreas measuring 11.77 mm in maximal diameter. Cadaver 2 received a total injection volume of 27cc with creation of peri-pancreatic space along the head and uncinate of the pancreas measuring 11.77 mm in maximal diameter. Cadaver 2 received a total injection volume of 27cc with creation of peri-pancreatic space along the head and uncinate of the pancreas measuring 11.77 mm in maximal diameter. The hydrogel was clearly visualized during EUS with hyperchogenic echogenicity and on post-procedure CT images without any artifacts in all cases.

Conclusion: EUS-guided delivery of hydrogel is feasible and results in an increase in the peri-pancreatic space in a cadaveric model. The hydrogel is clearly visualized on EUS and CT without significant artifacts. Further studies are warranted to evaluate feasibility, effectiveness and safety in a clinical model.

Disclosure of Interest: All authors have declared no conflicts of interest.
P1564 EX-VIVO RADIOFREQUENCY ABLATION OF PORCINE LIVER: A PROSPECTIVE STUDY OF EFFICACY OF A NEW SYSTEM

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Introduction: There are few published studies about the use of a novel radio-frequency (RF) system (EUSRA RF needle; VIVA RF generator; STARmed Co Ltd, Korea). With poor standardization of the procedure in terms of ablation powers and ablation times, it results in great heterogeneity of the results.

Aims & Methods: To standardize the radiofrequency ablation (RFA) procedure using this system performing ex-vivo tests on porcine liver in order to find the best ablation power and ablation time to produce the maximum size of coagulative necrosis at histological examination. The system consists in a radiofrequency generator delivering electric energy, a 19 Gauge needle (150 cm in length with a 10 mm monopolar electrode), a peristaltic pump (to perfuse the needle with chilled saline solution, maximizing the ablation volume without tissue charring), an isolating plate and a pedal to deliver RFA. Liver samples were treated at different powers: 10, 20, 30 and 40 Watts (W); each ablation power was applied for a duration of 1, 3, 5, 7 and 15 minutes, according to Fibonacci escalation dose scheme, used in phase I studies. We studied the macroscopically: the size (millimeters) of the globular treated area and the size of the coagulative necrosis; microscopically on an ex-vivo section of the porcine pancreas. We perform a retrospective review of all EUS cases for pancreatic neoplasms showing a clear correlation (phi 0.24). The system can produce larger zones of mild cellular alterations at lower ablation powers (10 W), increasing with the increase of ablation times, which is better for future in-vivo animal studies in order to assess the evolution of these zones (evolving into fibrosis? necrosis? recovering?).

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P1565 THROMBOEMBOLIC DISEASE DIAGNOSED BY ENDOSCOPIC ULTRASOUND IN PANCREATIC CANCER: A CASE SERIES

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Introduction: Malignant associated thromboembolic disease (TED) has a complex multifactorial pathogenesis. Tumor cells activate platelets and express procoagulant factors including tissue factor and thrombin; in addition, normal host tissues may express procoagulant activity in response to the tumor. Thrombotic risk varies substantially according to cancer location and pancreatic cancer is one of the leading causes. The clinical spectrum includes migratory superficial thrombophlebitis, arterial thrombosis, deep venous thrombosis, portal vein thrombosis and disseminated intravascular coagulation (DIC) resulting in the role of endoscopic ultrasound (EUS) diagnosing TED in pancreatic cancer patients.

Aims & Methods: We perform a retrospective review of all EUS cases for pancreatic cancer in two centers and assess all TED events diagnosed.

Results: In a period of 6 months, a total of 55 EUS for pancreatic neoplasms were performed in two centers. TED was present in 5 patients (9%): 3 were male and the mean age was 70 (range, 46–81). In 1 patient the EUS indication was a large abdominal mass whose origin was not clear, in the remaining 4 the indication was the pancreatic neoplasm. In all of them was performed EUS with fine-needle aspiration (FNA). EUS identified an intraperitoneal embolism (PE) and an inferior vena cava thrombosis (IVCT) with right atrial extension: 2 (3.6%) had recently been diagnosed by computed tomography (CT) but 3 (5.4%) were not previously known. In all these, CT confirmed diagnosis.

Table 1: Demographic, clinical and ultrasonographic characteristics of the patients.

<table>
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<th>Case</th>
<th>Age (years)</th>
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<th>Neoplasms</th>
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<th>TED confirmation?</th>
<th>TED previous?</th>
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<td>Yes</td>
<td>Yes</td>
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<td>Yes</td>
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<td>Yes</td>
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<td>Yes</td>
</tr>
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</table>

Conclusion: To the best of our knowledge, this is the first case series of EUS-based TED diagnosis in pancreatic cancer patients. This series underlines importance of a systematic, station approach EUS technique, namely in the mediastinal lymph nodes regardless the clinical indication. TED is a common complication of pancreatic cancer and has major therapeutic and prognostic implications.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P1566 THE ROLE OF EARLY ENDOSCOPIC ULTRASOUND FOLLOWING TRANSABDOMINAL ULTRASOUND IN PATIENTS WITH SUSPECTED BILIARY COLIC

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Introduction: Cholecodolithiasis is the most common cause of biliary pain, leading to hospitalisation and gallbladder surgery. Patients affected by cholecodolithiasis presents an incidence of cholecodolithiasis ranging from 8% to 20%. When the suspicion of cholecodolithias is confirmed, stones should be removed by ERCP, but this operative measure is associated with high rates of adverse events as post-ERCP pancreatitis, bleeding or perforation. A correct diagnosis of cholecodolithiasis, before ERCP, is mandatory to decrease the operative risk and health care costs. Endoscopic ultrasound (EUS) has a high sensitivity and specificity in the diagnosis of CBD stones and could substitute other imaging modalities as CT-scan or MRCP, when indicated.

Aims & Methods: The aim of our study was to assess the role of early EUS (<48 hours), in patients undergoing US in emergency room for suspected biliary colic. We retrospectively evaluated all the patients arrived at first aid for suspected biliary colic (i.e. right upper quadrant pain and/or epigastric region, associated with an elevation in serum ALT, AST, GGT, ALP, or total bilirubin, but in absence of amylase or lipase elevation). All patients, irrespective of the finding at admission, were performed an EUS within 48 hours since admission. Data are presented as proportions with 95%-CI and mean±standard deviation (SD). Correlation between categorical variables was evaluated by computing the “phi” coefficient. We computed the number needed to misdiagnose, i.e. the number of patients who need to be tested in order for one to be misdiagnosed by the test, as 1/(1-diagnostic accuracy). All the analyses were run with R (Statistical Software) and with a 5% significance level.

Results: Overall, from January 2016 to December 2016, 88 patients (56% female; mean age 64 ± 17 years) were admitted to our hospital for suspected biliary colic. We retrospectively evaluated all the patients arrived at first aid for suspected biliary colic. All the analyses were run with R (Statistical Software) and with a 5% significance level. Further, we documented common bile duct (CBD) stones in 58 (65%) patients, CBD sludge in 4 (5%) subjects, whereas no cholecodolithiasis was found in 26 (30%) patients. At EUS examination CBD stones were found in 70 (80%) patients. Comparing US to EUS, we found false negative results in 16 (18%) cases and false positive findings (i.e. identifying CBD stones not documented by EUS) in 8 (9%) patients. The two diagnostic procedures showed little correlation (phi=0.289). The number of...
patients needed to be tested by US in order to provide an incorrect diagnosis was 3.7 (95% CI: 2.6–5.5).

Conclusion: US performed in the emergency room has a low diagnostic performance compared to EUS, but remains a first-step approach in patients with right upper quadrant pain and/or in epigastric region, associated with an elevation in liver enzymes. Based on the results of our study, EUS performed within 48 hours from the admission allows an immediate correct endoscopic treatment with significant sparing of unnecessary operative procedures, reducing possible related complications and costs.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P1567 BILIOPANCREATIC RADIOFREQUENCY ABLATION: COMPARISON OF THE THREE CURRENTLY AVAILABLE DEVICES IN A PIG MODEL

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Introduction: Three devices are currently available to perform radiofrequency ablation (RFA) of biliopancreatic lesions. Data from animal models are scarce.

Aims & Methods: Radiofrequency ablation was performed in four live pigs on the common bile duct and the liver parenchyma using an endobiliary probe (endHBP), on the liver and pancreatic parenchyma using an RFA catheter through an echoendoscope and biopsy needle (EUS-RFA) and using a needle-knife to perform RFA (RFA) of biliopancreatic lesions. Data from animal models are scarce.

Results: In the common bile duct, the depth of ablation ranged from 215 mm (Power = 15 W, Time = 120 s) to 330 ± 43 mm (Power = 10 W, Time = 30 s), suggesting that power is the most important parameter in this location. Conversely, depth of ablation in the liver parenchyma using the endHBP probe ranged from 947 ± 237 mm (Power = 10 W, Time = 30 s) to 1960 ± 20 mm (Power = 10W, Time = 180 s), suggesting that time is the most important parameter for RFA in the liver. The EUS RFA probe in the liver parenchyma showed a tissue necrosis increasing with the power setting used, ranging from 1903 ± 451 mm (Power = 8 W, Time = 120 s) to 2457 ± 104 mm (Power = 12W, Time = 120 s). This was not observed in the pancreatic parenchyma, where tissue damage ranged from 3108 ± 373 mm (Power = 8, Time = 120s) to 2305 ± 78 mm (Power = 12, Time = 120s). The EUSRFA ablation of the liver parenchyma resulted in tissue damage from 1573 ± 245 mm (Power = 30w, Time = 11 s) to 1545 ± 120 mm (Power = 70 W, Time = 9 s). In the pancreas, ablation depth ranged from 3616 ± 475 mm (Power = 30s, Time = 15s) to 3805 ± 446 mm (Power = 70 s, Time = 30 s).

Conclusion: Power and time of ablation have different effects on the extent of tissue necrosis in the common bile duct, the hepatic and pancreatic parenchyma, depending on the type of catheter used to perform RFA. As indications for hepatic and pancreatic ablation tend to expand, specific ablation protocols should be developed for each tumor location and device.

Disclosure of Interest: All authors have declared no conflicts of interest.

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References

P1569 A RANDOMIZED CONTROL TRIAL ASSESSING THE CONTRAST ENHANCED GUIDED FINE NEEDLE ASPIRATION IN SOLID PANCREATIC NEOPLASMS

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4SOLID PANCREATIC NEOPLASMS CONTRAST ENHANCED GUIDED FINE NEEDLE ASPIRATION IN SOLID PANCREATIC NEOPLASMS

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Introduction: The preoperative differentiation of the solid pancreatic neoplasms by endoscopic ultrasound fine needle aspiration (EUS-FNA) remains around 90% and different needles or techniques of sampling has been used for improving the results. Data about the progress in diagnosis when the contrast harmonic enhanced (CH-EUS-FNA) is used are scarcely.

Aims & Methods: We aimed to assess the role of contrast-enhanced EUS-FNA compared to standard EUS-FNA in diagnosing the solid pancreatic neoplasms. Methods: Patients from one tertiary medical center with visible solid pancreatic mass on CT scan were included. EUS-FNA(one pass) and CH-EUS-FNA (one pass) were performed randomly in each patient by using a standard 22G needles, an Olympus-Aloka equipment and Sonovue as contrast agent. Core histology was assessed separately for each pass by the same pathologist blinded from the randomization process. The final diagnosis was based on the results of EUS-FNA and surgery, or the findings after 9 months’ follow-up.

Results: The final diagnosis of 40 patients included was adenocarcinoma (n = 36), neuroendocrine tumors (n = 2), chronic pancreatitis (n = 2). The lesions were located in the head of the pancreas (60%), body (32%) and tail (8%). The diagnostic sensitivity and specificity based on core histology was 89% and 94% in the CH-EUS-FNA passes and 86% and 91% in the EUS-FNA passes and the diagnostic value was significantly better in the CH-EUS-FNA group (p = 0.0046, t-test). The visual core size was not significant for the true-positive diagnosis of malignancy.

Conclusion: In a randomized control trial, CH-EUS-FNA improved significantly the diagnostic rate of solid pancreatic neoplasms over standard EUS-FNA. These techniques are complementary, not competitive, and they can be performed in the same session, resulting the increasing of the diagnostic rate with a minimum of passes.

Disclosure of Interest: All authors have declared no conflicts of interest.
P1570 EARLY CAPSULE ENDOSCOPY PROVIDES BETTER BLEEDING LOCALIZATION VALUE IN PATIENTS PRESENTING WITH NON-HEMATEMESIS GASTROINTESTINAL BLEEDING WHEN COMPARED TO CLINICAL SYMPTOMS ALONE

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Introduction: Traditionally, clinical symptoms such as melena were used as strong predictors for an upper GI bleeding source with primary evaluation with an EGD (esophagogastroduodenoscopy). Little consideration was given to the small bowel. It has been known for decades that melena can originate from the nose to the right colon and hematocrit can originate from the proximal gut to the rectum. Thus, current endoscopic approaches have limited localization value and diagnostic yields. We hypothesize capsule endoscopy (CCE) provides better localization of bleeding when compared to clinical symptoms alone.

Methods & Study: We compared the efficacy of localizing the source of bleed in early CCE versus SOC (standard of care) tests chosen based on clinical symptoms alone. This was a prospective single center randomized trial of 73 consecutive patients presenting to the University of Massachusetts Medical Center with NHGB (melena, hematochezia/anemia, or guaiac-positive stools/anemia). Exclusion criteria included presence of pacemaker, dementia, non-English speaking, hemodynamically significant bleeding. Patients were randomized to SOC arm versus early capsule (EC) deployment. The EC group received a primary diagnostic procedure based on clinical symptoms that was dictated by the gastroenterologist on service, who was at liberty to choose the procedure sequence as they felt appropriate.

Results: Out of 73 enrolled, 71 were included. 2 patients from the initial included group were excluded (one due to technical capsule failure and one was transferred from an outside hospital). Baseline characteristics were similar and depicted in Table 1. The EC group (n = 34) had localization of presumed source of bleeding in 21 (62%) of patients at the time of the first diagnostic procedure compared to 48.4% (n = 16) in the SOC group (p = 0.02). Active bleeding or stigmata of recent bleeding at the time of the first procedure was seen in 64.7% (n = 22) of patients in the EC groups compared to only 30% (n = 6) in the SOC group (p = 0.003). However, when melena was the only bleeding symptom in the SOC (n = 26) group, EGD was the most commonly chosen primary diagnostic procedure (n = 23), but was only diagnostic 52% of the time. After complete diagnostic evaluation in the SOC group, patients presenting with gastrointestinal symptoms more often than the other diagnostic approach, since it examines much more of the GI tract than EGD and COL alone. Detection of the anatomic site of bleeding allows for better therapeutic decisions.

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All other authors have declared no conflicts of interest.

P1571 MUCOSAL HEALING RATES INDUCED BY ADALIMUMAB IN ISOLATED SMALL BOWEL CROHN'S DISEASE: PROSPECTIVE EVALUATION BY CAPSULE ENDOSCOPY

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Introduction: Detecting mucosal barrier healing (MH) of isolated small bowel Crohn’s Disease (CD) induced by anti-tumor necrosis factor alpha agents are scarce.

Aims & Methods: 1) To evaluate MH rates by capsule endoscopy (CE) in patients with isolated SB inflammation treated with adalimumab (ADA). 2) To correlate MH with clinical and biological indices of remission. This was a prospective observational, single center study. CD patients with isolated (per CE) active (CDAI > 220) SB disease, who were recommended ADA therapy by their treating physician were consecutively recruited; first CE was performed prior to commencing ADA, and the second -14-week after starting ADA. All enrolles underwent a patency capsule study to confirm patency. Disease severity was assessed by the capsule endoscopy Crohn’s Disease activity index (CECDAI) score. MH was defined as CECDAI score <3.

Results: Out of 31 patients screened, 24 were eligible, and 22 completed the study (as two patients developed an allergic reaction to ADA and were withdrawn). Females: 12 (54.5%), median disease duration: 3 years (IQR 1–7), biological evaluation: 13 patients (61%) had lesions on the SOC exam. In our study, we confirmed MH was detected in 8/22 patients (36.4%), CDAI < 150 in 11/22 patients (50%), normal- ization of CRP in 7/22 patients (31.8%), and normalization of fecal calprotectin in 8/22 patients (36.4%). Inflammatory indices significantly decreased within 14 weeks of ADA treatment compared with baseline: median CECDAI 5 (1–16) vs 10 (5–20), p = 0.001; median CDAI 150.8 (109.8–211.5) vs 256 (240.5–232.0), p < 0.001; median CRP 0.14 (0.07–0.5) vs 1.1 (0.2–1.5) mg/dl, p = 0.002; median fecal calprotectin- 83 (80–139) vs 126 (61.5–266.5), pg/gram, p = 0.014. MH detected by CE did not correlate with normalization of either CDAI <150, CECDAI <3, or fecal calprotectin lower than 250.

Conclusion: ADA induced MH in 36% of CD patients with isolated active SB disease. MH did not correlate with either clinical or biological remission. Thus, further evaluation should be performed after 52 weeks of maintenance therapy.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1572 CORRELATION BETWEEN SMALL BOWEL MRI, Faecal Calprotectin and Capsule Endoscopy in the Investigation of Inflammatory Bowel Disease

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Introduction: Capsule endoscopy (CE) is widely used to investigate the small bowel (SB). However, patients with non-bleeding gastrointestinal (GI) disease (IBD) are considered to be at higher risk for capsule retention. The ESGE recommends using dedicated cross-sectional imaging to assess SB patency in patients with known Crohn’s Disease (CD) prior to CE. Evidence suggests that a combination of SB MRI with faecal calprotectin (FC) may potentially together may be more effective in assessing SB inflammation compared to an individual modality alone. We aimed to assess the effectiveness of this approach.

Aims & Methods: Retrospective, multicentre study; consecutive patients who had undergone both SB MRI and CE within 6 months of each other were included.

Results: Out of 540 screened, 282 underwent both CE and SB MRI at 4 centres in the United Kingdom, Israel and Portugal. Indications included suspected SB inflammation (n = 81), IBD reassessment (n = 21). Overall, there were 3 incomplete CEs, but no case of SB capsule retention. Of 82 SB MRIs, 4 patients had evidence of SB obstruction, 10 had SB thickening and/or inflammation, 3 had other findings (SB pneumatisos, polyps). 64/82 cases were normal and 1 study had poor quality, precluding any conclusion. Of the 4 cases with SB inflammation on MRI, 2 had SB inflammation on CE. Of the 10 patients with SB thickening and/or inflammation seen on MRI, 6 had corresponding CE findings; in particular, there were 2 cases with strictures on CE and 4 cases with mucosal inflammatory changes. 64 patients had normal SB MRI and 35 (54.7%) had a normal CE. 18/64 (28.1%) patients had mucosal inflammatory changes on CE; 2 of them had strictures which were eventually traversed by the capsule. 10 patients had other non-inflammation findings on CE. Of 18 patients with normal SB MRI, 10 had a raised FC (> 150 μg/g). 5 had borderline FC levels (50–100 μg/g). None of the patients in this group had normal FC levels; the mean FC was 637.5 ± 844.4 μg/g. In the group of patients with both normal SB MRI and CE, 16/35 had raised FC, 7 patients had borderline FC levels. The overall mean FC for the 5 patients with normal SB MRI was 266 ± 229 μg/g. The mean FC between patients with SB inflammation seen on CE and patients with normal SB MRI and CE was significantly different (p = 0.04).

Conclusion: A significant proportion (28.1%) of patients with normal SB MRI to investigate possible SB inflammation had CE findings showing SB inflammation, including 2 patients with strictures. However, no retention occurred in this group. Raised FC was significantly associated with CE findings despite normal SB MRI.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P1573 HOW MANY CAPSULE ENDOSCOPY STUDIES CAN BE READ IN A GIVEN SESSION BEFORE ACCURACY IS AFFECTED?

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Introduction: The interpretation of small bowel capsule endoscopy (SBCE) requires a high level of concentration. An abnormality may be present on just a few of the many thousands of images presented for interpretation. It is
unidentified whether fatigue affects the accuracy of SBCE reporting and how many SBCE can be read in one session.

Aims & Methods: Thirty-two participants (16 experienced SBCE readers and 16 novices) were invited to participate in this study. Each participant was asked to read 6 pre-selected SBCE studies consecutively. These studies were presented in a random order. All readings took place using the single view mode, readers were able to choose the frames per second viewed from a range of speeds. Fatigue was measured subjectively using a Likert scale and objectively using a computer-based psychomotor vigilance test. These measures were performed at prior to commencing the study and after every second capsule read. Accuracy in lesion detection was determined by comparison with a gold standard reading derived from the non-consecutive readings of two expert capsule readers. Accuracy was plotted against the order in which SBCE studies were read. The aim of this study was to determine whether fatigue influences accuracy of SBCE interpretation and how many cases can be read before accuracy declines.

Results: In keeping with existing literature, high intra-observer variability amongst the participants was observed, with experienced readers reaching kappa values of 0.51 with the gold standard and 0.08 amongst novices. As progressive SBCE studies were read the mean speed increased for both experts and novices, with a mean reduction of 10 minutes between the first and the last study read. This was associated with faster reading speeds selected in progressive studies read. Where accuracy was analysed with respect to the reading speed chosen, a negative correlation between increasing speed and accuracy was demonstrated, with 31% of lesions detected when read at 6–10 frames per second, compared to 15% when using the 22–28 speed. There was no significant change in accuracy with progressive capsule read when the group was analyzed as a whole. The accuracy of experienced readers declined after just one study read, from 38% to 27% and plateaued thereafter. Novice readers demonstrated no significant change in accuracy with the time points used tend towards improvement, perhaps indicating skills acquisition during the study.

Conclusion: The accuracy of SBCE reporting declines after one study reporting in a given period of time by expert SBCE readers. The optimal time interval between readings needs to be explored. This does not affect novice readers perhaps demonstrating skill acquisition.

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PI574 FEASIBILITY OF SAME-DAY COLON CAPSULE ENDOSCOPY (CCE) IN PATIENTS WITH INCOMPLETE COLONOSCOPY

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Introduction: Rates of incomplete colonoscopies (IC) range from 2–19%, requiring repeat procedures or radiological imaging which can often lead to diagnostic delays as well as increased inconvenience for the patient. Same-day CCE may allow one to avoid both ineffective and cost-effective mode of colonoscopy post IC.

Aims & Methods: We aimed to determine the feasibility of same-day CCE post incomplete colonoscopy. A prospective pilot study was performed without a contraindication to CCE with an IC for reasons other than poor bowel prep was offered the test following an appropriate recovery time of 1-hour post IC. Informed consent was obtained from all subjects. Upon ingestion of the capsule, the recording of IV methoclopramide was given to overcome the antimotility effects of fentanyl given during routine colonoscopy. Standard booster protocol for CCE was administered. Patient demographics, procedure indication, the number of cases can be read in one session, and patient satisfaction were recorded.

Results: To date, 40 same-day CCE have been completed. The mean age was 57 yrs (22–83 yrs) and 65% (26) were female. Indications for OC were; altered bowel habit 33% (n = 13), Iron deficiency anaemia 30% (n = 12), Inflammatory bowel Disease Assessment 15% (n = 6), PR bleeding 5% (n = 2), abdominal pain 5% (n = 2), poly surveillance 5% (n = 2), positive family history of CRC 5% (n = 2) and abnormal imaging 2% (n = 1). OC were incomplete due to excessive looping 40% (n = 16), patient intolerance 30% (n = 12) and severe diverticular disease 30% (n = 12). The mean sedation used during OC was 5 mg midazolam (range 3–10 mg) and 75 mcg of fentanyl (range 50–100 mcg). In all 84% (n = 34) of CCE were complete, however full colonic views were obtained in 94% (n = 37). Mean colonic passage time was 222 minutes and overall image quality was deemed to be excellent in 16% (n = 6), good in 31% (n = 12), adequate in 44% (n = 18) and poor in 9% (n = 4) of participants. Overall final scores were normal 25% (n = 10), polyps 38% (n = 15), inflammation 22% (n = 9), diverticular disease 25% (n = 10), adenoma 30% (n = 11), and diverticulitis 5% (n = 1). Amongst the patients who had polyps, 8 required polypectomy and the remaining 7 were put on a surveillance programme. Based on the CCE findings, 4 of the IB patients required treatment escalation. In terms of adverse events one patient reported abdominal pain during colonoscopy and one patient retained the capsule due to an inflammatory stricture.

Conclusion: CCE would appear to be feasible in the majority of patients and significantly detects colonic pathology.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

PI575 DEDICATED DIFFUSION WEIGHTED MR IMAGING FOR STAGING PERITONEAL METASTASES IN COLON CANCER: AN ACCURATE PREOPERATIVE SELECTION TOOL FOR CYTORDERUCTION SURGERY (CRS/HIPEC) CANDIDATES

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Introduction: Peritoneal carcinomatosis (PC) is a well-known mechanism of spread; it is the second-most frequent cause of death in colorectal cancer patients. However, the prognosis of PC patients has dramatically improved in recent years. Novel imaging techniques like preoperative accuracy of cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (CRS-HIPEC). 5-year survival rates of up to 50% are reported after CRS-HIPEC. Despite this survival gain, CRS-HIPEC has a considerable morbidity rate of up to 21%2. Obviously, patients with a limited life expectancy need to avoid pointless and costly aggressive surgical procedures. Hence, recognizing patients with a maximum risk-to-benefit ratio for the procedure is imperative. To select patients who could benefit from CRS-HIPEC the Peritoneal Cancer Index (PCI) is used. The PCI combines the size/portion of peritoneal tumours found out at surgery in 13 abdominal regions. Each of the 13 regions is scored for implant size on a scale of 0–3 (0 = no visible tumour implants; 1 = implants < 0.50 cm; 2 = 0.50–5.0 cm; 3 = > 5.0 cm). The PCI is the sum of the lesion scores from all 13 areas, and thus can vary between 0–39. The PCI is widely validated and is a quantitative prognostic indicator for long-term outcome. However, with this surgical staging procedure it is not always feasible to inspect all relevant peritoneal regions because of adhesions and/or tumour. So, there is a desperate need for a non-invasive imaging tool that could select those patients who will benefit from CRS-HIPEC. However, currently there is no validated imaging tool that can accurately predict the PCI.

Aims & Methods: Therefore, the aim of this study was to estimate the PCI preoperatively with diffusion weighted MRI (DW-MRI) and compare this with the PCI found at surgery to assess whether DW-MRI can be used to select CRS/HIPEC candidates. In this ongoing study twenty-four consecutively enrolled patients (April 2016–April 2017) with histologically proven peritoneal carcinomatosis from colorectal origin were included. Patients were excluded for exploratory laparoscopy and/or CRS/HIPEC and underwent preoperative dedicated DW-MRI (scanning time 30 min).

Two independent researchers prospectively determined the PCI on DW-MRI. Patients were categorized as low-risk (PCI 0–21) versus high-risk (PCI 22–39); in our center considered operable versus non-operable. Reference standard was PCI found at surgery. Furthermore, the both readers evaluated whether a R1 resection could be achieved on a 5-point scale combining PCI and other risk factors for an incomplete surgery, like invasion in hepatic hilum, mesenteric vessels, extensive pelvic invasion of liver metastases. Sensitivity and specificity of the test were calculated and receiver operating characteristic (ROC) curves were constructed. The area-under-the-curve (AUC) was calculated for each reader. Quadratic weighted kappa was used to evaluate the interobserver agreement.

Results: At surgery the mean PCI was 13.8 (range 0–34). For reader 1 the mean PCI was 13.8 (range 0–34). For reader 2 the mean PCI was 13.8 (range 0–34). For both readers evaluation the PCI was considered operable versus non-operable. Both readers categorized 23 out of 24 patients correctly (accuracy 96%) when compared to surgical findings. Both readers underestimated the same patient. The sensitivity and specificity for selecting patients with a PCI ≤ 22 was for both readers 100% and 75%, respectively. The interobserver agreement was perfect (k = 1.0). The AUC for predicting overall operability was 0.99 for reader 1 and 0.95 for reader 2.

Conclusion: These data suggest that DW-MRI is a robust and highly accurate tool to noninvasive selection of colorectal cancer patients who could benefit from CRS-HIPEC. Interestingly, no overstaging occurred with DW-MRI; this means that DW-MRI did not deprive patients from potential curative surgery. In addition, due to the lack of large studies concerning this subject, our ‘pilot study’ is one of the largest DW-MRI study in PC.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference
cases to obtain an automatic histological classification of colonic polyps. Our automatic histology prediction system is based on the segmentation of textural elements from polyp surface and their correlation with Kudo’s pit pattern classification. Textural elements are identified as bright regions in polyp surface and there are characterized according to their shape to tubular and circular: a high presence of tubular patterns is associated to an adenomatous histology whereas the absence of prominent tubular structures is associated to non-adenomatous. Taking this into account, we characterized segmented bright regions using a tubularity metric (Tub) designed to obtain low values for circular shapes and high values for tubular shapes of the ROIs. We tested our method in high definition (HD) white light polyp images which were obtained with a colonoscope Olympus C1F-H190 at Hospital Clinic in Barcelona. Neither conventional nor virtual chromoendoscopy were used. These images were selected to show as much variability in polyp appearance as possible. We used the mean of all Tub values for an image to classify it into two classes: Adenoma and Non-Adenoma. A ROC curve was constructed to select the optimal threshold value of Tub. Then, we compared the histology prediction provided by our system and the actual histology obtained after lesion removal.

Results: 51 polyp images were analyzed: 38 (74.5%) adenoma and 13 (25.5%) non-adenoma. Mean size of polyps was 14 ± 13 (range 1–40) and had the following morphology based on Paris classification: 5 (8.8%) 0-Ip, 27 (52.9%) 0-IIa and 16 (37.3%) 0-IIa. Mean Tub values were different for adenoma compared to Non-adenoma (19.5 ± 6.5 vs 14.1 ± 6.3; p = 0.013). An optimal threshold value of Tub = 13.14 to separate adenoma vs. non-adenoma was selected from the operating point of the ROC curve. With this value, our method was able to provide accurate histological diagnosis in 44 out of 51 images (86.3%) (table) with a Sensitivity, Specificity, PPV and NPV for the diagnosis of adenoma of 95%, 61%, 88% and 80%, respectively. On the other hand, processing of a single HD image took 2.7 seconds making feasible its use in the endoscopy room.

Conclusion: A computer vision system based on bright regions in the image has a high accuracy for on-line prediction of polyp histology during colonoscopy. Though the use of shape characterization is promising, the inclusion of other polyp characteristics (i.e. shape, color, vessels, . . .) as well as enlarging the validation database could improve the robustness of our methodology.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference
threshold of wall thickness for fibrosis was > 6.3 mm (specificity 100% and sensi-
tivity 89.6%). The cut-off value of ADC value was < 1.1 × 10⁻⁵ mm²/s⁻¹ with a sensitivity of 71.79% and specificity of 94.44% (AUC = 0.83).

Conclusion: The DWI sequence with ADC value can identify fibrosis in intestinal wall of COC and it is not always using the use of contrast medium.

Disclosure of Interest: All authors have declared no conflicts of interest.

### P1580 MOLECULAR IMAGING OF c-MET IN THE CLINICAL MANAGEMENT OF GASTROINTESTINAL CANCERS

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Introduction: The primary indication for c-Met targeted optical imaging agent EMI-137 is enhanced endoscopic detection of lesions during colorectal cancer screening, including flat lesions that are difficult to detect by normal white light endoscopy. We have evaluated the potential benefit of EMI-137 and analogues beyond colorectal cancer screening since c-Met is up-regulated in many other cancers.

Aims & Methods: We have synthesised analogues of EMI-137 where the fluores-
cent reporter was replaced by a radiosonde chelating moiety for PET imaging. The use of this agent alongside EMI-137 could enable the PET localization of the lesions prior to surgery guided by fluorescent signals. Through a systematic analysis of scientific literature databases, and the Human Protein Atlas, we have identified more than 13 different types of solid cancer that are amenable to PET imaging for which there is evidence for c-Met as a target. We believe that imaging of c-Met with EMI-137 in these indications has the potential to positively impact critical problems in the existing patient care path and reduce morbidity, mortality, and healthcare costs. We have assessed: 1) the healthcare problem, the impact on patient care path, and the likelihood of adoption by clinicians 2) the hardware landscape; whether imaging hardware required is commercially available or is being developed, and feedback from clinicians in the US and EU 3) our confidence in c-Met as a valid imaging target to address the healthcare problem.

Results: We have identified a number of promising applications within Digestive Oncology; gastric cancer, locally-advanced rectal cancer, and bile duct cancer surgery are all life-threatening indications with urgent healthcare problems that could be improved by utilising imaging of c-Met with EMI-137. Compatible imaging systems are commercially available for these indications. There is also strong evidence for c-Met as a biomarker in stratification in Barrett’s oesophagus (BO), a potentially precancerous lesion with the risk of progression to oesopha-
gal cancer. Progression rates are low and overall survival rates in BO patients are similar to the general population. However, due to the poor prognosis of oesophageal cancer, patients with BO lesions are managed by regular endoscopic surveillance and biopsy. This means that there is arguably a disproportionate healthcare burden related to the level of risk.

Conclusion: Gastric cancer, locally advanced rectal cancer, and bile duct cancer surgery all have strong evidence for c-Met as a valid target, and the healthcare problems are clear and widely recognized, with EMI-137 having the potential to help improve high intensive procedures in serious, life-threatening conditions. An imaging agent that enabled more accurate risk stratification of BO patients would lead to a change in patient management, with the potential to remove unnecessary biopsy and to reduce the frequency of surveillance.


### P1581 HOMEMADE FIXATION OF FULLY-COVERED SELF-EXPANDING METAL STENT

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Introduction: Esophageal self-expandable metal stents are currently used as an alternative for surgical treatment in esophageal neoplasia, benign strictures, fis-
tulas and anastomotic leaks. Migration is a common complication after stent placement and have higher rates when fully covered stents are employed. Covered stents prevent tumor ingrowth and can be removed easily, they can be used in the closure of fistulas and leaks. External fixation of the stent with Shim’s technique seems to be efficient in preventing stent migration, but has a high cost and it is not always available. Fixation by clipping or sutures has similar limitations. We developed a homemade technique for external fixation of the stent using dental floss to prevent dental stent to prevent stent migration. We present the results of this technique in a small cohort.

Aims & Methods: The present study enrolled sixteen patients with esophageal malignancies, anastomotic leaks, esophageal fistulas and extrinsic compres-
sion. The stents used in these patients were five partially covered and ten fully covered. We developed a homemade technique using dental floss for external fixation of the stent which prevent stent migration. We pull stripes of dental floss into the stent mesh and using a method similar to exchange of a nasobiliary drainage catheter, the dental floss is drawn out through the nose, tied a knot into it and its loose end is fixed to the patient’s earlobe.

Results: Upper gastrointestinal endoscopy was performed after two weeks and the proximal uncovered flange of the stent was evaluated. If it was embedding the esophageal mucosa and did not separate from the esophagus with air insuf-
flation, the external fixation was removed. Otherwise, the fixation was kept for another 2–4 weeks when a new endoscopic evaluation was performed. Patients were evaluated 15–30 days after stent placement. In cases of migration of the entire length of the stent into the stomach, the patient received a new stent and the same fixation method was employed. In cases of stents partially migrated through the cardia, the same stent was repositioned and fixed with dental floss stents as previously described.

Conclusion: According to the results we believe this homemade technique using dental floss for external fixation of stents is a simple and cheap method that can be applied and used to prevent stent migration.

Disclosure of Interest: All authors have declared no conflicts of interest.

### P1582 CLINICAL OUTCOME WHEN USING SELF EXPANDING METAL STENT IN OBSTRUCTIVE BRONCHOESOPHAGEAL CANCER IN 248 PATIENTS WITH 7 YEARS EXPERIENCE IN A TERTIARY CENTER

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Introduction: The reported incidence of colorectal cancer in Sweden in 2014 was 60-65/100,000 inhabitants and caused 25–30 deaths/100,000 [1]. Of all colorectal cancer, approximately 15–20% debutes with acute obstructive symptoms. Solid malignancy in these conditions (open surgery) have been shown to lead to mortality risk up to 20% and morbidity risk of 45–50%, followed by increased need for intensive care and more infections and stoma complications. Self-expanding Metal Stent (SEMS) for relieving malignant eosophageal obstruction is a treatment alternative for non-curative cases or for bridging the patient for later surgery. Studies have shown [2]clinical success of SEMS at 90%. An article from 2007 concludes that SEMS in acute colon obstruction has better results regarding sickness and side effects compared with acute open surgery and chemotherapy.

Aims & Methods: Our compilation covers the years 2010–16, when 248 SEMS interventions (53% men, 47% women, age 28–97) were performed at SU/Ostra Hospital. In 78% of cases, the obstruction was located below the left ilexare. In 80%, SEMS was made for palliative purposes.

Results: Technically, SEMS succeeded in 98% of cases and had clinical success in 90% of cases (absence in need of emergency surgery). Complications (colony perforation) occurred in 6% of the cases. Mortality within 30 days was 11% and within 90 days 22%. There were no 90-day deaths. There was no treatment failure with regard to 90-day mortality for the indication was palliative vs. bridging. 29 resp. 3%. Based on the clinical outcomes "success" vs "failure", the 90-day mortality rate was 19 resp. 55%.

Conclusion: Our interpretation is that SEMS is an effective method of acceptable safety regarding complications in acute malignant colon obstruction. The method is suitable for both intended intestinal relief for palliative purposes, as well as awaiting later curative measure (bridge to surgery).

Disclosure of Interest: All authors have declared no conflicts of interest.

References:

### P1583 ENDOSCOPIC TREATMENT OF ESOPHAGEAL FISTULAS

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Introduction: Tracheoesophageal fistulas are severe complications which com-
monly occur secondary to malignant tumors of the esophagus. Other causes include mediastinal or respiratory tract tumors, surgery, radiotherapy and trauma. Without treatment they often lead to pulmonary and gastroenterological complications, such as pneumonia, acute respiratory distress syndrome and poor nutrition. The purpose of this study was to assess the efficacy of endoscopic treat-
ment performed in our clinic for esophageal fistulas.

Aims & Methods: We performed a retrospective study on 43 patients admitted in our clinic between January 2015 and April 2017 for esophageal fistulas.

Results: The average age of the patients included in the study was 24 years old. The causes leading to the tracheoesophageal fistulas were the following: esophage-
al malignancy in 18 cases (41.8%), surgery in 8 cases (18.6%), respiratory tract malignancy in 6 cases (14%), gastric sleeve in 5 cases (14%), radiotherapy in 3 cases (7%) and trauma in 2 cases (4.6%). In every case, the treatment of choice was placement of fully-covered metallic stents. A number of 16 patients needed reintervention, with a mean of 2 reinterventions per patient. Regarding recurrent fistulas, endoclips were used in one case (2.3%), additional stenting in 11 cases

References:
Per patient, range 1–69 treatments) were performed in 135 patients (female 131/135 (97%) patients with a mean of 30.1 months (0 to 103).

OF SYMPTOMATIC ENTERIC STRICTURES IN CROHN’S DISEASE

Introduction:

Endoscopic treatment of enteric strictures in patients with Crohn’s disease (CD) is well established; however, long-term outcome is unknown.

Aims & Methods: All patients with CD, who had undergone endoscopic therapy of symptomatic strictures at Robert Bosch-Hospital Stuttgart from 2008–2017, were included in this retrospective cohort study. A follow-up was available for 131/135 (97%) patients with a mean of 30.1 months (0 to 103).

Results: A total of 452 endoscopic interventions (mean 3.4 per patient, median 2 per patient, range 1–69 treatments) were performed in 135 patients (female n = 67/male n = 68, mean age 47.5 years, BMI: 22.8 ± 4.98 kg/m², duration of illness: median 25.1 months). In 165 cases, the dominant stricture was located in the ileocecum, in 105 in the colon, esophagus (90), duodenum (54), upper intestine (26), lower intestine (11) or stomach (1). In 166 and 286 cases, there was an anastomotic and non-anastomotic stricture present, respectively. Treatment consisted of hydrostatic balloon dilatation (n = 447); bougienage (4), and ESEM (1). Dilatation was performed to a mean of 14 mm (SD: 2.4, range 7 to 24 mm). In seven cases complications occurred after endoscopic treatment (bleeding: n = 5; infection: n = 1); perforation: n = 1) which resulted in an extension of the hospital stay (n = 5), antibiotic therapy (1) and surgery (1). Immediate clinical success was observed in 438 of 452 of cases (96.9%). A follow-up.

Conclusion: Endoscopic dilation is effective and safe. Repetitive dilation is feasible with a significant reduction of clinical symptoms, and surgery was required in about 30% of patients at long-term follow-up.

Disclosure of Interest: All authors have declared no conflicts of interest.

References


P1568 EFFICACY AND COMPLICATIONS IN PALLITIVE OESOPHAGEAL STENTING, EXPERIENCES OF A TERTIARY REFERRAL CENTER IN THE UK

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Introduction: Palliative stenting is now established as a major treatment for dysphagia resulting from incurable oesophageal neoplasms. Palliative oesophageal stenting is associated with multiple possible complications after oesophageal stent insertion; most of these present with increasing dysphagia; however pain, bleeding, and reflux are also common. Although data on rates of various complications are available, there are no agreed standards to audit performance against, nor any requirement to do so. As this is a palliative procedure, success in symptom control is paramount; if this is not being achieved, then the appropriateness of the procedure must be questioned. As with any invasive procedure, complication rates are affected by multiple variables: technical, length and site of stricture, operator experience, patient co-morbidities and performance status. As a result of these variables, stated complication rates also vary. Only one study reported a rate of dysphagia (29%); migration occurred in 5–15% of cases, tumour ingrowth/overgrowth 5–20%, and food bolus obstruction in 5–15%. Quoted median survival ranged from 61–104 days, with a 30-day mortality of 20–28%.

Aims & Methods: Our aim was to scrutinise the efficacy and the safety of our palliative oesophageal stenting work. A retrospective study of all patients undergoing oesophageal stent insertion at our unit, between 01.01.2012 and 01.04.2016 was undertaken, looking for evidence of complications, repeat interventions, and for survival statistics after stent insertion. Patients who had undergone stent insertion for reasons other than oesophageal malignancy were excluded.

References


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P1555 EDOSOS INTRALESIONAL STEROID INJECTION IS EFFECTIVE IN THE TREATMENT OF BENIGN REFRACTORY OESOPHAGEAL STRICUTURE, A META-ANALYSIS

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Introduction: Endoscopic dilation is an effective treatment in oesophageal strictures, but recurrences may require frequent and repeated dilations in the long term. Several trials have been conducted to determine the efficacy of intralesional steroid injection in the treatment of benign refractory oesophageal strictures, since the first pediatric case series was published in 1969. However, a meta-analysis has not been carried out yet.

Aims & Methods: The aim of the analysis is to summarise the results and establish evidence in support or against the complementary treatment. A meta-analysis was performed using the preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P). Two reviewers conducted a comprehensive search on databases from inception to February 2016, to identify trials, comparing the efficacy of dilation combined with intralesional steroid injection. A meta-analysis was conducted on the data using the random-effects method by DerSimonian and Laird, because of the high level of the heterogeneity.

References


Results: Between 01.01.2012 and 01.04.2016, 152 patients were inserted in 125 patients in palliative oesophageal cancer patient; 104 patients had stent inserted once, 16 patients had twice, 4 patients had 3 times and 1 patient had 4 stent insertions. 69.6% were male and the median age at death was 79 years (SD 10.94). The reported histology for the 125 patients revealed, 85 (68%) adenocarcinoma, 35 (28%) squamous cell carcinoma, 5 (4%) lung cancer causing external compression of the oesophagus, 2 (1.6%) mesothelioma, 1 (0.8%) externally compressing spindle cell sarcoma, 1 (0.8%) metastatic adenocarcinoma from the colon, 1 (0.8%) externally compressing signet ring adenocarcinoma. Of these stent insertions 52 (34.2%) were documented to have going or recurrent dysphagia after the procedure, of which the causes were: tumour over- or ingrowth in 9 (5.9%); stent migration in 15 (9.9%); distal obstruction due to gastric folds 2 (1.3%), dysfunction of the anti-reflux valve in 3 (2.0%); and food bolus obstruction in 9 (6.0%). The indication for stent insertion was 2 (1.3%) benign obstruction and stent disintegration in 1 (0.7%) case. In 13 (8.6%) cases cause for dysphagia was not found or not investigated. 100 (65.8%) stent insertions resulted in complete resolution of the dysphagia. Repeat endoscopy was necessary in 34 (27.2%) patients, who had 98 repeat gastroscopies in total, to deal with minor complications of the stent insertion or to investigate dysphagia. In total there were 13 (8.7%) significant complications caused by the stent insertion of which 7 (4.6%) were bleeding, 2 (1.3%) were tracheo-oesophageal fistula formations, 1 (0.7%) was delayed perforation, 1 (0.7%) was a too short stent, 1 (0.7%) was a disintegrating stent and 1 (0.7%) was a compression of the bronchi. Median survival of the 125 patients after stent insertion was 96 days (SD 128) and 30-day mortality was 11.2% (14 patients). It is important to note that with retrospective data analysis, some data is not available, due to variations in recording at the time and a reliance on the patient to report symptoms to a clinician. Currently 2 patients are still alive.

Conclusion: Palliative stenting at this centre continues to be an effective treatment for patients with dysphagia from oesophageal cancer. On the whole, outcomes from stenting at this unit compare favourably with published data in terms of dysphagia, other complications, and mortality. Steps to improve post-procedure monitoring in the form of a “stent registry” with prospective collection of data by telephone or face-to-face follow-up could be useful in future service development.

Disclosure of Interest: All authors have declared no conflicts of interest.
available in many centers and have revolutionized the management of iatrogenic bowel vascular injuries. Aims & Methods: Evaluate the role of intervention radiology procedures to manage different post-cholecystectomy complications focused on the novel techniques to improve the final outcome. From June 2014 to June 2016, 30 patients presenting complications after cholecystectomy were referred to interventional radiology unit in our university hospital. They were 9 males and 21 females (age range: 18–66 years). Patients presented with biliary leaks (n = 12), benign biliary strictures with intrahepatic biliary dilations (n = 21), postoperative hernia (n = 2) and bleeding related to hepatic artery pseudo-aneurysm (n = 1). Different types of interventional procedures were performed, including: Percutaneous trans-hepatic drainage (PTD) (n = 16), surgical dilatation of benign stricture with increasing caliber dilators over 6 months followed by metallic stent procedures after catheter withdrawal (n = 6), biliary stenting with plastic stent (n = 2). Insertion of pigtail catheter (n = 15), preoperative progressive pneumo-peritoneum for their adhesiolysis effect to manage post-operative huge incisional hernias before their surgical repair (n = 1), and selective embolization of bleeding hepatic artery pseudo-aneurysm (n = 1) using tissue adhesive (n-Butyl 2 Cyaanoacrylate).

Results: All percutaneous procedures were technically successful. No recorded early or late complications. After manometric studies, all managed cases with biliary strictures did not show any clinical evidence of restenosis during 6 months follow-up. Overall, 14 out of 30 patients (46.7%) were only managed by different interventional radiology procedures. Second step surgical repair was needed for 13 patients (43.3%) and endoscopic managed for 3 patients (10%) with biliary leaks.

Conclusion: Minimally invasive interventions were valuable techniques in the management of different post-cholecystectomy complications. In fully equipped centers, expert multidisciplinary teams would achieve high cure rates for iatrogenic biliary injuries.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1590 WHAT IS THE ROLE OF ANGIOGRAPHY IN ACUTE COLONIC AND SMALL BOWEL BLEEDING?

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Introduction: Angiography is a diagnostic and therapeutic modality that is widely available for upper gastrointestinal bleeding but is used less frequently when the source of bleeding is placed distally to the Treitz angle.

Aims & Methods: To assess the usefulness of angiography in the diagnosis of colonial and small bowel bleeding and to determine the efficacy and complications of therapeutic procedures. Retrospective study; we included all patients with colonial and small bowel bleeding that were submitted to arteriography with or without embolization, admitted to the gastroenterology department of a tertiary hospital between February 2006 and November 2016. Statistics: Chi-square/ Fisher exact test, T-student.

Results: We reviewed 216 patients. Mâle evaluated, 63.6% male, mean age = 75 years (29–95). Angiography was done for: bleeding recurrence (36.2%), hemodynamic instability (33.3%), both (27.3%) or failure to endoscopic hemostasis (3%).

Conclusion: The role of angiography in the diagnosis of acute colonic and small bowel bleeding is still controversial but may offer therapeutic options in selected cases.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1592 PROPENSITY SCORE ANALYSIS OF 18-FDG PET/CT ENHANCED STAGING IN PATIENTS UNDERGOING SURGERY FOR OESOPHAGEAL CANCER

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Introduction: PET/CT has become an integral part of the staging pathway for oesophageal cancer and is usually performed before, during and after surgery.

Aims & Methods: Consecutively 120 patients undergoing oesophagectomy for cancer [median age 63 (31–80) yr., 395 male, 75 neoadjuvant therapy]; 60 did not proceed to surgery and were excluded. Postoperative morbidity and mortality occurred in 83 (69%; CD 3 in 27, 22.5%) and 4 (3.3%) patients respectively. ROC curve analysis showed oxygen uptake (peak V02) gave an area under the ROC of 0.66 (95% CI 0.55 to 0.77, p = 0.005); anaerobic threshold (AT) gave an area under the ROC of 0.62 (95% CI 0.51 to 0.74, p = 0.048) and optimum cut-off of 10.5ml/kg/min (sensitivity 60%, specificity 44%). Multivariable analysis revealed peak V02 to be the only independent factor to predict morbidity severity CD > 3 (OR 0.85, 95% CI 0.75–0.97, p = 0.018). Cumulative survival was associated with operative MSS (Chi2 4.892, DF 1, p = 0.027) but not with PET variables.

Conclusion: PET/CT is a significant predictor of morbidity after oesophagectomy with peak V02 the most important factor.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1593 PREDICTION OF LYMPH NODE METASTASIS FOR SUPERFICIAL ESOPHAGEAL CANCER WITH USING RANDOM FOREST ANALYSIS

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Introduction: Although surgical techniques and perioperative management for oesophageal cancer has been developed, it cannot be still safe to be performed oesophagectomy. Therefore, endoscopic submucosal dissection (ESD) for the superficial cancer has been increased. We also need to consider the risk of lymph node metastasis before treatment in each patient and the aim of this study is to predict lymph node metastasis for superficial esophageal cancer.

Aims & Methods: Predictive models can help to identify patients who are likely to develop lymph node metastases. This study is to predict lymph node metastasis for superficial esophageal cancer.
Aims & Methods: Seventy patients who were diagnosed as clinical T1a-MM, T1b-SM1 or T1b-SM2 and underwent esophagectomy at the Keio University, Tokyo, Japan between July 2000 and June 2016 were enrolled in this study. Patients who underwent esophagectomy as additional resections after ESD were included. We used random forest analysis to predict lymph node metastasis. Results: There were 62 men and 8 women in this study. The mean age of all patients was 62.8 ± 8.2 years. The main location of the tumor was in the middle thoracic esophagus (Upper: Middle; Lower; 13: 39: 18, respectively). 14 patients had lymph node metastasis in pathological findings; 2 patients (25%) were diagnosed as clinical T1a-MM, 2 patients (6.6%) were clinical T1b-SM1 and 10 patients (31.3%) were T1b-SM2. Random forest technique (2000 trees) resulted in an estimate of error rate of 25.7%. Lymph node metastasis was most associated with the factor of pathological T (relative importance 100%) followed by lymph node (98.9%) and T factor (95.9%). However, there were 3-6 months between the two fillings. The mean differences of the COPE-NVI scales were not statistically significant.

Conclusion: In our series, patients used Positive Attitude to manage everyday life (COPE-NVI scales). However, in order to improve them to positive attitude, some modifications are necessary. Disclosure of Interest: All authors have declared no conflicts of interest.

Comparison of manual counting to the computed methods showed mostly excellent accuracy of the obtained results using intraclass correlation with reliability analysis (ICC) and coefficient B with linear regression (B):

<table>
<thead>
<tr>
<th>mCRC</th>
<th>OvCa</th>
<th>HCC</th>
<th>PCa</th>
</tr>
</thead>
<tbody>
<tr>
<td>ZC</td>
<td>ICC  = 0.926, B = 0.368 ICC &lt; 0.978, B = 0.968 ICC &lt; 0.869, B = 0.621 ICC = 0.601, B = 1.20</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ISCC</td>
<td>ICC = 0.973, B = 0.851 ICC &lt; 0.992, B = 1.030 ICC = 0.990, B = 1.606 ICC = 0.934, B = 0.914</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IACCC</td>
<td>ICC = 0.896, B = 0.945 ICC &lt; 0.990, B = 0.606 ICC = 0.955, B = 0.723 ICC = 0.932, B = 1.32</td>
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Results: Quantification results from 2 blinded observers for reliable detection of hot spots were 0.949 in mCRC, 0.843 in OvCa, 0.805 in HCC and 0.957 in PCa. The ICC for the ratio of CD8+C in 1 hot spot compared to the average from 3 hot spots was consistent in all groups. The absolute cell count in 1 vs 3 hot spots was consistent in all groups. EORTC C30 functional scales are: PE2 (physical functioning), RF (role functioning), EF (emotional functioning), CF (cognitive functioning) and SF (social functioning). EORTC-C30 and COPE-NVI questionnaires. Thirty-two patients completed the questionnaires after surgery. Mean COPE-NVI scales were: SS = 22.3 (SD 9.5), AS = 23.2 (SD 4.8), PA = 30.8 (SD 7.9), P0 = 22.5 (SD 8.8), TO = 22.1 (SD 5.0). Overall, mean C30-QLQ was 72.9 (SD 16.3). Mean C30 functional scales were: PE2 = 80.8 (SD 16.6), RF = 85.0 (SD 20.7), EF = 81.5 (SD 17.0), CF = 87.4 (SD 14.0) and SF = 90.0 (SD 14.0). Avoidance Strategies score was negatively correlated with Social Function (rho = -0.60, p = 0.004). The remaining correlations between COPE-NVI scales, C30-QLQ and C30 functional scales were statistically not significant.

Conclusion: In our series, patients used Positive Attitude to manage everyday life (COPE-NVI scales). However, in order to improve them to positive attitude, some modifications are necessary. Disclosure of Interest: All authors have declared no conflicts of interest.
P1598 LIVER RESECTION IN OBSESE PATIENTS WITH HEPATOCELLULAR CARCINOMA

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Introduction: Obese disease has been recognized as a risk factor for hepatocellular carcinoma (HCC). On the other hand, there are few reports concerning liver resection (LR) in obese patients.

Aims & Methods: We performed curative LR in 471 patients with HCC between 2001 and 2015. In this study, we defined an obesity as no less than 25 of body mass index (BMI). We compared clinicopathological findings, operation details, and surgical outcomes of the obese and non-obese patients. Furthermore, we assessed the safety and the benefit of laparoscopic partial hepatectomy and left lateral segmentectomy in the obese patients.

Results: Among 471 patients, 123 patients (26.1%) were defined as obese. Among them, 20 patients (4.2%) showed no less than 30 of BMI. Diabetes, hypertension, and hyperlipidemia were significantly more common, and the patients with hepatic steatosis were positively associated in the obese patients group than in the non-obese patients group (p < 0.05). The two groups showed no differences in the liver function tests except the indocyanine green retention rate at 15 minutes. There were no significant differences between the two patients group in the number of tumors, diameter of tumor, prevalence of cirrhosis, frequency of portal invasion, the operative procedure, operative duration, blood loss, incidence of postoperative complications, postoperative hospital stay, and in-hospital mortality (3.3% vs. 1.4%). No significant difference was found in relapse-free survival rate, or overall survival rate between the two groups, too. Thirteen patients underwent laparoscopic surgery, and 34 patients had open surgery. The two groups showed no difference in the background, including BMI. However the operation time (265 min. vs. 397.5 min) and the postoperative hospital stay (14 days vs. 18 days) were significantly shorter, and the blood loss (50 ml vs. 600 ml) was less in the laparoscopic surgery group than in the open surgery group (p < 0.05).

Conclusion: Liver resection in the obese patients with HCC was safe, and laparoscopic liver resection might be more useful for reducing the surgical stress and reducing the hospital stay.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P1599 TIMING OF ELECTIVE CHOLECYSTECTOMY AFTER ACUTE CHOLECYSTITIS - A POPULATION-BASED STUDY

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Introduction: Acute cholecystectomy as treatment of acute cholecystitis is standard of care. However, many patients are still treated conservatively and undergo elective cholecystectomy 2 weeks following the primary admittance is postulated as a good timing for an elective surgery but there are no studies on the optimal timing for delayed cholecystectomy.

Aims & Methods: The aim of our study was to determine when it is most advantageous to perform a delayed surgery with respect to acute cholecystitis. All patients treated for acute cholecystitis in Sweden during the years of 2006 and 2013 were identified through the Swedish Inpatient Register. This cohort was cross-linked with the Swedish register for gallstone surgery. Cox regression was used for survival analysis. The impact of time from admission to surgery with regards to operative time, percentage of procedures completed with minimally invasive technique, peri and postoperative complications and bile duct injury or bile leakage was analysed with a multivariate logistic regression model.

Results: The years 2006 to 2013, 31091 patients were treated for acute cholecystitis in Sweden. After exclusion of patients that did not perform surgery, were not registered in GalRiks and that patients that were treated with acute cholecystectomy 5352 patients were identified that underwent planned surgery. In multivariate linear regression analysis with adjustment for gender and age the risk for peri- and postoperative complications, bile duct injuries and bile leakage and amount procedures not completed with minimally invasive technique decreases with time from the last hospitalization to surgery. All p-values < 0.05.

Conclusion: For those patients undergoing elective cholecystectomy after an acute cholecystitis the safety increases if surgery is performed later than 30 days after discharge.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1600 MIXED REALITY SURGERY USING CT-BASED PATIENT-SPECIFIC IMMOVABLE 3D HOMOLOGS ENHANCED SPATIAL AWARENESS IN HEPATO-PANCREATO-BILIARY AND GASTROINTESTINAL SURGERY

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Introduction: We developed a CT-based patient-specific holographic surgical simulation navigation system of immovable mixed reality (MR).

Aims & Methods: The aim of this study is to identify its benefit of simulating, analyzing and evaluating operative surgical treatment options in gastrointestinal and hepato-pancreato-biliary surgery. We used our original immersive MR application using HoloLens, that is a pair of MR smartglasses built-in high-magnification display. By reconstituting the patient-specific 3D surface polygons of each organ out of the patient’s MDCT images, MR anatomy was displayed on the grasses three-dimensionally during actual surgery. Based on the pair of MR smartglasses by satellite tracking. The gesture controlled manipulation by surgeons’ hands with surgical groves was useful for intraoperative anatomical references of tumors and vascular position under sterilized environment. It allowed the user to manipulate the spatial attributes of the virtual and real anatomies, which can enhance spatial awareness. The use of our systems reduced the length of the operation and discussion time.

MR navigation assistance could support complex procedures with the help of pre- and intraoperative imaging with better visualisation of the surgical anatomy and spatial awareness with visualisation of surgical instruments in relation to anatomical landmarks.

Conclusion: We report illustrative benefits of the immersive MR in surgical planning, simulation, education, and image-guided navigation. This could overcome the limitations of the conventional image-guided surgery.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

P1602 EFFICACY OF DOUBLE PIGTAIL STENT FOR POST OSEO-GASTRIC SURGICAL LEAKS NON LINKED TO BARIATRIC SURGERY: A PILOT BI-CENTRE RETROSPECTIVE STUDY

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Introduction: Post-surgical leaks are the first complication after non-bariatric oeso-gastric surgery in terms of frequency and morbidity. Anastomotic fistulae change the prognosis of the operated patient increasing the length of stay, increasing costs, increasing mortality and increasing risks of oncological recurrence. Surgery is still a possibility of treatment in particular in case of severe sepsis but the role of endoscopy or even of a new armamentarium of endotherapy dedicated to such complications. In cases of post laparoscopic sleeve gastrectomy leaks, a shift is ongoing between closure or diversion methods (Ovesco, clips, covered self expandable metal stents (SEMS)) and internal drainage (double pig tail stents). Two large studies have just reported a high efficiency and a low complication rate with internal drainage with double pig tail stents for post sleeve gastrectomy leaks. No data are available for such an endoscopic internal drainage in fistulas of the upper digestive tract non-linked to bariatric surgery. Here we report the results of a pilot bi-centre retrospective study.

Aims & Methods: A retrospective study of all upper digestive tract leaks non linked to bariatric surgery and treated by double pig-tail stent (DPTS) in two
Introduction: Abdominal compartment syndrome (ACS) is serious complication of big number of surgical interventions. According the data of the World Society of the Abdominal Compartment Syndrome (WSACS), rate of mortality without treatment is more than 90%, after treatment from 25% to 75% [1]. Patients with ruptured abdominal aortic aneurysms (rAAA) are the group of high risk regarding complication. Rate of incidence ACS at these patients is between 8% to 25%[2]. According to data of various authors, from one third to one half of them have died [3]. One of the main cause of this is the absence of good monitoring of intraabdominal pressure in this group of patients[4]. Currently, we have on one effective way of treatment: decompressive laparatomy [5]. But prophylaxis becomes more important point, if we take to attention mortality after start the develop of abdominal compartment.

Aims & Methods: We aimed to investigate the impact of implantation polypropylene mesh during all three years of follow-up on occurrence of ACS. We aimed to investigate the impact of implantation polypropylene mesh for other deseases, related with ACS and it severity. We aimed to investigate the impact of implantation polypropylene mesh for other deseases, related with it complication and mortality.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P1604 ESSENTIAL PERCUTANEOUS DRAINAGE (EPD) OF PERITONEAL COLLECTIONS AND ABSCESES SECONDARY TO BARIATRIC SURGERY LEAKS: THE PARADIGM SHIFT OF SEEING PERITONEUM AS AN ORGAN AMENABLE FOR FLEXIBLE PERITONEAL collections are dreaded complications. Laparoscopic or open surgery and percutaneous CT drainage are the current indications. Endoscopic management of pancreatic collections is a rationale for Endoscopic Peroral Drainage (EPD) approach in cases of BS leaks with abdominal collections.

Aims & Methods: The aim of this study is to evaluate utility and safety of EPD to treat peritoneal collections and abscesses secondary to BS leaks. Methods: This retrospective study included 65 consecutive patients from 2007 to 2015 at a single center (40 Sleeve gastrectomy, 25 gastric bypass) after 5 to 21 days from tertiary centers has been performed. DPTS are traced by the pharmacies of our two hospitals and all cases of DPTS were analysed thanks to the database of the pharmacies of our two hospitals since May 2014 (first DPTS used for non bar- iatric upper digestive tract fistula) or 10 french DPTS have been used according to the size of the fistula and the choice of the physician. Technical success was defined as the possibility to place the DPTS within the fistula. Clinical success was a composite endpoint combining clinical amelioration of the patient and healing of the fistula allowing the removal of the DPTS.

Results: 17 patients have been treated by DPTS from May 2014 to March 2017 for an upper digestive tract leaks non linked to bariatric surgery. Fistulas were linked to a levis-sanyt surgery in 8 patients (47%), total gastrectomy in 4 (23.5%), boerhaave syndrome in 2 (11.8%), endoscopic perforation in 2 (11.8%) and aortic surgery in 1 (5.9%). An infected collection was present in 16 patients (94%) and 11 (64.7%) suffer from a clinical sepsis. The mean delay between surgery and the diagnostic of fistula was 10 days and the delay of the diagnosis of fistula and the endoscopic drainage by DPTS was 16.4 days. DPTS were used alone in first intention in 11 cases (64.7%), in first intention in combination with a SEMS in 11.7% and in second intention after failure of a SEMS in 3 (11.7%). All patients had a technical success and 15 patients (88.8%) had a clinical success. The mean delay for refeeding after DPTS was 17 days. The mean ablation time of the DPTS was 73 days. 3 patients presented a complication (1 stenosis, 1 bleeding and 1 migration).

Conclusion: Endoscopic internal drainage using DPTS seems to be an interesting therapeutic option for upper digestive tract leaks non linked to bariatric surgery. DPTS are effective, safe, cheap and could replace SEMS not always well toler- ated and with a high rate of migration. Prospective multicenter studies are needed.
surgery. Patients presented heart rate over 120 bpm. Images from CT showed left side of the abdomen free from abdominal content. An Upper GI series was performed to localize the leak opening and enter to peritoneal cavity. Either 9.8 or 5.8 mm diameter gastroscopy were used. In 10 patients with orifices smaller than 5.8 mm balloon dilatation of the leak opening allowed peritoneal access. The technique of AL was performed in 100 (to 700ml). Sample was taken for bacterial cultures. The cavity was flushed and suctioned out with sterile saline solution (200 ml to 1000 ml). In cases of inadequate location surgical drains catheters were repositioned or replaced using endoscopic forces and snare. Failure in accomplishing lateral anastomosis after 3 attempts when the catheter was performed advancing with endoscopes through the leak all the way down to the skin. Once the tip of the endoscope was outside the peritoneum the latex drains were removed. Catheters were snared or grasped and pulled back into the peritoneum leaving the proximal end close to the fistula opening. Nineteen patients without surgical drainage systems one laparoscopic port was localized inside peritoneum and re-opened under endoscopic vision to allow drainage catheters placement. In 8 patients peritoneal adhesions were endoscopically liberated with endoscopic forces or knives to facilitate peritoneal navigation.

Results: Heart rate returned to normal within 24 hours and leukocytosis improved after 72 hours. In 50% of patients heart rate returned to normal immediately. Average time for the whole procedure was 45 minutes. Abdominal catheters were removed between 7 and 18 days once full resolution of the drainage was achieved. Twenty patients were discharged within the first 24 hours. The rest were discharged between 3 and 8 days. Partially covered SEMS were placed for 6 to 8 weeks leading to complete closure of leaks. There were no adverse events related.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1605 CLINICAL ASSESSMENT OF THE FAILING TO REVERSE A DIVERTING ILEOSTOMY
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Introduction: A diverting loop ileostomy with procedure of intestinal resections and colorectal anastomosis decreases morbidity from anastomotic leaks and may even reduce the risk of anastomotic leak as shown in recent studies. Reversal of a temporary ileostomy is considered a simple surgical procedure presenting with a low morbidity and mortality rates. However, ileostomy reversal may be associated with number of complications requiring reoperation, with anastomotic leak (AL) being most critical often leading to failure in restoration of digestive tract continuity.

Aims & Methods: The study aimed at evaluating the results of reversal of ileostomy in patients primarily operated on for colorectal cancer and inflammatory conditions. We assessed the frequency of failure following the surgical procedure of diverting loop ileostomy closure. The study was conducted at a tertiary referral center. 147 adult patients (89 men, mean age 50.5y ± 16.7y and 58 women, mean age 49.3y ± 16.9y) were enrolled to this study. All included patients underwent surgical closure of a temporary loop ileostomy at the Department of General and Colorectal Surgery, Lodz, Poland, between 2004 and 2014. The study was collected in a retrospective manner basing on hospital records. The analyzed parameters included length of hospitalization, gender, age, BMI, concomitant conditions, American Society of Anesthesiologists classification score (ASA) and the character of postoperative complications. Statistical analysis was used to evaluate the correlation between the variables and postoperative complications.

Results: AL as a postoperative complication with the need to create a new ostomy occurred in 15 patients (10.2%). Higher values of BMI and older age have been noted compared to noncomplicated surgeries (27.54 vs. 23.36 vs. 23.02 ± 3.96; p < 0.001; 54.53 ± 12.3 vs. 50.25 ± 15.95; p = 0.029 respectively). There was no significant correlation between patients’ gender and the incidence of AL (p = 0.087). The number of prior surgical procedures and ASA scale positively correlated with the prevalence of AL (p = 0.038; p = 0.003 respectively). There were no significant difference between patient with colorectal cancer and inflammatory conditions (p = 0.534). The average time interval from prior surgery to reversal of the stoma and AL occurrence were not related and did not reveal statistical significance (8.5 ± 4.41 vs. 7.24 ± 4.47; p = 0.25). Univariate logistic regression demonstrated that a BMI levels, patients’ age and average time interval from prior surgery to reversal procedure were significantly associated with number of complications requiring reoperation, with anastomotic leak (AL) being most critical often leading to failure in restoration of digestive tract continuity.

Conclusion: Postoperative complications is still a major issue related with failure of intestinal continuity restoration in patients undergoing loop ileostomy closure. Patients with elevated BMI, older age and shorter average time interval from prior surgery to reversal procedure present higher risk of failure in restoration of digestive tract continuity and the incidence rate was similar in patients operated primarily on for inflammatory conditions and colorectal cancer.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1606 BODY COMPOSITION AS A PREDICTOR OF MORBIDITY FOLLOWING BILIPANCREATIC CANCER SURGERY
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Introduction: The impact of body composition on the outcomes following pancreateicoduodenectomy is still unclear.

Aims & Methods: The aim of this study was to analyze the association between body composition the postoperative complications and 90-day mortality in patients undergoing bilipancreatic cancer surgery. Retrospective study of patients with pancreatic, ampullary or bile duct carcinoma that underwent surgery between March 2012 and October 2016. Body composition (skeletal muscle mass, body fat area, subcutaneous fat area and muscle radiation attenuation) was assessed in diagnostic or staging computed tomography (CT), in axial images at the level of the 3rd lumbar vertebra. Postoperative complications were recorded according to Clavien-Dindo classification and categorized as minor (grade I–IIIa) or major (grade IIIb–V).

Results: Fifty-nine patients were analyzed and 11 were excluded due to unavailable CT scan at our institution. Forty-eight were included, 28 were men, with a mean age of 70.5 ± 8.5 years. The incidence of major complications was 25% and 90-day mortality was 8.3%. On simple logistic regression of factors associated with major complications skeletal muscle area (OR 0.97, 95% CI 0.94–1.00, P = 0.09) and index (OR 0.91, 95% CI 0.81–1.00, P = 0.09) showed a trend for a protective effect. On multivariate logistic regression skeletal muscle area and radiation attenuation index were protective factors (OR 0.89, 95% CI 0.79–0.99, P = 0.05) and longer surgery (OR 1.01, 95% CI 0.99–1.03, P = 0.07) was associated with higher incidence of major complications. The receiver-operator characteristic (ROC) curve showed an acceptable power of discrimination of major complications using a model with skeletal muscle index and surgery duration as independent variables (area under the curve 0.736). On simple logistic regression surgery duration (OR 1.02, 95% CI 1.00–1.06, P = 0.05), visceral fat area (OR 1.02, 95% CI 1.00–1.04, P = 0.02) and AL level (OR 1.05, 95% CI 1.02–1.08, P = 0.04) were associated with higher 90-day mortality whereas muscle radiation attenuation had a protective effect (OR 0.88, 95% CI 0.76–0.99, P = 0.05).

Conclusion: These results suggest that low values of skeletal muscle and muscle radiation attenuation and high visceral fat area as well as high values of visceral fat and low skeletal muscle are associated with worse clinical outcomes following bilipancreatic cancer surgery.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1607 GASTROSCHISIS: A 16-YEAR STUDY
A.M. Bradeanu1, L. Balanescu2, I. Nenciu3

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Introduction: Gastrostomias is a ventral body wall defect tract which protrude mainly large and small intestines. The disease’s clinical course and prognosis is strongly related on both surgical techniques, severity of the defect, accompanying anomalies and complications.

Aims & Methods: We performed a retrospective study based on the analysis of patients records admitted to our hospital Neonatal Intensive Care Unit between January 2000 and December 2016. The aims of this study were to evaluate defect’s incidence, management and outcome of patients with gastrostomias in our institution.

Results: During the period 2000-2016 the overall incidence of gastrostomias in our NICU was 3.23% (140 cases out of 4,327). The abdominal wall gestational age was 35.5 weeks and the average birth weight was 2270 g. The abdominal wall defect was identified in antenatal period only in 15.4% of cases. Also, 23 patients (16.4%) presented other associated anomalies: 12 cases with urogenital anomalies, 5 cases with cardiac defects, 2 cases with neural tube defects. Surgical techniques performed for abdominal defect closure were: primary closure in 35 cases (25%), staged closure in 12 cases (8.57%), Gross technique in 44 cases (31.4%) and manual reduction and closure (Bianchi procedure) in 49 cases (35%). The average period of digestive pause was 12.9 days and the mean length of stay in NICU was 30.4 days. Patients were also ventilated for a average period of 4.6 days. The most frequent complication was late-onset sepsis (37.8%); also 26 neonates (18.5%) underwent surgical revision. The average mortality in our group was 33% but it constantly decreased over the years (from 84% in 2000 to 11% in 2016). Sepsis, prematurity, low birth weight and associated defects were identified as major risk factors for the unfavorable neonatal outcome.

Conclusion: The management of neonates with gastrostomias depends on several factors including the status of herniated organs, the size of abdominal cavity, the presence of other associated congenital anomalies and last but not least on the resources and experience of the neonatal interdisciplinary team. Significant changes occurred in the management of gastrostomias in our Unit and as consequence, the outcome of patients with gastrostomias has dramatically improved during the studied period.
Disclosure of Interest: All authors have declared no conflicts of interest.

References

WEDNESDAY, NOVEMBER 01, 2017
09:00-14:00
IBD III – HALL 7

P1608 ASSESSING THE EFFECT OF ETHNICITY ON URINARY METABOLIC PROFILES IN INFLAMMATORY BOWEL DISEASE

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Introduction: Urinary metabolic profiling has been shown to distinguish patients with inflammatory bowel disease (IBD) from healthy controls (HC), and also separate ulcerative colitis (UC) from Crohn’s disease (CD) in Caucasian (Cau) cohorts (1). Diet and lifestyle also have an effect on metabolic profiles (2), and these differ in patients from different ethnic backgrounds. Moreover, clinical phenotype varies between Caucasians and South Asians (SA)(3), however discriminatory metabolites have not been studied in different ethnic populations. The aim of this study was to compare the urinary metabolic profiles of IBD patients and healthy controls from Caucasian and South Asian backgrounds.

Aims & Methods: Samples from 405 IBD patients (283 Caucasian and 122 South Asian) and 137 healthy controls (98 Caucasian and 48 South Asian) were analysed by UPLC-QTOF MS. Clinical and dietary data were collected. Orthogonal partial least squares discriminant analysis (OPLS-DA) was performed to examine whether there were differences in metabolic data between Cau and SA. R2 (variance), Q2 (quality assessment) and p values (validity) for each model were described.

Abstract: P1608

<table>
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<th>South Asian (n and %)</th>
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<td>122</td>
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<tr>
<td>CD</td>
<td>160 (57%)</td>
<td>42 (34%)</td>
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<tr>
<td>UC</td>
<td>123 (43%)</td>
<td>80 (66%)</td>
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<td>Controls</td>
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<th>South Asian (n and %)</th>
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<td>122</td>
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<tr>
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<tr>
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<tr>
<td>Controls vs UC+</td>
<td>0.798</td>
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<tr>
<td>CD vs UC*</td>
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<tr>
<td>SA</td>
<td>SA</td>
</tr>
<tr>
<td>Controls vs CD+</td>
<td>N/A</td>
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<tr>
<td>Controls vs UC+</td>
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<td>CD vs UC*</td>
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P1609 EFFECTS OF ACUTE CHANGES IN FERMENTABLE FIBRE INTAKE ON REGIONAL COLONIC FERMENTATION AND TRANSIT IN PATIENTS WITH QUIESCENT ULCERATIVE COLITIS

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Introduction: Reduced saccharolytic fermentation has been described in patients with quiescent ulcerative colitis (UC). Such defects may differ across colonic regions along with acute variations in dietary fibre intake. These aspects deserve further study.

Aims & Methods: We aimed to define regional colonic fermentation by direct intestinal pH-transit profiling in patients with quiescent UC following acute variations in fermentable fiber intake. A randomized, double-blind, crossover trial was performed. Patients with quiescent UC (Partial Mayo Score ≤1; faecal calprotectin <150 μg/g) and healthy controls who were not taking any results showed that the phenotype of South Asian Crohn’s disease was not significantly different to Caucasian Crohn’s disease in this cohort. In the South Asian UC group there was more pancolitis (p = 0.051) and less proctitis (p = 0.008). There were more vegetarians in the South Asian group. OPLS-DA was able to separate patients with IBD from healthy controls, and also UC from Crohn’s disease, in the Caucasian cohort, but this separation could not be replicated in South Asians (negative Q2 values).

Conclusion: The separation between Caucasian and South Asian healthy controls may reflect differing lifestyles including diet. Caucasian IBD patients could be separated from healthy controls, and Crohn’s disease from UC, replicating previous studies. South Asian IBD patients could not be separated from healthy controls which may be due to lower numbers of South Asian patients in this study, and specifically less Crohn’s disease patients where stronger discriminating models have been shown in Crohn’s disease in previous studies. In Crohn’s disease, Caucasians and South Asians could be separated, but Caucasian and South Asian patients could not be distinguished in the UC cohort, possibly suggesting the metabolic milieu in Crohn’s disease is stronger and less influenced by the impact of ethnicity.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

*Montreal classification
+OPLS-DA model examining the differences in urinary metabolic profiles between these cohorts
+Q value cannot be calculated if OPLS-DA model has negative Q2 values
OPLS-DA models also separated South Asian healthy controls from Caucasians healthy controls, and South Asian Crohn’s disease from Caucasian Crohn’s disease, but in UC no robust model could be made.
antibiotics (including sulfasalazine), probiotics or fiber supplements were removed. At 7-day run-in, subjects were fed study meals high (11 g oligosaccharides, 2 g resistant starch) or low (<1 g) in fermentable fiber over a 12-h period before ingesting the pH-motility capsule, subjects then crossed over to the other diet 3 days after passage of the capsule. Endpoints were diet-associated differences in overall, caecal and distal colonic pH, and colonic transit time (CCT), taken as time between the ileocecal junction and capsule exit. Caecal pH was defined as the minimum pH following passage through the ileocecal junction whereas maximum pH was arbitrarily used as distal colonic pH.

Results: 15 UC patients (aged 24–72 y; 9 males) and 9 controls (aged 22–69 years, 4 males) were studied. A decrease in overall and distal colonic pH was observed in controls with high vs low fiber diet (Table 1). In UC patients, a high fermentable fiber intake reduced caecal pH but paradoxically tended to increase distal pH. A subserved for UC extent and changes in overall (r = 0.08; P < 0.001, Spearman’s correlation) and caecal pH (r = 0.53; P = 0.04) after a high fermentable fiber diet (Figure 1). No differences in CCT were observed between diets in either cohorts but subgroup analysis in the UC cohort showed heterogeneous responses to a high fermentable fiber diet: 64% patients had slower CCT whilst 36% had unchanged or faster CCT. In contrast, majority (63%) of controls had no changes in CCT after a high fiber diet.

Table 1: Colonic pH and transit responses to acute changes in fermentable fiber intake

<table>
<thead>
<tr>
<th>Overall mean pH (95% CI)</th>
<th>Mean caecal pH (95% CI)</th>
<th>Mean distal colonic pH (95% CI)</th>
<th>Median [ IQR ]</th>
<th>CCT (h)</th>
</tr>
</thead>
<tbody>
<tr>
<td>UC n = 15</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low fiber</td>
<td>6.4 (6.2–6.8)</td>
<td>5.6 (5.3–5.7)</td>
<td>7.9 (7.6–8.2)</td>
<td>17 [9–23]</td>
</tr>
<tr>
<td>High fiber</td>
<td>6.3 (6.0–6.5)</td>
<td>5.2 (5.0–5.4)</td>
<td>8.1 (7.8–8.4)</td>
<td>21 [16–39]</td>
</tr>
<tr>
<td>p-value</td>
<td>0.20</td>
<td>0.001</td>
<td>0.09</td>
<td>0.13</td>
</tr>
<tr>
<td>Healthy n = 9</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low fiber</td>
<td>6.9 (6.5–7.2)</td>
<td>5.5 (5.2–5.8)</td>
<td>8.2 (8.0–8.5)</td>
<td>16 [15–17]</td>
</tr>
<tr>
<td>High fiber</td>
<td>6.3 (6.0–6.5)</td>
<td>4.9 (4.5–4.9)</td>
<td>7.7 (7.4–8.0)</td>
<td>18 [15–32]</td>
</tr>
<tr>
<td>p-value</td>
<td>0.02</td>
<td>0.15</td>
<td>0.04</td>
<td>0.58</td>
</tr>
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</table>

1 paired t-test or 2Mann-Whitney test

Conclusion: A high fermentable fiber diet partially increased colonic fermentative activity in patients with quiescent UC compared to controls. Moreover, contrary to controls, UC patients exhibited an increase in distal pH and heterogeneous colonic transit responses after a high fermentable fiber intake. Our findings suggest that abnormalities in motility and regional defects in the function of the colonic microbiota exist despite quiescent disease.

Disclosure of Interest: C.K. Yao: The Department of Gastroenterology, Monash University benefits financially from the sales of a digital app and booklet on the low FODMAP diet.

R.E. Burgell: Rebecca has received consultancy fees from Allergan. The Department of Gastroenterology, Monash University benefits financially from the sales of a digital app and booklet on the low FODMAP diet.

J.S. Barrett: The Department of Gastroenterology, Monash University benefits financially from the sales of a digital app and booklet on the low FODMAP diet.

J.G. Muir: The Department of Gastroenterology, Monash University benefits financially from the sales of a digital app and booklet on the low FODMAP diet.

P.R. Gibson: PG has served as consultant or advisory member for AbbVie, Ferring, Janssen, Merck, Allergan, Pfizer, Celgene & Takeda; research support from AbbVie & Janssen; speaking honoraria for his institution from AbbVie, Janssen, Ferring, Takeda, Mylan & Pfizer.

All other authors have declared no conflicts of interest.

P1610 FECAL MICROBIAL DYSBIOSIS IN CHINESE PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Introduction: Microbiota dysbiosis in the gut has been suggested to play an important role in the pathogenesis of inflammatory bowel disease (IBD). In the present study, we sought to elucidate the effects of iron supplementation on hypoxia-mediated responses in the intestinal epithelium. For this purpose, serum starved Caco-2 monolayers were subjected to normoxia (21% O2) or hypoxia (0.2% O2) in the presence and absence of ferric ammonium citrate (FAC) and the iron chelator deferoxamine (DFO). Total RNA was isolated and changes in the expression of tumor necrosis factor (TNF), interleukin (IL)-1β, DMT-1, FPN and ferritin was assessed by real-time quantitative PCR. Western blot analysis was performed with antibodies against ferritin, p-NF-kB, IκBα, p-FOXO6, p-p38 and LC3. mRNA synthesis in Caco-2 cells under hypoxia was blocked using actinomycin D. Chromatin immunoprecipitation experiments were carried using antibodies against NF-κB and primers for promoter binding regions of TNF and IL-1β. Healthy volunteers (n = 10) were subjected to hypoxic conditions resembling an altitude of 4,000 m above sea level for 3 h using a hypobaric chamber. Serum samples were collected the day prior to hypoxia, and one day, one week and one month after hypoxia.

Introduction: Environmental hypoxia has been established to influence the development of inflammatory bowel disease (IBD). Adaptive responses to low oxygen tension are mediated through hypoxia inducible factor (HIFs), which are tightly regulated by oxygen and iron levels through the action of hemoxygenases. Dietary iron is mainly absorbed by duodenal enterocytes through the divalent metal transporter (DMT)-1. Once iron is inside the enterocytes, it is either sequestered into ferritin or transported out of the enterocyte into the circulation by ferroportin (FPN). Regulation of uptake, storage and export of iron is mediated by signals reflecting oxygen and intracellular iron levels in enterocytes, and systemic iron regulation is the liver hormone hepcidin, which regulates and is regulated by systemic iron levels. Hepcidin expression is induced by cytokines and results in anemia of inflammation.

Results: Hypoxia-induced the mRNA expression of TNF and IL-1β concomitantly with the iron transporters DMT-1 and FPN. In Caco-2 cells under hypoxia, hepcidin mRNA was induced p-mTOR and blocked autophagy. Iron overload enhanced decay of TNF, but not IL-1β mRNA. Iron also prevented binding of NF-κB to the promoter of TNF and IL-1β. Healthy volunteers presented reduced serum levels of iron, as well as transferrin saturation. Ferritin levels were unchanged indicating an increase of inflammation and suggesting enhanced intracellular iron accumulation in enterocytes following hypoxia.

Conclusion: Our results suggest that hypoxia-mediated iron uptake is crucial to counteract hypoxia-induced pro-inflammatory gene expression, and identify iron intracellular uptake and storage as a hypoxia protective mechanism to reduce mucosal inflammation.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference
**Introduction:** In both forms of inflammatory bowel disease (IBD), Crohn’s disease (CD) and ulcerative colitis (UC), inflammation of the gut wall is associated with extracellular tissue acidification. Low extracellular pH stimulates the family of proton-sensing G-protein coupled receptors (GPRCs); ovarian cancer G-protein coupled receptor 1 (GPR1), T-cell death-associated gene 8 (TDAG8) or G-protein coupled receptor 4 (GPR4), which activate specific signal transduction cascades. Recent studies reported a link between IBD and this family of pH-sensing receptors; in genome-wide association studies (GWAS), TDAG8 has been identified as an IBD-risk gene. The mechanism behind the influence on disease and IBD remains unclear. OGR1 and TDAG8 are both suggested to act in opposition by regulation of the inflammatory response; enhancing or inhibiting inflammatory pathways respectively, however the interplay between OGR1 and TDAG8 is unclear.

**Aims & Methods:** In this study we aimed to investigate the role of OGR1 in IBD patients. Expression of OGR1 in surgical specimens from non-IBD (n = 5), CD (n = 10) and UC (n = 10) patients was determined by immunohistochemistry, RT-qPCR and Western blotting. Clinical disease activity was assessed by the Harvey–Bradshaw Index (HBI) and the Modified Truelove and Witts activity index (MTWI)10 for CD and UC patients, respectively. Nonparametric Spearman’s rank correlation analysis was performed.

**Results:** OGR1 immunostaining of human surgical samples from non-IBD patients revealed OGR1 expression mainly in lamina propria cells, with weaker staining in epithelial cells. OGR1 staining in IBD patients was stronger compared to controls; however, in IBD patients OGR1 is highly expressed in both epithelial and lamina propria cells. Further, paired samples taken at the same time, from non-inflamed and inflamed intestinal tissue from IBD patients showed stronger OGR1 staining in the inflamed mucosa compared to the non-inflamed mucosa. Accordingly, mRNA and protein expression of OGR1 was significantly increased in IBD compared to non-IBD patients. Additionally, a significant positive correlation was observed between OGR1 expression and the clinical score in both the non-inflamed (r = 0.731, p = 0.0069) and the inflamed mucosa (r = 0.7698, p = 0.0054).

**Conclusion:** Expression of OGR1 is significantly increased in patients with IBD. OGR1 expression correlates with IBD disease activity, suggesting an active role for OGR1 in IBD pathogenesis. OGR1 appears to be a therapeutic target among the pH-sensing receptors involved in IBD.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**References:**

**TABLE 1:** Summary of Bacterial Taxonomic Findings in South Asians (SA) and Caucasians with ulcerative colitis. *Increase or decrease in SA relative to Caucasians.

<table>
<thead>
<tr>
<th>Phylum</th>
<th>Change*</th>
<th>Family</th>
<th>Change*</th>
<th>Genus</th>
<th>Change*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Actinobacteria</strong></td>
<td>Increased</td>
<td><strong>Bifidobacteriaceae</strong></td>
<td>Increased</td>
<td><strong>Bifidobacterium</strong></td>
<td>Increased</td>
</tr>
<tr>
<td><strong>Bacteroides</strong></td>
<td>Decreased</td>
<td><strong>Bacteroidales</strong></td>
<td>Decreased</td>
<td><strong>Barnesiellaceae</strong></td>
<td>Increased</td>
</tr>
<tr>
<td><strong>Firmicutes</strong></td>
<td>Decreased</td>
<td><strong>Clostridiales</strong></td>
<td>Decreased</td>
<td><strong>Clostridium</strong></td>
<td>Increased</td>
</tr>
<tr>
<td><strong>Streptococcus</strong></td>
<td>Increased</td>
<td><strong>Streptococcaceae</strong></td>
<td>Increased</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Streptococcus</strong></td>
<td>Increased</td>
<td><strong>Streptococcaceae</strong></td>
<td>Increased</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Ruminococcaceae</strong></td>
<td>Increased</td>
<td><strong>Ruminococcaceae</strong></td>
<td>Increased</td>
<td><strong>Ruminococcus</strong></td>
<td>Increased</td>
</tr>
<tr>
<td><strong>Ruminococcus</strong></td>
<td>Decreased</td>
<td><strong>Ruminococcaceae</strong></td>
<td>Decreased</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Bacteriodes</strong></td>
<td>Decreased</td>
<td><strong>Bacteroidales</strong></td>
<td>Decreased</td>
<td><strong>Bacteroidaceae</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Vellurnellaceae</strong></td>
<td>Increased</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Proteobacteria</strong></td>
<td>Increased</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Conclusion:** Increased **Bifidobacteria** and **Lactobacilli** in the SA group is consistent with the previous study. A possible explanation is the consumption of fermented foods in the SA group although there was no difference between healthy SA and Caucasian controls. There is a trend towards lower diversity in the SA group and reduced **Bacteroides** which are consistent with the UC dysbiosis described in the literature. Functional analysis of this unique microbial profile through metagenomic and metabolomic techniques may explain the different disease behaviour in the SA group.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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**Introduction:** There is evidence for vitamin D as an immunomodulator in patients with IBD, but results from clinical trials to date are inconclusive. It is uncertain whether vitamin D supplementation may affect the intestinal microbiota.

**Aims & Methods:** This study aimed to assess the effect of vitamin D replacement in deficient patients with and without ulcerative colitis (UC) on inflammation and faecal microbiota. Vitamin D was replaced over 8 weeks to patients with active UC, inactive UC, and non-IBD controls with baseline 25(OH) vitamin D < 30 nmol/L, and markers of inflammation and stool collected for microbiota analyses by next generation sequencing.

**Results:** Eight patients with active UC, 9 with inactive UC and 8 non-IBD controls received 40,000 units of vitamin D weekly for 8 weeks. No demographic differences were noted across the groups. Mean baseline 25(OH) vitamin D levels were 34 (range 12–49) nmol/L. Vitamin D supplementation increased mean 25(OH) vitamin D to 111 (range 71–158) nmol/L (P = 0.001), and reduced para-thyroid hormone levels from mean 4.3 to 3.3 pmol/L (p = 0.017). No change in baseline medications for UC took place in patients with UC, except for one patient with active UC who ceased his 5-aminosalicylic. Faecal calprotectin levels reduced from median 275 to 91 μg/g (p = 0.023) in patients with active colitis, but did not change in patients with inactive colitis or non-IBD controls. Similar improvements in albumin, platelet count and symptomatic disease activity indices were noted. No changes in overall bacterial diversity were noted. There was a trend towards an increase in abundance of *Ruminococcus gnavus* post vitamin D supplementation in active UC patients, but this did not reach statistical significance.

**Conclusion:** Vitamin D supplementation was associated with reduced intestinal inflammation in patients with active UC. A randomised controlled trial evaluating vitamin D in IBD is required along with further investigation of potential mechanisms by which vitamin D may alter specific microbial composition.

**Disclosure of Interest:** M. Garg: This work was supported by the European Crohn’s and Colitis Fellowship awarded to Dr Mayur Garg, and St Mark’s Association Grant awarded to Prof Ailsa Hart and Dr Mayur Garg. All other authors have declared no conflicts of interest.
**P1615** SUPPRESSION OF PHOSPHOLIPASE A2 OF INTESTINAL MICROBIAL STRAINS MINIMIZES MUCOSAL INFLAMMATION IN A GENETIC MOUSE MODEL OF ULCERATIVE COLITIS

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**Introduction:** Attack by commensal microbiota is one component for induction of inflammatory episodes in ulcerative colitis (UC). In UC, the mucus layer is intrinsically devoid of phosphatidylcholine (PC) resulting in low hydrophobicity, which facilitates bacterial invasion. Colonic ectophospholipase-carrying bacterial strains are likely candidates to break the PC mucus barrier. Therefore we aimed to evaluate the effect of phospholipase A2 (PLA2) inhibitors on inflammation in a genetic UC mouse model.

**Aims & Methods:** Attack by commensal microbiota is one component for induction of inflammatory episodes in ulcerative colitis (UC). In UC, the mucus layer is intrinsically devoid of phosphatidylcholine (PC) resulting in low hydrophobicity, which facilitates bacterial invasion. Colonic ectophospholipase-carrying bacterial strains are likely candidates to break the PC mucus barrier. Therefore we aimed to evaluate the effect of phospholipase A2 (PLA2) inhibitors on inflammation in a genetic UC mouse model.

**Results:** Luminal UDCA-LPE reduced the PLA2 activity in stool by 36.4%-8%. Concomitantly no inflammatory phenotype was observed when compared to knd2-/- mice not treated with UDCA-LPE. The improvement was documented in regard to stool consistency, calprotectin levels in stool, and macroscopic/analytic as well as histologic features of the mucosa. The pattern of colonic microbiota distribution obtained in the UC phenotype mice was reversed by UDCA-LPE to the control mice pattern. Construction of the bacterial ectophospholipase A2 activity improves mucosal inflammation in a genetic mouse model of UC. It is assumed that the remaining mucus PC shield is better preserved when luminal PLA2 is suppressed.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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**P1616** THE IMPACT OF THE RS8005161 POLYMORPHISM ON G PROTEIN-COUPLED RECEPTOR GPR65 (TDAG8) PH-ASSOCIATED SIGNALING IN INTESTINAL INFLAMMATION


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**Introduction:** Inflammatory bowel diseases (IBDs), Crohn’s disease (CD) and ulcerative colitis (UC), are typically associated with a loss of homeostasis in local pH. Genome-wide association studies (GWAS) identified over 240 non-overlapping single-nucleotide polymorphisms (SNP) associated with IBD, G-protein-coupled receptor 65 (GPR65) or Toll death associated gene 8 (TDAG8) has recently been reported to be a genetic risk factor for IBD. The gene of the lead SNP GPR65 SNP (rs8005161) within the GPR65 gene confers increased IBD risk. In response to extracellular acidification, GPR65 activates second messengers: cAMP, via the Gs signaling pathway, and G12/13/Rho signaling.

**Results:** Sequenced genotype frequency of rare homozygote rs8005161 in the SIBDCS was 1.17%, minor allele frequency (MAF) - 10.3%. The variant rs8005161 was more frequent in UC patients (M AF 14.53% vs 10.05% in the non-IBD group), whereas no statistically significant association with IBD, CD or UC was found for the other variants (GPR65 rs3742704, GALC rs1805078) by Taqman genotyping. No significant differences were observed in the cAMP production between IBD (WT/CC, CT, TT) and non-IBD (WT/CC) genotype carriers upon pH shift from 7.6 to 6.6. A decreased activation of GTPase Rhôo was detected in IBD (WT/CT, TT) patients as compared to non-IBD (WT/CC) patients (r=0.807), but no differences between rs8005161 TT, CT and CC patients was observed.

**Conclusion:** The minor T allele of the GPR65 associated SNP rs8005161 was significantly enriched in UC patients. Rhôo signaling was reduced in IBD patients as a result of a reduced activation of GTPase Rhôo signaling in IBD versus controls. However, no differences in cAMP signaling in IBD TT/CC subjects compared to healthy CC subjects were observed. Our results suggest impaired Rhôo signaling in IBD patients upon a pH shift, indicating a mechanistic explanation for increased IBD risk with GPR65 polymorphisms.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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**P1617** B2-STRUCTURING AND B3-PENETRATING PHENOTYPE IN CROHN’S DISEASE: CHALLENGE OF MACROPHAGES POPULATION AND WNT SIGNALING

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**Introduction:** Macrophages contribute to fibrosis through the release of different mediators and the pattern of secretion may vary according to their phenotype. Recent evidences have identified Wnt pathway as an emerging modulator of fibrosis.

**Aims & Methods:** The aim of the present study is to analyze the pattern of expression of macrophage markers and Wnt ligands in surgical resections from Crohn’s disease (CD) patients with different disease behavior. CD patients were categorized according to Montreal classification (age at diagnosis, location and behavior). mRNA was isolated from resections of patients presenting an structuring (B2) or a penetrating (B3) behavior or from patients with colorectal cancer (control). The expression of macrophage markers (CD206, CD86, iNOS, Argenae), Wnt ligands (Wnt1, Wnt2, Wnt3, Wnt4, Wnt5a, Wnt5b, Wnt6, Wnt7a, Wnt7b, Wnt8a, Wnt8b, Wnt9b, Wnt10a, Wnt10b and Wnt16) and DKK1 (inhibitor of Wnt signaling) was analyzed by RT-

**Results:** B3-patients seem to present a higher infiltration of macrophages since increased expression of markers classically used to detect pro-inflammatory (CD68) and regulatory/pro-resolving/pro-fibrotic phenotypes (CD206, ARG2) was detected in this group. These patients also presented a generalized increased expression of Wnt ligands together with augmented DKK1 mRNA levels. B2-patients showed a more complex situation with ligands that present increased (Wnt3), reduced (Wnt2B) or unchanged expression in the absence of significant variations in the levels of macrophage markers (Table). Table. Relative (G/A) mRNA expression (fold induction vs control group) of genes with detectable levels. Data are expressed as Mean±SEM with n ≥ 7 in all groups and analyzed by ANOVA + Keenan-Keuls test. (P< 0.05 vs control; #p < 0.05 vs B2).

**Conclusion:** Crohn’s disease patients presenting a structuring (B2) or a penetrating (B3) behavior undergoing surgical resection differ in the pattern of macrophage infiltration and Wnt signaling.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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**P1618** CD16 POSITIVE CELLS EXPRESS TGFβ AND MEDIATES MURINE INTESTINAL FIBROSIS


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**Introduction:** M2 macrophages play a key role in injury repair and fibrosis. We have reported that STAT6-dependent macrophages mediate mucosal repair after TNBS-induced acute colitis 3 and that, in a chronic model, STAT6-deficient animals accumulate macrophages expressing the CD16 marker that promote intestinal fibrosis 2.

**Aims & Methods:** We aim to analyze whether the expression of the pro-fibrotic mediator TGFβ is related with this macrophage phenotype and the relevance of these cells in murine intestinal fibrosis. Murine peritoneal macrophages obtained from both WT or STAT6 (-/-) mice were treated with IL-4 (20 ng/ml), IL-10 (10 ng/ml) or vehicle and the mRNA expression of CD16 and TGFβ was analyzed 72h later by qPCR. WT or STAT6 (-/-) mice were weekly administered with TNBs (0.5, 0.5, 0.75, 0.5, 1, and 1 mg, intrarectally) or saline and were sacrificed 7 weeks after the first TNBs administration. The mRNA expression of CD16, TGFβ, Vimentin, Coll1a1, a-SMA, MMP2 and TIMP1 was evaluated in murine intestinal mucosa by qPCR. In all cases results were expressed as fold induction vs vehicle and the correlation between different measurements was analyzed using Pearson’s correlation coefficient (r).

**Results:** A positive and significant correlation between CD16 mRNA and TGFβ mRNA was observed in isolated macrophages from WT mice (r = 0.637, P = 0.03) and STAT6 (-/-) mice (r = 0.677, P = 0.002) receiving different treatments. In the mucosa of WT and STAT6 mice the expression of TGFβ showed a significant positive correlation with CD16 mRNA (r = 0.60, P < 0.001), and with the expression of several fibrotic markers (vimentin: r = 0.637, P < 0.001; Colla1: r = 0.5101, P = 0.0003; a-SMA: r = 0.4126, P = 0.0048; MMP2: r = 0.5729, P = 0.0001; and TIMP1: r = 0.3958, P = 0.0071).

**Conclusion:** The expression of TGFβ is associated with CD16 positive cells and is involved in murine intestinal fibrosis.

**Disclosure of Interest:** All authors have declared no conflicts of interest.
Aims & Methods: The present study is to analyze the pattern of expression of macrophages and the expression of Wnt10b in human macrophages from clinical samples from Crohn’s disease (CD) patients with A2-stratifying and B3-penetrating behavior according to Montreal classification (age at diagnosis, location and behavior) as well as from non-inflamed tissue from cancer patients. Resections were immediately processed and lamina propria mononuclear cells characterized by flow cytometry. Macrophages were identified within singlet viable leukocytes as CD45 + CD14 + CD64 + . The percentage of CD206, CD16, CD163, CD86 and Wnt10b positive cells was analyzed in macrophages. Data are expressed as Mean±SEM % with n≥5 in all groups (P<0.05 vs control; Student's t test).

Results: The percentage of macrophages identified as CD45 + CD14 + CD64 + constituted the 0.22±0.03% of total events in the control mucosa while represented the 1.35±0.40% in the mucosa from CD patients (p<0.05). A high proportion of myofibroblasts/macrophages expressed CD206 in both, control (83.3±4.8%) and CD (89.6±3.9%). In these CD206+ cells, an increased expression of CD16 in CD mucosa was observed (Control: 34.5±6.8%; CD: 59.7±6.4%) while that of CD163 was similar in both groups (control: 72.8±8.4%; CD: 85.2±7.3%). The analysis of Wnt10b in CD206+ showed a significantly higher expression in CD patients (56.6±4.2%) than in control samples (30.1±10.4%). Additionally, CD86+ macrophages were more abundant in control (1.7±0.3) and CD (29.3±10.2) mucosa.

Conclusion: The mucosa of CD patients accumulate pro-inflammatory macrophages measured as CD86+ cells while those macrophages expressing the M2-marker CD206 after their phenotype increasing the expression of both, CD16 and CD163. This could be the profibrotic mediator Wnt10b.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

P1621 ANAEMIA PREVALENCE AND TREATMENT APPROACH FOR INFLAMMATORY BOWEL DISEASE
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Introduction: For inflammatory bowel disease (IBD), anaemia is the most frequently observed extra intestinal finding, prevalence of which varies from 6% to 74%. It’s of great importance to determine and treat anaemia as it lowers patients’ life quality and leads to labour loss. The main causes of anaemia in IBD are iron deficiency anaemia (IDA) and anaemia of chronic disease (ACD). In this study, we aim to specify the type and prevalence of anaemia along with a treatment approach for inflammatory bowel disease (IBD).

Aims & Methods: In this study, we specify the type and prevalence of anaemia along with a treatment approach for inflammatory bowel disease (IBD).

Results: We specified the following types of anaemia: IDA only (29.7%), IDA and ACD together (4.8%) while that of CD163 was similar in both groups (control: 72.8±8.4%; CD: 85.2±7.3%). The analysis of Wnt10b in CD206+ showed a significantly higher expression in CD patients (56.6±4.2%) than in control samples (30.1±10.4%). Additionally, CD86+ macrophages were more abundant in control (1.7±0.3) and CD (29.3±10.2) mucosa.

Conclusion: The mucosa of CD patients accumulate pro-inflammatory macrophages measured as CD86+ cells while those macrophages expressing the M2-marker CD206 after their phenotype increasing the expression of both, CD16 and CD163. This could be the profibrotic mediator Wnt10b.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

P1620 EXPRESSION OF WNT10B IN M2-MACROPHAGES FROM CROHN’S DISEASE PATIENTS
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Introduction: Intestinal fibrosis is a common complication of IBD and macrophages can contribute to fibrosis through the release of different mediators. We have recently reported that Wnt10b increases the deposition of collagen and promotes intestinal fibrosis in TNBS-treated mice (P015 ECCO 2017).

Aims & Methods: The aim of the present study is to analyze the pattern of expression of macrophages and the expression of Wnt10b in human macrophages from clinical samples from Crohn’s disease (CD) patients with A2-stratifying and B3-penetrating behavior according to Montreal classification (age at diagnosis, location and behavior) as well as from non-inflamed tissue from cancer patients. Resections were immediately processed and lamina propria mononuclear cells characterized by flow cytometry. Macrophages were identified within singlet viable leukocytes as CD45 + CD14 + CD64+. The percentage of CD206, CD16, CD163, CD86 and Wnt10b positive cells was analyzed in macrophages. Data are expressed as Mean±SEM % with n≥5 in all groups (P<0.05 vs control; Student’s t test).

Results: The percentage of macrophages identified as CD45 + CD14 + CD64+ constituted the 0.22±0.03% of total events in the control mucosa while represented the 1.35±0.40% in the mucosa from CD patients (p<0.05). A high proportion of myofibroblasts/macrophages expressed CD206 in both, control (83.3±4.8%) and CD (89.6±3.9%). In these CD206+ cells, an increased expression of CD16 in CD mucosa was observed (Control: 34.5±6.8%; CD: 59.7±6.4%) while that of CD163 was similar in both groups (control: 72.8±8.4%; CD: 85.2±7.3%). The analysis of Wnt10b in CD206+ showed a significantly higher expression in CD patients (56.6±4.2%) than in control samples (30.1±10.4%). Additionally, CD86+ macrophages were more abundant in control (1.7±0.3) and CD (29.3±10.2) mucosa.

Conclusion: The mucosa of CD patients accumulate pro-inflammatory macrophages measured as CD86+ cells while those macrophages expressing the M2-marker CD206 after their phenotype increasing the expression of both, CD16 and CD163. This could be the profibrotic mediator Wnt10b.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference
Conclusion: We found out that almost half of all IBD patients (50.3%), whom we followed up, had anaemia, the most frequent reason of which was IDA. Almost half of these patients received anaemia treatment. We should increase the treat- ment rate in our IBD patients that have anaemia.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1622 SUCCINATE RECEPTOR (SUCNR1) MEDiates INFLAMMATORY MURINE MODEL OF COLITIS

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Introduction: IBD is a chronic disorder of the gastrointestinal tract characterized by disruption of epithelial barrier function and gut inflammation. Evidence supports a relevant role of succinate, an intermediate of the tricarboxylic acid cycle1, in inflammation and the succinate receptor, SUCNR1, has been recently reported with rheumatoid arthritis2.

Aims & Methods: To analyze the role of SUCNR1 in a murine model of colitis induced by TNBS. WT or SUCNR1C11−/− mice received TNBS (3.5 mg/20g mice, intrarectally) or vehicle (EtOH 40%) and were weighed daily (results are expressed as percentage vs the weight at day 0 and mice were sacrificed 2 and 4 days after TNBS administration. Colon length and mucosal histology were evaluated. The mRNA expression levels of the inOS, Arginase I, COX-2, TNF-α, IL-1β, IL-6 and IL-10 was assessed by qPCR.

Results: Treatment of mice with TNBS induced a loss of body weight that peaked 4 days after TNBS administration. Colon length and mucosal histology were evaluated according to Wallace Score (1–10). The mRNA expression levels of iNOS, Arginase I, COX-2 (Table 1) were significantly different between TNBS-treated WT mice, as compared with TNBS-treated WT mice: a) the loss of body weight was significantly (P < 0.05) attenuated (96.99 ± 0.7% vs 91.78 ± 1.1%); b) the reduction in colon length was prevented (6.6 ± 0.2 vs 5.2 ± 0.2); and c) the mRNA expression was significantly (3.5 ± 0.2 vs 4.8 ± 0.5) increased two days after TNBS treatment. The increase in the expression of pro-inflammatory molecules was significantly prevented (P < 0.05) in TNBS-treated SUCNR1C11−/− mice compared with TNBS-treated WT mice.

Conclusion: Activation of the succinate receptor SUCNR1 mediates murine colitis. These findings highlight the biological significance of SUCNR1 and open the door to novel approaches for IBD treatment.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

Aims & Methods: Our aim was to investigate the role of ZIP7 in IBD initiation and progression. We investigated the expression of ZIP7 in the intestinal mucosa of IBD patients and in interleukin-10–deficient (Il10C11−/−) mice, and assessed the relation between ZIP7 and disease activity. ZIP7 upregulated downregulated lenivius was used to infect IEC6 and HEC cells, then we evaluated the expression of inflammatory factors, mucosal tight junction proteins (Occludin and ZO-1), and proteins related with endoplasmic reticulum stress (IRE1, XBP1, TRAF2, ASK1 and p-JNK). In addition, we used siRNA to silence IRE1 and SP600125 to inhibit the JNK pathway respectively, then evaluated the effect of endoplasmic reticulum stress on mucosal tight junction proteins.

Results: We found that ZIP7 was downregulated both in the intestinal mucosa of IBD patients and in Il10C11−/− mice, which was associated with disease activity. In IEC6 and HEC cells, the expression of mucosal tight junction proteins was consistent with the level of ZIP7, but the expression of inflammatory factors, mucosal tight junction proteins (Occludin and ZO-1), and proteins related with endoplasmic reticulum stress associated proteins were on the contrary. After the silence of IRE1 and the inhibition of JNK pathway, the expression of mucosal tight junction proteins was partly returned in ZIP7 downregulated cells.

Conclusion: ZIP7 induces disruption of the intestinal barrier, which was associated with activation of endoplasmic reticulum stress in IBD. It is expected to provide a novel mechanism of IBD and provide a new target for the treatment of IBD.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1624 EFFECT OF T CELL ACTIVATION AND INFLAMMATION ON THE INTERACTION BETWEEN T CELLS AND ENTERIC GLIAL CELLS

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Introduction: Enteric glia cells (EGC) are essential for intestinal homeostasis. In healthy intestines, EGC reduce IEB permeability and the reactive EGC functional impact on IEB permeability was studied (i) in vitro by grafting the treated rat EGC in colon wall of Sprague Dawley rats. In vivo colon wall grafting with control EGC did not modified the permeability whereas colon wall grafting with EGC preconditioned by TI significantly reduced

Results: Analyses reveal that non-activated T lymphocytes are capable of interacting with EGC. They also show that activation of T cells with anti-CD3/anti-CD28 antibodies increases the number of T lymphocytes interacting with EGC. Interestingly, an increased number of EGC-T cell interactions was observed after pretreatment of EGC with inflammatory stimuli. This phenomenon was also noted with activated T cells. Characterization of T cells show that both CD4 and CD8 cells are capable of contact with EGC.

Conclusion: Our present data reveal that EGC interact with T cells. These contacts are favored by T cell activation but also by EGC exposure to inflammatory cytokines. Further experiments are required to characterize these neuro-immune interactions but they suggest that EGC-T cell contact may play a crucial role in case of inflammatory bowel diseases. This work is supported by the Association François Aupetit.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1625 ENTERIC GLIAL CELLS REACTION TO INFLAMMATION IS LOST IN CROHN’S DISEASE

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Introduction: Enteric glial cells (EGC) are essential for intestinal epithelial barrier (IEB) homeostasis. In healthy intestines, EGC reduce IEB permeability and promote mucosal healing. In inflammatory bowel disease (IBD) such as Crohn’s Disease (CD) and Ulcerative Colitis (UC), both EGC phenotype and IEB functions are altered, but putative involvement of EGC in IBD pathogenesis remains unknown. If the astrocyte reactivity is well studied, the reaction of EGC in case of chronic inflammation is not well documented. We investigated whether EGC-IEB interactions are altered in an inflammatory environment and in IBD patients.

Aims & Methods: Rat EGC as well as human EGC from control, CD and UC patients were stimulated with the cytomix TI (TNFalpha + IL1beta + 100 ng/ml) or LPS for 2 or 4 days. Reactive EGC phenotype were characterized and reactive EGC functional impact on IEB permeability was studied (i) in vitro using human intestinal epithelial cells (IEC6) in a non-co-tact co-culture model, or (ii) in vivo by grafting the treated rat EGC in colon wall of Sprague Dawley rats.

Results: Rat and human control EGC induced a significant reduction of IEB permeability in vitro, whereas IBD EGC induced a significant increase of IEB permeability. IBD EGC were also used to characterize the subpopulations of T cells (CD4+, CD8+) that contact glial cells.

References

Aims & Methods: Our aim was to investigate the role of ZIP7 in IBD initiation and progression. We investigated the expression of ZIP7 in the intestinal mucosa of IBD patients and in interleukin-10–deficient (Il10C11−/−) mice, and assessed the relation between ZIP7 and disease activity. ZIP7 upregulated downregulated lenivius was used to infect IEC6 and HEC cells, then we evaluated the expression of inflammatory factors, mucosal tight junction proteins (Occludin and ZO-1), and proteins related with endoplasmic reticulum stress (IRE1, XBP1, TRAF2, ASK1 and p-JNK). In addition, we used siRNA to silence IRE1 and SP600125 to inhibit the JNK pathway respectively, then evaluated the effect of endoplasmic reticulum stress on mucosal tight junction proteins.

Results: We found that ZIP7 was downregulated both in the intestinal mucosa of IBD patients and in Il10C11−/− mice, which was associated with disease activity. In IEC6 and HEC cells, the expression of mucosal tight junction proteins was consistent with the level of ZIP7, but the expression of inflammatory factors, mucosal tight junction proteins (Occludin and ZO-1), and proteins related with endoplasmic reticulum stress associated proteins were on the contrary. After the silence of IRE1 and the inhibition of JNK pathway, the expression of mucosal tight junction proteins was partly returned in ZIP7 downregulated cells.

Conclusion: ZIP7 induces disruption of the intestinal barrier, which was associated with activation of endoplasmic reticulum stress in IBD. It is expected to provide a novel mechanism of IBD and provide a new target for the treatment of IBD.

Disclosure of Interest: All authors have declared no conflicts of interest.
**P1626** PROSTACYCLIN REVERSES COLITIS THROUGH THE DOWN REGULATION OF INTESTINAL EPITHELIAL PERMEABILITY

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**Introduction:** In inflammatory bowel disease (IBD) both intestinal epithelial barrier (IEB) permeability and PTGIS expression are altered. Nevertheless the role of the lipid mediator PG12 produced by PTGIS in IEB permeation is unknown. The present study concerns the control of IEB permeability by PG2 and its involvement in the development of colitis.

**Aims & Methods:** The role of PG12 production from control or IBD biopsies was established using high sensitivity liquid chromatography tandem mass spectrometry. Consequences of flolan PG12 analogous supplementation were evaluated in a DSS-induced mice model of colitis, measuring disease activity index (DAI), inflammation (pro-inflammatory cytokine mRNA) and IEB permeability (sulfonic acid flux). Molecular mechanisms involved were assessed by quantification of junctional and pro-proliferative pro-apoptotic protein expression (western blot and immunostaining). Eventually PG12 impact on reversing IEB breakdown was assessed ex vivo measuring permeability of mice or human mucosal explants treated with staurosporine apoptosis inducer, or permeability of IBD biopsies both treated or not with flolan.

**Results:** Biopsies from IBD patients had lower PG12 production compared to control patients, and addition of flolan reduced their permeability. In vivo PG12 supplementation significantly reduced DAI, and inflammation (Interferon mRNA) as well as reduced IEB permeability. DSS-induced cleavage of Caspase 3 is normalized by flolan.

**Conclusion:** This study not only presents a role of PG12 in controlling IEB permeability through the regulation of apoptosis mechanisms, but also reveals that increased permeability in IBD patients can be fixed by PG12 supplementation.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**Reference**

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**Introduction:** Ulcerative colitis (UC) is a clinical type of inflammatory bowel diseases. The pathogenesis of UC remains unclear. Nowadays the role of Th17 helpers type 17 (Th17) as well as cytokines they release is discussed in pathogenesis of autoimmune inflammation in UC.

**Aims & Methods:** The aim of study is to analyze the serum levels of following cytokines: interleukin (IL)-17A and F, 21, 22, 23, 10 in UC patients both in the acute stage of disease and remission. Forty eight UC patients in the acute stage and twenty patients in remission were included into the study. Serum cytokine levels were analyzed using multiplex immunoassay for Th17 cytokines (Bio-Rad, USA). Statistical analysis was performed using STATISTICA 6.0 Software Package. The control group consisted of 11 healthy volunteers.

**Results:** Statistically significant increase of IL-17A level (15 pg/ml [12.11;23.38]; 14.68 pg/ml [11.29;17.19] respectively) was observed in patients with UC both in acute stage and remission compared to controls (7.36 pg/ml [5.18;8.06]; p = 0.00007, p = 0.00029 respectively). The same trend was observed regarding IL-21, which median values were higher both in acute stage (156.51 pg/ml [133.44;233.53]) and remission (144.02 pg/ml [133.44;154.43]) compared to control group (98.31 pg/ml [89.14;124.86]), and showed statistically significant differences (p = 0.00077, p = 0.00054 respectively). Besides it was revealed that IL-17F and IL-22 were also higher in acute stage (136.5 pg/ml [68.05;228.185] and 3.76 pg/ml [1.55;8.33], respectively) compared to controls (48.7 pg/ml [38.7;87.6], and 2.6 pg/ml [1.7;3.2], respectively), however differences were not statistically significant (p = 0.06; p = 0.172, respectively). Increase of described cytokines levels could be a sign of Th17 functional overactivity suggesting autoimmune type of inflammation.Statistically significant increase of IL-10 in remission (27.99 pg/ml [17.53;33.55]) compared to controls (4.36 pg/ml [3.26;15.25], p = 0.0046) was found as well. IL-10 was also higher in patients with acute stage (21.93 [3.61;35.35]) compared to controls, however differences were not statistically significant (p = 0.065). IL-10 as an anti-inflammatory cytokine characterizes the activity of regulatory T-cells which suppress autoimmune inflammation. In addition, it was revealed that the level of IL-23 which stimulates Th17 differentiation was both higher in acute stage (258.4 pg/ml [55;367.49]) and remission (244.93 pg/ml [124.3;301.93]) compared to controls (124.3 pg/ml [107.9;296.04]), however differences were not statistically significant.

**Conclusion:** Increase of IL-17A, IL-17F, IL-21, IL-22 levels could be a sign of Th17 functional overactivity suggesting autoimmune type of inflammation. IL-17A and IL-21 produced by Th17 cells might be considered as markers of active autoimmune inflammation in UC patients.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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**Disclosure of Interest:** All authors have declared no conflicts of interest.
P1629 ANP32E IS INVOLVED IN THE STEROID-REFRACTORY UC GEMBER: A SYSTEMATIC APPROACH
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Introduction: The steroid-refractoriness is a common complication of ulcerative colitis (UC) with an unproven antirefractory mechanism of action (MoA) that has been implicated in corticosteroid failure. However, there are no conclusive studies on the molecular functions involved in UC steroid-refractoriness.
Aims & Methods: Therefore, we decided to know in depth the MoA related to the steroid-refractoriness of UC patients with UC treated with glucocorticoids. RNA from rectal biopsies was obtained before and on the 3rd day of glucocorticoid treatment. Then, whole-genome expression using microarrays (Illumina, USA) and profiles microRNA by sequencing (Illumina, USA) were analysed. After quality control, omics data were compared between phenotypes. The results of these comparisons were integrated into mathematical models generated by means of Systems Biology.
Results: These models reproduce the updated molecular interactions on glucocorticoids and UC, and integrating our experimental data, we identified a potential MoA that includes 64 key proteins, 18 of them capable of perfectly classifying patients with a good response to glucocorticoids and the non-responders. The biological functions of these proteins have been associated with inflammation (e.g. RelA), glucocorticoid receptor transcription (e.g. NR3C1 and NCOA3) and angiogenesis (e.g. VEGF), mainly. But among these 18 proteins, the ANP32E has never been related to either steroid-refractoriness or ulcerative colitis. ANP32E is a 30 kDa protein (A-type) that is part of the chromatin (flanking DNA regions recognized by the glucocorticoid receptor). Additional WB and immunofluorescence assays confirm differences in the intestinal levels of ANP32e and in the nuclear localization at baseline, between patients with drug refractory UC.
Conclusion: In conclusion, this study has identified a potential new MoA related to UC steroid-refractoriness involving chromatin remodeling modifications.
Disclosure of Interest: All authors have declared no conflicts of interest.

P1630 CO-HOUSING DSS TREATED MICE WITH HEALTHY MICE RESULTS IN FASTER NORMALIZATION OF THE INTestinal MICROBIOTA AND PROMOTES RECOVERY
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Introduction: The intestine is populated with myriads of bacteria, which form a complex ecosystem and have tremendous impact on our health. In inflammatory bowel disease (IBD), shifts in microbiota composition and a reduction in overall diversity (decreased Shannon index, \( p < 0.01 \)) and a marked shift in the composition of the microbiota (increased abundance of Verrucomicrobia, Cyanobacteria and some families of Firmicutes [mainly Clostridiae], although overall abundance of Firmicutes was decreased \( \text{p} < 0.01 \)) was observed between the percentage of expression of sulfomucins at surgery, at 6 or 12 months after ileo-colonic resection (1). In the present study, correlation between the percentage of expression of sulfomucins and clinical recurrence was evaluated for 5 years. Colonic phenotype of the ileum as assessed by the expression of sulfomucins (colon mucin-type) and saIomucins (small intestine mucin-type) (1). In the present study, correlation between the percentage of expression of sulfomucins and clinical recurrence was evaluated for 5 years. Statistical analysis: results expressed as median (range), correlations were assessed by the Spearman correlation test, differences between groups by the unpaired T test.
Results: After ileo-colonic resection, clinical follow up at 5 years was completed by 17/19 (89.4%) CD patients enrolled (12 males, age 41 [17–73]). The percentage of expression of sulfomucins (colon phenotype) as assessed in the ileal surgical specimens was significantly correlated with the CDAI score at 4 years \( (r = 0.62; \text{p} = 0.007) \) and at 5 years \( (r = 0.6; \text{p} = 0.010) \). Differently, in the ileal biopsies at 6 months with vs without clinical recurrence, both at 12 months \( (r = 0.53; \text{p} = 0.03) \) and at 5 years \( (r = 0.53; \text{p} = 0.02) \). The ileal expression of sulfomucins in the ileal biopsies at 12 months was higher in patients with vs without clinical postoperative recurrence at 2 years \( (40 [10–99] \text{vs} 5 [0–30]; \text{p} = 0.044) \). The expression of colon mucin-type in the ileal biopsies at 12 months was higher in patients with vs without clinical recurrence, both at 12 months \( (30 [1–40] \text{vs} 0 [0–35]; \text{p} = 0.02) \) and at 2 years \( (30 [0–40] \text{vs} 0 [0–33]; \text{p} = 0.029) \). No correlations were observed between the percentage of expression of sulfomucins at surgery, at 6 or 12 months and the haematochemical parameters considered.
Conclusion: In CD, colonic phenotype of the ileum as assessed by the expression of ileal sulfomucins, may represent a predictive marker of clinical recurrence after ileo-colonic resection for CD.
Disclosure of Interest: L. Biancone: The study was not supported by any grant nor funded and any of the below reported disclosures are related to the study. Lecture fees or Advisory Board: Zambon, MS&D, Takeda, Abbvie, Sofar, Ferring, Wassermann; F. Pallone: The study was not supported by any grant nor funded and any of the below reported disclosures are related to the study. Lecture fees from Tazbom, Takeda.
All other authors have declared no conflicts of interest.

References

P1631 ILEAL SULFOMUCINS PREDICT CLINICAL RECURRENCE AFTER ILEO-COLONIC RESECTION FOR CROHN’S DISEASE: A PROSPECTIVE STUDY AT 5 YEARS
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Introduction: In Crohn’s Disease (CD), colonic phenotype of the ileum has been reported in severe lesions, but not in CD ileum with no lesions or with early post-operative recurrence (1).
Aims & Methods: In a prospective study at 5 years, we aimed to address whether colonic phenotype of the ileum may represent a subclinical marker of clinical postoperative recurrence in CD. At this purpose, clinical recurrence was assessed yearly for 5 years in a cohort of CD patients with colonic phenotype of the ileum already defined at surgery, 6 and at 12 months after ileo-colonic resection (1). A cohort of CD patients with clinical recurrence already assessed and reported at 6 and 12 months after ileo-colonic resection (1), was clinically followed up for additional 4 years. In the 5 years follow up, indication for treatments, haematochemical, radiological and/or endoscopic assessments was given according to current European guidelines (2). Haematochemical assessments included whole blood count, ESR, serum CRP evaluation yearly for 5 years, with possible additional assessments, according to clinical indications. Clinical recurrence (CDAI > 150) was assessed yearly for 5 years. Colonic phenotype of the ileum was already reported at surgery, at 6 and 12 mos, according to the expression of sulfomucins (colon mucin-type) and saIomucins (small intestine mucin-type) (1). In the present study, correlation between the percentage of expression of sulfomucins and clinical recurrence was evaluated for 5 years. Statistical analysis: results expressed as median (range), correlations were assessed by the Spearman correlation test, differences between groups by the unpaired T test.
Results: After ileo-colonic resection, clinical follow up at 5 years was completed by 17/19 (89.4%) CD patients enrolled (12 males, age 41 [17–73]). The percentage of expression of sulfomucins (colon phenotype) as assessed in the ileal surgical specimens was significantly correlated with the CDAI score at 4 years \( (r = 0.62; \text{p} = 0.007) \) and at 5 years \( (r = 0.6; \text{p} = 0.010) \). Differently, in the ileal biopsies at 6 months with vs without clinical recurrence, both at 12 months \( (r = 0.53; \text{p} = 0.03) \) and at 5 years \( (r = 0.53; \text{p} = 0.02) \). The ileal expression of sulfomucins in the ileal biopsies at 12 months was higher in patients with vs without clinical postoperative recurrence at 2 years \( (40 [10–99] \text{vs} 5 [0–30]; \text{p} = 0.044) \). The expression of colon mucin-type in the ileal biopsies at 12 months was higher in patients with vs without clinical recurrence, both at 12 months \( (30 [1–40] \text{vs} 0 [0–35]; \text{p} = 0.02) \) and at 2 years \( (30 [0–40] \text{vs} 0 [0–33]; \text{p} = 0.029) \). No correlations were observed between the percentage of expression of sulfomucins at surgery, at 6 or 12 months and the haematochemical parameters considered.
Conclusion: In CD, colonic phenotype of the ileum as assessed by the expression of ileal sulfomucins, may represent a predictive marker of clinical recurrence after ileo-colonic resection for CD.
Disclosure of Interest: All authors have declared no conflicts of interest.
P1632 IMMUNOREACTIVITY OF A QUADRIVALENT INFLUENZA VACCINE AMONG PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Introduction: Immunization of a quadrivalent influenza vaccine (A/California/7/2009(H1N1)pdm09, A/Switzerland/9715293/2013(NIB-88) (H3N2), B/Phuket/3073/2013, and B/Texas/2/2013) began in the 2015/2016 season. We assessed the immunogenicity and booster effect of quadrivalent influenza vaccine for adult inflammatory bowel disease patients treated with immunosuppressive drugs and/or anti-TNF-α agents.

Aims & Methods: Single vaccination group and booster group were randomly assigned to adult patients with crohn’s disease or ulcerative colitis, and quadrivalent influenza vaccine was administered subcutaneously. Serum samples were collected at 3 points (before vaccination, 4 weeks after the first vaccination, and after the end of the influenza season) in the single group and 4 points in the booster group (before vaccination, 4 weeks after the first vaccination, 4 weeks after the second vaccination and after the end of the influenza season). Antibody titer against influenza A strains in patients who maintained blood concentrations (SP%: 0.82; B/Texas: p = 0.79; B/Phuket: p = 0.82; B/Texas: p = 0.84). In patients treated with infliximab, serum protection rate (SP%) and seroconversion rate (SC%) tended to be lower in Indian and Pakistani groups. UC incidence was significantly higher in the Pakistani and Caucasian groups. UC incidence was significantly higher in the Indian population compared to Caucasians and Pakistanis (p < 0.001). Data for disease phenotype (Montreal classification) was collected onto the Epicom database. Chi-squared test was used to detect differences in IBD incidence between ethnic groups. A p value < 0.05 was considered significant.

Results: A total of 132 patients with IBD were randomly assigned to single vaccination and booster groups. Eighteen patients received immunomodulatory monotherapy and 20 received anti-TNF-α single agent therapy. Nineteen patients received combination therapy of immunosuppressant and anti-TNF-α agents. No significant difference between the single vaccination group and booster group was observed (American indian: H1N1: p = 0.81; H3N2: p = 0.79; B/Phuket: p = 0.82; B/Texas: p = 0.84). In patients treated with infliximab, serum protection rate (SP%) and seroconversion rate (SC%) tended to be lower in Indian and Pakistani groups. UC incidence was significantly higher in the Pakistani and Caucasian groups. UC incidence was significantly higher in the Indian population compared to Caucasians and Pakistanis (p < 0.001). Data for disease phenotype was available for 160/219 patients with UC (24% E1, 42% E2 and 34% E3). There was no significant difference in disease extent between ethnic groups.

Conclusion: The incidence rates for IBD in seven urban populations in England are similar to recent data from Western Europe (IBD 18.5/100,000, UC 9.8/100,000 CD 6.3/100,000 and IBDU 2.4/100,000). Ethnic-adjusted incidence rates showed that Indians have higher incidence of UC than Caucasians and Pakistanis with highest observed incidence in Northwest London. These findings are consistent with previous data suggesting that Indians have a higher predisposition for UC. Genetic, environmental and dietary factors may be responsible for differences and further analyses are underway. Better understanding of the susceptibility of Indians to UC may lead to the underlying cause of UC.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

Abstract: P1633. Table 1: Incidence rates per 100,000 for inflammatory bowel disease, Crohn’s disease, ulcerative colitis and inflammatory bowel disease unclassified in England for patients aged 16 years or older in 2016/17. CD, Crohn’s disease; IBD, inflammatory bowel disease; IBDU, unclassified UC, ulcerative colitis.

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<th>Background population</th>
<th>Cauc</th>
<th>Ind</th>
<th>Pak</th>
<th>No. of cases</th>
<th>IBD crude</th>
<th>CD crude</th>
<th>UC crude</th>
<th>IBDU crude</th>
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<td>92,047</td>
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<td>3.64</td>
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<td>6.81</td>
<td>3.31</td>
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<td>5.0</td>
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<tr>
<td>All centres</td>
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<td>154,747</td>
<td>351</td>
<td>15.54 (95% CI 4.8-9.42)</td>
<td>4.80 (95% CI 1.1-8.90)</td>
<td>9.69 (95% CI 5.5-15.7)</td>
<td>1.01 (95% CI 0.4-3.6)</td>
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Incidence by Ethnicity

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<th>Ethnicity</th>
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<th>Pak</th>
<th>No. of cases</th>
<th>IBD crude</th>
<th>CD crude</th>
<th>UC crude</th>
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Introduction: The global incidence of inflammatory bowel disease (IBD) is increasing. Migration may influence disease epidemiology. The UK demographics are affected by sustained migration from South Asia. The incidence of UC in South Asians (SA) was previously reported as higher than the Caucasian population.1,2 These single centre studies were done over 20 years ago. The current epidemiology of IBD in the multiethnic UK is unknown.

Aims & Methods: We aimed to describe the UK incidence of IBD and distribution within ethnic groups. Census data (2011) was used for background population size, ethnic groups and to identify areas with high SA populations where Indians and Pakistanis were the predominant groups. The incidence was calculated by using the number of subjects in each ethnic group in the background population as the denominator. Adult patients (>16 years) with newly diagnosed IBD (fulfilling Copenhagen diagnostic criteria) were prospective recruited over one year in 7 catchment areas with high SA population. Data including demographics, ethnic codes and disease phenotype (Montreal classification) was collected onto the Epicom database. Chi-squared test was used to detect differences in IBD incidence between ethnic groups. A p value < 0.05 was considered significant.

Results: Over 1 year IBD was diagnosed in 351 cases: 219 ulcerative colitis (UC), 107 Crohn’s disease (CD) and 26 inflammatory bowel disease unclassified (IBDU). Collective crude incidence rates were 15.54/100,000 for IBD, 9.69/100,000 for UC, 4.80/100,000 for CD and 1.01/100,000 IBDU. (Table 1) Crude IBD incidence rates varied between populations: lowest was 6.81/100,000 in Pennine, North Manchester and highest 26.11/100,000 in Leicester. Overall incidence of UC was higher than CD (9.69/100,000 vs 4.80/100,000) and was consistent for all populations except Pennine (3.31/100,000 for CD and 2.76/100,000 UC). Of the total number of IBD cases recruited 298/351 were coded as Caucasian, Indian or Pakistani. IBD, UC and CD incidence was similar between Pakistani and Caucasian groups. UC incidence was significantly higher in the Indian population compared to Caucasians and Pakistanis (p < 0.001). Data for disease phenotype was available for 160/219 patients with UC (24% E1, 42% E2 and 34% E3). There was no significant difference in disease extent between ethnic groups.

Conclusion: The incidence rates for IBD in seven urban populations in England are similar to recent data from Western Europe (IBD 18.5/100,000, UC 9.8/100,000 CD 6.3/100,000 and IBDU 2.4/100,000). Ethnic-adjusted incidence rates showed that Indians have higher incidence of UC than Caucasians and Pakistanis with highest observed incidence in Northwest London. These findings are consistent with previous data suggesting that Indians have a higher predisposition for UC. Genetic, environmental and dietary factors may be responsible for differences and further analyses are underway. Better understanding of the susceptibility of Indians to UC may lead to the underlying cause of UC.

Disclosure of Interest: All authors have declared no conflicts of interest.
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Disclosure: The increasing incidence of anal canal (AC) carcinomas in men and women requires better knowledge on Human papillomavirus (HPV) infection at this site and its risk factors. Higher incidence of AC cancers in Crohn’s disease (CD) patients is strongly suggested in the literature, without knowledge on HPV involvement. A gastroenterology population offers the opportunity to study a mixed and non-sexually at risk selected population and to study anal HPV infection in CD patients.

Aims & Methods: The aim of the study was to assess AC HPV infection prevalence and risk factors in a gastroenterology population. The ‘Human PAPILLOMavirus ANaL infection’ - PAPILLAN- study took place in a French university hospital gastroenterology unit. Consecutive patients were prospectively recruited at the occasion of a colonoscopy, whatever the indication. On the day of colonoscopy, under local anesthesia, AC smear was sampled with a dedicated brush for molecular analysis. HPV detection and genotyping was performed with the INNO-LiPA assay. Risk factors for any HPV, and high risk (HR) HPV infection were assessed by bivariate and multivariate analysis after logistic regression.

Results: A total of 469 consecutive patients (median age 54 years, 52% women) had suitable anal swabs for HPV DNA detection. Among them 101 had initial anal bowel disease (IBD), 70 had CD. 112 patients had at least one immunosuppressive treatment for IBD or another condition. Overall 34% of the population had a detection of any HPV type in AC smears. HR HPV prevalence was 18%, LR HPV prevalence was 9% and HPV16 prevalence was 7%. Most prevalent HR HPV types were, by decreasing order: HPV16, HPV51, HPV52 and HPV39. Among all patients with HPV positive or HR HPV positive samples, 65.6% and 65.9% were women, respectively (p = 0.0001; p = 0.0035, compared to men). Regarding medical history, HR HPV and HPV16 prevalence were signif- icantly higher in Crohn’s disease patients (90%, p = 0.0051; 14%, p = 0.0072, compared to the rest of the study population). Eleven (12%) patients (50%) with perianal CD had an AC infection with any HPV. Multivariable analysis associated female gender and history of sexually transmitted disease with the presence of HPV, lifetime and past year number of sexual partners, active smoking and immuno- suppressive treatment (OR 5.3) with the presence of HR HPV.

Conclusion: We demonstrated that CD patients harbor more frequent AC infec- tion with HR HPVs and that gut colonization with ESBL-E is associated with an independent risk factor for HR HPV infection at this site. These findings strongly support prophylaxis with vaccination and adequate screening in our patients.

Disclosure of Interest: L. Vuitton: Speaker for Abbvie, Hospira, MSD, Ferring, Travel grants from MSD, Takeda Consulting fees from Ferrin, Abbvie
S. Koch: Speaker for Abbvie, MSD, Norgine, Olympus
All other authors have declared no conflicts of interest.
L. Platrasac: Speaker for Hospira, Abbvie, MSD

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Introduction: Extended spectrum beta-lactamase producing Enterobacteria (ESBL-E) is the most frequently found multi-resistant bacteria colonizing the gut of inflammatory bowel disease (IBD) patients. Changes in the micro- biome may act as a trigger in IBD inflammation process.

Aims & Methods: The aim of the study was to analyze whether gut colonization with Enterobacteria is associated with clinically relevant disease activity activity increase in ulcerative colitis (UC) and in Crohn’s disease (CD). All consecutive patients with confirmed UC and CD diagnosis, previously hospitalized in two largest tertiary medical care centres in Riga, Latvia during a 7-year period (2010-2016) were included in the study, interviewed, rectal swabs were collected, Enterobacteria were cultured and analyzed for ESBL presence according to EUCAST guidelines. To clinically evaluate disease activity UC patients were evaluated according to Mayo score, Montreal classification, adapted Truelove and Witts criteria and CD patients according to Crohn’s disease activity index (CDAI), suggested by ECCO IBD guidelines (2016).

Results: A total of 101 patients with UC and 47 patients with CD were tested for gut colonization with ESBL-E. We found that 12 (11.9%) of the UC patients and 5 (10.6%) of the CD patients were colonized with ESBL-E. Statistical signifi- cant differences were found in all UC clinical disease activity scores between patients with and without gut colonization with ESBL-E and showed tendency towards statistical significance in CD. The mean disease activity according to Mayo score in UC patients without ESBL-E colonization was 3.44 (SD = 2.07), whereas in patients with ESBL-E colonization it was 5.08 (SD = 2.84) (p = 0.015).

Most of the UC patients without ESBL-E colonization (n = 63; 70.8%) were in clinical remission, whereas half of the patients with ESBL-E colonization (n = 0;
50% had mild to moderate to severe disease activity, according to Montreal classification disease activity index section (p = 0.037). Most of the UC patients with out ESBL-E colonization (n = 81; 91%) had mild disease activity, whereas half of the patients with ESBL-E colonization (n = 6; 50%) had moderate disease activity, according to modified Truelove and Witt’s criteria (p < 0.001). Most of the CD patients without ESBL-E colonization (n = 38; 90%) had moderate disease activity, whereas most of the patients with ESBL-E colonization (n = 3; 60%) had severe disease activity, according to CDAI (p = 0.05).

Conclusion: Gut colonization with ESBL-E might increase disease activity in out-patients with IBD. Such clinical findings could be clinically relevant and help to improve diagnostic and treatment protocols for IBD patients, because eradication of ESBL producing bacteria might reduce IBD disease activity.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference
Table 1: Adherence to Questionnaires

<table>
<thead>
<tr>
<th>Questionnaires</th>
<th>Adherence over 6 months</th>
<th>First 3 months</th>
<th>Last 3 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daily symptom (SCCAI) questionnaire</td>
<td>76%</td>
<td>81%</td>
<td>72%</td>
</tr>
<tr>
<td>fortnightly QoL questionnaires</td>
<td>95%</td>
<td>96%</td>
<td>94%</td>
</tr>
<tr>
<td>IBD-Control 8, CUCQ8 and EQ-SD</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Once only demographic and outcome questionnaires</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
</tr>
</tbody>
</table>

Conclusion: Uptake of FCa home testing was 73% (48/66), median tests 4 (IQR 3, range 1–6). Median SUS score was 92.5 (IQR 15, range 45–100) which corresponds to a ‘superior product’. Qualitative interviews confirmed that TCUC was efficient, effective, easy to learn and well liked. Improvements suggested included optimisation of the graphical display on smartphones and decreasing the number of QoL questionnaires from three to one, with a preference for IBD-Control.

Disclosure of Interest: Patients with UC will collect digital data in real-time, with good adherence to symptom, QoL, outcome questionnaires and FCa home testing. Usability was classified as ‘superior’ but further improvements are possible. Larger studies are required to determine cost effectiveness.

Aims & Methods: We followed 198 IBD outpatients (144 CD and 54 UC) for 3 years to indentify potentional risk factors of unfavourable disease outcome. Baseline body composition were measured by bioelectrical impedance analysing (BIA) method to evaluate nutritional status. Penalized logistic regression was used for the multivariate modelling of the outcome, with two sets of - prespecified - predictor variables age, sex, CU/CD, BMI, FFMI.

Results: According to our results 19.2% of the patients (n = 38) were underweight (had BMI <18.5 kg/m²) and 29.8% (n = 59) had alarming low fat-free mass index (FFMI) and were at risk of sarcopenia. Overall 31.5% (n = 62) of the patients needed steroid therapy and 53.5% (n = 106) was given anti-TNF. Almost third of the participant (30.8%, n = 61) were hospitalized due to disease flair or its complication at least once during the follow-up time. The mean period of hospitalization was 19.14 ± 3.27 days. 20.2% (n = 40%) of all participants have undergone intestinal surgery. Hospitalization was positively associated with sarcopenia risk: alarming low FFMI was associated with an OR of 1.81 (95% CI: 1.33–4.47, p = 0.0046). The risk of operation was higher in patients with lower BMI: OR = 1.55 (95% CI: 1.05–2.29, p = 0.0278) for 5 units decrease; no other association was significant in the models.

Conclusion: Our results suggests that low BMI is a risk factor of surgery in inflammatory bowel disease patients. Furthermore alarming low FFMI is a predictor of need of hospitalization and that suggets more serious flares. Identification of malnutrition and altered body composition has notable importance in disease outcome among IBD patients.

Disclosu of Interest: All authors have declared no conflicts of interest.
P1643 
CONTRAST-ENHANCED ULTRASOUND IS HELPFUL IN THERAPEUTIC DECISION MAKING IN PATIENTS WITH STRICTURING CROHN’S DISEASE
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Introduction: The majority of Crohn’s disease (CD) develop structuring complications of the disease at some point. The proper selection of patients with potential benefit of therapy escalation is crucial in order to avoid unnecessary bowel disease resection in the affected bowel segment; at intravenous contrast-enhanced ultrasound (CEUS) has been shown to correlate with disease activity but there are no data available on the benefit of CEUS for the therapeutic decision making in this clinical setting.
Aims & Methods: The aim of the study was to evaluate the clinical outcomes of CD patients with structuring disease managed based on the CEUS findings. CD patients with structuring disease were recruited from two IBD centres between June 2015 and February 2017. Patients with penetrating disease complications were excluded. CEUS was performed at therapeutic step-up to antiTNF or intravenous immunosuppression (SonoVue, Bracco Imaging). Patients having rapid uptake (within 20 second after injection) were indicated for therapy escalation, patients without uptake with obstructive symptoms were referred for surgery; patients without uptake and no obstructive symptoms remained at the stable medication. In patients with the minimal follow-up of one year clinical and endoscopic remission was evaluated.
Results: In total, 27 patients were included (10 men; median age 37 yrs, range 23–67; 22 pts with ileo-coecal localization, 3 pts with multiple small bowel segments involvement, 2 with colonic disease). Seventeen patients (63%) had rapid uptake at the CEUS; 13 of these patients had therapy escalation (3 pts intensified or switched to another biological; 10 pts had therapy step-up to antiTNF or intravenous immunosuppression). Three remaining pts improved subsequently on stable therapy with antiTNF and one patient with longstanding symptomatic colonic stricture was referred for surgery. Ten patients (37%) had no rapid uptake at the CEUS; seven out of these pts had symptomatic strictureing without any changes in the medication. Three patients had no symptoms and no therapeutic changes were made. Twenty-five patients had follow-up longer than 12 months (median 18 months, range 13-23). In the group of patients with rapid uptake, all but two patients achieved sustained remission after therapy escalation. Two patients initially responded to therapy but have lost response and eventually needed surgery.
Conclusion: Contrast-enhanced ultrasound might be helpful in guiding the therapeutic decision making between surgery and therapy intensification in patients with stricturing Crohn’s disease.
Disclosure of Interest: All authors have declared no conflicts of interest.

P1644 
FERTILITY AND PREGNANCY IN IBD - OUR EXPERIENCES
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Introduction: Inflammatory bowel disease (IBD) commonly affects patients during their reproductive years, making the interaction between fertility, pregnancy, and IBD an important issue for both genders. As these are the reproductive years, patients and physicians often have concerns regarding the interaction between IBD, medications and surgery used to treat IBD, and reproduction, pregnancy outcomes, and neonatal outcomes.
Aims & Methods: The aim of the study was to determine IBD patient’s reproductive behaviour and evaluate the factors that affect family planning. Finally we investigated the factors that may affect the family planning decision in IBD patients. Family planning was not the subject of the study and none of these patients had recurrence at the surveillance colonoscopy at 12 months.
Conclusion: Contrast-enhanced ultrasound might be helpful in guiding the therapeutic decision making between surgery and therapy intensification in patients with stricturing Crohn’s disease.
Disclosure of Interest: All authors have declared no conflicts of interest.

P1645 
DIAGNOSTIC DELAY AND PREDICTIVE FACTORS FOR CROHN’S DISEASE IN AN ALGERIAN POPULATION
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Introduction: Crohn’s disease (CD) is a chronic inflammatory bowel disease whose diagnostic delay (DD) is highly variable. A delay in diagnosis of MC can result in severe damage. Rapid therapeutic response is dependent on the patient’s CD and the CD medication used.
Aims & Methods: All patients with certain or probable CD between 2004 and 2016 identified by The department’s inflammatory disease hospital registry were included. The socio-demographic characteristics collected included: the patient’s personal area at the time of diagnosis in urban, rural or semi-urban, distant from the nearest hospital (CH). Clinical symptoms and phenotype of CD to diagnosis according to the Montreal classification were collected
Results: Among 247 patients with CD; 90 had a median SD of 03 months. A DD > 7 months was considered a diagnostic delay observed in most patients is 157. In univariate and multivariate analysis at diagnosis, the female sex (54.25%), young age (37.24%), absence of emaciation (27%), presence of extra-digestive manifestations (25.91%) and Isolated lesions (L1) (34%) and penetrating phenotype (B3) (22.67%) were associated with significant delay. Factors Influencing SD may be a function of the country’s health system, but also linked to the particular clinical and evolutionary profile of the disease. The objective of this study was to measure the DD of CD, to describe its distribution and evolution over time and to The factors associated with a long DD (> Q3).
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Discussion of Interest: All authors have declared no conflicts of interest.

Reference
http://www.ibdcohorti.ch/

P1646 
TUBERCULOSIS IN INFLAMMATORY BOWEL DISEASE UNDER TUMOUR NECROSIS FACTOR ALPHA ANTAGONIST–THE RISK BEYOND SCREENING
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Introduction: Tumour necrosis factor alpha antagonist (anti-TNFα) has revolutionized the treatment of the inflammatory bowel disease (IBD). Considering that it plays a central role in immune-mediated modulation, there are some concerns about its safety and ongoing infectious treatment. The main patient-related reasons for “voluntary infertility” were fear of congenital abnormality secondary to medications of IBD (68%) and concern about genetic risk of IBD in child (56%). 50% of male and 75% of female patients were concerned about safety issues from conception do delivery. Pregnancy was planned in 77% of cases, the childbearing and delivery was without any complication. Prematurity and low birth weight occurred in 6-6 cases (10%-10%). IBD was in remission in most cases, during pregnancy 25% of the patients had flare. 40% of women could breastfeed their baby after 6 months.
Conclusion: The management of IBD in women during their reproductive years should include consideration of their family planning decisions, and education counseling regarding the overall safety of medications and the importance of medication adherence should occur prior to conception. Disease control prior to desired conception and throughout pregnancy is the most important factor to keep in mind when caring for the IBD patients. Educating the patients will help to achieve successful outcomes both for patients and babies.
Disclosure of Interest: All authors have declared no conflicts of interest.

References
Huang YW et al.: From conception to delivery: Managing the pregnant inflammatory bowel disease patient. World J Gastroenterol 2014 April 7; 20(13): 3495–3506
Aims & Methods: We intend to know the incidence of tuberculosis in IBD patients under anti-TNFα therapy in a single tertiary referral centre, analyzing the tuberculosis screening methods and demographic characteristics. IBD patients treated with anti-TNFα therapy between January 2000 and December 2016 were retrospectively analyzed.

Results: During this period 166 patients received anti-TNFα therapy. Before anti-TNFα treatment, screening for LT was performed through medical history, chest x-ray, tuberculin skin test (TST) and/or IGRA. Forty-two patients (25%) had a positive screening and received tuberculosis prophylaxis prior to anti-TNFα therapy. Seven patients (4.2%) developed tuberculosis while under anti-TNFα treatment (four women, mean age 44 ± 7 years and mean IBD duration 10 ± 8 years). Six of them had a negative LT screening (methods: 4 TST and 2 IGRA) and one patient had positive TST screening, been treated with isoniazid before starting anti-TNFα therapy. During screening, three patients were under immunosuppressive and one under corticosteroid therapy. In the IGRA negative screening patients, the diagnosis of tuberculosis occurred within the first 10 weeks after starting anti-TNFα therapy. There were five cases of miliary tuberculosis and two of pulmonary disease. Despite difficult diagnosis, all patients were treated successfully, six of whom needed hospitalization.

Conclusion: In our centre the incidence of tuberculosis in IBD patients under anti-TNFα therapy was 4.2% and most of them presenting with a severe disease pattern. The therapeutic regime of tuberculosis was effective and no mortality was recorded. All this patient had a previously negative screening, two of them with IGRA, been considered a high sensitivity and specificity screening method. Therefore, a surveillance strategy for IBD patients with anti-TNFα therapy is needed.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P1647 CAN A PATIENT RATE THE ACTIVITY OF THEIR CROHN'S DISEASE THROUGH A MOBILE APP? THE MEDICROHN STUDY
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Introduction: The MediCrohn study was designed to evaluate the level of agreement between the Harvey Bradshaw Index (HBI) translated into a patient-based questionnaire completed through a mobile app, and the original HBI questionnaire assessed by the clinician (considered as reference).

Aims & Methods: Patients completed the HBI score through a mobile app designed for both Android and iPhone devices and thereafter (<48 h later), the questionnaire was completed onsite by the gastroenterologist who was blinded for the patients’ responses. We assessed agreement between HBI scores of the clinician and patient on the total sum score and per item. HBI score <5 was considered as inactive disease.

Results: 135 patients participated in the study and completed the HBI trough a mobile app (mean age: 36.4 ± 8 years, 58% women). The proportion of agreement between clinician and patient assessment, both evaluating CD as active or in remission was 91.1%. Only in 12 cases (11%), the patient classified CD as active, whereas the physician evaluated it as inactive. No active cases remained undetected by the patient evaluation. Sensitivity, specificity, positive and negative predictive values are shown in Table. The highest agreement was seen for the questions: “abdominal mass” and “general well-being” whereas “number of liquid stools per day” was the item with the lowest agreement.

Patient Rate Clinician Assessment Clinician Assessment Total
| Active | 26 | 12 | 38 |
| Remission | 0 | 97 | 97 |
| Total | 26 | 109 | 135 |

Sensitivity (%) Specificity (%) PPV(%) NPV (%) Agreement
100 89 68 100 91.1% CI(95%)
P1649 EVALUATION OF MODIFIED MAYO ENDOSCOPIC SCORE AS A TOOL TO DETERMINE WHICH INPATIENT ULCERATIVE COLITIS EXTENSION, IN THE PREDICTION OF RELAPSE

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Introduction: Current endoscopic activity scores for Ulcerative Colitis (UC) do not take into account the extent of mucosal inflammation. Recently, two endoscopic scores that combine the assessment of severity and disease extension were developed, the Modified Mayo Endoscopic Score (MMES)1 and Degree of Ulcerative Colitis Burden of Luminal Inflammation (DUBLIN)2. Results: 82 patients were selected, 51.2% (n = 42) were female, mean age 49.4 ± 13.7 years. MMES ranged between 0–13.8 and DUBLIN between 0–9. MMES and DUBLIN scores presented good correlation (r = 0.945, p < 0.001). MMES was higher in patients with histoactivity defined by Nancy (3.7 ± 4.0 vs. 0.8 ± 1.5; p < 0.001) and Geboes (4.0 ± 4.2 vs. 1.3 ± 2.4; p = 0.005). DUBLIN was also higher in patients with histoactivity defined by Nancy (1.9 ± 2.1 vs. 0.5 ± 0.8; p = 0.001) and Geboes (2.0 ± 2.3 vs. 0.7 ± 1.2; p = 0.005). There was no significant association between both scores and analytically activity. Relapse occurred in 36.6% (n = 30) of patients, with a cumulative risk of 9.8, 18.4, 25.9, 31.5 and 42.0% at 12, 24, 36, 48 and 60 months, respectively. Mayo Endoscopic Subscore (MES) (p < 0.001), MMES (p = 0.001), DUBLIN (p = 0.001) and Nancy score (p = 0.001) presented a significant association with relapse. In multivariate analysis, MES (OR = 2.32; p < 0.001), MMES (OR = 1.19; p < 0.001) and DUBLIN (OR = 1.36; p < 0.001) were predictive of relapse independently from histoactivity. Areas under the ROC curve were: 0.71 (p < 0.0001) for MES, 0.75 (p = 0.001) for DUBLIN, and 0.001 for prediction of relapse, with MMES significantly higher than MES by a difference of 0.037 (0.002-0.072; p = 0.03). Conclusion: MMES and DUBLIN scores correlate with each other and with histoactivity. These scores act as independent predictors of relapse. MMES was superior to MES in the prediction of relapse.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P1650 USEFULNESS OF MAGNETIC RESONANCE ENTEROGRAPHY ON MEDICAL DECISION-MAKING IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE (IBD) AFTER A 1-YEAR FOLLOW-UP: A MULTICENTER STUDY

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Introduction: Magnetic resonance enterography (MRE) is an imaging technique recommended to determine and confirm the extension and activity of Crohns disease (CD) in the small bowel and discriminate penetrating disease and complications. MRE diagnosis allows to optimize medical treatment in IBD patients.

Aims & Methods: The aim of this study is to evaluate the impact of MRE on medical decision making in IBD patients and determine the maintenance of this new treatment along the time. Consecutive MRE studies performed in patients with confirmed or suspected Crohn’s disease between January 2011 and August 2014 were included in three centers. Medical charts were retrospectively reviewed. MRE indication, demographic and IBD data were collected at time of MRE. Three months after MRE, medical decision (conservative approach with maintenance therapy, significant change in medical therapy or surgery) was assessed. After twelve months of follow-up, the treatment decided after MRE was reviewed.

Results: A total of 474 MRE studies were performed and indications for MRE were: assessment of small bowel involvement in 40 (8.3%) patients with indeterminate colitis (IC) and 20 (4.2%) with suspected-IBD patients or evaluation of severity and extension of the disease in 414 (87.5%) CD patients (232 F; mean age 37 ± 13 years). Only 4 patients with suspected-IBD (4/20.2%) had involvement of small bowel on MRE confirming the CD diagnosis. Twenty-one patients with IC (21/40.52%) changed the diagnosis to CD. In 199/474 (40.5%) MRE determined a change on medical decision and 140 (70.3%) patients modified maintenance treatment because of MRE findings. Of them, 127 (63.8%) underwent “set-up” treatment by prescribing immunosuppressants (IS) (n = 45), anti-TNF agents (n = 22), anti-TNF escalation (n = 8), adding IS to anti-TNF agents (n = 9) and changing anti-TNF agents (n = 5). In addition, 13 (9.2%) patients underwent “top-down” therapy due to stop IS (n = 7), anti-TNF (n = 3) or anti-TNF de-escalation (n = 3). Surgery was indicated on 62 (62/196;31.1%) patients after MRE. After one year of follow-up, the medical decision was maintained in 65.4% (288/440) of patients.

Conclusion: RE is a very helpful tool for the medical management of CD patients. MRE provides major information to optimize treatment in the long-term of patients with active CD.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
1 Pariente et al, Gastroenterology 2015

P1651 CORRELATION BETWEEN THE LÉMANN INDEX AND THE INFLAMMATORY BOWEL DISEASE- DISABILITY INDEX IN CROHN’S DISEASE

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Introduction: Crohn’s disease (CD) is a chronic progressive destructive disease, resulting in cumulative structural bowel damage, which may predict long-term disability. The Lémann Index (LI) has been developed to measure CD-related bowel damage, including bowel surgery, presence of strictureing and penetrating lesions (Pariente and al, Gastroenterology 2015). The first Inflammatory Bowel Disease - Disability Index (IBD-DI) has recently been validated (Gower-Rousseau, Gut 2015).

Aims & Methods: The aim of the present study was (1) to identify factors associated with bowel damage and with disability in CD and (2) to evaluate the correlation between the LI and the IBD-DI. We performed a prospective study in the tertiary referral center of the Claude Huriez Hospital Lille from September 2016 to November 2016, including all consecutive CD outpatients.

Bowel damage was assessed by the LI calculated according to the published LI protocol. Abdominal and pelvic Magnetic resonance imaging (MRIs) were reviewed and red by the same couple of one gastroenterologist and one radiologist. The IBD-DI was also calculated for all patients. Factors associated with LI and IBD-DI levels were identified by means of bivariate analyses of variance. Results: 230 patients were prospectively and rigorously included. Median age was 34.0 (interquartile range [IQR]: 26.0–46.0) and median disease duration was 10.0 (IQR: 5.0–17.0) years. 65 patients (50%) underwent at least one resection surgery. The median LI was 10.8 (IQR: 0.6–17.5). Disease duration (p < 0.0001) and CD activity (p < 0.0001) were associated with higher LI scores. The correlation coefficient between the LI and the IBD-DI was 0.12 (0.002-0.072; p = 0.03).

Conclusion: MRE provides major information to optimize treatment in the long-term of patients with active CD.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
1 Pariente et al, Gastroenterology 2015
Introduction: The aetiology of Crohn’s disease (CD) and ulcerative colitis (UC) is not known. Recent data suggest a different cytokine profile between CD and UC.

Aims & Methods: The aim of this study was to analyse the expression of mRNA of proinflammatory, regulatory anti-inflammatory cytokines, chemokines and their ligands (IL-6,-8,-10,-12, IL-23, TNF-α, CCR1, -2, -3, -4, -5, -6, -7, -8, -9, -10, -11,-12, -13, -14, -15,-16, -17, -18, -19, -20, -21, -22, -23, -24, -25, -26, -27, -28, -29, -30, -31, -32, -33, -34,-35, -36, -37, -38), and transcription factor FoxP3 in the inflamed and non-inflamed intestinal biopsy samples of mucosa in IBD patients. We performed a cross-sectional study. The cohort consisted of 87 consecutive IBD patients (47 CD and 40 UC) who underwent colonoscopy at the IB centre of University Hospital Bratislava. We took biopsies from non-inflamed and if present also from inflamed mucosa from sigma (CD, UC) and terminal ileum (CD). mRNA was extracted from mucosal biopsy samples, isolated by a RLT buffer and PCR products were amplified using SYBR green method.

Results: In UC patients, we observed higher expression of IL-8 (p = 0.04), IL-23 (p = 0.019), TLR2 (p = 0.002), CCR1 (p = 0.007), CCR2 (p = 0.037), CCR5 (p ≤ 0.001), CD206 (p = 0.011), TNFα (p = 0.002) and IL-6 (p = 0.006) in the inflamed mucosa from sigma. In CD patients, we observed increased expression of IL-6 (p = 0.005), and IL-8 (p = 0.001) in the inflamed mucosa of a terminal ileum and decreased expression of CCL5. Also, in group of patients with CD we did not observe the difference of the expression of mRNA cytokines between the inflamed and non-inflamed mucosa of sigma.

Conclusion: There was a significant difference in the mRNA cytokine profiles between CD and UC patients.

Disclosure of Interest: All authors have declared no conflicts of interest.
**P1655 MONITORING OF LABORATORY PARAMETERS DURING THIOPURINE MAINTENANCE THERAPY IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE: AN UNNECESSARY BURDEN?**

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**Introduction:** Although thiopurine-induced myelotoxicity and hepatotoxicity rarely occur during maintenance thiopurine therapy for inflammatory bowel disease (IBD), current guidelines advise laboratory monitoring every 3 months. This study was performed to assess the current laboratory monitoring regimen in thiopurine maintenance therapy with regards to consequences of myelotoxicity and hepatotoxicity.

**Aims & Methods:** In this multicenter cohort study, we evaluated adult IBD patients with quiescent disease who were on maintenance thiopurine therapy between 2000–2016. Data collection started after 12 consecutive months of thiopurine treatment. The primary outcome was therapy adjustment, i.e. therapy cessation or dose reduction, due to myelotoxicity (leukocyte count \( < 4.0 \times 10^9/\text{l} \), platelet count \( < 150 \times 10^9/\text{l} \) and/or hepatotoxicity (alkaline phosphatase (AP), gamma-glutamyltransferase (γ-GT), alanine aminotransferase (ALT) and/or aspartate aminotransferase (AST) above the upper limit of normal (ULN)).}

**Results:** This study included 223 IBD patients (55% female, 64% with Crohn’s disease, mean age at diagnosis 27.2 years (SD 11.5)). Median follow-up was 3.2 years (IQR 1.9–4.7). The mean monitoring frequency was 3.3 assessments per treatment year (SD 1.8). Toxicity was observed in 445/2402 laboratory assessments (18.5%) in 120 patients. In total, 20 (0.8%) therapy adjustments were performed and 25 laboratory assessments (1.0%) led to additional diagnostic procedures. Myelotoxicity, observed in 244 assessments, led to 11 dose reductions and in 3 patients therapy was stopped. For hepatotoxicity, observed in 201 assessments, 2 dose reductions were performed and in 4 patients therapy was stopped. Ninety percent of observed toxicity were mild leukopenia (leukocyte count \( < 3.0 \times 10^9/\text{l} \)) or mild hepatotoxicity (\( < 2 \times \text{ULN} \)), primarily in the first years of treatment. Dose adjustments were more often associated with moderate leukopenia (leukocyte count \( < 3.0 \)) than with mild leukopenia (\( p < 0.01 \)). In total, 2 complications were recorded, 1 patient was hospitalized because of pancreatitis and received red blood cell transfusion, and 1 patient was treated for a CMV infection. Both patients presented with symptoms in clinic with preceding normal laboratory values. No mortality due to thiopurine-induced toxicity was observed.

**Conclusion:** Although mild toxicity is common during maintenance thiopurine therapy, adjustments based on laboratory assessments are rare. Therefore, a less intensive regimen to monitor thiopurine-induced toxicity should be considered.

**Disclosure of Interest:** N.K.H. de Boer: NaNne de Boer has received a research and travel grant from Takeda. DNA was submitted the work and served as principal investigator and consultant for TEVA.

C.J. van der Woude: CJW has served as a speaker and a consultant for Abbot, Abbvie, MSD and as a consultant for Shire and received funding from Janssen Biologics BV.

All other authors have declared no conflicts of interest.

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**P1656 ULTRASOUND ELASTICITY IMAGING PREDICTS THERAPEUTIC OUTCOMES IN PATIENTS WITH CROHN’S DISEASE TREATED WITH ANTI-TUMOR NECROSIS FACTOR ANTIBODIES**

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**Introduction:** Intestinal fibrosis represents one of the main sources of morbidity for patients with Crohn’s disease (CD), as its onset is associated with the development of CD-related complications which increase the likelihood of hospitalization and surgery. Ultrasound elasticity imaging (UEI) is a non-invasive ultrasonographic technique developed to evaluate tissue fibrosis by measuring tissue strain after application of a force. We have recently demonstrated that UEI can reliably detect severe ileal fibrosis in patients with Crohn’s disease. We therefore hypothesized that a more severe range of fibrosis might influence the therapeutic response to anti-tumor necrosis factor (TNF) treatment.

**Aims & Methods:** The aim of this explorative study was to assess the ability of UEI to predict therapeutic outcome in active CD patients treated with anti-TNF antibodies. 30 patients with ileal or ileocolonic CD (20 males, age 38.8 ± 14.5) initiating anti-TNF treatment were enrolled in the study. All patients completed the induction phase and underwent scheduled maintenance therapy with anti-TNF for 16.1 ± 8.5 months. Patients underwent bowel ultrasound and UEI at baseline and 14 weeks after initiation of anti-TNF. Bowel wall stiffness at UEI was quantified by calculating the strain ratio (SR) between the bowel wall and the surrounding mesenteric tissue. Receiver operating characteristic curve analysis was used to identify the best SR cut off able to predict surgery/bowel obstruction. Transmural healing at 14 weeks was defined as a bowel wall thickness ≤3 mm. Frequency of CD-related surgeries or hospitalizations due to bowel obstruction was recorded during the follow-up. The data are given as mean values ± standard deviation.

**Results:** Five patients (16.6%) underwent surgery or hospitalization for bowel obstruction during the follow up. Frequency of CD-related surgeries or hospitalizations was significantly greater in patients with SR ≥ 2 at baseline than in patients with SR < 2 (p = 0.02). A significant reduction in bowel thickness was observed after 14 weeks of anti-TNF treatment (from 5.8 ± 1.5 mm to 5.1 ± 1.7 mm, p < 0.05), while SR values remained unaltered (1.5 ± 1.3, p = 0.5). A significant inverse correlation was observed between values of strain ratio at baseline and thickness variations following anti-TNF therapy (p = 0.007). Eight out of 30 patients (27%) achieved transmural healing at 14 weeks. Baseline SR was significantly lower in patients with transmural healing than in patients not achieving this endpoint (1.06 ± 0.16 vs 1.67 ± 0.17, p < 0.05).

**Conclusion:** This explorative study shows that UEI is able to predict therapeutic outcomes, including CD-related surgeries and transmural healing, in patients with Crohn’s disease treated with anti-TNF therapy.

**Disclosure of Interest:** All authors have declared no conflicts of interest.
**P1657** CLINICAL CHARACTERISTICS OF RECTAL-SPARING ULCERATIVE COLITIS

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**Introduction:** Ulcerative colitis (UC) generally involves the entire large intestine except for the rectum to the ileocecal junction. However, some patients with moderate or severe UC lack any obvious rectal involvement (known as rectal-sparing [RS]-UC).

**Aims & Methods:** In this study, we evaluated the differences in the clinical characteristics between patients with rectal UC with or without RS. Of the 437 inpatients with rectal UC who achieved remission between April 2001 and September 2016 (follow-up period: 915±53 days, mean ± SD), 57 patients were classified as RS-UC and 340 patients without RS (standard [S]-UC) group. Patients of the two groups were compared for gender, age at onset, site of involvement, disease duration, pretreatment clinical activity index (CAI, Lichtiger score), Hb, C-reactive protein (CRP), total dose of prednisolone (PSSL) before the achievement of remission, duration of hospitalization, endoscopic and ultrasonographic features, UC endoscopic severity index (UCEIS), and relapse rates (RS). Of 1300, 300, 500, and 1000 days post-remission. Patients with RS were defined as those without any detectable rectal inflammation despite not receiving local treatment, such as rectal enemas or suppositories. Remission was defined as CAI ≤5.

**Results:** Relapse was defined as the need to restart remission induction therapy, such as intensive intravenous PSSL, initiation of treatment with biological agent, or readmission and dose escalation of tacrolimus to achieve a high blood trough level (≥2 ng/dl).

- **Results:** RS was observed in 57 (10.4%) patients. There were significant differences in CRP (RS-UC: 5.1±6.0, S-UC: 2.3±3.4 mg/L) and pretreatment endoscopic scores (Mayo: RS-UC: 2.7±0.3, S-UC: 2.4±0.5). UCEIS: RS-UC: 6.1±5.1 and S-UC between the two groups (P<0.05). There was no significant difference in the relapse rate at 100 days after remission (RS-UC: 18%, S-UC: 15%). However, the two groups showed significant differences in the relapse rates at 300 days (RS-UC: 38%, S-UC: 17%), 500 days (RS-UC: 50%, S-UC: 48%) and 1000 days (RS-UC: 77%, S-UC: 62%) after remission.

- **Conclusion:** Our results showed that RS is not an uncommon finding among patients with UC. Based on the higher CRP, endoscopic score, and relapse rates in the RS group, than the standard UC group, we recommend aggressive treatment in UC patients with RS.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**References**

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**P1658** EVALUATION OF COLONIC MUCOSA WITH FLEXIBLE SPECTRAL IMAGING COLOR ENHANCEMENT (FICE) IN PATIENTS WITH LONG TERM ULCERATIVE COLITIS DURING DYSPLASIA SCREENING

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**Introduction:** Ulcerative colitis (UC) associated colorectal cancer risk (CRC) is related to the age of onset and duration and anatomic extent of the disease. The risk of dysplasia increases with the duration of the disease (1). Current guidelines recommend beginning the surveillance colonoscopy after eight to ten years of disease; random biopsies should be obtained from 4 quadrants of every 10cm of the colon. In addition, any suspicious areas should be biopsied. Recent endoscopic imaging technologies provide a more detailed visualization of the superficial microstructure of the mucosa and vascularity. Thus it is possible to get targeted biopsies. The purpose of this study is to evaluate the image patterns of dysplasia change in ulcerative colitis, and their histopathological correlation, by using a virtual chromosendoscopy technique, FICE and to investigate the effectiveness of this technique.

**Aims & Methods:** The purpose of this study is; to evaluate the image patterns of dysplastic changes in ulcerative colitis, and their histopathological correlation, by using a virtual chromosendoscopy technique, FICE and to investigate the effectiveness of this technique. Eighteen follow-up patients of our inflammatory bowel disease polyclinic, with UC at least 8 years of disease history and who are in clinical remission were included to this study. Screening colonoscopy was performed to the patients included in the study. Entire colon and especially the dysplasia suspected areas visualised with standard endoscopy first, and then with FICE; random and targeted biopsies were taken. Image patterns were compared with histological diagnosis. Normal, colitis and polyp images acquired by FICE, were evaluated by seven endoscopists and statistical analysis was performed. **Results:** In a total of 18 patients, by evaluating 120 colonic segments, 1831 images were measured. Biopsy indication was found in 17 of 18 patients. Of the 17 patients, 6/17 were classified as RS-UC and 11/17 as S-UC. Of the 1831 images taken by FICE separately, from each areas of normal colonic mucosa, polypoid lesions and colitis. A total 584 biopsies were taken, 492 (84.2%) random and 92 (15.7%) targeted biopsies. While there were no dysplasia in random biopsies, microscopic dysplasia was detected in 3 diminutive polyps taken as targeted biopsy. The analysis of the FICE images by voting by seven endoscopists showed that, the best imaging channels are; 2, 6, 9 for normal mucosa; 3, 7, 9 for polyps; and 2, 3, 9 for colitis. When all the images are analyzed, channels 2 and 9, were found to be significantly different from other channels. When the most rated channels, and 9, were compared to the WLE, the FICE image is better for evaluation of the mucosal and vascular structure. However, there were no significant difference between channels 2 and 9.

**Conclusion:** There were no significant superiority of FICE, in dysplasia screening. Consistent with the literature in this study, we showed us that FICE image is better for detecting diminutive polyps, and evaluating surface patterns without magnification. In clinical remission in patients with UC, FICE can have a role in the assessment of the severity of inflammation. For this purpose, more clinical trials are needed. Our study is the first study in UC. Channels 2 and 9 are the best image channels of FICE in UC.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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**Introduction:** The gut microbiome is thought to be relevant to the pathogenesis of inflammatory bowel disease (IBD). We aimed to explore associations between microbial diversity and specific IBD endotypes as well as inflammatory disease activity in an inception cohort of treatment-naïve IBD patients as well as with inflammatory activity in symptomatic non-IBD patients and healthy controls. The term ‘dysbiosis’ expresses alterations in the gut microbial community.

**Aims & Methods:** Patients were grouped according to the international criteria, including endoscopic and histopathological assessment. Clinical disease activity in Crohn’s Disease (CD) patients was measured by the Harvey-Bradshaw index (HBI), and in ulcerative colitis (UC) patients by the Simple Clinical Colitis Activity Index (SCCAI). Inflammatory activity was assessed by CRP and faecal calprotectin (FCal), (IgCAL® ELISA, Buhlmann laboratories AG).

**Results:** Stool samples were collected within 60 days prior to and 14 days after the diagnosis, and stored at ~80 °C. Antibiotic treatment within the last two months was an exclusion criterion. Identifiable microbial profiles were generated by 16S RNA analyses, using the GA-mapTM Dysbiosis Test. Dysbiosis was defined as non, mild or severe (1). Differences in disease activity between levels of dysbiosis severity were analysed using ANOVA at a significance level of 0.05. Intra-group associations between inflammatory activity and log-transformed microbiota profiles were analysed using ANCOVA. P-values corrected for multiple testing, using Benjamini-Hochberg correction, are presented. Presenting stool samples were compared to stool samples of diarrhoea patients and healthy controls.

**Conclusion:** CRP was available for 52 CD, 74 UC, 10 IBD-U patients, and 88 symptomatic non-IBD patients. HBI was available for 50 CD patients, while SCCAI was available for 77 UC patients. Disease activity: No association was found between FCal and dysbiosis in UC patients (P =0.08), CD patients (P =0.22), and healthy controls (P =0.57). However, an association was found between FCal and dysbiosis in symptomatic non-IBD patients (P =0.04) and in healthy controls (P =0.005). An association was found between FCal and dysbiosis in CD patients (P =0.02), while not for UC and symptomatic non-IBD patients. No association was found between HBI and dysbiosis in CD patients (P =0.23), and between SCCAI and dysbiosis in UC patients (P =0.32). Microbiota: Increasing dysbiosis severity in UC, CD and non-IBD patients yielded lower abundance of Faecalibacterium prausnitzii, and higher abundance of Proteobacteria, a profile typically observed in gut inflammatory conditions. In addition, the commensal bacteria Bifidobacterium yielded lower abundance with increased dysbiosis severity in UC and non-IBD patients, and in combination with elevated levels of FCal and/or CRP in UC patients. In the healthy controls, increasing dysbiosis severity yielded higher abundance of Proteobacteria.

**Disclosure of Interest:** All M.K. Karlsson: Employee of Genetic Analysis AS. L. Finny: Employee of Genetic Analysis C. Casen: An employee of Genetic Analysis AS Other authors have declared no conflicts of interest.
P1660 SIMPLIFIED MR ENTEROCOLONOGRAPHY CAN BE USED ON ENDOSCOPY FUNDING FOR ACTIVITY ASSESSMENT OF CROHNS DISEASE
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Introduction: Crohns disease (CD) is a lifelong inflammatory bowel disease. Evaluating the extent and severity of the disease is critical to determine appropriate therapeutic strategies in patients with Crohn's disease. MR imaging is one of the most recommended technique for detection of large and small bowel lesions. Hence, we aimed to evaluate clinical utility of the 3-point MR enterocolonography (MRC) classification for assessing CD activity based on endoscopic findings.

Aims & Methods: A total of 120 patients (70 for derivation cohort and 50 for validation cohort) with CD was enrolled and undergone MREC and ileocolonoscopy or balloon-assisted enteroscopy (BAE). MREC was evaluated for each bowel segment: rectum, sigmoid, descending, transverse, ascending colon, terminal, proximal ileum, and jejunum, according to the consensus of two observers in the derivation phase, and independently by three observers in the validation phase, using a 5-point MREC classification based on a lexicon of MR findings. The conventional MR score, or MaRIA, was evaluated simultaneously. Areas under the receiver operating characteristic curves (AUCs) were obtained to assess the accuracy of discriminating deep ulcers. Inter-observer reproducibility was assessed using weighted Kappa coefficients.

Results: BAE was performed in 49 (70%) and 37 (74%) patients in the derivation and validation cohort, respectively. The AUCs of MREC classification were 89.0% in the derivation phase and 88.5, 81.0, and 77.3% for three observers in the validation phase, using a 5-point MREC classification based on a lexicon of MR findings. The conventional MR score, or MaRIA, was evaluated simultaneously. Areas under the receiver operating characteristic curves (AUCs) were obtained to assess the accuracy of discriminating deep ulcers. Inter-observer reproducibility was assessed using weighted Kappa coefficients.

Conclusion: For clinical use, radiological reporting systems should be simple and provide appropriate levels of accuracy and reproducibility. The 5-point MREC classification meets these requirements, and is useful for evaluating CD activity in the large bowel and small bowel segments.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1661 RISK FACTORS FOR METABOLIC SYNDROME AND ITS COMPONENTS IN INFLAMMATORY BOWEL DISEASE
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Introduction: Metabolic Syndrome (MetS) is a combination of biochemical and anthropometric disturbances and a recognized risk factor for cardiovascular disease. A higher prevalence of this condition has been previously reported in IBD patients, correlating to age as in the general population.

Aims & Methods: The aim of this study was to assess the effect of individual disease activity-related putative risk factors for MetS in a group of IBD patients, as well as any protective effects of treatment on MetS or its components. Consecutive IBD patients and age- and sex-matched controls were included during a 1-year period. MetS was diagnosed according to the “harmonized” criteria as the presence of >3 criteria among elevated waist circumference, blood pressure, blood glucose, serum triglycerides, or reduced HDL levels. All subjects underwent colonoscopy; endoscopic disease activity was assessed according to SES-CD and Mayo endoscopic scores. CRP, fecal calprotectin (FC), hemoglobin and ferritin levels were also measured.

Results: We enrolled 145 consecutive IBD patients (53 Crohn’s disease and 92 ulcerative colitis; 58 M:87 F; mean age 51±18 yrs) and 250 age- and sex-matched controls. Overall, MetS prevalence was 37% in IBD and 21.6% in controls (OR=2.1, 95%CI:1.32–3.39). Prevalence according to sex or disease type did not show significant differences. At multivariate analysis, age and BMI >25 were associated to an increased probability for a positive MetS status both in IBD (OR=3.41, and OR=6.01) and controls (respectively OR=3.47 and OR=3.74). In patients under 50 years, age (OR=1.24), CRP (OR=1.9) and FC (OR=1.35) positivity were associated to MetS status, while a BMI >25 increased risk at any age (<50ys OR=3.8, >50ys OR=1.56). Interestingly, anti-TNFα treatment was not associated to MetS status at any age. Interestingly, anti-TNFα treatment was protective in both groups, but reached statistical significance only in older subjects (OR=0.08). Regarding individual MetS components, in the <50ys subgroup, age and CRP positivity associated with an impaired glycemic (respectively, OR=1.15 and OR=2.28) and lipidemic status (respectively, OR=1.23 and OR=2.3). In older patients, CRP positivity only associated to impaired HDL status (OR=5.41). Importantly, anti-TNFα treatment favourably associated to HDL status (OR=0.2).

Conclusion: MetS prevalence is increased in IBD compared to healthy controls at any age. Patients with increased BMI and/or inflammatory markers are at higher risk for MetS, while anti-TNFα agents appear to be protective. The components associated to MetS are differently distributed according to age, with the inflammatory ones prevailing in subjects <50 years and metabolic disturbances in older patients. These results indicate that MetS and its related long-term neoplastic and cardiovascular complications may reduce MetS occurrence and associated risks in subjects >50 years, in younger patients more effective inflammation control measures may prevent MetS and its related long-term neoplastic and cardiovascular complications.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1662 C-REACTIVE PROTEIN/ALBUMIN RATIO IS A GOOD PREDICTOR OF RESPONSE TO INTRAVERSE CORTICOSTEROIDS IN ACUTE SEVERE ULCERATIVE COLITIS
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Introduction: Patients with acute severe ulcerative colitis (ASUC) have a high risk of response medical therapy or colectomy. Recently, the C-reactive protein (CRP)/albumin ratio on admission, to predict response to intravenous corticosteroids in patients with ASUC. Retrospective assessment of systematically hospitalized patients with first episode of ASUC, who required intravenous corticosteroids. Demographic, clinical, laboratory and endoscopic variables were evaluated on admission. The response to intravenous corticosteroids was defined as clinical and endoscopic improvement in at least 75% of patients and patients who required rescue medical therapy with infliximab or cyclosporine has been instituted. The accuracy of CRP/albumin ratio in predicting non-response to intravenous corticosteroids was assessed by the area under the ROC curve (AUC).

Results: 51 patients were included, 30 (58.8%) of them female, with a mean age 34.3±14.5 years. Twelve patients (23.5%) required medical rescue therapy. No patient underwent colectomy. The presence of deep ulcers and a shorter evolution of the disease were associated with a lack of response to intravenous corticosteroids, p<0.001 and p=0.008, respectively. Patients with no response to intravenous corticosteroids had higher CRP admission values and lower albumin values, compared to patients with response, 111 vs 67.5 (mg/L), p=0.028, 2.8 vs 3.5 (g/dL), p=0.005, respectively. The CRP/albumin ratio was 51.4% higher in unresponsive patients 40.06 vs 22.14, p=0.022, showing a good accuracy for predicting non-response to intravenous corticosteroids with an AUC of 0.746, p=0.01.

Conclusion: A high value of CRP/albumin ratio was significantly associated with the lack of response to intravenous corticosteroids, at the 3rd day of treatment. This index may also better risk stratification on admission, of patients with acute severe ulcerative colitis.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1663 INSUFFICIENT VARIATION OF MEDIUM CORPOSCULAR VOLUME (MCV) IN INFLAMMATORY BOWEL DISEASE UNDER THYPOPURINES PREDICTS DIFFICULTY IN ACHIEVING MUCOSAL HEALING AND COMBINATION WITH ANTI-TNF - THE OTHER SIDE OF THE MCV FLOW STUDY
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Introduction: The MCV flow study confirmed the association ΔMCV ≥7fl at week 26-28 of Azathioprine monotherapy (mAzA) with favourable outcomes in a Portuguese IBD population.

Aims & Methods: For this work, our aims were to evaluate the need for step-up therapy in those under mAzA with ΔMCV ≤7 and to identify predictors of combined deep remission outcomes (DeepRem), at the same timepoint, for the patients who subsequently began combination therapy with Anti-TNF (AzaExperienced + Anti-TNF). Evaluation of patients under mAzA with ΔVGM < 7 at key timepoint week 26-28 treatment, included for The MCV flow study. Demographic characterization and severity of pre-treatment disease was evaluated (Montreal classification, previous surgery status, Mayo score and Crohn’s disease activity index (CDAI)). ΔMCV’s association with DeepRem (Steroid-free clinical remission (CDAI ≤150, Mayo < 2) + mucosal healing (MH)+C-reactive protein (CRP) <10) and need for biological therapy at the end of week 26-28 was verified. ΔMCV was also an independent predictor in patients who subsequently started combination therapy. Statistical: Chi-square test; Binary logistic regression.

Results: A total of 106 IBD patients were evaluated [56.6% women, mean age 39±15.2 years; 58 ad, 14% operated] at week 26-28 of mAzA. Identified strong association between an average ΔVGM ≥ 7 (n=70; 66%) with DeepRem (p < 0.05), while a ΔVGM < 7 was associated with biological therapy need (p < 0.05). 45 patients were later started with Anti-TNF therapy

Reference
Aims & Methods: The aim of this prospective study was to evaluate whether elevated FC values can predict short-term clinical and/or endoscopic relapse. We enrolled 60 IBD patients (30 ulcerative colitis - UC, 30 Crohn’s disease - CD) who were in remission and endoscopically normal. FC was measured using quantitative immunochromatographic point-of-care test (Quantum Blue® Calprotectin, Bühlmann Laboratories AG, Switzerland). Patients were followed-up by FC examination and clinical activity assessment every second month until relapse or up to 24 months. Histocolonoscopy was performed at inclusion and at the time of clinical relapse.

Results: During the follow-up 36 (60%) relapsed and 24 (40%) remained in remission. The mean time to relapse in all patients was 13.9 (range 2-20) months. Significant association in median FC levels was seen 2 months (p < 0.001) before endoscopic relapse. ROC analysis indicated that a cut-off of >0.95 µg/mL (OR 24, 95% CI = 5.117, p = 0.001) in mean FC values 2 months before relapse could predict relapse in UC patients with 83.3% sensitivity and 82.9% specificity. In CD patients a cut-off parameter of >1.55 µg/mL (OR 193, 95% CI = 22.1682, p < 0.001) could predict relapse within two months with 91.7% sensitivity and 94.6% specificity. Constantly normal FC values during the follow-up were predictive for deep remission.

Conclusion: It is seen that FC elevates two months before clinical and/or endoscopic relapse. FC is a suitable marker for predicting relapse and building a follow-up strategy for IBD patients in clinical practice.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
be required to obtain a 2x2 contingency table. Pooled analysis was done using a random-effects model. Subgroup analysis was performed at real-time Kudo pit pattern based and real-time CLE for characterization of visible lesions. Heterogeneity was assessed using Chi squared and I^2 statistics.

Conclusion: Our search strategy identified 172 studies of which only 20 met the inclusion criteria. The pooled results are outlined in the table. Real-time CLE and magnification endoscopy had the best performance characteristics. However there was a lot of heterogeneity in the results. Most CLE and magnification studies were single centre, single expert user which could explain these results. CLE studies were also affected by attrition bias with some studies reporting non-interpretable mages in a significant proportion.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1669 ENDOCUTIC FINDINGS AND COLONOSCOPIC PERFORATION IN MICROSCOPIC COLITIS: A SYSTEMATIC REVIEW OF THE LITERATURE

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Introduction: Microscopic colitis (MC) is a clinical syndrome of severe watery diarrhoea with few or no endoscopic abnormalities. The incidence of MC is reportedly similar to that of other inflammatory bowel diseases. The need for histological confirmation of MC frequently guides reimbursement health policies. With the advent of high-definition (HD) coloscopes, the incidence of distinct endoscopic findings reported in MC has risen. This has the potential to improve diagnosis times, increase cost-effectiveness of MC management and diminish the workload and costs of busy modern endoscopy units.

Aims & Methods: Publications on distinct endoscopic findings in MC available until 31st March 2017 were searched systematically (electronic and manual) in PubMed. The following search terms/descriptors were used: collagenous colitis(CC) OR lymphoid colitis(LC) AND endoscopy, colonoscopy, findings, microscopic colitis, erythema, macrovascular structure, abnormalities. An additional search for MC AND perforation was made.

Results: Eighty (n = 80) articles, predominantly single case reports (n = 45), were retrieved. Overall, 1,582 (4,119 female: 61.6:14.1) years patient(pts) with MC and endoscopic findings were reported. The majority of articles (n = 62) were on CC (756 pts; 77.5% female). We identified 16 papers comprising 779 pts (68.9% female) with LC and 7 articles describing 47 pts (72.3% female) confirmed to have MC. The youngest patient was 10 and the oldest 97 years old. Aside from diarrhoea, symptoms included abdominal pain, weight loss, bloating, flatulence and oedema. In the study group we found 616 (38.9%) pts with macroscopic findings. The most common colonic findings were non-ulcerous lesions i.e. pseudomembranes, a variable degree of vascularule pruning & dwindling, mucosal lacerations & abnormalities such as erythema/edema/nodularity, or surface textural alteration (n = 537; 87.2% pts). Isolated linear ulcerations were identified in 5 pts(0.8%) and in conjunction with non-ulcer lesions in 74 pts(12.9%). The location of endoscopic findings was not reported in 26 articles. Distinct endoscopic findings were described in the left (descending, sigmoid, rectum –23/20/10 studies), right (cecum, ascending–7/21 studies) & transverse colon (14), as well as duodenum (7) and terminal ileum (2). Colonic perforation was reported in 9 patients (0.57%).

Conclusion: Endoscopic findings are recognized with increased frequency in pts with MC. This could improve MC diagnosis by prompting a more extensive biopsy protocol in such cases and an earlier initiation of treatment. Procedure-related perforation has been reported in this group, therefore, cautious air insufflation is advisable when endoscopic findings are recognised.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P1670 PREVALENCE AND QUANTITATIVE ASSESSMENT OF LIVER STEATOSIS IN INFLAMMATORY BOWEL DISEASE PATIENTS

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Introduction: It is well recognized that patients with inflammatory bowel disease (IBD) are at risk for nonalcoholic fatty liver disease (NAFLD). Our aim was to evaluate the prevalence and to quantify hepatic steatosis in IBD patients using the controlled attenuation parameter (CAP).

Aims & Methods: We prospectively recruited all IBD patients presenting for a disease flare or follow-up visit in our clinic, during a 18 month period. Patients were considered as alcohol intake if they have more than 20 g/day and those with coexisting viral hepatitis were excluded from analysis. Clinical characteristics and laboratory data were recorded. Hepatic steatosis was evaluated by conventional ultrasound, hepatic steatosis index (HSI) and transient elastography with CAP (Fibroscan, Echo chiff, Paris). Significant steatosis (S ≥ 1) was defined for a CAP value over 236 [1], and the cut-off of HSI for detecting NAFLD was set at ≥ 36 [2].

Results: Altogether 62 IBD patients (35 ulcerative colitis, UC and 27 Crohn’s disease, CD), mean age 45 ± 15 years, 50% female, were included in the analysis. The two groups (UC, CD) were similar regarding disease activity (remission/flare/48.5/53.1% in the UC group, 55.6/44.4% in the CD group), BMI (24.1 and 24.5 kg/m2), and disease duration (21 and 21.1 months). Hepatitis B and C virus infections were excluded (HBsAg 498 and 513 mg/dL). UC patients had higher mean cholesterol values (205.9 vs. 176.4 mg/dL) and 11% of them were diabetic (compared to none in the CD group). Mean CAP was higher in CD compared to UC—246 vs. 225 dB/m, while HSI was 4.9 for UC patients versus 3.4 for IBS. As expected, UC patients had higher FIB-4 score (21/32, 35.3%) and CAP even more (23/62, 37.1%), yielding an 8% detection rate. NAFLD-IBD patients were more likely to have CD phenotype, history of resection, and longer disease duration.

Conclusion: In our cohort, about one in three IBD patients had fatty liver disease, as quantified by CAP. Diagnostic performance of CAP was better than conventional ultrasound and HSI in detecting fatty liver in IBD patients.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P1671 INTESTINAL MICROBIOTA BIOMARKERS AS A NEW TOOL TO SUPPORT IRREVERSIBLE BOWEL SYNDROME DIAGNOSTICS

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Introduction: Irritable Bowel Syndrome (IBS) is a common gastrointestinal disorder that affects around 11% of global population. Despite the high prevalence of IBS, the cause of this disorder remains unknown and the criteria used to diagnose IBS are still unclear. In recent years, disturbances in the intestinal microbiota have been associated to the pathophysiology of IBS. Recently, two accurately defined Firmicutes (Fpra) and Eubacterium rectale (Eco) have been shown to discriminate between Inflammatory Bowel disease (IBD) and Healthy subjects (H). Therefore, the purpose of this study was to verify the capability of Fpra and Eco abundances to distinguish among healthy subjects, IBS, and IBD patients, in order to create a non-invasive system of diagnostic support for IBS patients.

Aims & Methods: A cohort consisting of 33 H and 14 IBS was enrolled. IBS patients were separated by subtypes: IBS with constipation (C-IBS), IBS with diarrhea (D-IBS), and alternating IBS (A-IBS). Rome IV criteria were used to diagnose IBS patients. Moreover, 29 ulcerative colitis (UC) and 15 Crohn’s disease (CD) patients were also included. All subjects were recruited by the Gastroenterology Services of the Hospital Universitari Dr. Josep Trueta (Girona) and Hospital Universitari de Bellvitge (Hospitalat del Llobregat, Spain). Fpra total and Eco abundances were quantified by qPCR.

Results: We found lower abundance values of Fpra in IBS patients when compared with H (P = 0.005). In contrast, Eco abundance was higher in IBS patients, although the differences observed were not significant (P = 0.221). When comparing among subtypes of IBS (C-IBS, D-IBS, and A-IBS) no significant differences were observed, although Fpra abundance was lower in C-IBS. We also used Fpra in combination with Eco as a complementary indicator of dysbiosis (Ratio Fpra/Eco). This ratio allows a good discrimination between H and IBS (FDR = 0.04). When it comes to discrimination between IBS and IBD patients, significant differences were observed in Fpra/Eco ratio between UC and IBS patients (P = 0.008), but not between IBS and CD patients (P = 0.775). Concerning disorders different to IBS, significant differences were also observed between D-IBS and CD (P > 0.001), between H and UC (P = 0.037), and between CD and UC (P = 0.027).

Conclusion: Fpra abundance is a good biomarker to discriminate between healthy subjects and IBS patients. The use of Fpra/Eco ratio allows to distinguish IBS from H and UC patients. In contrast, none of the used biomarkers was able to differentiate IBS and CD patients. These results show that IBS and CD patients share similar dysbiosis parameters opening the need of further study to stabilize any eventual pathogenic link.

Disclosure of Interest: All authors have declared no conflicts of interest.

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1Department of Inflammatory Bowel Disease and IBD and Irritable bowel syndrome (IBS) may present in a similar manner [1] [2]. Measuring faecal calprotectin concentration is often recommended to rule out inflammatory bowel disease, however, there are no tests to positively diagnose irritable bowel syndrome and invasive tests are still used to rule out other pathologies [3, 4]. There is a chance, therefore, for novel, non-invasive diseasespecific biomarkers. Volatile organic compounds (VOCs), originating from physiological metabolic processes in the human body, are excreted as waste products through stool samples. For this reason, several biological, non-invasive, simple and low-cost biomarker studies of inflammation that are useful in clinical practice for both diagnostic screening and therapeutic or course response monitoring are being evaluated in recent years Evolution of the disease. In this sense, stool markers, and especially calprotectin, have become of great importance in recent years as screening to select patients requiring more diagnostic studies and as a marker of activity for therapeutic follow-up [5]. Can the VOCs from stool samples show differences between ulcerative colitis and Crohn’s disease.

Aims & Methods: Five healthy individuals (control group- CON) and nineteen patients diagnosed with IBS were selected for the analysis of their stool VOCs. Healthy participants Healthy control samples (Control) (n = 5) were collected from healthy volunteers working in the Digestive Diseases Area and they were defined as healthy volunteers based in a group of CD-UC-CON where was analyzed 10 CD patients, 9 UC patients, and 5 controls with 455 samples. Data from stool samples was obtained using eNose MOOSY32 [6].

Results: Figure 1 shows the scatter 3D plot with three voltage parameters for the group UC-CON. These results show that IBS and CD patients from H and UC patients. In contrast, none of the used biomarkers was able to differentiate HBD and CD patients. These results show that IBS and CD patients share similar dysbiosis parameters opening the need of further study to stabilize any eventual pathogenic link.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
2. Five healthy individuals (control group- CON) and nineteen patients diagnosed with IBS were selected for the analysis of their stool VOCs. Healthy participants Healthy control samples (Control) (n = 5) were collected from healthy volunteers working in the Digestive Diseases Area and they were defined as healthy volunteers based in a group of CD-UC-CON where was analyzed 10 CD patients, 9 UC patients, and 5 controls with 455 samples. Data from stool samples was obtained using eNose MOOSY32 [6].

Table: Different algorithms test for matrix classification by WEKA software. Classification Relative absolute error

<table>
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<th>MLPL</th>
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<th>Test</th>
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<td>89.7%</td>
<td>17.1%</td>
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</tbody>
</table>

Conclusion: In this preliminary research to distinguish between Ulcerative Colitis and Crohn’s disease, the best algorithm for patient’s classification was the MLP with 30% to train and 70% to test. Although the high classifications result it is hoped is useful. The authors have declared no conflicts of interest.

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P1673 CZECH REGISTRY OF INFLAMMATORY BOWEL DISEASE PATIENTS ON BIOLOGICAL THERAPY: RESULTS FROM THE FIRST YEAR

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Introduction: Czech Registry of Inflammatory Bowel Disease (IBD) Patients on Biological Therapy (CREdIT) was launched in March, 2016 in order to collect and analyze the data from Czech centers appointed to provide biological therapy to IBD patients.

Aims & Methods: The objective is to provide information on the CREdIT registry after its first year of operation. Basic demographic data (sex, age, diagnosis, Montreal classification or disease extent) were collected together with information on disease activity, therapeutic regimen, concomitant medication and adverse events. Patients who began biologic therapy prior to enrolment into the registry as well as those who start their treatment are included, and labeled as “retrospective” and “prospective” cohort, respectively.

Results: Among 30 centers providing biological therapy to patients with Crohn’s disease (CD) and ulcerative colitis (UC) in the Czech Republic, 24 participated as of 1st of March 2017. The centres enrolled 2129 IBD patients (CD, 1595; 74.9%; UC, 505, 23.7%; IBD-U, 29, 1.4%), with median of 63 (range 4-528) patients per center. Majority belong to the retrospective cohort (65%), the remaining 35% represent the prospective cohort. According to the latest data check, patients are treated with infliximab (1273, 59.8%), adalimumab (739, 34.7%), vedolizumab (73, 3.4%), and golimumab (42, 2%). Treatment intensification on disease activity, therapeutic regimen, concomitant medication and adverse events.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

P1675 COST EFFECTIVENESS OF IBDC FACIAL CALPROTECTIN AS A SURROGATE MARKER OF MUCOSAL HEALING POST INDUCTION OF BIOLOGICAL AGENTS IN INFLAMMATORY BOWEL DISEASE

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Introduction: Traditionally in our unit all IBD patients started on anti-TNF therapy are followed up at 3 months and we aim to do a colonoscopy at 6 months to assess for mucosal healing. Recently we have started using a relatively new technology, called IBDoc, which allows testing the faecal calprotectin at home using a smartphone application and the results are automatically updated in our database.

Aims & Methods: We aimed to evaluate the cost effectiveness of using IBDoc faecal calprotectin post induction of biological agents. The data was collected retrospectively from ourIBDoc data base. All patients that were commenced on anti-TNF therapy for IBD and trained in using IBDoc at home were included. IBDoc faecal calprotectin was tested at 3 and 6 month post induction of biological agents.

Results: Total number included in the study was 131 patients. 40% had normal calprotectin at 3 month saving 53 follow up clinic visits (cost of clinical visit 128 euro) and 75% had a normal faecal calprotectin at 6 months saving 40 routine colonoscopy (cost of colonoscopy 337 euro). 78 patients had a raised faecal calprotectin at 3 month, of which 28% had a normal faecal calprotectin at 6 months saving 22 follow-up colonoscopy. In total 53 clinical visits and 62 colonoscopies were avoided.

Conclusion: This study demonstrate a significant cost effectiveness of using IBDoc faecal calprotectin post induction of anti-TNF therapy, as well as reducing the waiting time for both clinic visits and colonoscopies.

Disclosure of Interest: G. El-Saffi: Abbvie
All other authors have declared no conflicts of interest.

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P1676 DOSE OPTIMISATION OF INFliximAB: COMPARATIVE STUDY OF A RAPID TEST AND AN ESTABLISHED ELISA METHOD

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Introduction: In patients with inflammatory bowel diseases (IBDs), comprising Crohn’s disease (CD) and Ulcerative colitis (UC), a patient-tailored therapy is an unmet need that requires accurate monitoring of the intestinal disease activity.

We demonstrated recently, that the expression of microRNA (miR)-320a follows the disease activity in murine colitis models1. In this prospective study we evaluated the potential of miR-320a as a biomarker to monitor the disease activity in IBD patients as well as its potential to distinguish UC/CD from infectious colitis.

Aims & Methods: The miR-320a was measured by qRT-PCR analysis in peripheral blood samples from 36 CD and 54 UC patients with acute flare of disease (n = 51) and in remission (n = 37) as well as in healthy control patients (n = 20) and in patients with infectious colitis (n = 9). Disease activity was assessed clinically applying the Crohn’s disease activity index (CDAI) and the partial Mayo score (pMayo) for UC patients as well as the simple endoscopic score Crohn’s disease (SES-CD) and the endoscopic Mayo score (eMayo) to score endoscopic disease activity.

Results: Both in CD and in UC patients, miR-320a expression in remission was significantly increased as compared to healthy controls (49 ± 8.7 ± 17 vs. 17 ± 3; both p < 0.001) but distinctly reduced as in CD/UC patients with acute flare (1718 ± 488; p = 0.006; 531 ± 107, p = 0.001). In CD patients with acute clinical flare (CDAI > 220), miR-320a expression level were significantly increased as compared to CD patients in clinical remission (CDAI < 15, 267 ± 637 vs. 57 ± 9; p < 0.001) and showed a strong correlation with endoscopic disease activity (r = 0.70). Similarly, in UC patients, miR-320a also revealed a significant increase in patients with low (pMayo 3-4), moderate (pMayo 5-6) and severe clinical disease activity (pMayo > 6) as compared to UC patients in remission (259 ± 47; 281 ± 26; 1090 ± 204 vs.76 ± 13, all p < 0.001).

Conclusion: The miR-320a expression in peripheral blood from IBD patients followed the clinical and endoscopic disease activity and may distinguish between IBD and infectious colitis. Therefore, miR-320a might serve as biomarker to non-invasively assess the disease activity in IBD patients.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
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P1677 RISK FACTORS ASSOCIATED WITH A HIGH RISK OF COLORECTAL CANCER IN PATIENTS WITH ULCERATIVE COLITIS. PRELIMINARY RESULTS FROM THE IBSEN COHORT

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Aims & Methods: Our aim was to evaluate how individual disease variables contribute to the development of colorectal cancer. A population-based inception cohort of patients with ulcerative colitis patients diagnosed between 1990–1994 have been prospectively followed at one, five, 10 and 20 years after inclusion. In this cohort of patients with ulcerative colitis patients diagnosed between 1990–1994, 239 patients were included (table 1). A total of 135 serum sample from patients with CD and UC. IFX concentration in serum samples were determined using a well established IFX-specific ELISA assay (Promonitor®) and the test assay Quantum Blue®. According to the manufacturer, the lower and upper limits of quantification are: In the Quantum Blue assay 0.4 μg/ml and 20 μg/ml respectively In the Promonitor assay 0.035 μg/ml and 14.4 μg/ml respectively. All statistics were carried out using the statistical programs IBM SPSS statistics 21 and Epidat version 4.2.

Results: The IFX levels measured by the point-of-care method were higher than those measured by established ELISA (Promonitor level: mean 4.67, median 3.2 s.d. d. 4.39 (0.035–14.4)); Quantum Blue level mean 6.31; median 3.75 s.d. 6.27 (0.4–20). The intraclass correlation coefficients were 0.81 (p < 0.001). The standard ELISA had a high (r = 0.89) and significant (p < 0.001 correlation with the Quantum Blue® assay. A Bland-Altman analysis showed a bias of 1.88% confirming the overall excellent correlation of the two methods. The results for each measurement stratified according to a common accepted therapeutic strategy are listed in Table 1. The agreement was excellent in 7 μg/ml lower than 3 and higher than 7 with a high agreement. We estimated a simplified score to convert the “point-of-care” level into “Promonitor” level and facilitate dose management: *Nivel de Promonitor = 0.793 + 0.615*Nivel QB*.

Conclusion: Our aim was to evaluate the clinical usefulness of establishing a simplified score to convert the “point-of-care” level into “Promonitor” level and facilitate dose management.

P1679 THE ADDITION OF AN IMMUNOSUPPRESSANT IS AN EFFECTIVE OPTIMIZATION STRATEGY AFTER LOSS OF RESPONSE TO ANTI-TNF ALPHA MONOTHERAPY IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE: A TWO-YEAR STUDY

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Introduction: In patients with inflammatory bowel disease (IBD) the addition of an immunosuppressant (IM) after loss of response to anti-TNF alpha monother- apy is regarded as an emerging strategy of therapeutic optimization. However, few clinical data have been reported to date.

Aims & Methods: The aim of this study was to evaluate efficacy and tolerability of a “selective” combination therapy in patients with IBD. All consecutive patients with loss of response to anti-TNF alpha monotherapy despite an intensive dose optimization who added an IM from October 2014 to October 2016 were entered in a prospectively maintained database. The steroid-free remission and the clinical response, this latter defined as a clinical improvement (reduction of Harvey-Bradshaw Index ≥ 3 for Crohn’s disease and of Mayo Partial Score ≥ 2 for ulcerative colitis compared with baseline) with a concomitant reduction of steroid dosage compared with baseline and discontinuation within twelve weeks, were considered as responses. Few clinical data have been reported to date.

Results: Among 630 patients treated with biologics during the study period, 46 (33 Crohn’s disease and 13 ulcerative colitis) were included (table 1). A total of 31 patients (67.4%) were treated with an intravenous anti-TNFz (infliximab, as originator product or biosimilar), while 15 (32.6%) with a subcutaneous anti-TNFz agent (10 adalimumab and 5 golimumab). The mean doses of thiopurines used in combination therapy were below those regarded as therapeutic in IBD, methylxanthine was mostly employed at a dose of 15 mg/week, and all patients treated with mycophenolate mofetil were able to tolerate the target dose of 1500 mg/day. The mean duration of follow-up was 12.8 ± 7.3 months. Twenty-one patients (45.7%) remained on combination therapy at the end of follow-up: 15 (32.6%) maintained a steroid-free remission, and 6 patients (13.0%) achieved a clinical response.

All patients who experienced a treatment success, median value of C-reactive protein decreased from the baseline to the end of follow-up (13.2 vs. 3.0, p = 0.01; normal values < 5 mg/L). Adverse events leading to treatment discontinuation were reported in 8 out of 46 patients (17.4%).
Table 1

<table>
<thead>
<tr>
<th>Variable</th>
<th>N = 46</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years), mean ± S.D.</td>
<td>45.6 ± 13.0</td>
</tr>
<tr>
<td>Male gender, n (%)</td>
<td>22 (47.8%)</td>
</tr>
<tr>
<td>Smokers, n (%) Never Current Ex</td>
<td>4 (8.7%)</td>
</tr>
<tr>
<td>2 (4.3%)</td>
<td></td>
</tr>
<tr>
<td>Type of Disease, n (%)</td>
<td></td>
</tr>
<tr>
<td>Crohn's Disease Ulcerative Colitis</td>
<td>33 (71.7%)</td>
</tr>
<tr>
<td>Duration of disease, mean ± S.D.</td>
<td>12.4 ± 8.4</td>
</tr>
<tr>
<td>Localisation of the disease, n (%)</td>
<td>10 (30.4%)</td>
</tr>
<tr>
<td>Crohn's Disease Ileal</td>
<td>18 (54.5%)</td>
</tr>
<tr>
<td>Disease involvement Ulcerative Colitis Proctitis Left-sided Extensive</td>
<td>3 (9.1%)</td>
</tr>
<tr>
<td>Extraintestinal manifestations, n (%)</td>
<td>2 (4.3%)</td>
</tr>
<tr>
<td>6 (18.2%)</td>
<td></td>
</tr>
<tr>
<td>Extraintestinal manifestations, n (%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>Concurrent prednisone at baseline, n (%)</td>
<td>6 (14.3%)</td>
</tr>
<tr>
<td>Line of anti-TNF therapy, n (%)</td>
<td>15 (45.5%)</td>
</tr>
<tr>
<td>First Second Third</td>
<td>14 (42.4%)</td>
</tr>
<tr>
<td>Experienced to the IM used in combination therapy, n (%)</td>
<td>4 (12.1%)</td>
</tr>
<tr>
<td>Time between start of anti-TNF therapy and addition of IM (months), median (IQR)</td>
<td>13 (28.3%)</td>
</tr>
<tr>
<td>Exposed to the IM used in combination therapy, n (%)</td>
<td>7 (15.3%)</td>
</tr>
<tr>
<td>Combination therapy, n (%)</td>
<td></td>
</tr>
<tr>
<td>IFX + AZA IFX + 6-MP</td>
<td>11 (46.2%)</td>
</tr>
<tr>
<td>2 (4.3%)</td>
<td></td>
</tr>
<tr>
<td>IFX + MTX IFX + MMF TOTAL IV</td>
<td>5 (21.7%)</td>
</tr>
<tr>
<td>ADA + AZA</td>
<td>10 (43.5%)</td>
</tr>
<tr>
<td>ADA + MTX GOL + AZA + GOL TOTAL SC</td>
<td>13 (28.3%)</td>
</tr>
</tbody>
</table>

Conclusion: In patients with IBD the addition of an immunosuppressant is an effective and safe optimization strategy after loss of response to anti-TNF alpha monotherapy. Low doses of IM are sufficient to achieve a clinical response in this setting.

Disclosure of Interest: F.S. Macaluso: Lecture grants from MSD and Takeda Pharmaceuticals.
S. Renna: advisory board member for AbbVie and MSD; lecture grants from AbbVie, MSD, Takeda Pharmaceuticals, Zambon.
M. Cottoni: Received financial support for the organization of a second level Master degree in inflammatory bowel disease from AbbVie, MSD, Takeda Pharmaceuticals, and Sofar.
A. Orlando: Advisory board member for AbbVie, MSD, Takeda Pharmaceuticals; lecture grants from AbbVie, MSD, Takeda Pharmaceuticals, Sofar, Chiesi.

All authors have declared no conflicts of interest.

P1680 CORRELATION BETWEEN EXTRA-INTESTINAL MANIFESTATIONS AND ANTI-DRUG ANTIBODIES DEVELOPMENT IN CROHN'S DISEASE PATIENTS

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Introduction: Extra-Intestinal Manifestations (EIM) are frequently (up to 40%) encountered in patients with Crohn’s Disease (CD). Commonly, their presence is associated to a more severe degree of luminal disease and lower response to conventional therapy (i.e. immunosuppressants). Drug trough levels are associated with biological drug response, while the role of Anti-drug Antibodies (AAA) is still debated. Moreover, the predicting factors associated with AAA development have not been thoroughly studied yet. To the best of our knowledge, there are no studies correlating the presence of EIM and AAA development.

Aims & Methods: The aim of our prospective study was to identify an association between the presence of EIM and the development of AAA in CD patients treated with biological therapy. We prospectively enrolled 60 CD patients (32 males, median age = 46y, range = 21–72) treated either with adalimumab (ADA n 39, 63%; IFX n 21, 35%) with a median follow-up of 80 (range 14–206) weeks. Blood samples were drawn at standardized time points assessed using an homogenous mobility shift assay (HMSA; Prometheus Lab, San Diego, United States).

Results: ADA were detected in 27 (45%) patients and their development has proved to be more frequent in subjects treated with IFX rather than those in therapy with ADA (n 14, 66.6% vs 13, 33.3%, P = 0.017). EIM were observed in 26 (43.3%) patients, without any significant difference between ADA and IFX patients (n 17, 51.5% vs n 9, 42.9%, P = 1). We found that ADA treated patients with EIM were more likely to develop AAA (n = 9, 52.9% versus n = 4, 18.2%, P = 0.039) while no statistically significant association between EIM and AAA development was observed in IFX treated patients (n = 5, 55.5% versus n = 9, 75%, P = 0.64).

Conclusion: We found that ADA-treated patients with EIM tend to develop more frequently AAA. Assuming that the presence of AAA reduces the effectiveness of biological therapy, the presence of EIM may be considered a predictive factor for loss of response to biological therapy with anti-tumor necrosis factor alpha drugs.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1681 THE PRESENCE OF IRRITABLE BOWEL SYNDROME-TYPE SYMPTOMS IN MICROSCOPIC COLITIS IS ASSOCIATED WITH INCREASED PSYCHOLOGICAL COMORBIDITY AND IMPAIRED QUALITY OF LIFE

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Introduction: Patients with microscopic colitis (MC) often present with abdominal pain and diarrhoea1, and small cross-sectional surveys suggest that up to one-third may meet diagnostic criteria for irritable bowel syndrome (IBS)2. However, the impact of IBS-type symptoms in patients with MC, in terms of their effect on psychological health and quality of life has not been assessed. Aims & Methods: We conducted a cross-sectional survey of individuals with MC. We analysed demographic data, symptoms that met the Rome III criteria for IBS, mood (via hospital anxiety and depression scale (HADS)) and somatoform-type behaviour (via patient health questionnaire-15 (PHQ-15)) and quality of life (QOL) (via SF-36) in order to determine risk factors for, and impact of, IBS-type symptoms in patients with MC.

Results: In total, 157 individuals with MC returned completed questionnaires, 53 (36.0%) of whom met the Rome III diagnostic criteria for IBS. The commonest IBS subtypes in MC were collagenous colitis (52.9%, n = 83), followed by lymphocytic colitis (38.2%, n = 60), and MC-not otherwise specified (8.9%, n = 14). Individuals meeting the Rome III criteria for IBS had significantly higher levels of anxiety (HADS-anxiety score 8.6 vs. 5.0, P = 0.001), depression (HADS-depression score 6.1 vs. 3.5, P = 0.001), and somatoform-type behaviour (PHQ-15 score 12.5 vs. 7.9, P < 0.001) compared with individuals who did not. Individuals meeting the Rome III criteria scored significantly worse on all domains of the SF-36, except for physical functioning. There were also trends towards these individuals being younger (65 years vs. 69.2 years, P = 0.011) or taking proton-pump inhibitors (58.5%, n = 31 vs 42.4%, n = 39, P = 0.062).

Conclusion: More than one-third of individuals with MC met diagnostic criteria for IBS and these individuals reported higher levels of anxiety, depression, and somatisation plus impaired quality of life. Management strategies for these symptoms are required.

Disclosure of Interest: J.S. Kane: This work was supported by an investigator-initiated grant from Dr. Falk Pharma UK Ltd. A.C. Ford: This work was supported by an investigator-initiated grant from Falk Pharma UK Ltd. All other authors have declared no conflicts of interest.

References
TREATMENT IN CROHN’S DISEASE PATIENTS ARE NOT CORRELATED TO RESPONSE TO USTEKINUMAB

P1683 TROUCH LEVELS AND ANTIBODIES TO USTEKINUMAB ARE NOT CORRELATED TO RESPONSE TO USTEKINUMAB TREATMENT IN CROHN’S DISEASE PATIENTS

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Introduction: Ustekinumab (UST) has been shown to be effective in refractory Crohn’s disease (CD) in phase III trials. The aim of the present study was to prospectively evaluate the association between UST trough levels and anti-ustekinumab antibodies, with the response and remission to induction and maintenance UST treatment in CD patients.

Aims: We performed a prospective study including all CD patients refractory to anti-TNF who received subcutaneous UST from September 2015 to November 2016 in the tertiary French referral center of Gastroenterology in Cliniques Universitaires de Lille. During induction patients received 90mg of SC UST at week 0, 4 and 12. During the maintenance phase patients received 90 mg of SC UST every 8 weeks that could be optimized by shortening injection 77% of patients received concomitant immunosuppressant and 42% received corticosteroids. At the end of the induction phase (week 12) clinical response was observed in 57% patients. There was no significant difference in mean UST trough levels in patients who responded to UST induction (median 1160 ng/ml; IQR: 603–1644) as compared to patients who did not respond (median 1556 ng/ml; IQR: 494–2758, p = 0.24). Forty-three (90%) patients received at least 4 injections of UST, with 12 patients who were optimized at the time of dosages. Clinical response was observed in 30.4% (70%) patients. Median UST concentration in clinical responder was 1359 ng/ml (IQR: 554–2086) and 2392 ng/ml in non-responder (IQR: 1496–3494), with no significant difference between the two groups of patients (p = 0.20). UST antibodies were undetectable for the 48 patients.

Conclusion: We confirmed that UST treatment is effective in the majority of CD patients refractory to anti-TNF agents. Median trough levels to UST are not correlated to response and remission to UST induction and maintenance treatment, with no antibodies developed against UST.

Disclosure of Interest: All authors have declared no conflicts of interest.

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Introduction: Inflammatory bowel diseases (IBDs) are chronic conditions characterized by elevated costs (both direct and indirect). Over the last years also a significant healthcare burden associated with IBD has emerged, due to an increasing use of biological therapies and hospitalization costs. Despite the creation of local or regional databases in Italy data regarding healthcare expenditure are lacking.

Aims: The aim of this study was to evaluate costs comprehensive of biological treatments and hospitalizations in a series of patients with ulcerative colitis (UC) and Crohn’s disease (CD) and their correlation with demographic and clinical variables. Disease severity was evaluated by clinical scores (partial Mayo score for UC, Harvey Brashaw Index for CD). We analyzed retrospectively patients treated by biologics referred to our IBD Unit between May 2015 and April 2016 who underwent at least six months follow-up (last visit October 2016). As regards biological therapies costs burdens our Centre pharmacy for each drug (Infliximab, Adalimumab, Golimumab, Vedolizumab) and for single patient were evaluated. About hospitalizations the average costs of hospital care specific for a department through fares for homogeneous groups of patients i.e. Diagnosis-Related Group (DRG) were collected. The mean overall monthly expenditure for each case was then evaluated.

Results: We collected clinical-economical data of 142 patients in biological treatment for IBD, with no significative differences between UC and Crohn’s disease. The results show the positive correlation between the number of hospitalizations and the average costs per patient. The amount of costs for hospitalizations amounts for more than 80% of the total costs. We analyzed in groups different for sex and age and disease activity only the last one was associated with increased costs with R² = 0.84 for UC and 0.95 for CD. The cost increases in patients with more lines of therapy in UC (not in CD) but the difference wasn’t significative.

Conclusion: In our study the main cost is due to biological therapy but the subjects enrolled were the most severe in comparison to the whole IBD population under conventional therapy. No differences were found between the type of biologic administered and the way of administration (intravenous or subcutaneous) so the therapeutical choice could be driven by clinical reasons and not only economic ones.

Disclosure of Interest: All authors have declared no conflicts of interest.

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Introduction: Useklinumab (UST) has been shown to be effective in refractory Crohn’s disease (CD) in phase III trials. The aim of the present study was to prospectively evaluate the association between UST trough levels and anti-ustekinumab antibodies, with the response and remission to induction and maintenance UST treatment in CD patients.

Aims: We performed a prospective study including all CD patients refractory to anti-TNF who received subcutaneous UST from September 2015 to November 2016 in the tertiary French referral center of Gastroenterology in Cliniques Universitaires de Lille. During induction patients received 90mg of SC UST at week 0, 4 and 12. During the maintenance phase patients received 90 mg of SC UST every 8 weeks that could be optimized by shortening injection interval to every 4 weeks in case of loss of response. Clinical response was defined by decrease Harvey Bradshaw Index (HBI) by 3 points, clinical remission by HBI < 5, loss of response by new increase of HBI. UST trough levels and anti-ustekinumab antibodies were correlated with Hb and transferrin saturation (13.63 /C6 26.50 vs 17.75, p = 0.003), previous surgery (OR 2.845 95% CI 1.111–7.284, p = 0.02) and pene-trating pattern in CD (OR 8.252 95% CI 1.289–52.919, P < 0.001). Hb and CRP had a negative correlation (p = 0.016, p = 0.022). In UC, CRP and FC normalization was associ-cated to transferin saturation (13.63 /C6 1.66 vs 12.47 ≥ 1.38, p = 0.005 and 51.33 ≥ 26.0 vs 27.63 ≥ 9.96, p = 0.048). There was no difference in the parameters evaluated comparing groups 1 and 2. There was also no significative difference in the variation of Hb and iron values after treatment with ferric saccharate and ferric carboxymaltose.

Conclusion: In a population of patients with IB, iron deficiency was the main cause of anaemia and the two forms of intravenous iron replacement were equally effective. In the group of patients with UC, elevated CRP was associated with anaemia.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
Introduction: The monitoring of appropriateness, costs, and clinical outcomes of biological therapy in inflammatory bowel disease (IBD) is a relevant need. Aims & Methods: We aimed to evaluate all these issues in Sicily through a web-based network of all prescribing centers. The Sicilian Network for Inflammatory Bowel Disease (SN-IBD) is composed by a super Hub coordinator centre and a Harvey-Bradshaw Index (HBI) for UC, and to a Harvey-Bradshaw Index (HBI) for CD.

As clinical end-point, we set remission (corresponding to a Mayo Partial Score <2) for UC, and to a Harvey-Bradshaw Index (HBI) for CD, and response (reduction of mean stool frequency and/or stools/day/week), clinical response (defined as 50% reduction of mean stool frequency/day/week), and clinical remission (defined as no effect on anti-TNF despite the fact that 2 patient had even tested both anti-TNF agents. In the cases that failed anti-TNF, further treatment with vedolizumab (n = 14) did not gain clinical remission despite the use of a third anti-TNF agent (certolizumab pegol). Four patients had an adverse event (vomiting, anxiety, fatigue and eczema—all reversible). Two patients had a serious adverse event (septicemia).

Results: From January 2013 to January 2017, 1578 patients were included. Incident cases were 1151 (808 Crohn’s disease [CD], 335 ulcerative colitis [UC], no significant difference in efficacy was observed between IFX originator (n = 5) and its generic (n = 10) at both 12 and 52 weeks; however, this results could be influenced by the preference of ADA as first-line anti-TNF drug in CD. IFX in UC was superior to GOL and ADA at 52 weeks; once again, this result could be influenced by the preference of IFX as first-line anti-TNF agent in UC; no difference was found between GOL and IFX in UC. Being naive to biologics is a relevant predictor of response in both CD and UC at any time point. No significant difference in efficacy was observed between IFX originator and biosimilars.

Conclusion: In one of the largest “real-life” series of IBD patients on biological therapy reported to date, ADA in CD had a higher success compared to IFX at both 12 and 52 weeks; however, this results could be influenced by the preference of ADA as first-line anti-TNF drug in CD. IFX in UC was superior to GOL and ADA at 52 weeks; once again, this result could be influenced by the preference of IFX as first-line anti-TNF agent in UC; no difference was found between GOL and IFX in UC. Being naive to biologics is a relevant predictor of response in both CD and UC at any time point. No significant difference in efficacy was observed between IFX originator and biosimilars.

Disclosure of Interest: A. Orlando: Advisory board member for AbbVie, MSD, Takeda Pharmaceuticals; lecture grants from AbbVie, MSD, Takeda Pharmaceuticals, Sofar, Chiesi. F.S. Macaluso: Lecture grants from MSD and Takeda Pharmaceuticals. All other authors have declared no conflicts of interest.
P1687 BENEFICIAL EFFECT OF A LOW FODMAPS DIET IN DIFFERENT INTESTINAL DISORDERS

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Introduction: Recent studies have shown that FODMAPs (Fermentable Oligosaccharides, Disaccharides, Monosaccharides, and Polyols)-free diet is effective in subjects with Irritable Bowel Syndrome (IBS). Patients with Inflammatory Bowel Diseases (IBD), and celiac disease (CD) can experience functional gastrointestinal symptoms unrelated to inflammation, but data about the use of low FODMAPs diet in these settings is still scarce.

Aims & Methods: To evaluate the usefulness of a low FODMAPs diet on patients with IBS, non-active IBD, and CD on strict gluten-free diet (GFD), we performed a dietetic interventional prospective study evaluating the effect of a low FODMAPs diet on subjects affected by IBS, CD following at least a 1-year-GFD and IBD who had been experiencing gastrointestinal symptoms without signs of active inflammation. Each subject was put on a low FODMAPs diet after being evaluated by filling out questionnaires concerning on quality of life and symptoms experienced (IBS-SSS and SF-36), and was re-evaluated twice, first after 1 month and second after 3 months.

Results: 127 subjects were enrolled: 56 with IBS, 30 with IBD and 41 with CD. The analysis of the IBS-SSS survey showed that abdominal symptoms improved after 1 month of low FODMAPs diet in all subjects, with statistically significant difference within each group at T0 (average score in IBS: 293 ± 137 SD, average score in IBD: 206 ± 86 SD, average score in CD: 222 ± 65 SD, p < 0.0001). Furthermore, by analysing the SF-36 questionnaire, while we did not observe any significant difference between the three groups, in terms of response to diet (p = NS), we observed a clinical improvement from T0 to T3, after the start of the diet, for most of the questionnaire’s domains.

Conclusion: A low FODMAPs diet could be a valid option to counter abdominal symptoms in patients with IBS, non-active IBD or CD on GFD, and, thus improve their quality of life and social relations.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1688 EFFICACY OF VEDOLIZUMAB ON INTESTINAL AND ARTICULAR SYMPTOMS: REAL-LIFE DATA FROM THE SICILIAN NETWORK FOR INFLAMMATORY BOWEL DISEASE (SN-IBD)

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Introduction: Vedolizumab (VDZ) is a new biologic agent approved for the treatment of adult patients with moderately to severely active ulcerative colitis (UC) and Crohn’s disease (CD).

Aims & Method: The Sicilian Network for Inflammatory Bowel Disease (SN-IBD) is composed by all Sicilian centres prescribing biologics. These centres continuously enter in a web based software all real-life data about pre-scriptions and outcomes of biological therapy in patients with inflammatory bowel disease (IBD). Herein we report data on efficacy of VDZ on intestinal and articular symptoms after 10 and 24 weeks of treatment. As clinical end-point, we set steroid-free remission (corresponding to a Mayo Partial Score < 2 for UC, and to a Harvey-Bradshaw Index < 5 for CD), and clinical response (reduction of Harvey-Bradshaw Index ≥ 3 for CD and Mayo Partial Score ≥ 2 for UC compared with baseline with a concomitant reduction of steroids dosage at week 10, and complete discontinuation at week 24).

Results: From July 2016 to April 2017, 163 patients (84 with CD and 79 with UC) were included (table 1). At week 10, a steroid-free remission was obtained in 71 patients (43.6%), while a clinical response in 37 (22.7%). Out of 71 patients reaching 24 weeks of follow-up, 29 (40.8%) were in steroid-free remission, and 10 (14.1%) had a clinical response. No significant difference in terms of clinical benefit (rate of remission plus clinical response) among patients with UC and CD was reported at week 10 (68.4% vs. 64.3%, respectively; p = 0.58) and at week 24 (54.3% vs. 55.6%, respectively; p = 0.91), and no difference was observed comparing naïve and non naïve patients, neither at week 10 (61.5% vs. 67.7%, respectively; p = 0.48) nor at week 24 (30.0% vs. 39.9%, respectively; p = 0.11). At multiple regression analysis, a longer duration of disease (OR 0.961, p = 0.047) and presence of steroid-dependence (OR 0.189, p = 0.033) were predictors of reduced rates of clinical benefit at week 10, while a lower serum level of C-reactive protein at baseline (OR 0.950, p = 0.031) was predictor of clinical benefit at week 24. An improvement of articular symptoms was reported in 39.5% of patients with active spondyloarthritis at baseline at week 10, and in 45.4% of patients at week 24. The only factor associated with articular response was the coexistence of clinical benefit on intestinal symptoms, both at week 10 (OR 8.471, p = 0.05) and week 24 (OR 5.600, p = 0.08). Three inductions or flares of spondyloarthritis during treatment with VDZ were reported.

Table 1

<table>
<thead>
<tr>
<th>Variable</th>
<th>N = 163</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years), mean ± S.D.</td>
<td>50.6 ± 16.0</td>
</tr>
<tr>
<td>Male gender, n (%)</td>
<td>94 (57.7%)</td>
</tr>
<tr>
<td>Smokers, n (%) Never Current Ex</td>
<td>134 (82.2%)</td>
</tr>
<tr>
<td>Type of Disease, n (%) Crohn’s Disease Ulcerative Colitis</td>
<td>84 (51.5%)</td>
</tr>
<tr>
<td>Duration of disease, mean ± S.D.</td>
<td>79 (48.5%)</td>
</tr>
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<td>Localization of the disease, n (%) Crohn’s Disease ileal Heelocic Colic Upper gastrointestinal tract</td>
<td>50 (59.5%)</td>
</tr>
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<td>Previous resections (Crohn’s Disease), n (%)</td>
<td>51 (60.7%)</td>
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<td>Disease Activity Harvey-Bradshaw Index, Crohn’s Disease - mean ± S.D. Mayo Partial score, Ulcerative Colitis - mean ± S.D. C-Reactive Protein, mean ± S.D. (n.v. &lt; 5mg/L)</td>
<td>3.9 ± 2.4</td>
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<tr>
<td>Endoscopy within three months of initiation of VDZ (n=)</td>
<td>7.6 ± 7.5</td>
</tr>
<tr>
<td>Indication for treatment with VDZ, Failure of anti TNFα therapy Contraindications to anti-TNFα therapy</td>
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<td>Steroid-dependent, n (%)</td>
<td>144 (88.3%)</td>
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<td>Systemic steroids at baseline, n (%)</td>
<td>103 (63.2%)</td>
</tr>
<tr>
<td>Concurrent therapy with immunosuppressant, n (%)</td>
<td>13 (8.0%)</td>
</tr>
</tbody>
</table>

Conclusion: In this large cohort of Sicilian IBD patients, VDZ showed good efficacy after 10 and 24 weeks of treatment, particularly in those with a shorter duration of disease and a limited inflammatory burden. A subset of patients reported improvement also on articular symptoms, probably as a consequence of the concomitant control of gut inflammation.

Disclosure of Interest: F.S. Macaluso: Lecture grants from MSD and Takeda Pharmaceuticals; lecture grants from AbbVie, MSD, Takeda Pharmaceuticals, Zambon. M. Cottone: financial support for the organization of a second level Master degree in inflammatory bowel disease from AbbVie, MSD, Takeda Pharmaceuticals and Sofar. A. Orlando: Advisory board member for AbbVie, MSD, Takeda Pharmaceuticals; lecture grants from AbbVie, MSD, Takeda Pharmaceuticals, Sofar, Chiesi. All other authors have declared no conflicts of interest.
P1689 POSITIVE PHARMACOKINETIC EFFECT OF AZATHIOPRINE CO-MEDICATION ON INFlixIMAB TROUGH LEVELS IS DOSE-DEPENDENT
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Introduction: Combined immune suppression of anti-tumour necrosis factor (antiTNF) biologicals and thiopurines is superior to respective monotherapies in remission induction and maintenance of response in inflammatory bowel disease (IBD) due to the mutually positive pharmacokinetic effect of thiopurines on antiTNF levels and vice versa. It has been suggested that for this synergistic effect, reduced dose of thiopurines might be sufficient but the data supporting this hypothesis are still limited.

Aims & Methods: The aim of the study was to assess the differences of infliximab trough levels according to the dose of concomitantly used thiopurines. All IBD patients treated with infliximab (Remicade®) in two IBD centres between November 2015 and April 2017 were eligible. Infliximab trough levels were routinely measured in all patients with maintenance infliximab therapy using commercially available ELISA kit (Ridscreen®, R-Biopharm). All patients in remission with stable dose regimen of 5mg/kg every 8 weeks at the time of the first assessment of infliximab trough levels were identified retrospectively from the medical records. The differences in the proportion of patients with adequate trough levels (3–12 µg/mL) between patients on infliximab monotherapy, reduced (below 2mg/kg) azathioprine (AZA) dose vs. full (2 to 2.5 mg/kg) AZA dose were analyzed statistically.

Results: Out of a total of 214 IBD patients treated with infliximab, there were 154 in remission at the time of the first assessment of infliximab trough levels. After excluding patients with previously intensified dose regimen, 125 patients were further investigated. Among these 125 pts, 41 pts (33%) were on infliximab monotherapy, 58 pts (46%) were using combined immune suppression with a reduced dose of AZA and 26 (21%) were using the full AZA dose concomitantly with infliximab. Both groups, patients with infliximab monotherapy as well as patients using the reduced AZA dose had significantly lower percentage of patients with therapeutic levels of infliximab compared with the group using the full dose AZA co-medication (41% vs. 64% vs. 81%; infliximab monotherapy, reduced AZA dose and full AZA dose, respectively; p<0.001 for both comparisons, infliximab monotherapy vs. reduced AZA dose vs. full AZA dose).

Conclusion: The proportion of patients with adequate infliximab trough levels is significantly higher in patients with full dose of concomitant azathioprine compared with the patients using a reduced dose of azathioprine. Thus, in order to maximize the chances for sustained benefit from infliximab maintenance treatment, the combined immune suppression should comprise full dose of azathioprine.

Disclosure of Interest: Z. Zelínkova: Speaker’s fee from Abbvie, MSD, Takeda, Janssen
All other authors have declared no conflicts of interest.

References

P1690 G60 FULLERENES ATTENUATE THE INTENSITY OF COLON DAMAGE AND EXTRA-INTESTINAL MANIFESTATIONS ON RATS WITH ACUTE ULCERATIVE COLITIS MODEL
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Introduction: The primary drugs used for inflammatory bowel disease (IBD) treatment have some adverse effects and often are ineffective, so the need for more potent and more reliable medications is clear. A significant role at all the stages of the inflammatory process is attributed to reactive oxygen species, therefore the use of antioxidants is a promising direction of the IBD therapy.

Aims & Methods: C60 fullerene are the effective free radicals scavengers [1], therefore the evaluation of possible protective properties of water-soluble pristine C60 fullerene using the simulation of acute ulcerative colitis (UC) in rats was aimed to be discovered. The pristine C60 fullerene aqueous colloidal solution (C60-FAS; initial concentration 0.15 mg/ml) was prepared according to the protocols described before [2]. UC was simulated by acetic acid intracolonic instillation. C60-FAS was intraperitoneally or intrarectally applied at dose of 0.5 mg/kg C60 daily for 2 times after UC induction. The colon injury was estimated semi-quantitatively on macro- and light microscopy levels using 10- and 14-grade score, respectively, and the grade of total injury (GTI) was calculated. Permeability of colon epithelium was estimated by phenol red dye daily excretion. The states of the colon, liver, pancreas and spleen were assessed by histological (hematoxylin-eosin staining) and biochemical (plasma blood liver enzymes activity) methods, quantitative blood indices were calculated and leukograms were analyzed.

Results: Colon wall edema, hyperemia and hemorrhage on bowel internal surface, ulcers of different size, epithelium desquamation and inflammatory features manifested by submucosa lymphoid and histiocyte infiltration and extravasation appeared under UC condition. Therapy with G60 FULLERENES MANIFESTATION IN INFLUXIMAB TROUGH LEVELS IS DOSE-DEPENDENT

Conclusion: G60-FAS corrects local and systemic morphofunctional changes, conditioned by the induction of acute UC. The protective properties of C60 fullerene against bowel, hematopoietic system and liver due to its local application are more expressed compared to their systemic one, but their impact on pancreas is controversial. Thus, water-soluble pristine C60 fullerene could be used as efficient therapeutic agents at ulcerative colitis.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
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Introduction: Tacrolimus, a calcineurin inhibitor, has been shown to be safe and effective when used as salvage therapy for steroid-refractory ulcerative colitis (UC). Its pharmacological effect has been reported to be dependent on trough level in blood, though little is known regarding predictive factors in relation to the clinical efficacy of tacrolimus in UC patients.

Aims & Methods: The aim of this study was to identify factors related to prediction of short- and long-time efficacy of tacrolimus for UC. We retrospectively reviewed the medical records of patients with moderate to severe steroid-refractory UC who were treated with tacrolimus as induction therapy at Shimane University Hospital between January 2010 and March 2016. Oral tacrolimus was administered at a whole-blood trough level of 10–15 ng/mL to induce remission and then 5–10 ng/mL to maintain remission. Following tacrolimus therapy for 3 months, patients in clinical remission were given azathioprine for maintenance at an appropriate dosage. Using the Rachmilewitz clinical activity index (CAI), clinical remission was defined as a score of ≤4. Predictive factors associated with short- and long-term tacrolimus efficacy were analyzed by evaluating various clinical parameters.

Results: Thirty-six patients received oral tacrolimus for induction, of whom 22 (61.1%) and 27 (75%) experienced clinical remission at 2 and 12 weeks, respectively, after starting therapy. In order to achieve short-term efficacy, the remission rate at 2 weeks was significantly associated with CAI at 2 weeks. Interestingly, of the 22 patients in clinical remission within 2 weeks, 21 (95.5%) remained in remission at 12 weeks. In contrast, only 6 of 14 (42.9%) who did not achieve clinical remission at 2 weeks were not in clinical remission at 12 weeks. For evaluating the long-term efficacy of tacrolimus induction therapy, relapse-free periods were assessed using the Kaplan-Meier method. The relapse-free rate at 48 weeks was higher in patients who achieved clinical remission within 2 weeks compared to those without remission at that time point (79.0% vs. 60.0%).

Conclusion: Tacrolimus induction therapy was effective for patients with moderate-to-severe steroid-refractory UC. Our results clearly indicate that clinical remission achievement within 2 weeks is useful for predicting both short- and long-term outcomes in UC patients treated with that therapy.

Disclosure of Interest: All authors have declared no conflicts of interest.

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Introduction: Early clinical remission by week 2 predicts good short- and long-term efficacy of tacrolimus therapy in patients with moderate-to-severe steroid-refractory ulcerative colitis.

P1691 EARLY CLINICAL REMISSION BY WEEK 2 PREDICTS GOOD SHORT- AND LONG-TERM EFFICACY OF TACROLIMUS THERAPY IN PATIENTS WITH MODERATE TO SEVERE STEROID-REFRACTORY ULCERATIVE COLITIS
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P1692 INFLIXIMAB (IFX) IN MODERATE TO SEVERE ULCERATIVE COLITIS (UC): COMPARISON BETWEEN SCHEDULED TREATMENT STRATEGY AND BRIDGE STRATEGY
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Introduction: UC is a potentially severe disease that carries an increased risk of complications and colectomy. Immunosuppressant and biological therapies are relevant tools for complex patients. The ACCENT study showed that in Crohn’s disease (CD), scheduled IFX infusions vs. episodic are associated with greater efficacy. However, the difficulties of economic access had conditioned to our IBD center, to use IFX in moderate to severe UC as a bridge to thiopurines in 6 mp/aza naïve. In UC, the mentioned strategy was sufficiently compared with a regimen of scheduled IFX treatment, that currently we use.

Aims: Similarly to be compared in moderate to severe UC the results of induction with IFX (in thiopurine naïve pts) continuing with 6 mp/aza maintenance vs. similar induction followed by scheduled IFX maintenance strategy.

We included a cohort of moderate to severe UC treated with IFX in an IBD center (2006 to 2015) comparing results between IFX bridge followed by thiopurines (re-induction when available for moderate to severe relapse) vs. scheduled IFX (w/ 2.6, w/ 8 and w/ 12 interval infusions maintenance).

Conclusion: Kaplan Meier/Log rank test: a) Cumulative incidence of colectomy (difference is 7.46% (p = 0.06) in re-induced pts. b) survival time relapse free, c) survival time corticosteroid free.

Disclosure of Interest: All authors have declared no conflicts of interest

P1693 ILLNESS PERCEPTIONS, COPING STRATEGIES, OUTCOMES AND THEIR CHANGES OVER TIME IN IBD PATIENTS WITH ARTHROPATHIES: A 12-MONTH FOLLOW-UP STUDY
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Introduction: Arthropathies are the most common extra-intestinal manifestation (EIM) in patients with inflammatory bowel disease (IBD). Psychological and behavioural factors, including illness perceptions and coping strategies, perceived by IBD patients with arthropathies may differ from patients without arthropathies and may change during follow-up. Understanding these differences and changes over time, creates knowledge for health care professionals about interventions that may be effective in IBD patients with arthropathies.

Aims & Methods: This longitudinal follow-up study evaluates the differences in illness perceptions, cognitive and emotions regarding a disease and coping strategies (behavioral efforts and strategies to deal with a chronic disease) and illness outcomes between IBD patients with and without arthropathies, and examines the changes of these variables in IBD patients with arthropathies after 12 months.

In total, 204 IBD patients with (n=123) and without (n=81) arthropathies completed questionnaires at baseline and after 1 year follow-up to assess illness perceptions (Revised Illness Perception Questionnaire), coping strategies (Coping with Rheumatic Stressors Questionnaire) and illness outcomes including quality of life (Short Form-36), and activity and work impairment (Work Productivity Activity Index). Linear regression analyses were used to assess the impact of arthropathies on illness perceptions, coping and illness outcomes compared with IBD patients without arthropathies. Mixed model analyses were used to evaluate the change of these variables in IBD patients with arthropathies over time.

Results: Linear regression models demonstrated that arthropathies in IBD were associated with the illness perceptions stronger ‘illness identity’ (β = 0.31 (95% CI 0.31-0.36); p < 0.001), stronger ‘cyclical timeline’ (β = 0.33 (95% CI 0.33-0.34); p = 0.001), more ‘concerning disease’ (β = 0.20 (95% CI 0.16-0.22); p = 0.006), stronger ‘emotional representations’ (β = 0.27 (95% CI 0.20-0.35); p = 0.002) than without arthropathies.

Disclosure of Interest: All authors have declared no conflicts of interest

P1694 INFliximab Biosimilar CT-P13 Therapy is Effective in Maintaining Endoscopically Remission in Ulcerative Colitis Patients: Results from a Multicenter Observational Cohort
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Introduction: CT-P13, the first biosimilar monoclonal antibody to infliximab (IFX) has previously been confirmed to be efficacious in inducing mucosal healing in ulcerative colitis (UC) patients.

Aims & Methods: The aim of this study was to evaluate the efficacy of CT-P13 therapy in maintaining mucosal healing in UC. Patients diagnosed with UC, who were administered CT-P13 from June 2014 at 4 Hungarian and one Czech IBD Centre were prospectively enrolled. Sigmoidoscopy was performed at week 14 and week 54 to assess mucosal healing. Mucosal healing was defined as Mayo endoscopic subscore of 0 or 1. Complete mucosal healing was defined as Mayo endoscopic subscore of 0. CT-P13 trough levels, antibody positivity, serum inflammatory markers as CRP level, fecal calprotectin were assessed at the time of induction and during follow-up and at weeks 14 and 54, previous use of anti TNF drug and the need of dose intensification as possible predictive factors for mucosal healing at week 54 were evaluated. Relevant data of seventy-five UC patients were included in the study of which 74 patients completed the induction therapy and 54 patients had already completed the 54 week treatment period. Mucosal healing was shown in 55.4% of the patients at week 14 and in 61.7% at week 54 (p = 0.033). Complete mucosal healing was present in 24.3% at week 14, but in 36.8% at week 54. The positive interventions including cognitive behavioural therapy (CBT) or physical exercise.

Disclosure of Interest: All authors have declared no conflicts of interest

P1695 THE USE OF ANTI-TNFs IN INDUCING CLINICAL RESPONSE AND REMISSION IN ULCEARTIVE COLITIS: A COMPARATIVE ANALYSIS IN THE REAL-LIFE EXPERIENCE OF A SINGLE REFERRAL CENTER
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Introduction: Anti-tumor necrosis factor (anti-TNF) agents, infliximab (IFX) and more recently adalimumab (ADA) and golimumab (GOL), have been shown effective and safe in the treatment of moderate-to-severe ulcerative colitis
were treated with IFX (p < 0.001). ADA and GOL were more often used as a second-line or third-line. The principal indication for steroid-resistant patients was IFX. No significant difference was observed between IFX and ADA both at week 8 (p = 0.18; response IFX p = 0.08) and at week 16 (p = 0.5; remission p = 0.97), though there was a trend towards a higher rate of response at week 8 with IFX (79% vs 64%). IFX and ADA were more effective than GOL at week 8 (response IFX vs GOL p = 0.020; remission: ADA vs GOL p = 0.027). At week 16 only IFX seems to be more effective than GOL in inducing clinical response (p = 0.048) but not remission. No significant difference among the three drugs was observed in patients naïve to anti-TNFs. Treatment was discontinued in 2 patient in IFX group and in 6 patients in GOL group and in 6 patients with ADA because of persistent disease activity.

Conclusion: This single-center study shows that IFX is more effective than both in the induction (8 weeks) and in the maintenance of response (16 weeks). ADA is more effective than GOL in inducing remission at 8 weeks but no significant difference is observed in the medium-term. However, GOL was used mainly as a second or third-line. In naïve patients, efficacy among anti-TNFs is comparable. Our results may help clinicians in the choice of an anti-TNF in UC. We should prefer in steroid-resistant patients to get a faster response, ADA and GOL should be the first option in steroid-dependent patients naïve to anti-TNFs.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

P6196 REAL WORLD SAFETY OF VEDOLIZUMAB IN INFLAMMATORY BOWEL DISEASE: A META-ANALYSIS
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2Agopoulos Markus Hospital, Frankfurt/Germany
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4King Abdulaziz University, Jeddah/Saudi Arabia
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Introduction: Vedolizumab (VDZ), a gut-selective monoclonal anti-a4ß7-integrin antibody, is used for treatment of Crohn’s disease (CD) and ulcerative colitis (UC). Data from large real-world cohorts can further characterise safety events not fully elucidated in a clinical trial setting, such as the risk of serious infections, as identified with anti-tumour necrosis factor-alpha (TNFα) therapy in the TNFα blockade/anti-TNFα/ENCORE® trials.

Aims & Methods: We conducted a systematic review and meta-analysis of real-world safety outcomes reported for VDZ in UC and CD. MEDLINE-, Cochrane-, and EMBASE-indexed publications and conference abstracts (n ≥ 10) from May 1, 2014–January 10, 2017 were searched for studies reporting real-world VDZ safety outcomes. Reports for patients <18 years of age or for off-label VDZ use were excluded. A meta-analysis was conducted using the DerSimonian-Laird random effects method to obtain a weighted mean of adverse events (AE) rates.

Results: Two hundred and eighty published studies were identified, with 33 reporting safety rates on 2857 VDZ-treated patients (CD: 1532; UC: 829; unspecified/other: 36; three studies [n=460] did not report individual UC/CD data) over a VDZ exposure/follow-up period ranging 0.5–18 months (20 studies). Among included studies, the mean age of patients ranged from 21 to 67 years, with mean disease duration ranging from 7 to 16 years. Most VDZ-treated patients (62–100%) had prior exposure to ≥1 anti-TNFα therapy and 6–64% of VDZ-treated patients were receiving concomitant corticosteroids and immunomodulators. The most common non-infectious AEs were acute or acnec-like lesions (7%; 95% confidence interval [CI] 3–11%), fatigue (6%; 95% CI 3–15%) and arthropalgia (5%; 95% CI 3–10%) (Table 1). The most common infectious AEs were upper respiratory tract infections (6%; 95% CI 3–9%) and sinusits (4%; 95% CI 1–19%) (Table 1). Infusion-reaction-related occurred in 2% (95% CI 1–4%) of patients (n = 811), and malignancies were reported in <1% of patients (<1–4%; 2 studies). Overall, the pooled AE rate reported in VDZ-treated patients was 21% (95% CI 14–32%); 10% (95% CI 6–16%) for infections, 8% (95% CI 6–10%) for serious infections and 7% (95% CI 3–13%) for serious infections (Table 1).

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

Table 1: Pooled real-world adverse event rates of vedolizumab in inflammatory bowel disease

<table>
<thead>
<tr>
<th>Event</th>
<th>n</th>
<th>Rate, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acne or acne-like lesions</td>
<td>290</td>
<td>7.2</td>
</tr>
<tr>
<td>Fatigue</td>
<td>569</td>
<td>6.3</td>
</tr>
<tr>
<td>Arthropalgia</td>
<td>1356</td>
<td>5.2</td>
</tr>
<tr>
<td>Exacerbation of IBD symptoms</td>
<td>674</td>
<td>4.9</td>
</tr>
<tr>
<td>Muscle pains</td>
<td>147</td>
<td>4.8</td>
</tr>
<tr>
<td>Headache</td>
<td>937</td>
<td>4.7</td>
</tr>
<tr>
<td>Dizziness</td>
<td>222</td>
<td>4.5</td>
</tr>
<tr>
<td>Cough</td>
<td>185</td>
<td>4.0</td>
</tr>
<tr>
<td>Other skin and subcutaneous-related</td>
<td>900</td>
<td>3.7</td>
</tr>
<tr>
<td>Nausea</td>
<td>623</td>
<td>3.2</td>
</tr>
<tr>
<td>Paroxysm</td>
<td>526</td>
<td>2.9</td>
</tr>
<tr>
<td>Respiratory, thoracic and mediastinal-related</td>
<td>70</td>
<td>2.9</td>
</tr>
<tr>
<td>Hives</td>
<td>146</td>
<td>2.1</td>
</tr>
<tr>
<td>Liver-related</td>
<td>468</td>
<td>2.0</td>
</tr>
<tr>
<td>Memory impairment</td>
<td>136</td>
<td>2.0</td>
</tr>
<tr>
<td>Other musculoskeletal and connective tissue-related</td>
<td>498</td>
<td>2.0</td>
</tr>
<tr>
<td>Infectious adverse events (≥2% of patients)</td>
<td>960</td>
<td>6.0</td>
</tr>
<tr>
<td>Upper respiratory tract infection</td>
<td>960</td>
<td>6.0</td>
</tr>
<tr>
<td>Sinusitis</td>
<td>576</td>
<td>4.2</td>
</tr>
<tr>
<td>Other respiratory infections</td>
<td>328</td>
<td>3.1</td>
</tr>
<tr>
<td>Genitourinary tract infections</td>
<td>409</td>
<td>3.0</td>
</tr>
<tr>
<td>Flu or flu-like infection</td>
<td>450</td>
<td>2.8</td>
</tr>
<tr>
<td>Perianal abscesses</td>
<td>284</td>
<td>2.5</td>
</tr>
<tr>
<td>Clostridium difficile</td>
<td>1101</td>
<td>2.1</td>
</tr>
<tr>
<td>Folliculitis</td>
<td>146</td>
<td>2.1</td>
</tr>
<tr>
<td>Adverse events</td>
<td>1243</td>
<td>21.3</td>
</tr>
<tr>
<td>Serious adverse events</td>
<td>832</td>
<td>7.7</td>
</tr>
<tr>
<td>Infections</td>
<td>906</td>
<td>6.9</td>
</tr>
<tr>
<td>Serious infections</td>
<td>832</td>
<td>6.7</td>
</tr>
</tbody>
</table>

*Includes paradoxical skin manifestations, acne, generalised exanthematous pustulosis, dry skin, erythema nodosum, palmar erythema. Includes spontaneous nausea. Includes liver test abnormalities (transaminis transientis), drug-induced liver injury (not specified). Includes severe musculoskeletal syndrome, exacerbation of pre-existing enteropatic arthritis. Includes pneumonia, lower respiratory tract infections, respiratory tract infection (not specified).

Conclusion: Pooled analysis of AE rates across multiple studies support the favourable, long-term benefit-risk profile of VDZ in real-world clinical practice, with low rates of infusion-related reactions, serious infections and malignancies reported, and no identification of new safety signals. These results are consistent with integrated safety data reported for VDZ in six clinical trials (>4000 patient-years), despite the selection of complex patients failing previous immunosuppressive or biologic therapies. Limitations of incidental reporting in real-world studies include potential underestimates of AE rates and the reporting of AEs not regularly observed in clinical trials; for example, due to the variability in concomitant medication use and sub-optimal screening of prior infections.

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A744

United European Gastroenterology Journal 5(5S)
Introduction:

Although many biologies (Bs) have been approved for the treatment of ulcerative colitis (UC) patients who have responded inadequately to conventional therapy, the selection of Bs is controversial due to the lack of head-to-head trials. Indirect economic comparisons of these costly drugs are available from National Healthcare perspectives that are not the Italian ones.

Aims & Methods:
The objective is to evaluate cost-utility of Bs for the treatment of refractory moderate-to-severe UC both in Italy and in the Lombardy Region. A Markov model (considering 3 transition states: remission, clinical response, relapse) is constructed using the software R (a R markovchain-package) to evaluate incremental cost-utility ratios (ICUR) of adalimumab (ADA), infliximab (IFX), infliximab biosimilar (IFX-B), golimumab (GOL) and vedolizumab (VED) treatments of patients over a 10-year time horizon from the perspective of the Italian (N) and Lombardy Region (R) healthcare system. Clinical parameters were derived from clinical trials. Costs (actualised by -1.5%) were obtained from the National database and Regional public tender. Utility was expressed as QALY (Quality Adjusted Life Years).

Results:
 Costs per treatment were different from a N and R perspective (ADA -55%; IFX -16.7%; IFX-B -29.6%; GOL -9.6%; VED -10%). Direct healthcare costs (treatment cost, visits, lab tests, hospital admissions) were calculated over 10 years of treatment per patient: ADA (N: 114,227, R: 110,438), IFX (N: 130,955, R: 103,081), IFX-B (N: 110,438; R: 78,852, -28.6%), GOL (N: 118,602, R: 96,923, -18.3%), VED (N: 113,852, R: 102,932, -9.6%) with associated QALY respectively of 6.68, 6.66, 6.66, 6.70, 7.02. From a N perspective, IFX-B was dominating compared to all other treatments. The ICUR of VED/IFX-B was 49,483 for 10 years (willingness to pay €490/QALY). From a R perspective, ADA was dominating compared to all other treatments. The ICUR of VED/ADA was 101,818 for 10 years (€102,932/QALY).

Conclusion:
National and Regional cost-utility analyses produced different results. As Regional price discounts can occur, local analysis is needed to estimate the economic impact of therapies to ensure optimal choice.

Disclosure of Interest:
All authors have declared no conflicts of interest.

References

P1697 COST-UTILITY ANALYSES OF BIOLOGICS FOR REFRACTORY ULCERATIVE COLITIS
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Introduction:
Although many biologies (Bs) have been approved for the treatment of ulcerative colitis (UC) patients who have responded inadequately to conventional therapy, the selection of Bs is controversial due to the lack of head-to-head trials. Indirect economic comparisons of these costly drugs are available from National Healthcare perspectives that are not the Italian ones.

Aims & Methods:
The objective is to evaluate cost-utility of Bs for the treatment of refractory moderate-to-severe UC both in Italy and in the Lombardy Region. A Markov model (considering 3 transition states: remission, clinical response, relapse) is constructed using the software R (a R markovchain-package) to evaluate incremental cost-utility ratios (ICUR) of adalimumab (ADA), infliximab (IFX), infliximab biosimilar (IFX-B), golimumab (GOL) and vedolizumab (VED) treatments of patients over a 10-year time horizon from the perspective of the Italian (N) and Lombardy Region (R) healthcare system. Clinical parameters were derived from clinical trials. Costs (actualised by -1.5%) were obtained from the National database and Regional public tender. Utility was expressed as QALY (Quality Adjusted Life Years).

Results:
 Costs per treatment were different from a N and R perspective (ADA -55%; IFX -16.7%; IFX-B -29.6%; GOL -9.6%; VED -10%). Direct healthcare costs (treatment cost, visits, lab tests, hospital admissions) were calculated over 10 years of treatment per patient: ADA (N: 114,227, R: 110,438), IFX (N: 130,955, R: 103,081), IFX-B (N: 110,438; R: 78,852, -28.6%), GOL (N: 118,602, R: 96,923, -18.3%), VED (N: 113,852, R: 102,932, -9.6%) with associated QALY respectively of 6.68, 6.66, 6.66, 6.70, 7.02. From a N perspective, IFX-B was dominating compared to all other treatments. The ICUR of VED/IFX-B was 49,483 for 10 years (willingness to pay €490/QALY). From a R perspective, ADA was dominating compared to all other treatments. The ICUR of VED/ADA was 101,818 for 10 years (€102,932/QALY).

Conclusion:
National and Regional cost-utility analyses produced different results. As Regional price discounts can occur, local analysis is needed to estimate the economic impact of therapies to ensure optimal choice.

Disclosure of Interest:
All authors have declared no conflicts of interest.

References

P1698 ENDOSCOPIC SUBMUCOSAL DISSECTION OF ULCERATIVE COLITIS-ASSOCIATED DYSPLASIA: A SINGLE CENTER-BASED EXPERIENCE
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Introduction:
Dysplasia is considered as the precursor of colitis-associated cancer in the long standing ulcerative colitis (UC). Although endoscopic submucosal dissection (ESD) has been suggested as an endoscopic resection technique for non-polyoid dysplasia, only a few studies investigated the feasibility of ESD as a treatment option of non-polyoid dysplasia.

Aims & Methods:
We aimed to investigate the feasibility of ESD for the resection of ulcerative colitis-associated dysplasia (UCAD) in UC. From August 2009 to January 2017, 19 UC patients with low grade dysplasia (LGD), high grade dysplasia (HGD) or early colon cancer were admitted for ESD and their medical records were retrospectively reviewed.

Results:
Mean age of the 19 patients was 55.5±15.4 years and mean duration between UC diagnosis and dysplasia detection was 13.7±6.5 years. Nine were male. Five of 19 patients directly underwent colectomy without ESD trial due to non-lifting sign (n=4) or surface ulceration (n=1). Of these, preoperative single HGD (n=3) or ECC (n=1) patients showing non-lifting sign were diagnosed as invasive cancer and a single preoperative LGD case with non-lifting sign had multifocal LGDs in the colectomy specimen. As a result, ESD was performed for 14 of 19 patients. Major and minor axes of the lesion was 23.4±9.0mm and 18.1±9.1 mm, respectively. The lesions were located at the rectum (n=9), sigmoid colon (n=2), descending colon (n=1), and transverse colon (n=1). The gross morphologic showed Paris IIa (n=7), IIb (n=4), Is (n=1), and Ib+Is (n=2). No lesions contained ulcerations. The borders were distinct in 6 and vague but endoscopically assumable in 8 cases. Mean UC endoscopic index of severity of the surrounding mucosa was 0.3±0.1. Mean resection time was 54.8±25.7 minutes. En bloc resection and R0 resection rates was 92.9% and 71.4%, respectively. There was no perforation or clinically significant bleeding.

Mean hospitalization period after ESD was 1.14±0.36 days. Final histology of ESD specimens revealed 1 indefinite for dysplasia (IND), 1 sessile serrated adenoma/poly, 7 LGDs, 3 HGDs, and 1 intramucosal adenocarcinoma. Synchronous lesions were present in 5 patients. Synchronous dysplasia in 4 patients were removed endoscopically. However, colectomy was done in one patient having synchronous adenocarcinoma and endoresection by ESD and the other developed both metachronous and recurrent LGDs at 8 months after ESD.

Conclusion:
According to our ESD series for dysplasia, ESD seems to be feasible for the endoscopic resection of UC-associated dysplasia. However, meticulous surveillance colonoscopy is mandatory to monitor local recurrence and metachronous dysplasia. Non-lift sign and surface ulceration are highly suggestive of invasive colitic cancer.

Disclosure of Interest:
All authors have declared no conflicts of interest.

References
clinical scoring as compared to only half of the low-producers, but statistical significance was not reached due to the small number of patients (high: 101% vs. low: 50%, p = 0.167). However, remission rates after 6 weeks were significantly higher in high-producers compared to low-producers: (high: 80% vs. low: 0% remission; p = 0.048). Secondary endpoints showed no significant difference in the two groups.

Conclusion: Quantification of TNF-expression in PBMCs and the resulting classification in low- and high-producers could be a potential predictive marker for response to anti-TNF-treatment in IBD patients.

Disclosure of Interest: D. Lissner: Donata Lissner received a research grant from Pfizer and lecture fees from Falk and Abbvie. B. Siegmund: Britta Siegmund received a research grant from Pfizer, served as consultant for Janssen, MSD, Abbvie, Takeda, Hospira and received lecture fees from Abbvie, Falk, Ferring, MSD, Merck, Takeda; all money went to the institution.

All other authors have declared no conflicts of interest.

P1701 EVALUATION OF CONCOMITANT CORTICOSTEROID AND VEDOLIZUMAB USE IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE (IBD) IN REAL-LIFE CLINICAL PRACTICE

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Objective: To analyze vedolizumab use in inflammatory bowel disease (IBD) patients who were on concomitant corticosteroids at the time of initiating vedolizumab treatment. The main aim of the study was to analyze vedolizumab treatment of IBD patients who received at least one vedolizumab infusion since 2014. Key data collection points were at baseline, week 14 and month 6 of vedolizumab treatment. The main aim of the study was to analyze vedolizumab treatment persistence in patients with Crohn’s disease (CD) and ulcerative colitis (UC).

Methods: We included 50 patients (mean age 45.5 y; male 56%) with Crohn's disease (CD, n = 26) and Ulcerative colitis (UC, n = 24). 44 (88%) IBD patients had previous anti-TNF therapy. Baseline median HBI was 8 (5–16) and median pM Mayo was 6 (5–7). Median VTL (Interquartile range, IQR) at weeks 6, 10 and 14 were 38.6 (20.3–53.5), 25.4 (13.4–45.6) and 17.7 (10.1–33.7) ug/ml, respectively. VTL measured at week 6 were significantly higher in clinical responders as compared to non-responders: median (IQR) 55.8 (46–64.1) vs 33.3 (13.4–20.6) ug/ml, p = 0.04. Week 6 VTL were also higher in CRP responders (<5 mg/l): median (IQR) 48.1 (32.5–55.8) vs 32.8 (19.7–44.3) ug/ml, p = 0.04. Week 6 VTL were inversely correlated with CRP (rho = −0.39, p = 0.006). By ROC curve analysis cut-off identified as 44.3 ug/ml for clinical response at week 6 (AUC 0.677, sensitivity 61.9%, specificity 79.3%, p = 0.02). Week 6 VTL were significantly higher in IBD patients in clinical remission at their last follow-up (mean 20 weeks) compared to non-remitters: median (IQR) 55.8 (46–64.1) vs 33.3 (25.9–40.4) ug/ml, p = 0.0035. The ROC curve analysis identified a cut off of 44.3 ug/ml (AUC 0.813 sensitivity 88.9%, specificity 73.2%, p = 0.0006). Week 14 VTL were also significantly higher in IBD patients in clinical remission at 22 weeks compared to non-remitters: median (IQR) 38.3 (20.5–49.8) vs 13.4 (8.4–20.6) ug/ml, p = 0.0035. The cut off identified by ROC curve analysis for this outcome was 16.4 ug/ml (AUC 0.820 sensitivity 100% specificity 63%, p = 0.0019). AVA were detected in 2% of patients at week 6, in 5.9% at week 10 and in 4.5% at week 14 and were not correlated with clinical response.

Conclusion: These preliminary data suggest that obtaining a VTL of 44.3 ug/ml after the first 2 Vedolizumab infusions is correlated with early clinical and biological (CRP) response and with clinical remission at a mean follow-up of 20 weeks. Week 14 VTL are correlated with clinical remission at week 22 and the identified cut off is 16.4 ug/ml. Immunogenicity of Vedolizumab is low in these patients.


All other authors have declared no conflicts of interest.
P1703 EFFICACY, SAFETY AND LONG-TERM OUTCOME OF ENDOSCOPIC DILATION THERAPY FOR PRIMARY CROHN’S DISEASE STRICSTURES OF THE UPPER GASTROINTESTINAL TRACT—AN INTERNATIONAL MULTICENTER COMBINED ANALYSIS

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Introduction: Strictures in Crohn’s disease (CD) may occur in different segments along the gastrointestinal (GI) tract. In contrast to ileocolic strictures, endoscopic balloon dilation (EBD) is a potential treatment option for the treatment of upper gastrointestinal (UGI) tract strictures that is rarely reported. We therefore performed a comprehensive efficacy and safety analysis of EBD for CD-associated strictures in this multi-centre cohort study.

Aims & Methods: Individual patients characteristics were retrieved from electronic case report forms. Upper GI tract was defined as esophagus, stomach and duodenum up to the ligament of Treitz. Time-to-event analysis was performed to assess symptom recurrence, re-dilation or surgery. Kaplan-Meier estimates were used for survival analysis. For the multivariable Cox regression models, all variables that were available for at least 85% of subjects were considered for inclusion and the score method was used to choose the best model with two factors for each outcome.

Results: A total of 73 CD patients and 127 performed dilation procedures were included. Stricture location were: duodenum n = 46, stomach n = 14; esophagus n = 9; stomach and duodenum n = 4. Technical success rate was 94.1%, resulting in clinical efficacy in 88.9% of patients. Major complications, defined as perforation, bleeding or dilation-related surgery, occurred in 2.9% of all procedures. During a median follow up period of 36 months, 89.4% of patients underwent re-dilation and 29.8% required surgical intervention. The multivariable Cox regression analyses indicated that a younger age at diagnosis was associated with symptom recurrences (HR 0.82 (0.71, 0.95), p = 0.003). In a Cox model that included 13 selected variables and rank correlation showed no relationship between adherence to 5-ASA and the risk factors for each outcome.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P1704 AMINOSALICYLATES FOR MAINTENANCE THERAPY IN ULCERATIVE COLITIS: IS THE ADHERENCE REALLY IMPORTANT?

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5Department Of Gastroenterology, Hepatology & Nutrition, Digestive Diseases and Nutrition Institute, University Hospital Zurich, Zurich/Switzerland
6Department Of Gastroenterology, Hepatology & Nutrition, Digestive Diseases and Nutrition Institute, University Hospital Zurich, Zurich/Switzerland
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Introduction: The goal of maintenance therapy in Ulcerative Colitis (UC) is to keep clinical and endoscopic steroid-free remission. 5-aminosalicylate (5-ASA) represents the first line maintenance therapy1. Non-adherence to 5-ASA is associated with an increased risk of disease relapse, colorectal cancer and worsening of quality of life2. Adherence rate has been analysed in several studies with controversial results3-4.

Aims & Methods: The aim of this study is to quantify the prevalence of adherence to 5-ASA, to identify risk factors to non-adherence and its correlation with the clinical disease. Observational, analytical retrospective, single tertiary centre, cohort study of all UC patients followed-up in our IBD unit, until January 2016, with 5-ASA maintenance treatment prescribed by an electronic management program. Adherence was considered when 80% of the prescribed 5-ASA was dispensed at pharmacy and if patients were prescribed 5-ASA or a higher median age (52 (±11) vs 43 (±13), p = 0.001) and received more non-UC chronic drugs (OR = 2.3, 95CI = 1.5–3.4, p = 0.001). The independent variables, age and intake of other non-UC drugs, included in the multivariate analysis reached a predictive capacity of 65% outcomes of adherence. There was no significant reduction in the risk of moderate-severe flares that required corticosteroid therapy when comparing both adherent and non-adherent groups and rank correlation showed no relationship between adherence to 5-ASA and the risk factors of the univariable analysis. A Spearman’s rank coefficient analysis was performed to correlate percentage of adherence with relapse rate.

Results: The study cohort included 433 patients, 55% males with a median age at the first 5-ASA prescription analysed of 49 years (IQR 39–61). 17% had a proctitis, 31% a left-side colitis and 52% an extended disease. 30% of patients suffered from extraintestinal manifestations and 8 from a complication. The mean dose of 5-ASA taken was 2.6 g/day (range 0.7–4.8) distributed in a daily dose of 3 (±1) of the patients. Adherence prevalence to 5-ASA was 65%. Adherent patients had a higher median age (52 (±11) vs 43 (±13), p = 0.001) and received more non-UC chronic drugs (OR = 2.3, 95CI = 1.5–3.4, p = 0.001). The independent variables, age and intake of other non-UC drugs, included in the multivariate analysis reached a predictive capacity of 65% outcomes of adherence. There was no significant reduction in the risk of moderate-severe flares that required corticosteroid therapy when comparing both adherent and non-adherent groups and rank correlation showed no relationship between adherence to 5-ASA and the risk factors of the univariable analysis. A Spearman’s rank coefficient analysis was performed to correlate percentage of adherence with relapse rate.

Adherence to 5-ASA in our population is low. Older patients that take other non-UC chronic treatments show higher adherence. With a one year prescribed and dispensed analysis, non-adherence to 5-ASA is not related with a higher risk of flares that require corticosteroid therapy. Patients treated with adjuvant maintenance therapy, show better results throughout the course of the disease.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

References

Table 1 Continued

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>ICC cohort CD (N=146)</th>
<th>GEMINI 1 (N=1455)</th>
<th>ICC cohort UC (N=890)</th>
<th>GEMINI 2 (N=895)</th>
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</thead>
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<tr>
<td>Colon only</td>
<td>36 (24.7)</td>
<td>336 (28.3)</td>
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</tr>
<tr>
<td>Beun and colon</td>
<td>56 (38.4)</td>
<td>618 (55.4)</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Beun and upper GI</td>
<td>11 (7.5)</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Beun and colon and upper GI</td>
<td>4 (2.7)</td>
<td>–</td>
<td>–</td>
<td>–</td>
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<tr>
<td>Disease behavior</td>
<td></td>
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<td></td>
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<tr>
<td>Immunosuppressant inflammatory</td>
<td>89 (61)</td>
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<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Structuring</td>
<td>35 (24)</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Penetrating</td>
<td>12 (8.2)</td>
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<td>–</td>
<td>–</td>
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<tr>
<td>Perianal fistula</td>
<td>13 (8.9)</td>
<td>–</td>
<td>–</td>
<td>–</td>
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<tr>
<td>Disease location UC, n (%)</td>
<td>116 (13.0)</td>
<td>448 (50.1)</td>
<td>331 (37.0)</td>
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</tr>
<tr>
<td>Concomitant medications - no. (%)</td>
<td>5 (6.3)</td>
<td>–</td>
<td>–</td>
<td>–</td>
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<tr>
<td>Glucocorticosteroids only</td>
<td>59 (40.4)</td>
<td>383 (34.2)</td>
<td>37 (46.3)</td>
<td>332 (37.1)</td>
</tr>
<tr>
<td>Immunosuppressive agents only</td>
<td>28 (19.2)</td>
<td>181 (16.2)</td>
<td>12 (15)</td>
<td>159 (17.8)</td>
</tr>
<tr>
<td>Both immunosuppressive and corticosteroid</td>
<td>16 (11)</td>
<td>14 (17.5)</td>
<td>–</td>
<td>149 (16.6)</td>
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<tr>
<td>Prior TNF antagonist therapy (%)</td>
<td>–</td>
<td>–</td>
<td>–</td>
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<tr>
<td>Corticosteroid No glucocorticosteroids or immunosuppressive agents</td>
<td>43 (29.5)</td>
<td>189 (17.0)</td>
<td>21 (25.3)</td>
<td>255 (28.5)</td>
</tr>
<tr>
<td>Prior IBD surgery (%)</td>
<td>72 (49.3)</td>
<td>466 (41.8)</td>
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<td>–</td>
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<tr>
<td>Perianal surgery (%)</td>
<td>27 (18.5)</td>
<td>–</td>
<td>–</td>
<td>–</td>
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<tr>
<td>IPAA (%)</td>
<td>3 (3.8)</td>
<td>–</td>
<td>–</td>
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</tbody>
</table>

Conclusion: The ICC developed a uniform web-based registry to study post-marketing safety and effectiveness of novel IBD-drugs. A feasibility study with 230 patients starting vedolizumab showed successful data-capture, managing, and reporting with the ICC-case series in 6 centres. Table 1 shows clear differences between baseline characteristics of real-life Dutch patients and patients in the GEMINI studies underlying the importance of country specific post-marketing data.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P1707 SIX-YEAR EFFICACY AND SAFETY OF AZATHIOPRINE TREATMENT IN THE MAINTENANCE OF STEROID-FREE REMISSION IN INFLAMMATORY BOWEL DISEASE PATIENTS
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Introduction: Azathioprine (AZA) and thiopurine are widely used for induction and maintenance of remission in patients steroid-resistant or dependent with inflammatory bowel disease (IBD). The treatment must be withdrawn in 5–30% of patients due to the occurrence of adverse events.

Aims & Methods: Aim of this study has been to investigate its efficacy and safety in maintaining steroid-free remission in steroid dependent IBD patients six year after the institution of treatment. Data from consecutive IBD outpatients referred in our Institution, between 1985–2015, were reviewed and all patients treated with AZA were included in this retrospective study. AZA was administered at the recommended dose of 2–2.5mg/kg. Blood chemistry was analysed before administration of the drug, every 10–15 days for the first 3 months and then every 1–2 months following the institution of treatment.

Results: Out of 2722 consecutive IBD outpatients visited in the index period, AZA was prescribed to 415 patients, 227 (54.7%) were affected by Crohn’s disease (CD) and 188 (45.3%) by ulcerative colitis (UC). One hundred and fifty-eight patients with a follow-up <72 months were excluded from the study. Two hundred and fifty-seven patients were evaluated, 143 (55.6%) with CD and 114 (44.4%) with UC. One hundred and forty-two (55.2%) were male

Table 1: Baseline characteristics of ICC cohort and GEMINI trials

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>ICC cohort CD (N=146)</th>
<th>GEMINI 1 (N=1115)</th>
<th>ICC cohort UC (N=890)</th>
<th>GEMINI 2 (N=895)</th>
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</thead>
<tbody>
<tr>
<td>Age - yr</td>
<td>39 ± 13.7</td>
<td>36.1 ± 12.1</td>
<td>43.7 ± 16.5</td>
<td>40.3 ± 13.3</td>
</tr>
<tr>
<td>Male, no. (%)</td>
<td>520 (46.6)</td>
<td>506 (62.5)</td>
<td>525 (58.2)</td>
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</tr>
<tr>
<td>Current smoker - no. (%)</td>
<td>38 (25.9)</td>
<td>206 (26.7)</td>
<td>1 (1.3)</td>
<td>55 (6.1)</td>
</tr>
<tr>
<td>Disease duration-yr</td>
<td>13.6 ± 12.5</td>
<td>9.0 ± 7.8</td>
<td>8.6 ± 7.8</td>
<td>6.9 ± 6.4</td>
</tr>
<tr>
<td>Median CRP - mg/L (IQR)</td>
<td>7 (4–20)</td>
<td>11.5</td>
<td>6 (2–15)</td>
<td>–</td>
</tr>
<tr>
<td>Median fecal calprotectine - ug/g (IQR)</td>
<td>881 (287–1800)</td>
<td>686.0</td>
<td>1551 (441–2519)</td>
<td>899 (414–2127)</td>
</tr>
<tr>
<td>Disease location CD, n(%)</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Beun only</td>
<td>31 (21.2)</td>
<td>181 (16.2)</td>
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</tbody>
</table>

(continued)
and 115 (44.8%) female (average age of 35.68 ± 14.22 SD years, range 14–74 y.). Six years after the institution of treatment, 130 (50.6%) patients still were in steroid-free remission (85 CD vs 45 UC, 59.5% and 39.5%, respectively, p = 0.0017), 71 (27.6%) had a relapse requiring retreatment with steroids (29 CD vs 42 UC, 20.3% and 36.6%, respectively, p = 0.0048), 56 (21.8%) discontinued the treatment due to side effects (29 CD vs 27 UC, 20.2% and 23.7%, respectively). Loss of response from 1st to 6th year of follow-up was low, about 20%.

**Conclusion:** Six years after the onset of treatment 56% of patients did not require further steroid courses. After the first year loss of response was low in five subsequent years. In the present series the maintenance of steroid-free remission was significantly higher in CD than in UC patients. The occurrence of side effects leading to the withdrawal of AZA treatment has been low.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**P1708 CLINICAL EFFICACY AND SAFETY OF ANTI-TNF THERAPY IN INFLAMMATORY BOWEL DISEASE IN THE ELDERLY: A UK TERTIARY REFERRAL CENTRE EXPERIENCE**

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**Introduction:** Many patients, especially the elderly or those with comorbidities, are excluded from clinical drug trials and little real-life data exists on the safety and efficacy of anti-TNF.

**Aims & Methods:** We aimed to compare the clinical efficacy and safety of anti-TNF therapy in patients over 60 years in a tertiary IBD centre in London, UK. We interrogated our IBD biobanks database from January 2009 to November 2015 and performed retrospective data analysis until end of follow up in April 2017. Data was collected on demographics, endoscopy, calprotectin, CRP, clinical scores, serious infections, malignancy, drug levels and anti-drug antibodies. Patients with an age of ≥60 when starting anti-TNF therapy were identified and <60 comparators were selected at random in a 2:1 ratio. Primary endpoints: week 14 and week 54 steroid free clinical remission (Harvey Bradshaw Index < 5 or Simple Colitis Activity index < 3) Secondary endpoint: proportion of patients remaining on anti-TNF at the end of follow up

**Results:** See table.

**Conclusion:** Only a small number of ≥60 patients started anti-TNF (29 out of greater than 650). This may reflect our local population or that clinicians favour non anti-TNF therapies in this elder group. Overall there was similar clinical efficacy at weeks 14 and 54 of anti-TNF therapy between the ‘young’ and ‘old’ groups. There was a higher discontinuation rate after 1 year of therapy in the older group (p = 0.043). There were more adverse events in the older group (7/29) including 3 new cancer diagnoses compared with the younger group (3/58). 4 patients had detectable anti-drug antibodies in the older group despite 2 of them having therapeutic thiopurine suggesting that the elderly may have more immunogenicity than the young. Further studies with more patients across multiple sites are required to clarify safety and efficacy in the elderly.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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**Abstract No: P1709 TACROLIMUS IN REFRACTORY ULCERATIVE COLITIS-12 MONTH OUTCOME IN A SINGLE-CENTRE UK DISTRICT HOSPITAL**

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**Introduction:** Rescue therapy is required for patients with moderate - severe ulcerative colitis (UC) who have failed to respond to steroids and thiopurines. Anti-Tumour Necrosis Factor agents (Anti-TNFs) are widely used before considering a colectomy. Calcineurin inhibitors such as ciclosporin and Tacrolimus may be considered as alternatives to biologics. There have been some case series in assessing the use of Tacrolimus in such patients although the United Kingdom experience is limited. (1, 2)

**Aims & Methods:** We aimed to review the outcome of patients who received Tacrolimus as rescue and subsequent maintenance therapy for refractory symptoms of UC. This was a retrospective single-centre case review series. All patients who were refractory to standard medical therapies and being considered for a colectomy were reviewed by a Gastroenterologist with an interest in Inflammatory Bowel Disease. Demographic data, indications for treatment, clinical course and outcomes were reviewed from Electronic Patient Records (EPR).

**Results:** Fourteen patients (F = 6; mean age of 54 years) received Tacrolimus. 8 patients (57%) had evidence of pancolitis and six patients (43%) had distal colitis. All patients had previously received thiopurines and 11 patients (78.6%) had also received anti-TNFs. Three patients declined Anti-TNF treatment. All patients were steroid-dependent prior to commencing Tacrolimus. One patient received ciclosporin before the switch. The remaining 13 patients were initiated on Tacrolimus in the out-patient setting at a starting dose of 0.1 mg/kg/day in 2 divided doses. Patients took Tacrolimus for a mean period of 18.8 months (range: 2 months to 49 months). Eight patients (57%) achieved a steroid-free remission within 6 months. An additional 3 patients (23%) had a clinical response within 6 months, but required one course of steroids during this time period. Three patients (23%) failed to respond to Tacrolimus; 1 patient remains steroid-dependent and does not wish to proceed to surgery, 1 patient was switched to infliximab and 1 patient proceeded at 10 months to have an elective subtotal colectomy. Tacrolimus was withdrawn in all 3 non-responders. Of the 11 (78.6%) initial responders, 12-month outcome included withdrawal of Tacrolimus in 7 patients (63.6%). Reasons for withdrawal included: n = 1 renal impairment; n = 1 started on infliximab; n = 3 referred for leucapharesis; n = 1 re-started on Azathioprine and n = 1 referred for proctocolectomy. Three patients (21.4%) remain in steroid-free clinical remission with a good quality of life and

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**Table:**

<table>
<thead>
<tr>
<th>Category</th>
<th>&lt;60 years</th>
<th>≥60 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>n = 58</td>
<td>n = 29</td>
</tr>
<tr>
<td>Week 14</td>
<td>28/41 (68.3%)</td>
<td>8/16 (50%)</td>
</tr>
<tr>
<td>Week 54</td>
<td>24/40 (60%)</td>
<td>8/15 (53.3%)</td>
</tr>
<tr>
<td>Remain on anti-TNF at week 54</td>
<td>46/58 (79.3%)</td>
<td>23/28 (82.1%)</td>
</tr>
<tr>
<td>Reasons for stopping anti-TNF before week 54</td>
<td>7 primary non-response 2 secondary loss of response with detectable anti-drug antibodies 1 infusion reaction 1 clinical &amp; endoscopic remission</td>
<td>2 primary non-response 2 secondary loss of response with detectable anti-drug antibodies 1 infusion reaction</td>
</tr>
<tr>
<td>Remain on anti-TNF at end of follow up (April 2017)</td>
<td>38/58 (65.5%)</td>
<td>12/29 (41.4%) p &lt; 0.05</td>
</tr>
<tr>
<td>Reasons for stopping biologic during study period</td>
<td>8 primary non-response 4 secondary loss of response 3 secondary loss of response with detectable anti-drug antibodies 1 infusion reaction 1 clinical and endoscopic remission 2 infections (skin and respiratory) 1 stopped attending</td>
<td>4 primary non-response 2 secondary loss of response 3 secondary loss of response with detectable anti-drug antibodies 1 infusion reaction 1 clinical and endoscopic remission 1 infection (ophthalmic) 1 new diagnosis cancer (colorectal) 1 severe fatigue 1 peripheral neuropathy 1 moved away 1 stopped attending</td>
</tr>
<tr>
<td>Length of time on anti-TNF if stopped (months)</td>
<td>Range: 3–73 Median: 12</td>
<td>Range: 3–63 Median: 18</td>
</tr>
<tr>
<td>Anti-drug antibodies detectable during follow up</td>
<td>3/58 (5.2%) - 3 infliximab weeks 14, 34 and 76 no concomitant 1 subtherapeutic TGNs 1 prior exposure to infliximab</td>
<td>4/29 (15.8%) - 3 infliximab, 1 adalimumab weeks 14, 48, 52 and 54 concomitant with therapeutic TGNs 2 no concomitant exposure to infliximab</td>
</tr>
<tr>
<td>Adverse events throughout follow up</td>
<td>1 new diagnosis cancer (testicular) 1 infusion reaction 1 infection (dental abscess)</td>
<td>3 new diagnosis cancer (prostate, colorectal &amp; thyroid) 1 spontaneous ileal perforation requiring emergency surgery 1 infusion reaction 2 infections (chest infection and shingles)</td>
</tr>
</tbody>
</table>
Introduction: Adalimumab (ADA) and golimumab (GOL) are effective in the induction and maintenance treatment of moderate-to-severe ulcerative colitis (UC). No comparable data between the 2 drugs are available up to now. Therefore, the aim of the present study was to analyze the efficacy of ADA and GOL in patients (pts) with moderate-to-severe UC.

Aims & Methods: We reported the Sicilian Network experience on the comparative efficacy of ADA and GOL in patients (pts) with moderate-to-severe UC. From June 2015 until April 2017, 191 consecutive pts with moderate to severe UC were treated with ADA or GOL. The efficacy was evaluated at 8 week and at the end of the follow up considering “clinical response” (reduction of at least 2 points of Partial Mayo Score with concomitant steroid reduction or discontinuation) and “clinical remission” (Partial Mayo Score <2 without steroids). The presence of clinical response or clinical remission was defined as “clinical benefit”. Endoscopic Mayo Score was evaluated. These real life data confirmed the efficacy of subcutaneous anti-TNFα in the treatment of moderate to severe UC, ADA resulted to be more effective than GOL in inducing and maintaining clinical benefit.

Disclosure of Interest: All authors have declared no conflicts of interest.

References:
who completed first 14 weeks of treatment and confirming it as a safe drug. Anti TNФ is more likely to avoid colonic ectasia.

Disclosure of Interest: D. Pugliese: Lecture fees from AbbVie and Takeda. M. Allocca: Speaker’s fees from Janssen, Pfizer Consultant’s fee: Nikkiso Europe M. Di Girolamo: Speaker for AbbVie and Takeda All other authors have declared no conflicts of interest.

References

P1712 PREVALENCE OF CIPROFLOXACIN RESISTANCE IN INFLAMMATORY BOWEL DISEASE PATIENTS WITH GUT COLONIZATION WITH EXTENDED SPECTRUM BETA-LACTAMASE PRODUCING ENTEROBACTERIA ACCORDING TO BACTERIAL PLASMID GENES

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Introduction: Ciprofloxacin is one of the most frequently used antibiotics in hospitalized inflammatory bowel disease (IBD) patients. Also discrepancies between clinical guidelines and real clinical situations are observed in terms of antibiotic use in patients with IBD. In the last few years an emerging resistance to ciprofloxacin, ranging from 43% to 82%, has been described in extended spectrum beta-lactamase producing bacteria (ESBL-E) colonizing the gut. 1, 2

Aims & Methods: The objective of this study was to evaluate the gut colonization with ESBL-E in IBD patients, determine the resistance to ciprofloxacin and bacterial plasmid genes associated with that. Rectal swabs were collected from all consecutive patients with confirmed ulcerative colitis (UC) and Crohn’s disease (CD) hospitalized in two largest tertiary medical care centers in Riga, Latvia during a 7-year period (2010-2016). Enterobacteria were cultured and screened for ESBL presence according to EUCAST guidelines, resistance to ciprofloxacin and bacterial plasmid genes CTX-M, TEM and SHV were detected.

Results: A total of 148 patients with confirmed IBD diagnosis were included in the study: 67 (45.4%) had UC (47.3% with CD). We found that 12 (12%) of the UC patients and 5 (11%) of the CD patients were colonized with ESBL-E. The isolated ESBL producing strains from UC patients included Escherichia coli (n=10), Klebsiella oxytoca (n=1) and Escherichia hermanii (n=1). The isolated ESBL producing strains from CD patients included only Escherichia coli (n=5). The isolated bacterial plasmid genes associated with ESBL production in UC included CTX-M (n=11; 92%), TEM (n=4; 33%), SHV (n=1; 8%), in CD – CTX-M (n=4; 80%) and TEM (n=3; 60%). In UC 6 (50%) and in CD 1 (20%) out of patients colonized with ESBL-E were resistant to ciprofloxacin. In 1 case of the ciprofloxacin resistance CTX-M, TEM and SHV gene combination was observed, in 1 case CTX-M and TEM gene combination was observed, in 4 cases only CTX-M gene was present and in 1 case only TEM gene was present.

Conclusion: Higher gut colonization rate with ESBL-E in IBD patients, mostly with E. coli, expressing CTX-M gene was found comparing with the literature. 2. Higher resistance to ciprofloxacin was found in ESBL-E isolated from UC patients, compared to UC patients. 3. CTX-M and TEM genes are associated with resistance to ciprofloxacin.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P1714 PREDICTIVE FACTORS OF RESPONSE TO ANTI-TNF A TREATMENT OF COMPLEX ANO-PERINEAL FISTULAS IN CROHN’S DISEASE

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Conclusion: The general sample of health insurance beneficiaries’ database provides a unique representative sample to analyze and describe real-life usage of anti-TNF in Crohn’s disease patients in France. Aims: Recruitment of each patient.

Disclosure of Interest: None declared.

References
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Introduction: Anti-TNFs are well-established in therapeutic management of Crohn’s disease (CD). Real-life data on their pattern of use in a French clinical setting are, however, limited to this day.

Aims & Methods: The objective of this study was to examine for characteristics of CD patients and anti-TNF use in a real-life setting in France through the general sample of health insurance beneficiaries (EGB database) which includes reimbursable data from a sampled 1/97th of the French population. A cohort of 1280 patients with CD in the EGB database between 01/01/2010 and 31/02/2014 was retrospectively constituted, of which 189 (14.8%) initiated an anti-TNF treatment during that period and were studied for the analysis. An additional analysis was performed based on French hospital discharge data (medical information systems program [PMSI]) from 8142 CD patients to compare results from the EGB database but only support infliximab use due to its exclusive hospital availability in France (adalimumab can be prescribed in both hospital and retail markets).

Results: 48.7% of anti-TNF treated patients were male and the mean age at the initiation of an anti-TNF treatment was 38 years. The mean duration between diagnosis and start of treatment was 7.2 years, for an ALD [Long Term Illness] assignment to an ALD. Concomitant treatments such as corticosteroids and immunosuppressants were prescribed at least once in 63% and 47% of patients respectively. Around 35% of patients initiated a treatment with infliximab and 43% with adalimumab. Results at 12 months after anti-TNF initiation are presented in the table below:

Table 1: Anti-TNF use in patients initiating an anti-TNF treatment with at least 12 months of follow-up At 12 months, 13.6% of patients underwent surgery. Results from the hospital discharge database confirmed some of our observations. Optimization rate for infliximab 12 months after initiation was similar (33.5% at 12 months for infliximab). Treatment discontinuation rates were also within the same range observed and stable over time, with 10% of patients discontinuing infliximab treatment each year and a discontinuation rate after 12 months of treatment of 27.2%.

Anti-TNF use at 12 months after initiation N Results
Drug survival rate for the first line anti-TNF 108 69.8% [62.3–76.1] Survival rate for the first line adalimumab 47 71.7% [59.9–80.6]
Survival rate for first line infliximab 61 66.3% [55.9–74.8]
Anti-TNF dose optimization rate 85 41.5% [34.5–49.3]
Dose optimization rate for adalimumab 53 33.6% [25.2–43.8]
Dose optimization rate for infliximab 63 38.2% [30.1–47.8]
Switch rate to another anti-TNF 126 17.5% [12.6–24.1]
Switch rate from adalimumab to infliximab 70 13.6% [8.1–22.4]
Switch rate from infliximab to adalimumab 88 14.9% [9.6–23.0]
Anti-TNF treatment discontinuation rate 108 31.4% [25.0–38.9]
Discontinuation rate for adalimumab 47 28.2% [19.4–40.0]
Discontinuation rate for infliximab 61 33.7% [25.2–44.0]

Conclusion: A total of 49 patients had complex APF treated with anti-TNF in Crohn’s disease patients in France. Aims: Recruitment of each patient.

Disclosure of Interest: None declared.

References

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achieved clinical remission, 31% a partial clinical response and 12% a primary failure. Maintenance of a clinical response after a year of anti-TNF-α treatment. After a mean time of 13 months, 42% of the patients had a loss of response. The analytical study found that the absence of recto-colonic involvement, CRP negativity and normalization of platelet count under treatment and achievement of clinical remission after the induction phase were predictive factors of long-term good response to anti-TNF-α treatment. Clinical remission after the induction phase was the only independent predictive factor of long-term remission under maintenance treatment after multivariate analysis. However, previous studies assessing early therapeutic adaptation and patient involvement could better evaluate this perspective in the event of a partial clinical response. In addition, rectal involvement and recto-vascular fistulas are factors of poor response for which aggressive and specific treatment is essential.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1715 COMPARISON OF ORIGINAL AND BIOSIMILAR INFLEXIMAB IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE: A RETROSPECTIVE AND MULTICENTRIC STUDY IN SPAIN

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Introduction: The management of chronic inflammatory bowel disease (IBD) has experienced significant advance with the development of biologic therapy. Infliximab (IFX) was the first monoclonal antibody approved for IBD. The patent expiry of biologics and their relatively high costs that result in a significant economic burden on the healthcare system, has led to the development of biosimilar agents. The biosimilar IFX has been authorised for use in all the indications as the reference IFX. The demonstration of biosimilar IFX efficacy and safety equivalence was based on two pivotal clinical trials in rheumatic diseases. As a result of the extrapolation to IBD, there is growing controversy regarding the appropriate use of biosimilar IFX. The efficacy and safety of infliximab reference in inducing and maintaining remission in IBD has been extensively proven in clinical trials. However, the role of biosimilar IFX, has not been systematically investigated in clinical practice.

Aims & Methods: We aimed to compare the safety and efficacy in inducing and maintaining remission in IBD, between the reference IFX group and biosimilar IFX group. This retrospective, multicenter study was carried out at 4 tertiary hospitals (Hospital 10 de March 3 to December 2013) and all the data included in the analysis included patients from cohorts of consecutive patients. One cohort composed of patients who were started original IFX since 2013. The second cohort included patients who were treated from the introduction of biosimilar IFX. Adverse events (AEs), demographic, clinical, endoscopic and laboratory data were collected on all patients. Efficacy was assessed according to response and remission at 14th, 34th week. For CU, response was defined as a decrease in partial Mayo score of 2 or more from baseline and a partial Mayo score of 1 or less was used to remission. For CD, response was defined as a decrease in Harvey-Bradshaw score of 3 or more from baseline, and a Harvey-Bradshaw score of 4 or less was used to remission. We used Student’s t for independent samples and Chi-square test. Time to withdrawal due to adverse effects was estimated using Kaplan-Meier survival analysis, and the log rank test was used to test for treatment group differences.

Results: The analysis included 346 consecutive IBD patients. 104 treated with original IFX and 242 with biosimilar IFX. 103 patients were diagnosed with UC, 238 with CD and 5 with indeterminate colitis. Overall median follow-up was 21 months. Baseline clinical activity scores were not significantly different among the 2 groups. Frequency of concomitant azathioprine and systemic steroids were not different among both groups. Patients in biosimilar infliximab group were more likely to experience previous biologic treatment failure (29.2% versus 20.2% in the original IFX, p = 0.0163). There were no significant differences in patients achieving response and remission at weeks 14 and 54. There were no significant differences in rate of withdrawals among the 2 groups (37.1% versus 38% for biosimilar IFX, p = 0.811). There were no significant differences in cumulative discontinuation rate due to AEs in original IFX and biosimilar IFX (42.42, (95% CI 39.49-45.34) months versus 44.61 (95% CI 42.66-46.56) months, log-rank test p = 0.292).

Conclusion: The study experience showed similar efficacy and safety profile of biosimilar IFX compared to original IFX.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1716 DOES SEVERE ENDOSCOPIC COLITIS PREDICT STEROID REFRACTORY DISEASE IN ACUTE SEVERE COLITIS?

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Introduction: Acute severe Colitis (ASC) is a severe complication of inflammatory bowel disease (IBD), for which there is no consensus definition. Its diagnosis is performed on clinico-biological and endoscopic criteria. Low endoscopy is essentially a tool for the positive diagnosis of ASC as well as for the diagnosis of IBD.

Aims & Methods: The objective of this study is to describe the endoscopic aspect of ASC and its interest in therapeutic management in our series of 48 cases it is a prospective descriptive and analytical study of a series of 48 cases of acute severe colitis (ASC) collected during a period of 3 years (2014-2016) in the gastroenterology department.

Results: The average age of our patients is 39.8 years with extremes ranging from 14 to 58 years, a female predominance was found with a sex ratio, M/F = 0.77. The ASC was inaugural in 20 (41.66%), while 28 cases (58.33%) are known to have IBD, with 24 cases of UC (58.7%). Initial endoscopy was performed in all patients. The average time to perform endoscopy (from the onset of symptoms) was 37 days (2 to 75 days). Severe endoscopic aspects were present in 30 patients: deep ulcer (29 cases), spontaneous bleeding (4 cases), friability (4 cases). Other endoscopic lesions found were erythema (12 cases), erosions (5 cases), superficial ulcer (25 cases), pseudo polyps (14 cases), contact bleeding (27 cases). Biopsy was performed in all patients, histology was in favor of UC in 64.58% cases. CMV viral inclusions were found in 2.08% of cases. First-line medical treatment is based mainly on parenteral corticosteroid therapy, has been established in all cases. A second-line treatment with anti-TNF was introduced in 5 cases (10.41%) while surgical treatment was introduced in 15 cases (31.25%) of which 12 cases had severe endoscopic colitis. steroid refractory disease was associated with endoscopic severe colitis (p = 0.04). In mono-varied analysis, endoscopic severe colitis was found in patients with sex ratio greater than females (53.6 vs 43.3). With a statistically significant difference p = 0.020.

Conclusion: Endoscopy in ASC occupies an important place to specify the morphological severity and thus make the positive diagnosis, the severe endoscopic colitis constitutes one of the predictive elements of steroid refractory disease requiring the use of a second therapeutic palliation.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1717 BASELINE CALPROTECTIN DOES NOT PREDICT RESPONSE TO BIOLOGICAL THERAPY IN ULCERATIVE COLITIS

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Introduction: Response to biological drugs in ulcerative colitis (UC) is variable with induction response rates of 64.5% (vs 29.3% for placebo), 50.4% (vs 34.6% for placebo), 51.0% (vs 30.3% for placebo), 47.1% (vs 25.5% for placebo) for infliximab, adalimumab, golimumab and vedolizumab, respectively. Apart from prior exposure to anti-tumour necrosis factor (anti-TNF) agents and concurrent immunomodulatory therapy, predictors of clinical response and remission to biological therapy are not yet well defined. We sought to investigate the utility of baseline faecal calprotectin (FC) and early change in FC in predicting clinical response and remission to biological therapy in UC.

Aims & Methods: Patients who were commenced on any biological therapy for UC and had a baseline FC at the time of commencement were included in this retrospective study. Disease activity was monitored serially by calculation of Simple Clinical Colitis Activity Index (SCCAI) or by Physician global assessment (PGA) or by treatment persistence. Clinical response was defined as decrease in SCCAI ≤ 3 or a decrease in PGA score to one point below baseline. The ability of FC and fold change in FC to predict response and remission at 6 months was estimated using Mann-Whitney test.

Results: A total of 94 patients were commenced on biological therapy of who 70 had an active disease and commenced vedolizumab with a mean age of 41.8 (SD: ±18.2). Fifty-one (72%) and 39 (55%) patients commencing anti-TNF therapy were on concurrent immunomodulators (IM) and steroids respectively compared to 9 (38%) and 16 (67%) patients respectively for vedolizumab. Sixty-one (85%) patients treated with vedolizumab and anti-TNF agents were severely UC (72.2% and 73.5% respectively. The calprotectin values were similar for responders (482.5 (750 (IQR 330-1300) n = 16) and non-responders (400 (107, 2100) [n = 5]) to vedolizumab (P = 0.56). Similarly, responders (909 (13, 2100) [n = 26]) and non-responders (850 (240, 2100) [n = 13]) to anti-TNF agents had comparable calprotectin values at baseline, P = 0.93.

Conclusion: In a single-centre series of biologic treated UC patients, baseline FC did not predict clinical response at 6 months. Disclosure of Interest: S. Subramanian: Advice report member for Abbvie, Janssen and Behringer-ingleheim On speaker bureau for Dr Falk, Abbvie and MSD. All other authors have declared no conflicts of interest.
P1718 EIGHT YEARS EXPERIENCE OF DRUG EFFICACY IN CROHN'S DISEASE PATIENTS: A PROSPECTIVE MULTICENTER REAL-LIFE STUDY
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Introduction: The prevalence of Crohn’s disease is important for planning of health care and allocation of clinical resources. In 2005, a National Patient’s Registry in Poland was established to collect demographic and clinical data. The aim of the study was assess the efficacy and tolerance of different medications in real-life treatment during the study period, data regarding medical treatment were collected from Registry.
Aims & Methods: The aim of the study was to assess and compare the efficacy of medications in reference to demographic and disease data and disease location and behaviour. The study included 6030 of patients who have been enrolled to the Polish National CD Patient’s Registry, conducted in 9 gastroenterology centers in Poland. Patient’s phenotype according to: Montreal classification, demographics, smoking, alcohol consumption, extraintestinal manifestation and medical treatment have been evaluated. The impact of demographic factors on the use of drugs from different groups (mesalamine, prednisone, azathioprine, methotrexate, anti-TNF, ) and medications efficacy and tolerance was assessed. The efficacy assessment was evaluated according to subjective 4-step scale. Similarly treatment tolerance was assessed according to 2-step scale.
Results: No gender effects were observed on the use or efficacy of individual drug classes, although greater tolerability of prednisone and azathioprine was observed in men (respectively 95.56 vs 93.82 and 93.94 vs. 91.65, both p < 0.05). Smoking did not affect the effectiveness and tolerability of the used medications. However surprisingly fewer smokers were treated with azathioprine, methotrexate, and anti-TNF in comparison to non-smokers (38 vs 45%, 0.5 vs 1.55%, 0.5 vs 11%, all p < 0.05). In patient’s declaring casual alcohol use, the efficacy and tolerability of prednison was significantly better than in patients declaring abstinence (89 vs 84 and 96 vs 93%; p < 0.05). Referring to the Montreal classification, efficacy of mesalamine, prednisone and azathioprine was significantly higher in A1 group with the lowest in A2 patients (A1: 90, A2:83, A3: 86 for prednisone, p < 0.05). Regarding relation to localization of the disease, the efficacy of treatment with immunosuppressive agents (azathioprine and methotrexate) in L3 was significantly lower compared with L1 and L2, despite of increased use of immunosuppressive drugs in L1 (76 vs 82%, p < 0.05). As predicted, the use of immunosuppressive and anti-TNF drugs was higher in complicated disease behavior (B2 and B3) than in B1, however efficacy of infliximab was similar in B1 in comparison to others (B3: 15.5% B1: 7% of infliximab use).
Conclusion: This is the first study comparing efficacy and tolerability of treatment methods used in “real-life” practice in Poland during last 8 years. Most observations are in compliance with data from clinical trials. Positive effect of casual alcohol consumption on efficacy of medications requires further observation. Interestingly some unexpected relationships, concerning similar efficacy of infliximab in different disease behavior was found. This effect requires also further observations in regards to more frequent use of anti-TNF drugs in last years.
Disclosure of Interest: All authors have declared no conflicts of interest.

P1719 EFFICACY OF VEDOLIZUMAB INDUCTION THERAPY IN PATIENTS WITH SEVERE, THERAPEUTIC RESISTANT INFLAMMATORY BOWEL DISEASE
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Introduction: Vedolizumab (VDZ) is the first gut-specific monoclonal antibody alternative to anti-tumor necrosis factor alpha therapy in patients with moderate-to-severe inflammatory bowel disease (IBD). It has been registered since 2016 in Hungary, but currently the high treatment costs are considerably limiting the availability of VDZ. All newly initiated VDZ therapy is individualized, it should be approved by the steering committee of five Hungarian IBD-specialists. This results in that VDZ therapy is available exclusively for patients in whom conventional treatment was ineffective or contraindicated.
Aims & Methods: The aim of our non-interventional prospective study was to assess the efficacy of induction VDZ therapy in 41 patients with Crohn’s disease (CD) and 25 with ulcerative colitis (UC) received VDZ induction therapy between September 2016 and April 2017 in Hungary. Efficacy of induction therapy was assessed based on the changes of activity indices on week 14.
Results: Of 41 enrolled IBD patients were therapeutic failure or intolerant for infliximab and/or adalimumab therapy. The mean age was 38.6 years (range 18–67; median 40) and the average disease duration was 11.7 years (range 1–36; median 10). In 16 cases moderate and in 25 cases severe disease activity was observed. Extraintestinal manifestations occurred in patients, and in cases the IBD was associated with primary sclerosing cholangitis (PSC). Rate of the therapeutic responders for VDZ induction therapy was 80.49% (N = 33). Complete clinical remission was observed in 19 cases (46.34%) 8 cases (19.51%) of which were steroid-free remission. In one case VDZ therapy had to be interrupted due to development of IBD associated colorectal cancer and in one case due to MCV infection.
Conclusion: Our results suggest that induction VDZ therapy is effective and it is a safe therapeutic option in anti-tumor necrosis factor alpha failure or intolerant IBD patients with moderate or severe disease activity.
Disclosure of Interest: All authors have declared no conflicts of interest.

P1720 OUTCOMES OF TREATMENT FOR LATENT TUBERCULOSIS INFECTION IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE RECEIVING BIOLOGIC THERAPY
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Introduction: Tuberculosis (TB) reactivation is of particular concern in patients with inflammatory bowel disease (IBD) treated with biologic therapies. Screening for latent tuberculosis infection (LTBI) is indicated prior to initiating treatment. In patients with IBD, the development of LTBI is more common. Several studies have suggested the risk of reactivation following treatment for LTBI the risk of reactivation still exists. The efficacy of LTBI treatment in IBD patients receiving biologic therapy and the timing of biologic therapy initiation has not been extensively studied.
Aims & Methods: In order to evaluate the effectiveness of LTBI treatment in IBD patients receiving biologic, we conducted a retrospective review of all IBD patients diagnosed with LTBI following a tuberculin skin test (PPD) or interferon gamma release assay (IGRA) and who received biologic therapy between January 1996 and August 2016. LTBI was extracted included in the study. Their mean age was 38.3 ± 14.4 years and 68.6% were male (Table 1). The median time from diagnosis of IBD to LTBI was 9 years (0–48 years). Prior IBD therapies included corticosteroids (86%), aminosalicylates (83%), other immunosuppressants (69%). At least 43% of patients have been previously exposed to at least 1 biologic agent. The most common LTBI treatment regimen was isoniazid (INH) for 9 months (n = 26, 74%). Biologic therapy used were infliximab (n = 14, 40%), adalimumab (n = 10, 29%), vedolizumab (n = 7, 20%), and certolizumab pegol (n = 4, 11%). Combination therapy with an immunomodulator and a biologic agent was administered in 57% of cases (n = 20). All patients were treated for LTBI and the majority (83%) was treated prior to
starting biologic therapy. The median time from initiation of LTBI treatment to biologic was 43 days (IQR 19–34). The mean duration of follow-up was 2.9 ± 3.3 years. The median calculated annual risk of developing active TB without treatment was 0.52% (0.08%–1.3%). Of the cohort studied, only one patient taking adalimumab monotherapy after completing 6 months of INH therapy developed reactivation of TB. The estimated TB reactivation rate in our cohort was 0.98 cases per 100 patient-years of follow up.

**Table 1:** Cohort Characteristics and Estimated Post-treatment Tuberculosis Reactivation Rate

<table>
<thead>
<tr>
<th>Description</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Age</td>
<td>38.3 (±14.4) years</td>
</tr>
<tr>
<td>Male Sex</td>
<td>24/35 patients</td>
</tr>
<tr>
<td>Type of Inflammatory Bowel Disease (IBD)</td>
<td>Ulcerative Colitis (23%) Crohn’s Disease (77%)</td>
</tr>
<tr>
<td>Mean Time since IBD</td>
<td>9 years (range: 0–48)</td>
</tr>
<tr>
<td>Diagnosis</td>
<td>Inflamixim (40%), Adalimumab (29%), Vedikuzumab (20%), Islonizad (INH) for 9-months</td>
</tr>
<tr>
<td>Therapy</td>
<td>Isoniazid (INH) for 9-months</td>
</tr>
<tr>
<td>Median time to initiate biologic therapy</td>
<td>43 days (range: 4–3653)</td>
</tr>
<tr>
<td>Mean duration of follow-up</td>
<td>2.9 ± 3.3 years</td>
</tr>
<tr>
<td>Mean Pre-treatment Risk of Development of IBD Tuberculosis</td>
<td>0.52%/year (range: 0.08%–1.3%/year)</td>
</tr>
<tr>
<td>Estimated Post-treatment Tuberculosis</td>
<td>0.98 cases per 100 patient-years</td>
</tr>
<tr>
<td>Reactivation Rate</td>
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</table>

**Conclusion:** Treatment for LTBI in patients with IBD treated with biologics is effective, but does not eliminate the risk of reactivation, which occurred at a rate of 0.98 cases per 100 patient-years in our cohort. Additional studies with extended follow-up are warranted to further characterize the efficacy of LTBI treatment in these patients.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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**P1721 CLINICAL CHARACTERISTICS AND MANAGEMENT OF CROHN’S DISEASE IN PATIENTS WITH RESIDUAL DISEASE AFTER SURGERY COMPARED WITH CURATIVE SURGERY. RESULTS FROM PRACTICROHN STUDY**


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**Introduction:** Resection in Crohn’s disease (CD) intends to be a curative surgery, but the presence of a damaged gut. The aim of our study was to describe the characteristics and management of patients with residual disease after surgery (RD) and to compare these with patients with curative surgery (CS) in post operative CD patients.

**Aims & Methods:** PRACTICROHN was a retrospective study that included adult patients from 26 Spanish hospitals who underwent CD-related ileocolonic resection with ileocolic or ileorectal anastomosis between January 2007 and December 2010. Clinical data was retrospectively collected from clinical charts. RD was defined when lesions were still present after surgical resection. Postoperative recurrence (POR) was defined by clinical symptoms (diarrhea, abdominal pain) and endoscopic Rutgeerts score ≥2, and/or CT or MRI confirmation of disease activity. Categorical variables were compared with the χ2 test or Fisher’s exact test Kaplan-Meier method was used to assess time to clinical recurrence and a log-rank test to obtain statistical significance.

**Results:** Three hundred and sixty-four patients were analyzed (mean age 40 years [SD 13.5%] 50% men). Of these, 27 (7.5%) had RD after surgery. Median age at diagnosis was shorter in patients with RD than CS: 23 (IQR 19–34) years vs 29 (IQR 23–40), p = 0.02. At the time of resection BI (+) behavior was more frequent in RD than in CS: 6 (22%) vs 26 (8%), p = 0.05; and location was mainly L1+L4 in CS (190, 57%) and L3+L4 in RD (19.70%), p = 0.02. Four (16%) patients in RD were receiving immunomodulators at the time of surgery vs 132 (41%) of CS. p = 0.02. More patients in RD vs CS presented postoperative complications (12 (44%) vs 87 (26%), p = 0.06) as well as hospitalizations the first year after surgery (10 (37%) vs 42 (12%) p = 0.001). No differences in smoking habit, perianal disease or length of resection were found between the two groups. More patients were performed an endoscopy within the first year after surgery in the RD vs CS:16 (59%) vs 122 (36%), p = 0.03 but no difference in prophylactic treatment were found in RD vs CS groups. POR was more frequent among patients with RD (69% vs. 29%, OR = 0.001). Median time to POR was longer in patients who received prophylaxis vs those who didn’t received it (698 vs 392 days; p = 0.41) in CS and in RD presented POR with median time to POR being longer in patients who received prophylaxis (no median found vs 1529 days) p = 0.04. Table 1.

**Conclusion:** Residual disease is a rare situation after intestinal resection in CD. Patients with residual disease after surgery, are more frequently followed-up endoscopically within the first year. Conversely, similar proactive recurrence prevention was observed compared to curative surgery. In the case of residual disease although prophylactic treatment is useful, most of the patients will present POR. RD is a factor of poor poor prognosis in post-operative CD patients.

**Disclosure of Interest:** L. Cea-Calvo: MSD employee C. Romero: msd employee B. Juliá De Páramo: MSD employee All other authors have declared no conflicts of interest.

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**P1722 SEVERITY OF BILE ACID MALABSORPTION CORRELATES WITH LENGTH OF ILEAL RESECTION IN CROHN’S DISEASE**

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**Introduction:** Bile acid malabsorption (BAM) is a common cause of diarrhea in Crohn’s disease (CD) patients with ileal resection and can lead to complications such as renal and biliary stone disease. BAM is usually diagnosed by selenium labelled homotaurocholic acid test (75SeHCAT) but its availability is limited. Thus, a large proportion of resected CD patients either remain undiagnosed or subject to empirical therapy. There is a paucity of studies examining the correlation between length of ileal resection and severity of BAM which will be of particular use to clinicians with no recourse to diagnostic testing for BAM.

**Aims & Methods:** We identified all CD patients with a prior surgical resection who underwent 75SeHCAT testing at our institute. Testing was based on the treating clinician’s discretion. The length of resected ileum was recorded from histopathology report. We conducted a Spearman’s correlation test to check for correlation between length of resected ileum and percentage retention on 75SeHCAT. Response to bile salt sequestrant and 75SeHCAT retention values was tested using Mann-Whitney test.

**Results:** A total of 97 patients were treated with a mean age of 46.4 (SD 14.5). The median length of resected ileum was 22.5 cms (range 1.5–95 cms) with a median of 1 resection (range 1–4). Overall, 90 patients (92.8%) had 75SeHCAT retention values of <5%, 5 (5.2%) patients between 5–10% and only 2 patients had values of >15%. There was moderate correlation between 75SeHCAT retention and length of ileal resection (Spearman’s rho: 0.4041, P < 0.001). Data on response to treatment was available for 60 patients, of who 41 (42%) responded and 19 (19%) failed to respond to bile salt sequestrants. The 75SeHCAT retention values was comparable among responders (median 0.02%, range 0.1–6.6) and non-responders (median 0.02%, range 0.1–6.6, Mann-Whitney test, P = 0.72).

**Conclusion:** There was moderate correlation between length of ileal resection and severity of BAM as defined by 75SeHCAT retention values. Response to bile salt sequestrant therapy was not dependent on 75SeHCAT retention values.

**Disclosure of Interest:** S. Subramaniam: Advice report member for Abbvie, Janssen and Behringer-ingeilheim On speaker bureau for Dr Falk, Abbvie and MSD.

All other authors have declared no conflicts of interest.
P1723 A MICROBIAL SIGNATURE OF PSYCHOLOGICAL DISTRESS IN IRritable BOWEl SYndrome

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Introduction: Irritable Bowel Syndrome (IBS) is associated with alterations along the brain-gut-microbiota axis. Previous studies have suggested a parallel segregation of microbial features with psychological burden in IBS (1,2,3).

Aims & Methods: This study aimed at examining microbial correlates of psychological distress, anxiety, depression and stress perception. 16S rRNA fecal microbial analyses (Illumina MiSeq, V1-2 amplified from total DNA) in 48 IBS patients (Rome-III criteria, mean age 42 years, 35 female subjects, 25 diarrhoea-predominant, 22 constipation-dominant and 18 alternating-type IBS). Assessment of psychological and clinical variables with validated questionnaires, microbial analysis via qHIME. Machine learning to predict psychological distress through a composite model of bacterial features. Correlational analysis and comparisons in bacterial abundance among subgroups defined by thresholds in psychological variables.

Results: Thirty-one patients (65%) showed psychological distress, 22 (31%) anxiety, and 10 (17%) depression. Psychological distress was uncorrelated with IBS severity (Spearman’s ρ = 0.05, p = 0.736). Microbial beta diversity was significantly associated with distress and depression (q = 0.044 each). A random forest model using 148 microbial estimators was able to correctly classify patients regarding presence of psychological distress (AUROC = 0.98). Patients exceeding thresholds of distress, anxiety, depression and stress perception showed significantly higher abundances of Proteobacteria (LDA = 2.5). Patients with anxiety were characterized by higher abundances of Bacteroidaceae (LDA = 3.0). Differentially abundant with Lachnospiraceae (q = 0.05, p = 0.018), anxiety positively with Anaerostipes (ρ = 0.65, q = 0.001).

Conclusion: A microbial signature accurately predicted the presence of psychological distress. Psychological variables significantly segregated gut microbial features, underscoring the role of brain-gut-microbiota interaction in IBS. Supported by Austrian Society of Gastroenterology and Hepatology (ÖGGH) and funds of the Oesterreichische Nationalbank, Fund project number: 16506.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P1724 SACCHAROMYCITES BOULARDII CNCM I-745 LOWERS FECAL CHOLIC ACID CONCENTRATIONS DURING ANTIBIOTHERAPY IN HEALTHy VOLUNTEERS: A NEW MECHANISM IN THE PROTECTION AGAINST CLOSTRIDIUM DIFFICILE INFECTION

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Introduction: Saccharomyces boulardii (SB) CNCM I-745 demonstrated clinical efficacy in the secondary prevention of post-antibiotic Clostridium difficile infection (CDI), but the mechanism remains unclear. Cholic acid (CA) is a primary bile acid (BA), synthesized by the liver which triggers the germination of C. difficile spores in the intestine. Physiologically, the gut microbiota transforms primary BAs (cholic acid and chenodeoxycholic) into secondary (deoxycholic and lithocholic). CA loses its germinating properties after transformation and appears to become protective against CDI. The goals of this work in healthy volunteers (HV) were to: 1) Describe the effect of antibiotics on the quantity of ‘germination’ primary BA including CA in human stools 2) Describe whether SB enhances transformation to ‘protective’ secondary BA in human.

Aims & Methods: This work was an ancillary of a previous study conducted in 4 groups of HV at Beth Israel Deaconess Medical Center and Harvard Medical School, Boston, Massachusetts. The previous results of this work showed that SB CNCM I-745 can modulate shifts in the microbiota and reduces diarrhea during an antibiotic therapy. Group 1 (n = 12) received SB CNCM I-745 500 mg twice daily for 14 days. Group 2 (n = 12) received Amoxicillin-Clavulanate (AC) (875/125 mg twice daily) for 7 days. Group 3 (n = 12) received AC for 7 days and SB for 14 days. Group 4 (n = 12) did not receive any treatment. Groups 1, 2, 3 had successive stool samples at D-28, 0, 3, 7, 10, 13, 21. Group 4 had stool samples at D0, 7 and 21. The fecal concentrations of 28 BAs were measured by HPLC-MS, and expressed as % of total. An ANOVA was performed.

Results: AC alone (group 2) significantly reduced the rate of fecal secondary BA at day 7 compared to control (group 4) (54.8 ± 10.1 vs 83.1 ± 7.4%, p = 0.017). In group 3 (AC plus SB), the decrease in secondary BA rate was significantly less than AC (71.23 ± 7.4 vs 57.80 ± 9%, p = 0.04), and this difference was prolonged over time. Similarly, the AC+SB group showed a significantly lower (and sustained) increase in CA than in the AC alone group.

Conclusion: Antibiotics alter the transformation of BA by microbial enzymes into secondary BAs. Probiotics may reverse this transformation. Cholic Acid rates, a primary BA which facilitates C. difficile spore germination in vitro, increases in stool during antibiotic therapy. The concomitant administration of SB during AC treatment significantly reduces this CA peak. These results highlight new human data on a potential mechanism for post-antibiotic CDI: alteration of the microbiota can encourage germination of C. difficile spores via increased CA concentrations and reduced concentrations of secondary BAs. The effectiveness of SB in preventing recurrent CDI may be explained, in part, through modulation of microbiota changes that influence the balance of pro- and anti-germination BA concentrations.

Disclosure of Interest: H. Duboc: I worked with Biocodex as an advisor for the development of a free smartphone App for patients suffering of constipation.

K. Kelly: Scientific advisor and consultant to: Merck, Seres Therapeutics and Summit.

All other authors have declared no conflicts of interest.

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1. Castellari, M., Warren, R. L., Freeman, J. D., Dorelioni, L., Krzywinski, M., Strachan, P., Barnes, R., W. G., Fischbach, M. A. & Holt, A. 2012. Fusobacterium nucleatum infection is prevalent in human colorectal adenomas and cancers, some specific bacterium have been identified as a related factor. Recent studies have reported a high abundance of Fusobacterium nucleatum (F. nucleatum) in colorectal cancer (CRC) subjects compared to normal subjects12. F. nucleatum is also known as a pathogenic species of oral microbiota, but it is not known if F. nucleatum plays a role in other part of the digestive tract. F. nucleatum may affect metabolic pathways for the carcinogenesis1. We examined whether there is relationship between F. nucleatum oral cavity and CRC.

Aims & Methods: We assessed the abundance of Fusobacterium in CRC, colorectal mucosa and saliva. We extracted DNA from mucosal biopsies and measured bacterial levels by quantitative PCR of the 16S ribosomal RNA gene. We also investigated the homology of F. nucleatum in oral cavity and CRC.

Results: In 51 CRC cases, Fusobacterium positivity was significantly higher in CRC compared to controls (p < 0.05). Fusobacterium was more detected in CRC (12.9%) than in normal tissue (7.6%) respectively. The detection rate of F. nucleatum was 96% in saliva and 95% in CRC by next-generation sequencing. A total of 15 patients with CRC were included to check the homology of F. nucleatum in saliva and CRC. From the 15 patients, 9 were F. nucleatum-positive in saliva (60%) and 8 from these patients were F. nucleatum-positive in saliva. From these patients who were F. nucleatum-positive in saliva and CRC, we next looked for the results of AP-PCR and 6 patients have shown common band patterns.

Conclusion: The results support a link between the abundance of F. nucleatum in oral cavity and CRC. Our data also indicate that there may be a route from the oral cavity to the CRC in F. nucleatum positive cases. We are now identifying DNA sequences, specific for the objective strains.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
P1727 HUMAN MILK Oligosaccharides: A NEW STRATEGY AGAINST POST-ANTIBIOTIC CLOSTRIDIUM DIFFICILE INFECTION?

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Introduction: Human Milk Oligosaccharides (HMOs) are a family of complex carbohydrates found in high concentrations in human milk and which are now becoming commercially available. In clinical studies, in both infants and adults, HMOs powerfully and specifically modulate the gut microbiota by increasing bifidobacteria and reducing certain pathogenic bacteria (1,2). Also, HMO bacterial consumption results in the production of beneficial metabolites such as short chain fatty acids and decrease pH compared to a control with no added HMOs. Additionally, HMOs reduced the level of C. difficile in some cases completely eraditing C. difficile below detection limits. This antimicrobial effect of HMOs on C. difficile was pH-independent, hence another mechanism is causing the anti-pathogenic activity of HMOs.

Conclusion: Conclusively, the results show that HMOs can impact C. difficile infection in an in vitro system, which suggests HMOs as a potential approach to reduce risk of antibiotic associated diarrhoea and post-antibiotic C. difficile infection.


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P1728 CHANGES IN GUT MICROBIOTA ASSOCIATED WITH AGING IN OBESE INDIVIDUALS

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Introduction: It has been reported that the composition of human gut microbiota changes with aging, body mass index (BMI), diet and other environmental factors. In particular, the relationship between gut microbiota and obesity has been underlined frequently because intervention in the microbiota may reduce body fat. In this study, we investigated the relationship between obesity and composition of gut microbiota in healthy Japanese population.

Aims & Methods: Participants were 1,082 healthy Japanese adults (410 males, 672 females) who participated in the Iwaki Health Promotion Project in 2014. Faecal samples were analysed by 16S rRNA gene-targeted sequencing to determine family composition of gut microbiota. They were classified into obese group (BMI ≥ 25) and normal weight group (BMI < 25) according to Japanese standard and were stratified into 7 age groups, 19-29, 30-39, 40-49, 50-59, 60-69, 70-79 and 80-90. The family composition of gut microbiota in each age group was compared between obese and normal group.

Results: There were 235 obese participants, and 847 normal ones. The proportion of Bacteroidaceae decreased substantially, and Ruminococcaceae increasing slightly with aging in obese group. The proportion of Bifidobacteriaceae, Lachnospiraceae and Porphyromonadaceae decreased gradually with aging in both groups.

Conclusion: Changes in composition of gut microbiota with aging were different between obese and normal group. Some previous researches observed differences of gut microbiota between obese and normal group, but many of the researches did not take aging into consideration. Our study indicated that different intervention stratified with age could be needed.

Disclosure of Interest: All authors have declared no conflicts of interest.

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P1729 CARBOXYLIC AND AMINO ACIDS MIXTURE IDENTICAL TO THE METABOLITES OF THE PROBIOTIC ESCHERICHIA COLI AS A756 INDUCES BACTERIOCIN SYNTHESIS IN PROBIOTIC LACTOBACILLUS HELVETICUS D75 AND D76 STRAINS AND ENHANCES THEIR ANTIMICROBIAL ACTIVITY AGAINST TEST PATHOGENS

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Introduction: The production of bacteriocins is considered as the key metabolic function of gut microbiota and as the inherent property of probiotic strains. Bacteriocins and metabolites of probiotic microorganisms (metabiotics) can optimize host-specific physiological functions related to human health.

Aims & Methods: This study aims to: (a) detect the bacteriocin genes of probiotic strains Lactobacillus helveticus D75 (NCBI Reference Sequence NZ_CP020029.1) and Lactobacillus helveticus D76 (NCBI Reference Sequence NZ_CP016827.1) and (b) evaluate in vitro effects of the carboxylic and amino acids mixture identical to the metabolites of the probiotic Escherichia coli strain A756 (components 25% acetic acid, 0.007% L-cysteine, 10% L-helveticin of Lactobacillus helveticus D75 and Lactobacillus helveticus D76). The variation in antimicrobial activity of Lactobacillus helveticus D75 and Lactobacillus helveticus D76 was estimated by the microdilution method. The identification of bacteriocin genes was performed by PCR using helveticin J gene primers. Amplified fragments were sequenced using ABI PRISM® 310 Genetic Analyzer and were analyzed using NCBI/BLASTX.

Results: The identical sequences of 537 bp homologous to gene fragment of helveticin of Lactobacillus helveticus DPC 4371 (lhv_1632 gene) were detected.
in DNA of both probiotic strains. Sequencing of these fragments showed differ-
ences compared to the reference DNA of DPC 4571 strain (A instead of G at position 46, C instead of T at position 249 and A instead of T at position 537), but all these replacements do not lead to changes in the amino acid sequence of a bacteriocin. For Lactobacillus acidophilus D76 another bacteriocin gene fragment of 283 bp was identified (in addition to 537 bp fragment). The latter had 95% homology with the helveticin J gene of Lactobacillus helveticus R0052 (R0052_09025 gene). In NCBI BLASTX database the sequences homolo-
gous to the helveticin gene of Lactobacillus helveticus DPC 4571 were found in 17 Lactobacillus species related to Lactobacillus acidophilus, Lactobacillus amylovorans, Lactobacillus crispatus, Lactobacillus gallinarum, Lactobacillus helveticus and Lactobacillus kitasatosan. The addition of the carboxylic and amino acids mixture (Actioflor®-S) results in 2-2.5-fold enhanced antimicrobial activity of both tested probiotic Lactobacillus strains against test pathogens (Lactobacillus coli D75 and Salmonella Enteritidis 209), most likely due to an increase in bacteriocin gene expression.

Conclusion: Study shows that there are at least two bacteriocins in Lactobacillus helveticus D76 and one bacteriocin in Lactobacillus helveticus D75. Carboxylic ac and amino acids mixture identical to the metabolites of the probiotic Escherichia coli strain M17 probably induces bacteriocin synthesis in probiotic strains Lactobacillus helveticus D75 and Lactobacillus helveticus D76 and enhances their antimicrobial activity against test pathogens Escherichia coli D75 and Salmonella Enteritidis 209, most likely due to an increase in bacteriocin gene expression.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
3. Fernandez B, Le Lay C, Jean J, Fliss I. Growth, acid production and bacteri-

unsolved. In our institution, we gastroenterologists perform interventional radiology for the feasibility rule out an upper GI source.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1735 GLASGOW-BLACHFORD SCORE ACCURATELY PREDICTS THE NEED OF TRANSFUSION IN ACUTE LOWER GASTROINTESTINAL BLEEDING. A DIAGNOSTIC ACCURACY EVALUATION STUDY

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Introduction: The incidence of acute lower gastrointestinal bleeding (LGB) is increasing in Western countries, but the predictors of its outcome are not well studied to be defined.

Aims & Methods: The aim of this study was to compare the accuracy of Glasgow-Blachford score (GBS) with three available risk scores (State, Velayos and Newman) for predicting the need of any clinical intervention (endoscopic therapy or surgery) in patients admitted for acute LGB. A retrospective study from January 2013 to December 2015 in a university tertiary care hospital. Patients with acute LGB were identified using the International Classification of Diseases (9th Revision) and Clinical Modification codes for admission diagnosis. Scores were retrospectively calculated according to clinical reports data. Area under the receiver operating characteristic curve (AUROC), sensitivity, specificity, positive and negative predictive values were calculated for four scores. Also the best cut-off of each score was chosen from using the AUROC curve values. Results: A total of 298 (51% men) consecutive patients with acute LGB were identified. Median age was 76.1 years (range 25.4–96.5), 201 (67.4%) of patients were older than 70 years. Five patients (1.7%) died, 18 (6%) developed recurrent bleeding, 89 (29.9%) needed transfusion, 30 (12.1%) received endoscopic therapy, and 3 (1%) underwent transcatheter arterial embolization. No patients required any surgical intervention. AUROC of GBS score was 0.87 (95%CI:0.82–0.91) for the need of transfusion, and 0.82 (95%CI:0.76–0.87) for the need of any clinical intervention. AUROC for the need of transfusion and clinical intervention were 0.68 (95%CI:0.61–0.74) and 0.67 (95%CI:0.60–0.73) for the Strate score, 0.77 (95%CI:0.71–0.83) and 0.74 (95%CI:0.68–0.80) for the Velayos score and 0.78 (95%CI:0.72–0.85) and 0.74 (95%CI:0.68–0.81) for the Newman score, respectively. GBS was significantly more accurate than LGB risk scores for predicting the need of transfusion. Although AUROC of GBS was also numerically better for predicting the need of any clinical intervention, the difference was only significant when comparing with the Strate score. All the risk scores were more accurate for determining the need for transfusion than for the need of clinical intervention. Sensitivity, specificity and positive and negative predictive values for each score are shown in table 1.

Table 1: Prediction values of the different scores for detecting the need of transfusion (TRF) or clinical intervention (CI). 1Best cut-off scores for Blachford score were 6 for transfusion and 4 for clinical intervention. Values are expressed as%.

<table>
<thead>
<tr>
<th>Score</th>
<th>TRF 5 TRF 3p TRF PPV TRF NPV CI 1 SCI 3p CI PPV CI NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blachford*</td>
<td>80 78 61 90</td>
</tr>
<tr>
<td>Strate &gt; 1</td>
<td>69 58 41 81</td>
</tr>
<tr>
<td>Velayos &gt; 0</td>
<td>95 46 41 96</td>
</tr>
<tr>
<td>Newman &gt; 192</td>
<td>40 39 93</td>
</tr>
</tbody>
</table>

Conclusion: The GBS was superior to the 3 LGB risk scores for predicting the need for transfusion and clinical intervention. The GBS may be an useful tool for risk stratification in acute LGB.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1734 ACCURACY OF THE NASOGASTRIC TUBE AND THE BUN/CREATININE RATIO FOR DISTINGUISHING BETWEEN UPPER AND LOWER SOURCES OF GASTROINTESTINAL BLEEDING. A SYSTEMATIC REVIEW

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Introduction: The insertion of a nasogastric tube (NGT) and assessment of the BUN/creatinine ratio were recommended as initial measures to distinguish between upper and lower gastrointestinal bleeding (American College of Gastroenterology 2016). As the nasogastroscope is one of the most bothersome interventions for the patient, we evaluated the evidence supporting these recommendations.

Aims & Methods: The aim of the study was to identify the diagnostic accuracy (sensitivity, specificity, positive predictive value, negative predictive value and likelihood ratios) of the NGT and the BUN/creatinine ratio for distinguishing between upper and lower sources of gastrointestinal (GI) bleeding. We conducted a systematic review of the literature in order to identify studies assessing the diagnostic accuracy of the NGT or BUN/creatinine in patients with melena, hematochezia or rectorrhagia without hemorrhages. The search was performed in November 2016 in five data bases (Pubmed, Scopus, Web of Science, Cochran Plus Library and OpenGrey).

Results: Four studies met the selection criteria (two evaluating the NGT, one BUN/creat and one both). The two methods had a low sensitivity for detecting upper GI bleeding source. Both a positive NGT aspiration and BUN/creatinine ratio above 30 markedly increased the probability of an upper GI source with a positive likelihood ratio ranging from 2 to 11. Unfortunately, the sensitivity of both tests for upper GI bleeding was very low (negative likelihood ratios around 0.3). Characteristics and results of the studies selected are shown in table 1.

Table 1: Characteristics and results of the studies

<table>
<thead>
<tr>
<th>Study/period</th>
<th>Design/Period</th>
<th>Sample size/Tests</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>Predictive positive value (%)</th>
<th>Predictive negative value (%)</th>
<th>Negative Likelihood ratio</th>
<th>Positive Likelihood ratio</th>
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</thead>
<tbody>
<tr>
<td>Richards 1990</td>
<td>Retrospective 1983–1990</td>
<td>126 BUN/creatinine (Cut off ≥30)</td>
<td>37</td>
<td>100</td>
<td>100</td>
<td>53</td>
<td>0.63</td>
<td>++++++</td>
</tr>
<tr>
<td>Aljebreen 2004</td>
<td>Retrospective 1999–2001</td>
<td>520 NGT</td>
<td>68</td>
<td>54</td>
<td>41</td>
<td>78</td>
<td>0.61</td>
<td>1.44</td>
</tr>
<tr>
<td>Witting 2006</td>
<td>Retrospective 1997–2002</td>
<td>352 BUN/creatinine (Cut off ≥30) NGT</td>
<td>94</td>
<td>91</td>
<td>81</td>
<td>81</td>
<td>0.65 0.56</td>
<td>6.4 11.1</td>
</tr>
<tr>
<td>Kessel 2016</td>
<td>Retrospective 2011–2014</td>
<td>386 NGT</td>
<td>28</td>
<td>86</td>
<td>99</td>
<td>2</td>
<td>0.84</td>
<td>2</td>
</tr>
</tbody>
</table>

Conclusion: Neither test reliably rules out an upper GI source of bleeding. Therefore, in cases of uncertainty, an upper GI endoscopy will be necessary to make a definite diagnosis.

Disclosure of Interest: All authors have declared no conflicts of interest.

Table 1: Characteristics and results of the studies

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P1736 ACUTE LOWER GASTROINTESTINAL BLEEDING IN PATIENTS TREATED WITH NON-VITAMIN K ANTAGONIST ORAL ANTICOAGULANTS COMPARED WITH WARFARIN IN CLINICAL PRACTICE: CHARACTERISTICS AND CLINICAL OUTCOME

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Introduction: Acute lower gastrointestinal bleeding (ALGB) occurs in patients taking anticoagulants either warfarin or non Vitamin K oral anticoagulants (NOACs). The use of NOACs has been increasing compared with warfarin in recent years. We investigated patients with ALGB on anticoagulation therapy and we analyzed characteristics, management and clinical outcome in patients treated with NOACs versus warfarin.

Aims & Methods: All patients with ALGB on anticoagulation therapy treated in our hospital during a seven year period were evaluated. Characteristics and clinical outcome were compared between patients on warfarin and patients on NOACs.

Results: Out of 587 patients with ALGB, 43 (7.3%) were on NOACs and 68 (11.6%) on warfarin with an age range of 75.9 (2.9) vs 77.1 (1.9). The bleeding site was in the small bowel in 2/43 and 6/68 respectively. Causes of bleeding were not different between the two groups except for polyps/neoplasia (8/43 vs 6/68, p=0.003). Endoscopic hemostasis was more commonly needed in patients on NOACs versus warfarin (17/43 vs 8/68, p=0.049). Blood transfusions and need for other interventions (embolization and/or surgery) were not different. Also recurrence of bleeding (4/43 vs 11/68) and mortality (3/43 vs 6/68) were low and not statistically different between the two groups.

Conclusion: ALGB in patients on NOACs although presents some differences it has a similar clinical outcome to patients with ALGB on warfarin.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P1737 NOBLADS - THE NEW RISK SCORE TO PREDICT THE SEVERITY OF ACUTE LOWER GASTROINTESTINAL BLEEDING

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Aims & Methods: We aimed to evaluate the accuracy of the NOBLADS score to predict severe LGIB and the outcome of patients admitted by LGIB. We performed a retrospective, observational and unicentric study. Including patients admitted for acute LGIB and submitted to endoscopic evaluation between January/2015 and March/2016. LGIB was classified as severe if ≥2 units of erythrocyte concentrate (UCE) were required and/or if hematoctit drop ≥20%. Total score ranges from 0-8; when total score is ≥2, it is considered high risk for severe LGIB.

Introduction: A new risk score for acute lower gastrointestinal bleeding (LGIB) has recently been validated, based on 8 admission criteria–nonsteroidal anti-inflammatory drugs use, absence of diarrhea, absence of abdominal tenderness, score >10 on abdominal pain score, platelet count ≤150 platelets/µL, systolic blood pressure <90 mmHg, serum creatinine ≥1.5 mg/dL, disease score ≥2 (Charlson comorbidity index) and syncope (NOBLADS). Results: 173 patients were included (male: 50.3%, mean age: 69 ± 17 years), with LGIB managed by hematocita (91.9%) or melena. Endoscopic evaluation was performed 1.7 ± 2 days after admission, with the most frequent findings being diverticular hemorrhage (n=53) and ischemic colitis (n=29); no lesions were found in 8.3% of cases. Thirty-three patients required intervention (endoscopic n=27, radiological n=2, surgical n=4) and 36 (20.8%) repeated endoscopic intervention. 28.9% of patients presented severe LGIB and the NOBLADS score determined the severity of LGIB with an under the curve value of 0.92 ± 0.018. Overall, higher score values were associated with a requirement for transfusion support, intervention and longer hospitalization (p<0.001 for trend test). Patients at high risk for severe LGIB (score ≥2, n=39) presented a significantly higher number of transfused UCEs (3.6 vs 0.08, p<0.001), intervention (38% vs 13%, p<0.001) and days of hospitalization (12.8 vs 3 days, p<0.001).

Conclusion: The NOBLADS score is simple and quick to apply. It predicts with high accuracy the risk of severe LGIB and allows to identify patients that are more likely to require transfusional support, intervention and prolonged hospitalization. In clinical practice, NOBLADS score may be useful to select on admission patients who will benefit from hospitalization or from earlier intervention.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference
Takuya Inoue, Clinical features of post-polypectomy bleeding associated with heparin bridging therapy; *Dietetic Endoscopy* 2014:26:243–249

**P1740 RISK OF COLORECTAL CANCER IN ASYMPTOMATIC INDIVIDUALS WHOSE FIRST DEGREE RELATIVES WERE AFFECTED BY CRC AT DIFFERENT AGES OF ONSET: A SYSTEMATIC REVIEW AND META-ANALYSIS OF 9.28 MILLION SUBJECTS**

J.L. Huang, M. C. Wong, C. Chan, J. Lin, W. W. Cheung, M. Liang, Y. Fang, C. Yu, E. Fung
*Chinese University of Hong Kong, Hong Kong/Hong Kong Prc*

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**Introduction:** The current literature is mixed regarding whether first-degree relatives (FDRs) of patients who suffered from colorectal cancer (CRC) at much earlier age are at substantially increased risk of CRC. Aim & Methods: The present systematic review and meta-analysis examined the CRC risk conferred by family history of CRC in FDRs according to their age of onset. We searched Ovid Medline, EMBASE and grey literature from their inception to December 2016, and included all screening studies that investigated the relative family history of CRC and incidence/prevalence of CRC. Two reviewers independently worked on selection, assessment and data extraction of eligible articles. A random effects meta-analysis was employed to pool relative risks (RR) and odds ratios. Subgroup analyses were performed according to the age of onset of CRC in FDRs of asymptomatic subjects (<40 vs. ≥40; ≤50 vs. ≥50: <60 vs. ≥60 years). Statistical heterogeneity was assessed by the I² statistic. Publication bias was evaluated by an inverted funnel plot analysis with Begg’s regression model.

**Results:** Fifty-six case-control and seven cohort studies involving 9.28 million subjects were included in the analysis. A family history of CRC in FDRs of asymptomatic subjects conferred a significantly higher risk of CRC (RR = 1.76, 95% CI = 1.57–1.97; p < .001, I² = 95.7%). Earlier age of onset of CRC in FDRs was associated with significantly higher risk of CRC in index subjects (RR = 3.29, 95% CI. 1.67–6.49 for ≤40 vs. RR = 1.42, 95% CI. 1.24–1.62 for ≥40 years, p = 0.017; RR = 2.81, 95% CI. 1.94–4.07 for ≤50 years vs. RR = 1.47, 95% CI. 1.28–1.69 for ≥50 years, p = 0.001). The Begg’s test did not identify any publication bias (Kendall’s tau = 0.122, p = 0.159).

**Conclusion:** A family history of CRC in FDRs whose age of onset is earlier than 40 or 50 years conferred a significantly higher risk of CRC to asymptomatic individuals, implying that age of onset could potentially enhance the discriminatory capability of CRC prediction scores.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**P1741 IS THERE ANY DIFFERENCE IN RISK OF COLORECTAL CANCER AMONG ASYMPTOMATIC SUBJECTS WHOSE SIBLINGS VS. PARENTS WERE AFFECTED? A SYSTEMATIC REVIEW AND META-ANALYSIS**

J.L. Huang, M. C. Wong, C. Chan, J. Lin, W. W. Cheung, M. Liang, Y. Fang, D. Fung, C. Yu
*Chinese University of Hong Kong, Hong Kong/Hong Kong Prc*

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**Introduction:** Few studies compared the risk of colorectal cancer (CRC) among individuals with probands who were parents, siblings, and those with two or more probands. Aim & Methods: This systematic review and meta-analysis tested the hypothesis that the risk of CRC conferred by family history of CRC in parents vs. siblings vs. ≥2 first-degree relatives (FDRs) was similar. The Ovid Medline, EMBASE and grey literature were searched from their inception to December 2016, and all screening studies that examined the association between detection of CRC and family history of CRC in FDR were included. Two reviewers independently searched, assessed and extracted data from eligible studies. The relative risks (RR) and odds ratios were pooled based on a random effects meta-analysis. We conducted subgroup analyses according to the identity of FDRs affected (parents vs. siblings vs. ≥2 FDRs), and examined statistical heterogeneity by the I² statistic. Potential publication bias was explored by funnel plot analysis with Begg’s regression test.

**Results:** We identified 56 case-control and 7 cohort studies, consisting of 9.28 million subjects who were finally included in the meta-analysis. Asymptomatic individuals with siblings affected (RR = 2.44, 95% CI = 1.90–3.13); parents affected (RR = 2.18, 95% CI = 1.95–2.45) and ≥2 FDRs affected (RR = 2.68, 95% CI = 1.39–5.18) had statistically similar risk of CRC. We did not identify any publication bias based on the Begg’s regression test (p = 0.159).

**Conclusion:** The risk of CRC was similar among subjects whose siblings; parents or ≥2 FDRs were affected by CRC. Information on the identity of the FDRs affected does not seem to be necessary when the risk of CRC in asymptomatic individuals is predicted.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**P1742 GILBERT SYNDROME IS NOT THAT INNOCENT?**

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2Tel-Aviv Sourasky Medical Center, Tel Aviv/Israel

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**Introduction:** Gilbert’s syndrome is considered to be entirely benign. Some studies have shown a reduced risk for cardiovascular disease (CVD). There is conflicting data regarding cancer risk among Gilbert patients. Aims & Methods: We aimed to evaluate the association of Gilbert syndrome with CVD and cancer. Clinical and epidemiological data was obtained from consecutive healthy subjects undergoing annual screening at the Integrated Cancer Prevention Center in Tel Aviv. The annual check-up includes: thorough examination by specialists in internal medicine, surgery, dermatology, plastic surgery, OBGYN, urology, oncology, oral surgery, gastroenterology. Blood work (smac 24, blood count, TSH, CRP, PSA), vaginal, PSA and mammography (>40yrs), LDCT in heavy smokers and all needed imaging when clinically indicated. Peripheral blood DNA was extracted from all subjects. Gilbert syndrome was determined by clinical criteria (normal liver function tests but mild elevation in unconjugated bilirubin < 3mg/dl without any hemolysis. In the majority of the cases the diagnosis was confirmed genetically by the homozygous mutation (TA)7TA7 in the promoter region of UGT1A1 enzyme. Prevalence of CVD and cancer were compared between subjects with/without Gilbert syndrome. Mortality data was obtained from the Israeli ministry of health and cancer incidence from the Israeli registry.

**Results:** A total of 6258 (49%) men and 6461 (51%) women, mean age 47.0 ± 11.5 years, were included of which 1.019 had clinical Gilbert. Gilbert was significantly more common among men (11.5% versus 4.6% P < 0.001). The rate of Gilbert disease was equal in Sephardic and Ashkenazi Jews. Malignancy and CVD were diagnosed in 678 (5.3%) and 1.837 (14.4%) subjects respectively. The prevalence of any CVD was significantly higher in the Gilbert group (OR 1.23 95% CI 1.04–1.46 p = 0.017), as was non-hypertension (OR 1.37 95% CI 1.12–1.68 p = 0.003) and CVA (1.1% versus 0.6% p = 0.06). Higher rate of kidney and bladder cancers (2.64, 1.22–5.70, p = 0.019) was also observed in the Gilbert group. In contrast, the prevalence of breast cancer was much lower among the Gilbert patients (0.36% vs 0.97%, P = 0.034).

**Conclusion:** In Israel Gilbert syndrome is not that innocent. In a large cohort it seems to be associated with increased risk of hypertension, CVD and CVA. Bladder cancer is higher but females are protected from breast cancer. Further studies are mandated in order to better understand these findings and determine proper screening and surveillance practices in Gilbert disease.

**Disclosure of Interest:** N. Arber: Bayer Bio-view Gi-View Micro-medie Check-cap All other authors have declared no conflicts of interest.

**P1743 CHARACTERISTICS AND PREDICTORS OF INTERVAL CANCER: A CASE-CONTROL STUDY**

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2Stony Brook University Hospital, New York/United States of America

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**Introduction:** Interval colorectal cancer is largely related to a poor endoscopic performance (missed lesions, incorrect resection margins or different polyps) contributing to the development of the polyp (accelerated growth). Thus, quality endoscopic measures and Lynch syndrome were highly investigated for their association with interval cancer. However, most reports came from the Western world and not the Middle East, and differences in ethnicity or environmental factors might potentially have impact on the biology of tumor progression. In addition, patient-related factors were less investigated for their association with interval cancer. The aim of this study was thus to assess tumor and patient characteristics and predictors of interval cancer in a population from Israel.

**Aims & Methods:** This retrospective cohort study included all patients that were diagnosed with colon cancer in our institution between 2005–2014. Cases included patients with a previous colonoscopy within 1–10 years before the diagnosis of cancer, with either negative or insignificant findings or benign polyps. Only full colonoscopies with at fair or good preparation were included. Interval cancer was defined on an individual basis, when cancer occurred within the recommended surveillance interval according to accepted guidelines. Cases were further stratified according to time since index colonoscopy (<3, 3-10) years). Positive controls were cancer patients without previous colonoscopy, and "negative" controls were sex- and age-matched patients with two negative colonoscopies within the study period who were randomly selected on a 1:1 ratio. Tumor characteristics (location, staging) and patient-related factors (age, gender, positive family history of colon cancer, aspirin use, diabetes, diverticulosis) were compared between cases and control groups.

**Disclosure of Interest:** No conflicts of interest were declared.
Aims: To identify the metabolic risk factors associated with colorectal neoplasia (advanced adenomas and cancers) and evaluated their impact in colorectal cancer screening. Prospective, multicenter study was performed from January 2013 to December 2015 at eight high-quality colonoscopy centers. Aims & Methods: We retrospectively analyzed colonoscopy data of 2338 and 2636 patients, respectively, using standard quality control criteria. Risk factors, and colonoscopic pathologic findings were assessed in patients with metabolic syndrome (target group) who underwent preventive colonoscopy (FIT positive or screening colonoscopy). This data was compared with consecutive controls (without metabolic syndrome). We used the screening population criteria (asymptomatic, without family or personal history of colorectal neoplasia).

Results: 1500 individuals were enrolled; 726 persons (494 men, 68%) in the target group (metabolic syndrome) and 774 persons (353 men, 46%) in the control group (without metabolic syndrome). The significantly higher prevalence of advanced adenomas was observed in the target group (18%; 95% CI 15–21%) compared to the control group (9%; 95% CI 7–11%; OR 1.8; p=0.002). Similarly, the prevalence of all adenomas was higher in the target group (48%; 95% CI 44–51%) than in the control group (35%; 95% CI 32–38%); however, the difference was not statistically significant (p=0.179). Individuals with isolated high cardiovascular risk (SCORE >10%) had higher prevalence of both non-advanced adenomas (51%; 95% CI 46–56%; p=0.037) and advanced adenomas (22%, 95% CI 18–26%; p=0.049) compared to the individuals with isolated DM2. Advanced adenomas were more likely in patients aged 65–75 years.

Conclusion: Colorectal neoplasia is positively associated with metabolic syndrome. Cardiovascular risk factors (SCORE >10%) is a stronger risk factor than the presence of diabetes mellitus type 2. Individuals with SCORE >10% should be considered as a risk group of colorectal cancer. Based on our findings, colonoscopy is the primary screening method is appropriate. This project has been supported by the Czech Ministry of Health grant NT 13673 and MO 1012.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P1747 CONTRIBUTION OF GERMLINE MUTATIONS TO NON FAMILIAL EARLY ONSET CANCERS

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Introduction: Early onset gastroenterological cancers lacking a positive family history are an increasingly worrisome entity. On one hand, early onset is the cornerstone of genetically determined oncological problems, but on the other negative family history does not support the suspect of familial syndromes.

Aims & Methods: We addressed the contribution of germline mutations to non familial early onset cancers. Patients with pancreatic, gastric, esophageal, duodenal and colorectal cancers were enrolled from 2015 to 2017 at the Gastrointestinal Personalized Medicine unit. Eligibility criteria were the juvenile onset and the negativity for clinical criteria of hereditary cancer syndromes. Early onset colorectal cancer was defined as <45 yrs for the other cancers, the threshold was defined at 50. Eligible patients provided informed consent. Genes were sequenced by means of a validated Next Generation Sequencing panel of oncological susceptibility genes and confirmed by means of Sanger sequencing.

Results: Among 12 colorectal cancer patients (7F, 5M), NGS analysis showed 2: MSH2 and MSH6 occurring de novo, given the absence of family history; 3 variants of unknown significance (VUS) (2 MSH2 and 1 MLH1); and 7 were negative. Age-stratification revealed that, among those <35 years (n = 4), 1 had MSH2 gene mutation and 3 were negative. In the 36-40 age group (n = 3), 1 had a MSH2 VUS and 2 were negative. In the age group 41-45 (n = 5), MSH6 mutation and 2 VUS were found, alongside 2 negative results. Among the colorectal cancers, 17% of patients had a de novo mutation of Lynch Syndrome, 25% had a VUS, and 58% were negative.

Conclusion: A significant percentage (17%) of early onset colorectal cancers resulted in Lynch Syndrome even when family history is not suggestive of hereditary cancer. We reliably infer the determinant role of genetics, even when the family history does not support the hypothesis. Elsewhere, our results suggest that the already known susceptibility genes seldom contribute to sporadic early onset cancers. Other genes and mechanisms may explain the early onset phenotype. Our data show that NGS is often non conclusive in early onset GI cancers, and further development is needed to better classify VUS (25%).

Disclosure of Interest: All authors have declared no conflicts of interest.

P1748 IMPACT OF COLIBACTIN-PRODUCING ESCHERICHIA COLI ON IMMUNE MICROENVIRONMENT IN PRECLINICAL COLORECTAL CANCER MODELS

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Introduction: Colibactin producing E. coli strain (11G5), non pathogenic properties on CRC murine models. Aim of this work was to evaluate the impact of chronical infection by colibactin-producing E. coli on CRC carcinogenesis process.

Aims & Methods: Mice were infected or non-infected mice. These results can be linked with our in vivo optical imaging observations and our results about the increase of neutrophils chemo-attractants CXCL1 and CCL20 measured by qRT-PCR after infection. Analysis of T cells, macrophages, B cells and myeloid suppressive cells are in progress.

Conclusion: Here we can observe an increase of lymphoid follicle associated with tumor volume after colibactin-producing E. coli infection. Our first results suggest that neutrophils can be one of the immune cells implicated in this process. This work shows a link between immune microenvironment, pathogenic E. coli and tumor development.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1749 INVESTIGATING THE DIRECT INTERACTION BETWEEN CD24 AND β-CATENIN IN INTESTINAL TUMORIGENESIS

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Introduction: CD24 is a glycosylphosphatidylinositol-linked protein that functions as an adhesion molecule and is overexpressed at an early stage of CRC (Sagiv et al., 2006). The Wnt/β-catenin signaling pathway plays an important role in the CRC carcinogenesis process. C57BL6/J mice carrying the ApcMin mutation develop ~24±3.7 adenomas and several carcinomas in the small intestine by the age of 16 weeks compared to the ~7±1.7 polyps that ApcMin/CD24−/− (double KO) mice developed. Mice colonscopy showed a significant reduction in the number and size of polyps upon depletion of CD24 alleles. The ApcMin mice displayed severe spleenomegaly (355±68 mg) compared (141±49 mg) in double KO mice similar to WT mice. Hb level in the ApCMin was 5.8±2.5, significantly lower than in the double KO mice (8.2±0.9) and their WT littermate.

Aims & Methods: We aimed to study the cellular interactions between CD24 and β-catenin, and effects of their interaction on intestinal tumorigenesis. CD24-inducible 293T-Rex cells previously developed in our lab (Shapira et al., 2011) and SW480 CRC cells stably transduced with CD24 (Naumov et al., 2014) were used to study this interaction in vitro. Co-immunoprecipitation and immunofluorescence staining were used to investigate the interaction between the two proteins. Far western blotting (FWB) analysis was used to confirm this direct interaction by probing the standard WB membrane with the purified CD24 protein.

Results: In vitro: Western blotting analyses showed that expression of CD24 in 293T-Rex cells induced the activation of β-catenin, while down-regulation of CD24 in SW480 cells caused a decrease in the level of active β-catenin. Cyttoplasmic/nuclear fractionation showed that more active β-catenin entered the cell. It was in cells that expressed higher levels of control (clone 4). In addition, in both cell lines, TOP/FOP luciferase reporter assay showed a significant increase in Luciferase activity upon CD24 expression induction. Co-immunoprecipitation studies of CD24 and β-catenin indicated that these two proteins might be interacting. In addition, in HEK-293T cells and SW480 cells, immunofluorescent staining of CD24 and β-catenin showed that these two proteins co-localize on the cellular membrane. Furthermore, far western blotting analysis suggests that a direct interaction between the proteins exist.

Conclusion: 1. CD24 plays a major role in intestinal tumorigenesis. 2. CD24 interacts with the Wnt pathway by activating β-catenin. 3. CD24 interacts directly with β-catenin. 4. Down-regulation of CD24 may be an important aim in the therapy of CRC.

Disclosure of Interest: N. Arber: Bio-view Micro-Medic Check-cap Gi-View Bayer. All other authors have declared no conflicts of interest.

Reference

P1750 YM155 AS AN INHIBITOR OF CANCER STEMNESS SIMULTANEOUSLY INHIBITS AUTOPHOSPHORYLATION OF EGFR AND G9A-MEDIATED STEMNESS IN EGFR-POSITIVE CANCER CELLS

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Introduction: Cancer stem cells survive as the leading reason to tumor recurrence after tumor repressive treatments. Therefore, it is worth discovering specific and efficient inhibitors against cancer stemness for applications in reducing tumor recurrence. Previously, literature has indicated that YM155 can significantly reduce the formation of gastric cancer and suppress EGFR activity. However, the pharmaceutical mechanism of YM155 is not completely clear.

Aims & Methods: The aim of this study attempted to investigate the potential mechanism of YM155 against cancer stemness in EGFR-positive cancers. The tumorspheres derived from EGFR-mutant HCC827 and EGFR-wild-type HCT116 and A549 cells expressing higher cancer stemness markers, CD133, were used as cancer stemness models.

Results: We found that higher EGFR autophosphorylation (Y1068) in HCC827-, A549-, and HCT116-derived tumorspheres compared to the parental cells, which induced tumorsphere formation through activating G9α-mediated stemness property. YM155 was demonstrated to inhibit the tumorsphere formation by unexpectedly blocking the autophosphorylation of EGFR and G9α-mediated stemness pathway. The chemical and genetic inhibitions of EGFR and G9α revealed the significant role of EGFR-G9α pathway in maintaining the cancer stemness property.

Conclusion: In conclusion, this study not only revealed that EGFR triggered the formation of tumorspheres through elevating the G9α-mediated stemness, but also demonstrated that YM155 inhibited the formation of tumorspheres by simultaneously blocking autophosphorylation of EGFR and activity of G9α as a potent anti-stemness agent against EGFR-positive cancers.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P1754 FGF14 IS A FUNCTIONAL TUMOR SUPPRESSOR VIA INHIBITING AMPK/mTOR PATHWAY IN COLORECTAL CANCER

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Introduction: Promoter hypermethylation-induced epigenetic silencing of tumor related genes played a key role in the initiation and development of colorectal cancer (CRC). Using Methylated DNA Immunoprecipitation (MeDIP), we identified that Fibroblast Growth Factor 14 (FGF14) was preferentially methylated in CRC.

Aims & Methods: We aimed to investigate the epigenetic regulation and biological function of FGF14 in CRC. The expression of FGF14 in 10 CRC cell lines and 24 pairs of CRC tissues and paired adjacent normal tissues by real-time PCR. CRC cells were treated with DNA demethylating agent 5-aza-2'-deoxycytidine (5-Aza). The methylated status of FGF14 in CRC cell lines and CRC tissues were determined by real-time MSP. The biological function of FGF14 in CRC was interrogated by cell viability assay, colony formation, immunofluorescence and flow cytometry, as well as in vivo study.

Conclusion: FGF14 was downregulated or silenced in all (10/10) CRC cell lines, while it was frequently expressed in normal colon tissues. The expression of FGF14 was significantly lower in primary CRCs as compared to their adjacent normal tissues (P < 0.01). The loss of FGF14 gene expression was restored by treatment with DNA demethylating agent 5-Aza. Re-expression of FGF14 in CRC cell lines inhibited colony formation, suppressed cell viability, and induced cell apoptosis via AMPK/mTOR pathway, accompanied with enhanced protein expression of cleaved caspase-3, cleaved caspase-7, cleaved caspase-9 and PARP. In xenograft mouse model, overexpression of FGF14 significantly reduced tumor growth (P < 0.001).

Conclusion: FGF14, which induces cell apoptosis via AMPK/mTOR pathway, is a novel tumor suppressor down-regulated by epigenetic inactivation.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
P1755 CHARACTERISTICS OF HYPERMUTATOR IN DIGESTIVE SYSTEM CANCERS
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Introduction: A cancer with a number of somatic mutations is defined as “hypermutator”, and shows therapeutic features, such as high sensitivity to immune checkpoint inhibitor. However, to date, analyses of hypermutator have not been done with a large number of cases.

Aims & Methods: The aim of this study is to analyze the incidences and characteristics of hypermutator in digestive system cancers. We analyzed somatic mutation in digestive system cancers in 1145 cases (age: 67.4±11.3 yrs., M:F=755:390), those underwent surgery after full informed consent during 2014 to 2015. Genomewide sequencing was performed on 47 inherited cancer-associated genes and 411 cancer-associated genes using next generation sequencer (Iontorrent. Precise trimmer, Alientrimmer dk). We confirmed hypermutator by DNA sequencing and microarray analysis.

Results: The 1145 subjects included 583 colorectal cancers (CRC), 229 gastric cancers (GC), 103 metastatic liver tumors, 100 hepatocellular carcinomas (HCC), 45 pancreatic cancer, 23 GISTs, 15 esophageal cancers, and 411 cancer-associated genes using next generation sequencer.

Conclusion: Hypermutator was recognized in 5–10% of digestive system cancers, associated with a somatic mutation of mismatch repair genes. Further research is needed to clarify the characteristics of hypermutator in digestive organs in the therapeutic aspects.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1756 UNBIASED ANALYSIS OF REGULATION OF TRANSCRIPTION FACTORS UPON ER STRESS IN THE LS174T COLORECTAL CANCER CELL LINE EXPLORES CTBP2 AS A POTENTIAL REGULATOR OF STEMNESS
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Introduction: In the intestinal epithelium, stem cells are located at the bottom of the crypt and their maintenance and differentiation is essential for sufficient cell maintenance using a transcriptomics approach. On thapsigargin treated LS174T cells, a cell line with a transcriptomic profile resembling intestinal stem cells, we performed a TF DNA-binding assay (catTFRE) in which TFs present in the cell are bound to plasmid DNA, co-extracted and quantified using mass-spectrometry. We confirmed downregulation using immunoblot in colorectal cancer cell lines. Additionally, we examined CtBP2 expression in colorectal cancer cell lines. Additionally, we examined CtBP2 expression in colorectal cancer cell lines.

Methods: The aim of this study is to analyze the incidence and characteristics of hypermutator in digestive system cancers. We analyzed somatic mutation in digestive system cancers in 1145 cases (age: 67.4±11.3 yrs., M:F=755:390), those underwent surgery after full informed consent during 2014 to 2015. Genomewide sequencing was performed on 47 inherited cancer-associated genes and 411 cancer-associated genes using next generation sequencer (Iontorrent. Precise trimmer, Alientrimmer dk). We confirmed hypermutator by DNA sequencing and microarray analysis.

Results: The 1145 subjects included 583 colorectal cancers (CRC), 229 gastric cancers (GC), 103 metastatic liver tumors, 100 hepatocellular carcinomas (HCC), 45 pancreatic cancer, 23 GISTs, 15 esophageal cancers, and 411 cancer-associated genes using next generation sequencer.

Conclusion: Hypermutator was recognized in 5–10% of digestive system cancers, associated with a somatic mutation of mismatch repair genes. Further research is needed to clarify the characteristics of hypermutator in digestive organs in the therapeutic aspects.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1757 MICROBIOTA A NEW INDICATOR OF COLORECTAL CANCER (CRC) HETEROGENEITY
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Introduction: Location and somatic gene signature of CRCs may impact prognosis and thereby response. A relative specific CRC-related dysbiosis has been characterized.

Aims & Methods: The aim was to characterize colon microbiota in CRC patients regarding location, gene markers and outcome. Patients (N = 173) signed consent for stool DNA (metagenome shotgun sequencing on Illumina HiSeq (2014) analysis of stool DNA: 72 CRC (53 sporadic-S, 19 Lynch-L), 87 asymptomatic subjects (normal colonoscopy), 14 first degree healthy relatives from Lynch families. "MOCA1" pipeline was used, library sorted (Pherd quality score 20 Alignment score > 40). After extraction of < 5% of human genes or phage sequences. Quality sequences were aligned (REFMG v.0.1) and most abundant genes constructed (MBMA program v.0.1). The Shuman program (shuman.c3bi.pasteur.fr) was used. The number of bacteria was estimated (REFMG program). The linear model (GLM) was implemented in the DESeq2 R kit. Differences between Control (N = 87) and CRCs (N = 69), between L (N = 19) and S CRCs(N = 50), and between LCRCC (N = 19) and Healthy Lynch relatives were obtained after interaction of age, BMI and gender was considered (GLM model). The p < 0.1 value was retained as a cut-off (Benjamini and Hochberg).

Results: There was no difference for gender, age (p = 0.08) and BMI (p = 0.187) in the L and S CRCs. Significant differences were observed between Normal and CRCs, C-CRC and L-CRC, L-CRC and first degree relatives based on the common component (similarity of sequences); 13 species differentiated Normal and CRCs and two were more prevalent in L-CRCs. The panels of bacteria linked with location, MSI, Ras mutations, methylation phenotypes and survival were identified. No significant link was observed with TNM Staging (I (N = 17, 2L and 15S), II (N = 12, 5L and 7B), III (N = 20, 10L, 10B), IV (N = 22.1L, 21S). DFS might be dysbiosis dependent.

Conclusion: CRC dysbiosis is location-dependent. Several bacteria are associated with Ras mutation, MSI, and methylation status. They may directly or through epigenetic changes impact the prognosis. Microbiota signature should be taken in consideration in trials.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

P1758 EPIGENETIC SILENCING OF SMOC1 IS ASSOCIATED WITH DEVELOPMENT OF COLORECTAL TRADITIONAL SERRATED ADENOMAS
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Introduction: Colorectal serrated lesions (SLS) include hyperplastic polyp (HP), traditional serrated adenoma (TSA) and sessile serrated adenoma (SSA/p). SSA/Ps are well-known precursors of colorectal cancer (CRC) characterized by BRAF mutation and microsatellite instability (MSI), whereas the molecular characteristics of TSAs are not fully understood.

Methods: The aim of this study is to analyze the incidence and characteristics of hypermutator in digestive system cancers. We analyzed somatic mutation in digestive system cancers in 1145 cases (age: 67.4±11.3 yrs., M:F=755:390), those underwent surgery after full informed consent during 2014 to 2015. Genomewide sequencing was performed on 47 inherited cancer-associated genes and 411 cancer-associated genes using next generation sequencer (Iontorrent. Precise trimmer, Alientrimmer dk). We confirmed hypermutator by DNA sequencing and microarray analysis.

Results: The 1145 subjects included 583 colorectal cancers (CRC), 229 gastric cancers (GC), 103 metastatic liver tumors, 100 hepatocellular carcinomas (HCC), 45 pancreatic cancer, 23 GISTs, 15 esophageal cancers, and 411 cancer-associated genes using next generation sequencer.

Conclusion: Using an unbiased transcriptomics approach we identified transcription factors that are lost on protein level upon ER stress. Furthermore, our data suggests that the significant loss of the transcriptional regulator CtBP2 contributes to intestinal epithelial stem cell differentiation.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
Aims & Methods: We aimed to identify epigenetic alterations associated with the development of TSAs and to clarify the associations between clinical, pathological and molecular characteristics in colorectal lesions. The genome-wide DNA methylation status in TSAs consisting of protruding and flat components was identified. The significance of identified genes and CIMP markers (MINT1, -2, -12, -31, p16 and MLH1) and BRAF/KRAS mutations were analyzed in 847 colorectal lesions and 61 samples of normal colonic tissue. Effects of ectopic expression on CRC cell growth in a preclinical setting in TSA were identified. Methylation of CDK4, SMOC1 and CIMP markers in TSAs and SSA, but significantly downregulated in TSAs. Immunohistochemical analysis showed that CDK4 was expressed in normal colon and SSA/Ps, but is significantly downregulated in TSAs. Analysis of colorectal lesions revealed that SMOC1 is strongly associated with CIMP methylation and CIMP-low.

Conclusion: Methylation of SMOC1 is associated with CIMP-low development but is rarely observed in SSA/Ps. Immunohistochemical analysis of SMOC1 may be a useful marker to discriminate between SSA/Ps and TSAs. Our data suggests SMOC1 methylation may play a role in the neoplastic pathways arising in TSAs.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1759 DEVELOPMENT AND VALIDATION OF PREDICTIVE MODEL FOR PARTICIPATION IN COLORECTAL CANCER SCREENING IN KOREA

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Introduction: The number of individuals partaking in colorectal cancer (CRC) screening still remains to be low even after the implementation of the Korean Government’s National Cancer Screening Program for CRC. The aim of this study is to identify factors associated with partaking in CRC.

Aims & Methods: The Korean National Health and Nutrition Examination Survey (KNHANES) 2007 ~ 2010 datasets were used to develop a CRC screening participation screening score. 10,577 individuals aged ≥50 who completed the survey and not previously diagnosed with CRC were selected. Both logistic regression (LR) analysis and artificial neural network (ANN) were used to develop predictive models. Multilayer perception ANN was constructed based on 16 clinical variables. We then validated the models using the KNHANES 2011 and 2012 (n = 9956) datasets and compared them with each other.

Results: Out of 10,527 individuals selected, 57.0% (n = 6003) responded unscreened for CRC. Among various demographic and socioeconomic factors, including age, gender and education, level, private health insurance, self-reported depression, self-reported health status, and residence were found to be independently associated with CRC screening participation. LR analysis produced screening score (range 0–10.3), and a cutoff point of ≥5.5 defined 49% as unscreened for CRC and yielded area under the curve (AUC) of 0.626. When validated with KNHANES 2011 and 2012 datasets, the AUC of the defined LR model was 0.663, meanwhile the AUC of ANN based predictive model was 0.743.

Conclusion: The ANN produced better performing model than LR analysis based model in identifying population with low CRC screening participation. Sensible approaches should be implemented to encourage partaking in CRC screening in the identified individuals.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1760 CD24 PREDICTIVE LEVELS- A SIMPLE NOVEL BLOOD TEST FOR EARLY DETECTION OF COLORECTAL CANCER

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Introduction: Background: CD24, a mucin-like cell surface molecule, highly expressed in solid tumors and hematological malignancies (HM) (Gastro 2006, Clin Can Res 2007, Can Res 2008). nLab was found to inhibit the growth CD24 cancer cells (Gastro 2009). We have shown that a simple non-invasive blood test evaluating CD24 levels on PBL had good sensitivity and specificity for detecting colorectal neoplasia in subjects undergoing screening colonoscopy (Kraus et al., 2009).

Aims & Methods: We aimed to improve a simple, noninvasive blood test that can efficiently identify individuals with different types of cancer. Blood was taken from patients with various malignancies (CRC, Pancreatic Cancer (PC), gastric cancer (GC), sarcoma and HM), that was confirmed by histology. Age, gender and ethnich matched healthy individuals served as controls. Hemoglobin and hematocrit were measured. They underwent a thorough and extensive workout at the Integrated Cancer prevention center at Tel Aviv Medical Center (Eur J Intern Med. 2013) All samples were collected and processed identically. For each sample, 20,000 leukocytes were analyzed by flow cytomtery. An internal template data has been generated using gates within the software to create a hierarchical population tree at the beginning of the screen. All additional analyses were accomplished after data acquisition have been completed. The template file include compensation adjustment, which is uniformly applied to all the data collected in order to minimize fluorescence overlap among detection channels.

Results: The novel assay was improved significantly, distinguished healthy from CRC (Fig.1a) (P < 0.013), PC (Fig.1b) (P < 0.018), biliary tract (P < 0.45E-12), HM (Fig.1c) (P < 0.013), Brain (Fig.1d) (P < 0.013), MDS (P < 0.1) and Lymphoma (P < 2E-07) patients. CD24 expression levels were higher by up to 25% in cancer cases as compared to normal subjects. The sensitivity and specificity for CRC were 72.4% and 77.4%, and for PC 70.6% and 75.9%, respectively.

The positive (PPV) and negative predictive (NPV) values of CD24 for the detection of CRC was 38% and 94.8%, and for PC 17.1% and 97.3%, respectively. Specificity and sensitivity for HM were also statistically significant (data not shown). The CD24 test could not discriminate between patients with cervical, stomach and lung cancers and healthy subjects.

Conclusion: Conclusions: CD24 expression in PBLs is a promising blood test for the early detection of CRC. PC and HM.

Disclosure of Interest: N. Arber: Bayer Bio-view Gi-View Micro-medico Check-cap
All other authors have declared no conflicts of interest.

P1761 FACTORS ASSOCIATED WITH OPTIMIZING PREPARATION FOR COLONOSCOPY USING SPLIT DOSE PICOLAX

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Introduction: Colonoscopy is considered the gold standard for prevention and early detection of colorectal cancer (CRC), however its effectiveness is directly related to quality of bowel preparation. Two of the quality measures of colonoscopy,ecal intubation rate and adenoma detection rate, are both associated with adequate bowel preparation. Data on factors associated with quality of preparation using Picolax® are limited.

Aims & Methods: We aimed to evaluate factors associated with a good bowel preparation using Picolax® (Sodium picosulfate/magnesium citrate) in the Israeli heterogeneous population. Consecutive outpatients referred for colonoscopy were prospectively assessed by a nurse practitioner filling out a questionnaire. Hemoglobin, thyroid function test, drinking behavior during the course of preparation using gates within the software to create a hierarchical population tree at the beginning of the screen. All additional analyses were accomplished after data acquisition have been completed. The template file include compensation adjustment, which is uniformly applied to all the data collected in order to minimize fluorescence overlap among detection channels.

Results: The number of individuals partaking in colorectal cancer (CRC) screening still remains to be low even after the implementation of the Korean Government’s National Cancer Screening Program for CRC. The aim of this study is to identify factors associated with partaking in CRC.

Aims & Methods: The Korean National Health and Nutrition Examination Survey (KNHANES) 2007 ~ 2010 datasets were used to develop a CRC screening participation screening score. 10,577 individuals aged ≥50 who completed the survey and not previously diagnosed with CRC were selected. Both logistic regression (LR) analysis and artificial neural network (ANN) were used to develop predictive models. Multilayer perception ANN was constructed based on 16 clinical variables. We then validated the models using the KNHANES 2011 and 2012 (n = 9956) datasets and compared them with each other.

Results: Out of 10,527 individuals selected, 57.0% (n = 6003) responded unscreened for CRC. Among various demographic and socioeconomic factors, including age, gender, ethnicity, including age, gender, ethnicity, and education, level, private health insurance, self-reported depression, self-reported health status, and residence were found to be independently associated with CRC screening participation. LR analysis produced screening score (range 0–10.3), and a cutoff point of ≥5.5 defined 49% as unscreened for CRC and yielded area under the curve (AUC) of 0.626. When validated with KNHANES 2011 and 2012 datasets, the AUC of the defined LR model was 0.663, meanwhile the AUC of ANN based predictive model was 0.743.

Conclusion: The ANN produced better performing model than LR analysis based model in identifying population with low CRC screening participation. Sensible approaches should be implemented to encourage partaking in CRC screening in the identified individuals.

Disclosure of Interest: All authors have declared no conflicts of interest.
Conclusion: Diabetics require a more intense bowel preparation aided by Bisacodyl which helps others. Those without both doses of bisacodyl 8 hours and preparation should end no later than 8 hours prior to colonoscopy. Patients should be instructed to drink a minimum of 8 glasses of water with each dose of picolax.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1762 IMPROVED ADENOMA DETECTION WITH ELUXEO LINKED COLOR IMAGING (LCI) AS COMPARED TO CONVENTIONAL WHITE-LIGHT HIGH-DEFINITION COLONOSCOPY–A RANDOMIZED CONTROLLED TRIAL

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Introduction: Colonoscopy is the gold standard method of colorectal cancer and polyp screening, but polyps are missed during a colonoscopic examination at a rate that varies from 6% to 27%. Improved adenoma detection rates can be achieved with optimized endoscopic visualization methods. A recently developed new Fujinon endoscope system, Eluxeo carries a new function of electronic chromoendoscopy, Linked Color Imaging (LCI), that enhances the coloring and visualization of membranes and is in high contrast which are difficult to see with the conventional endoscopes. In our prospective randomized study, we evaluated the effectiveness of LCI, a new endoscopic visualization technique that may enhance image quality to improve colonic adenoma detection.

Aims & Methods: Up till now 247 eligible patients, older than 54 years, admitted for screening outpatient colonoscopy were randomly enrolled to undergo high-definition white-light colonoscopy (WLC) or LCI colonoscopy during instrument withdrawal. The colonoscopic procedures were performed by three experienced endoscopists using the 7000 processor with the conventional high-definition Fujinon EC 590z or a new EC 760z VS Eluxeo colonoscope. All of the colonoscopic procedures were made under Propofol deep sedation guided by an anesthesiologist team. The minimum withdrawal time was defined as more than 6 minutes. All colonoscopies were routinely assisted with pure CO2 insufflation. The primary outcome parameter of our study was to assess and compare the polyp and adenoma detection rate with the two endoscopic techniques.

Results: A total of 247 patients were randomized (mean age 58.7 years), 101 patients enrolled in the WLC group and 146 patients in the LCI group. No significant differences have been observed in the patient demographics and colonoscopy withdrawal time between the two groups. Patients having both colorectal polyps and adenomas were detected more frequently in the LCI group than in the control group: 60.9% and 43.8% versus 55.4% and 33.6% respectively, however, this was not statistically significant (p = 0.32 and 0.16). In contrast, the total number of adenomas relative to the total number of polyps detected with LCI withdrawal were significantly higher than with conventional WLC: 105 vs. 124 adenomas, respectively (p < 0.0005).

Conclusion: The LCI enhancement of the Fujinon Eluxeo colonoscopy system was superior to the conventional HD-WLC in detecting patients with colonic adenomas, which was mainly due to the ability of the more sensitive detection of minute (less than 5 mm) adenomas.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1763 COMPREHENSIVE ANALYSIS OF LONG NON-CODING RNAs WITH CHARACTERISTIC EXPRESSION LEVEL ALTERATION IN COLORECTAL ADENOMAS AND CANCERS

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Introduction: Long non-coding RNAs (lncRNAs) play role in colorectal cancer (CRC) development, however, lncRNA expression profile in CRC and its relation to the epigenetic regulatory system still remain incomplete.

Aims & Methods: We aimed the perform whole genomic lncRNA expression profiling and the analysis of underlying functional interactions of aberrantly expressed lncRNAs. lncRNA expression levels were analyzed on 60 colonic biopsy samples (20 CRCs, 20 adenomas, 20 normals) by Human Transcriptome Microarray (HTA) 2.0. Expression alteration of certain candidates was verified by qPCR. Furthermore, in silico validation was performed on HGU133 Plus 2.0 array data and also on TCGA COAD dataset. miRNA targets prediction was performed on miRcode algorithm and miRNA expression was analyzed on miRnome 3.0 Arachnoid exacrine lncRNA-miRNA coexpression pattern analysis was also performed.

Results: According to HTA results in adenomas 12 lncRNAs (e.g. LIN00278) were upregulated and 6 lncRNAs (e.g. RP11.749D18.1) were downregulated compared to normals, while in CRCs 1 lncRNA (UCAI) was overexpressed and 8 lncRNAs (e.g. LIN00350) were underexpressed compared to adenomas (p < 0.05; `-2 ≤ Fc ≤ 2). In CRC samples 8 lncRNAs (e.g. AC123023.1) were overexpressed and 9 lncRNAs (e.g. RP13-497K6.1) were downregulated compared to normals. 42% of lncRNAs upregulated in CRC samples showed transcriptional regulation in adenomas (p < 0.05; `-0.6 ≤ Fc ≤ 2), while 42% of lncRNAs (p < 0.05; `-2 ≤ Fc ≤ 2) in adenomas were upregulated. In CRC samples 32 lncRNAs were downregulated (LIN01133). In line with aberrant expression of certain lncRNAs in tumors, miRNA and mRNA targets expression showed systematic alterations, e.g. UCA1 upregulation in CRC samples in parallel with miR-1 downregulation accompanied by CMET target mRNA overexpression (p < 0.05).

Conclusion: The defined lncRNA sets (e.g. UCAT1, UCA1) may have a regulatory role in adenoma and CRC development and in tumor cell growth pathways. A subset of CRC-associated lncRNAs showed significant differential expression in colorectal adenomas, which raise the possibility to develop potential adenoma specific markers and achieve early detection of colon lesions.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1764 AI-ANTITRYPSIN (SERPIN-A1) AS A PUTATIVE BIOMARKER FOR COLORECTAL CANCER

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Introduction: Serine protease inhibitors (Serpins) play an important role in the regulation of proteolytic cascades of different tissues. KLK14, acting via PAR-2, represents an auto- crine/paracrine regulator of colon tumorigenesis and alpha1-antitrypsin is a natural inhibitor of KLK14. Therefore its role in regulating the proteolytic cascade in colorectal tumorigenesis is of great importance.

Aims & Methods: The aim of this study was to analyze AI-antitrypsin (AAT) expression in tissue samples at different stages in the process of colorectal cancer development. We examined a total of 245 colon samples. Of those, there were 101 colorectal carcinoma tissues, for 70 of which paired normal mucosa was also examined. A total of 74 colorectal adenomas were examined. Quantitative real time PCR was used to measure AAT expression. Clinical evaluation of AAT levels was demonstrated in terms of disease-free survival (DFS) and overall survival (OS).

Results: Alpha-antitrypsin expression was found to be significantly associated with shorter disease-free survival stage (p = 0.028). On contrary, proportional hazard regression model using univariate analysis revealed that high status alpha-antitrypsin expression is a significant factor for disease-free survival (DFS) (p = 0.002) and overall survival (OS) (p = 0.026) in patients with colorectal cancer. Kaplan-Meier survival curves demonstrated that low alpha-antitrypsin expression is significantly associated with longer DFS (p = 0.001) as well as OS (p = 0.021).

Conclusion: Our data suggests that alpha-antitrypsin expression could be considered as a potential biomarker of unfavorable prognosis for colorectal cancer.

Disclosure of Interest: All authors have declared no conflicts of interest.

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P1765 DIFFERENTIATION BETWEEN NEoplastIC AND NON-neoplastIC DIMINUTIVE COLORECTAL POLyps WITH FUJINON ELUXEO-BLI VS RICc ELECTRONIC CHROMOENDoSCOPY–A RANDOMIZED PROspective STUDY

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Introduction: Real-time differentiation between neoplastic and non-neoplastic colorectal lesions may be crucial during colonoscopy. While adenomas are
neoplastic, and therefore should be resected, hyperplastic polyposis never turn malignant and do not require specific endoscopic therapy. The aim of our prospective, randomized study was to distinguish subcentimeter hyperplastic and adenomatous polyps based on Fujinon FICE versus Eluxeo BLI electronic chromoendoscopic technology with high-definition colonoscopy with and without optical zoom magnification.

Aims & Methods: In order to create a digital and visual picture library of polyps, patients undergoing screening or diagnostic colonoscopy were considered for inclusion. Patients with at least one histologically verified <10mm polyp were included. A short (20sec) video-clips and at least one still picture of each polyp without and with 50x optical zoom at standard white-light (WLI), and with FICE-light or BLI-light were recorded with Fujinon EC 590Z and EC760Z endoscopes and stored in an anonymized database. Once the video-library was completed each of our 5 colonoscopic experts (ML, SLM, OL, DZS, and SZA) independently and randomly reviewed all of the cases with a standardized electronic questionnaire. In each case, all of the observers had to assess the color, the vascularization and the surface of the polyps, and the pit pattern was also assessed. A Kudo classification system was used to assign polyps to one of five groups: 1) Type I (non-neoplastic polyp), 2) Type II (adenomatous polyp), 3) Type III (adenocarcinoma), 4) Type IV (metastatic tumor), and 5) Type V (other). The sensitivity, specificity and accuracy of EC-V1 for diagnosis of hyperplastic polyp were 88.9%, 98.5% and 97.7%, respectively. As regards the sensitivity, specificity and accuracy of EC-V3 for diagnosis of SMm cancer without vessel permeation does not metastasize. In contrast, SMm lesions show a substantial proportion (i.e. methylen blue dye) is always required. Since dye staining complicates the procedure, the new observation method without use of dye has been strongly desired. On the other hand, EC with NBI (EC-NBI) allows ultra-magnified microvessels observation without using any dye solution.

Aims & Methods: The aim of this study was to validate the evidence whether the observation of surface microvessels using EC-NBI was useful in predicting the histopathology of colorectal lesions. The study included 438 patients who underwent complete colonoscopy and endoscopic or surgical treatment between April 2006 and June 2015. A total of 576 lesions (45 Non-neoplastic polyps, 304 adenomas, 71 intramucosal cancer, 21 slightly invasive submucosal cancer (SMs) and 135 massively invasive submucosal cancer) were retrospectively evaluated. We used the Kudo classification for the degree of submucosal invasion and classified cancers accordingly. SMs cancer without vessel permeation does not metastasize. In contrast, SMm lesions show a substantial proportion (~10%) of lymph node metastases. We named the ultra-magnified microvessels findings as endoscopic vascular pattern (EVP) and pattern classified into the following 3 groups: EVP-1, the surface microvessels were very fine obscure; EVP-2, the surface microvessels were more clearly shown and showed a regular vessel network, and their caliber and arrangement were uniform; and EVP-3, the surface microvessels were thick, and their caliber and arrangement were not homogenous. Results: The sensitivity, specificity and accuracy of EVP-3 for diagnosis of hyperplastic polyp were 88.9%, 98.5% and 97.7%, respectively. As regards the sensitivity, specificity and accuracy of EVP-3 for diagnosis of SMm were 82.2%, 98.0% and 94.3%, respectively.

Conclusion: Endoscopic vascular pattern was helpful in predicting the histopathology of colorectal lesions.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

P1767 CONSIDERATION OF RECTAL NEUROENDOCRINE TUMOR (NET) IN OUR HOSPITAL
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Introduction: Rectal NETs are recommended to undergo endoscopic therapy, those with a tumour diameter of ≤10mm and up to the deep submucosal layer. However, no clear guideline has been established on the radical criteria and additional resection. Prognosis of the disease is also unclear. The validity of the diagnosis and treatment recommended in the guideline for rectal NETs will be examined in the cases treated at our hospital.

Aims & Methods: We examined the macroscopic features, pathological features, treatment methods, and prognosis of 22 patients diagnosed as having a rectal NET and treated at our hospital between 2007 and May 2016.

Results: The mean age of the patients was 65.2 years (range, 49–88 years); male-to-female ratio, 15:7; diagnosis opportunity, 21 asymptomatic cases and 1

and/or investigation. While miss rates for endoscopic and imaging modalities were low, 19% of missed cancer diagnosis were due to lack of appropriate investigations following outpatient or inpatient review for colorectal alarm symptoms or IDA; this might be improved by increasing specialist inpatient in-reach services and senior review of outpatient cases.

Disclosure of Interest: All authors have declared no conflicts of interest.

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P1767 ENDOCYTOSCOPIC VASCULAR PATTERN FOR COLORECTAL LESION IS HELPFUL IN PREDICTING PATHOLOGICAL DIAGNOSIS
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Introduction: Till now, narrow-band imaging (NBI) could make it possible to analyze the surface microvessels of colorectal lesions for differentiating neoplasms from non-neoplasms and for predicting the histopathological diagnosis. The electronic chromoendoscopy (EC) is the next generation of ultramagnification endoscopy that allow visualization of the glandular structure and cellular atypia. EC has visualized living tumor cells in vivo and obtained an ultra-magnification pathological image simply by applying the scope to the target mucosa during an endoscopic examination. However, in colorectal Villous adenoma and right-sided colorectal cancer.


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Introduction: Colorectal cancer (CRC) is the 4th commonest cancer in the UK but the diagnosis is often delayed until new symptoms appeared for development of bowel cancer screening. However not all patients are eligible for this. Furthermore, colorectal investigations have the potential to miss the diagnosis and this was regarded as gold standard. The overall accuracy with WLI versus FICE versus BLI technology of the 5 experts without zoom and with 50x optical zoom to differentiate between hyperplastic and adenomatous lesions was 77.62% and 84.31%, vs. 74.58% and 83.90% vs. 88.84%, respectively. There was an excellent correlation between the histopathological results and our Kudo classification with both FICE and BLI technology. Both 50x times optical zoom and BLI technology were independently and significantly improved our confidence rate that was associated with a more precise histological prediction as compared to non-zoom, WLI or FICE endoscopic polyp assessment.

Conclusion: The new electronic chromooendoscopic technology with Eluxeo BLI significantly improved the reliability of the prediction, and supported for colorectal investigations in the diagnosis of non-neoplastic polyps with Eluxeo BLI electronic chromoendoscopy provide a potential for real-time endoscopic diagnosis of hyperplastic polyps to support ressect and discharge strategy. (Study was supported by ECT grant GINOP 2.1.1.-15-2015-00128)

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

P1766 HOW FREQUENTLY DO SECONDARY CARE CLINICIANS MISS COLORECTAL CANCER?
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Introduction: The aim of this study was to validate the evidence whether the observation of surface microvessels using EC-NBI was useful in predicting the histopathology of colorectal lesions. The study included 438 patients who underwent complete colonoscopy and endoscopic or surgical treatment between April 2006 and June 2015. A total of 576 lesions (45 Non-neoplastic polyps, 304 adenomas, 71 intramucosal cancer, 21 slightly invasive submucosal cancer (SMs) and 135 massively invasive submucosal cancer) were retrospectively evaluated. We used the Kudo classification for the degree of submucosal invasion and classified cancers accordingly. SMs cancer without vessel permeation does not metastasize. In contrast, SMm lesions show a substantial proportion (~10%) of lymph node metastases. We named the ultra-magnified microvessels findings as endoscopic vascular pattern (EVP) and pattern classified into the following 3 groups: EVP-1, the surface microvessels were very fine obscure; EVP-2, the surface microvessels were more clearly shown and showed a regular vessel network, and their caliber and arrangement were uniform; and EVP-3, the surface microvessels were thick, and their caliber and arrangement were not homogenous.

Results: The sensitivity, specificity and accuracy of EVP-3 for diagnosis of hyperplastic polyp were 88.9%, 98.5% and 97.7%, respectively. As regards the sensitivity, specificity and accuracy of EVP-3 for diagnosis of SMm were 82.2%, 98.0% and 94.3%, respectively.

Conclusion: Endoscopic vascular pattern was helpful in predicting the histopathology of colorectal lesions.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference
symptomatic condition (lumbago); lesion site (Rs/Ra/Rb); 1/2/19 cases; mean tumor size: presence of biopsy sample; biopsy grade; I/II/III/IV cases; 11/14 (78.5%); presence:absence of endoscopic ultrasonography, 11/11 cases; and M3/M4/M5, 1/1/91 cases. The TNM classification of the cases was as follows: T1a, 16 cases; T1b, 5 cases; T2, 1 case; N1, 1 case; and M1, 1 case. The treatment was determined by the protocol of the endoscopic resection group/endoscopic mucosal resection with ligation/endoscopic mucosal resection/endoscopic submucosal dissection/surgery/drug therapy in 5/7/2/1/1 case. Of 19 endoscopic treatment cases, 15 corresponded to a tumor diameter of ≤10 mm, with negative resection margin and vascular invasion as criteria for curative resection, and 3 cases of unknown stumps were recognised. In the EMRL group, all cases were negative. In all the cases except the case of other-disease death, it elapsed without recurrence. Both surgical cases showed a positive vascular invasion, and one case was a confirmed N1, but neither of the patients survived without a relapse. In the case with hepatic and bone metastases, medication was administered, and the effect was temporarily effective, but the patient died a year and a half later.

Conclusion: Endoscopic treatments are considered appropriate for rectal NETs with a tumor diameter ≤10 mm, using fluorescence endoscopic technique, with minimal metastases, and not >10 mm in diameter. Among the treatment options, EMRL is considered useful and well tolerated. However, follow-up observation and case accumulation seem necessary to determine the long-term prognosis in NET, which may recur after years.

Disclosure of Interest: All authors have declared no conflicts of interest.

**References**


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**P1769** SELECTIVE ERADICATION OF K-RAS MUTATED CANCER CELLS BY DELIVERY OF BACTERIAL TOXINS

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Introduction: Inactivation of TP53 is the most frequent genetic damage in human cancer. In addition, hyperactivation of the RAS pathway is common in many human malignancies (Lung (LC)~40%, pancreatic (PC)>95%) and colorectal cancer (CRC)~50%). Despite multiple attempts, targeting these pathways for the treatment of cancer, for example through the development of RAS pathway inhibitors has not proven to be effective thus far. Herein, we propose to exploit the hyperactive RAS pathway and TP53 mutation status of human cancer to deliver targeted antimodeler therapy. We previously reported that a recombinant adeno virus, carrying a pro-apoptotic gene (PUMA) under the regulation of c/EBPδ (PY4) was effective in killing cancer cells expressing the hyperactive RAS cells harboring hyperactive RAS (Giladi et al., 2007). Furthermore, we had shown, both in vitro and in vivo, that replacing the pro-apoptotic gene with a bacterial toxin can improve the efficacy of this system (Shapira et al., 2015).

Aims & Methods: We aimed to establish a tight regulated dual system by expressing a toxin under PY4 elements in cancer cells, while sparing normal cells by expressing the anti-toxin under p53 responsive elements (RGC) specifically in non-malignant cells. Adenoviral vectors carrying the toxin (PY4-MaxF-mcherry) and an anti-toxin (RGC-mCherry) were cloned into an E1/E3 human type5 adenoviral vector. Virus particles were produced in 293E cells and purified by the End Point Dilution Assay and their potency was tested in vitro. Cell death was measured qualitatively by using the fluorescent microscopy and was quantified by the enzymatic MTT assay. Human colorectal, pancreatic, lung and triple negative breast cancer cell lines engineered and fused to the lentivirus envelope. Cell death was measured qualitatively by using the fluorescent microscopy and was quantified by the enzymatic MTT assay. Human colorectal, pancreatic, lung and triple negative breast cancer cell lines harboring mutated Ras. Those three constructs were cloned into a ''first generation'' lentivirus (LV) and pseudotyped with the lentivirus envelope. The anti-CD24 antibody fragment has a high affinity and specificity toward CD24, allowing targeted precision of viral transduction (Figure 1). These Lentivirus particles contain DNA molecules with flanked LTRs allowing their integration into the CD24 expressing target cells DNA and formation of double-strand breaks due to the action of the integrase enzyme whose activity was stimulated by the IN derived peptides. Massive cell death was induced upon exposure of the infected cells to the IN peptide compared to the control peptide.

Conclusion: The use of IN derived peptides together with the CD24-targeted lentiviruses approach suggests a novel strategy to specifically promote death of CD24-expressing cancer cells.


All authors have declared no conflicts of interest.

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**P1771** ILF3 STABILIZES AND ACTIVATES EGFR-MEDIATED G9A PATHWAY FOR MAINTAINING CANCER STEMNESS PROPERTY IN EGFR-POSITIVE CANCERS

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Introduction: A specific inhibitor of interleukin enhancer binding factor 3 (ILF3), YM155, suppresses EGFR phosphorylation and signal transduction involving in the formation of cancer stemness tumourospheres in vitro, suggesting that ILF3 as an oncogene participates in the maintaining of cancer stem cell property through stabilizing EGFR-mediated stemness pathway. Since cancer stemness cells is the leading reason for tumor recurrence in the tumor repressive treatments, and EGFR enhances the formation of cancer stemness, it is worthy of investigating the function of ILF3 for maintaining the cancer stemness property in the EGFR-positive cancers.

Aims & Methods: The tumourspheres derived from EGFR-wild-type and KRAS-mutant colorectal HCT116 and lung A549 cells expressing higher cancer stemness markers, CD133, were used as cancer stemness models in this study. YM155 was utilized to test the putative growth inhibiting involving in the formation of tumourospheres as the cancer stemness markers. Meanwhile, the differentiating stemness markers were also compared between ILF3-knockdowned and the control shLuc cells. Then, the protein level and phosphorylation of EGFR were investigated in the YM155-treated and ILF3-knockdowned cells. The results showed that EGFR was regulated and stabilized by ILF3. The ILF3-knockdowned cells were also transplanted into SCID mice for evaluating the function of ILF3 in vivo.

Results: We found that higher EGFR autophosphorylation (Y1068) in HCC116- and A549-derived tumourospheres compared to the parental cells. The results of RNAseq evaluated that CD133 was a positive stemness marker, whereas MARCH4 as a negative marker. Knockdown of ILF3 reduced the cell proliferation in the A549 cells in vitro and in vivo, demonstrating that ILF3 was an oncogene involving in cancer cell survival. Moreover, inhibition of ILF3 by YM155 blocked the autophosphorylation of EGFR and inhibited the EGFR-downstream G9a activation, leading to a reduction of stemness property. Moreover, Knockdown of G9a reduced the CD133 expression and increased MARCH4 expression, revealing that G9a was essential for maintaining for cancer stemness property in the EGFR-positive cancers.

Conclusion: In conclusion, this study demonstrated that ILF3 played an important role maintaining the EGFR-mediated stemness pathway in cancer stemness tumourospheres, and that ILF3/stabilized and phosphorylated EGFR to enhance the activation of G9a, leading to increasing CD133 and decrease MARCH4 expressions. Therefore, we suggested that the ILF3 inhibitor, YM155, was potential for utilization in cancer therapy against the EGFR-positive cancers.

Disclosure of Interest: All authors have declared no conflicts of interest.

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**P1770** USE OF A COMBINATION OF LENTIVIRUS PARTICLES AND A SPECIFIC PEPTIDE FOR ERADICATION OF CD24-EXPRESSING

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Introduction: Lentiviral replication is driven by a molecular motor consisting of the reverse transcriptase, protease and integrase (IN). The genomic RNA of the virus is used to produce a copy of viral DNA by reverse transcription, and the integrase catalyses the covalent insertion of this DNA into the chromosomes of the infected cells. Integration of the viral DNA—which is 9 kilobase pairs (kb) long when packaged in retroviral capsids—is random and can result in cellular mutagenesis. Perturbation of the viral integration process could cleavage and ligation resulting in the appearance of double-stranded breaks in the host genome that eventually leads to apoptosis. CD24 is a heavily glycosylated cell-surface GPI-anchored protein. We have previously shown that CD24 is an important player in the multistep process of GI carcinogenesis (Gastro 2006, Clin Can Res 2007, Can Res 2008) as well as in many other human malignancies (Cervical, Bladder, Squamous squamous cell carcinoma, Glioma, Breast etc.).

Aims & Methods: We aimed to develop and specifically direct lentiviruses to eradicate CD24-expressing cancer cells. We hypothesized that selective eradication could be achieved through a combination of cleavage and ligation resulting in the appearance of double-stranded breaks in the host genome that eventually leads to apoptosis. CD24 is a heavily glycosylated cell-surface GPI-anchored protein. We have previously shown that CD24 is an important player in the multistep process of GI carcinogenesis (Gastro 2006, Clin Can Res 2007, Can Res 2008) as well as in many other human malignancies (Cervical, Bladder, Squamous squamous cell carcinoma, Glioma, Breast etc.).

Conclusion: The use of IN derived peptides together with the CD24-targeted lentiviruses approach suggests a novel strategy to specifically promote death of CD24-expressing cancer cells.


All authors have declared no conflicts of interest.

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**References**

P1772 EFFICACY AND SAFETY OF TWELVE CHEMPREVENTIVE REGIMENS FOR THE RECURRENT OF COLORECTAL ADENOMAS: A NETWORK META-ANALYSIS

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Introduction: Although various pharmacological agents have been trialed for recurrent colorectal adenomas, their comparative effectiveness remains unknown. We conducted both direct and indirect comparisons of twelve chemopreventive agents for recurrent colorectal adenomas.

Aims & Methods: MEDLINE, EMBASE, Scopus, Web of Science, and Cochrane Central Register of Controlled Trials, and ClinicalTrials.gov were searched up to May 1, 2016. RCTs were assessed by a random-effects model within a Bayesian framework. Agents for each outcomes were ranked by surface under the cumulative ranking area (SURCA). This study is registered with PROSPERO, number CRD42016041923.

Results: 33 RCTs were eligible, enrolling 44,647 participants treated by twelve regimens: 9 aspirin and other NSAIDs, 11 antioxidants, 4 dietary supplements, 3 calcium, 4 folic acid, 2 calcium plus antioxidants, 2 aspirin plus folic acid and 1 aspirin.

Conclusion: In this network meta-analysis, aspirin was more effective than placebo in both pairwise and network comparisons, these agents include NSAIDs, antioxidants, dietary supplements, calcium as well as folic acid.

Disclosure of Interest: All authors have declared no conflicts of interest.

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Results: The human and mouse CRC cell lines tested displayed varying levels of sensitivity to EPA (IC₅₀ range: 19.1 ± 2.2 μM to 242 ± 2 μM). HT29 cells were sensitive to EPA in CRC cells. Human and mouse CRC cell lines were screened for their sensitivity to EPA by MTT assay in vitro (n = 3). The MC38/MC38r and CT26/MC38r cell lines expressed COX2, indicating that COX2 is required for tumour growth in mice without affecting normal tissue. Oncotarget 7: 7096–7109.

P1774 PROGNOSTIC ROLE OF GLASGOW PROGNOSTIC SCORE IN PATIENTS WITH COLORECTAL CANCER: EVIDENCE FROM COCHRANE DATABASE STUDIES

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Introduction: Colorectal cancer (CRC) is the third most common cancer world wide. The Glasgow Prognostic Score (GPS) is a simple tool that likely influences understanding of the cancer and treatment of patients with CRC. However, GPS was not defined for patients with CRC, who, with its ability to predict survival, could be useful for patients with CRC. The GPS was also widely studied, but the results were controversial.

Aims & Methods: To investigate the correlation between GPS and prognosis of patients with CRC to further clarify its clinical significance. We performed a comprehensive and systematic search of databases and other sources, and we identified six eligible studies. The results of the six studies were similar and consistent, and the inheritability of the GPS was high. The GPS was more useful for predicting survival among patients with CRC.
P175 COST EFFECTIVENESS OF THE FIRST SURVEILLANCE COLONOSCOPY IN POPULATION WITH ADVANCED COLORECTAL POLYPS OR MULTIPLE POLYPS FROM COLORECTAL CANCER SCREENING PROGRAM

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Introduction: The implementation of the CRC screening program has generated an increase in surveillance colonoscopies. However, the intermediate-high risk group that included advanced lesions (size ≥10 mm, villous component or high-grade dysplasia) or the presence of 3 or more polyps, has a low incidence of metachronous risk lesions when performing colonoscopy at 3 years according to the current recommendations. Identifying predictors of metachronous lesions would provide a better risk stratification and improve the efficiency of surveillance programs.

Aims & Methods: We aimed to identify the cost effectiveness of the first surveillance colonoscopy and the predictive factors of metachronous lesions at 3 years in individuals with advanced lesions or ≥3 polyps detected at baseline screening colonoscopy. This was an analysis of all cases with advanced polyps and/or multiplicity from CRC screening program population of Barcelona detected at baseline colonoscopy during the years 2010-2011 and with a performed colonoscopy after 3 years. Epidemiological and clinical data of all individuals were collected as well as the morphological data of all polyps. For the statistical study, a bivariate analysis and logistic regression were performed.

Results: 638 cases were identified, with mean age of 64 years. 342 were men (62.6%). 23.8% required more than one colonoscopy for the complete removal of all the polyps. A complete surveillance colonoscopy at 3 years was performed in 518 cases (82%) with an average surveillance time of 38 months [15-75]. Mean fecal hemoglobin was 440 nmol/g. 51.8% suffered from hypertension, 15% from diabetes mellitus, 46.5% from dyslipidemia and 12.3% from chronic obstructive pulmonary disease. 45.8% of individuals were overweight (BMI ≥25) and 34.7% were obese (BMI ≥30). Surveillance colonoscopy was normal or with low-risk polyps in 420 cases (80.1%); and advanced polyps or multiplicity were identified in 98 cases (18.3%) in 73 advanced adenoma in 59 cases (11.4%), ≥3 adenomas in 62 cases (11%) and ≥3 small adenomas and/or serrated in 71 cases (13.7%). The presence of ≥3 adenomas and/or serrated polyps was the only variable that was associated with increased risk of the diagnosis of advanced adenomatous or serrated lesions in surveillance colonoscopy (p < 0.001).

Conclusion: In individuals with advanced polyps and/or multiplicity the incidence of metachronous risk lesions at 3 years is low. Assessment a quality baseline colonoscopy with complete removal of all the polyps could allow to increase the interval of surveillance, maintaining and ensuring the compliance of the surveillance in 3 years in the cases with multiplicity in the baseline colonoscopy.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P177 POPULATION-BASED COLORECTAL CANCER SCREENING IN THE CZECH REPUBLIC–FIRST RESULTS OF THE NEW PROGRAM SETTINGS

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Introduction: The organized non-population based National Colorectal Cancer (CRC) Screening Program in the Czech Republic has been running since year 2000. In January 2014, the transition to population based setting has been implemented. Currently, the annual immunochromatographic FIT (FIT) is offered at the age 50-54, followed by FIT+ colonoscopy, if positive. In age of 55, there is a choice of either FIT biannually or screening colonoscopy in 10 years’ interval.

Aims & Methods: Main aim was to assess the impact of the first 30 months of the population-based CRC screening program on the target population participation and colorectal neoplasia detection. The data from National Reference Center (health insurance companies database) and Preventive Colonoscopies Registry in years 2013 (non-population based settings) and 2014-2015 (population-based settings) were evaluated and compared.

Results: In year 2014, there were 1,500,897 individuals (53% of all CRC screening target population) invited to FIT or colonoscopy, with 17.3% response. It resulted in the coverage increase by 4.3 percent points in comparison with year 2013 (11% in year 2014). The CRC screening coverage continued in year 2015 with the target population participation at 33.1%. This has influenced the increase of number of detected adenomas (by 42%) and cancers (by 20%) detection in year 2014. In year 2015, all the results remained stable (details resulted in the table).

Disclosure of Interest: All authors have declared no conflicts of interest.

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Introduction: Colorectal Endoscopic Submucosal Dissection (ESD) is recommended for superficial neoplastic lesions at high risk of submucosal invasion. ESD allows an en-bloc resection but ESD experience is still limited in Western centers.

Aims & Methods: The aim of this retrospective study was to evaluate technical and clinical outcomes of colorectal ESD, in a single tertiary European center. We retrospectively analyzed all consecutive patients treated by ESD for colorectal lesion at Humanitas Research Hospital (Milan, Italy) from January 2011 to September 2016. The primary outcomes were technical success, defined as en-bloc resection and clinical success, defined as curative resection (R0) without need for surgery. Secondary study outcomes were complication rate and ade- nona/carcinoma recurrence. Complications were divided in early (<24 hours) and delayed (>24 hours) and included bleeding and perforation. Recurrences were identified as the presence of adenoma or carcinoma at the endoscopic follow-up performed at 6 months, 1, 3 and 5 years. Data were analyzed by STATA 14 statistical software.

Results: A total of 185 lesions in 185 patients (M/F 97/89, mean age 67.6 ± 11.5). Lesions were located in the rectum (64.3%), left colon (9.7%), transverse (11.9%) and cecum (14%). Mean lesion size was 39.3 ± 1.2 mm. A high-grade dysplasia was found in 64 (34.6%), high-grade dysplasia (HGD) in 78 (42.2%) and adenocarcinoma in 42 (22.7%) cases. Only 1 NET (0.5%) was found. En bloc resection was achieved in 88% of lesions. Clinical success (R0) was obtained in 84.8% of lesions. The follow-up was going on in the remaining 28 patients (15.2%) needed surgery for unfavorable histology. A total of 12 complications were reported: 10 early complications (8 perforations and 2 bleeding) and 2 delayed complications (1 bleeding and 1 perforation). All but one adverse events were managed endoscopically. Surgery was required in the only case of delayed perforation. All patients untreated with surgery (n = 156) underwent follow-up evaluation. In particular, all patients had 6 months follow up, 97 patients had 1 y follow-up, 26 patients had 3 y follow-up, 9 patients had 5 y follow-up. Adenoma recurrences were found in 3.8% at 6 months and in 2% at 1 year. We did not find any adenoma recurrence at 3 years and 5 years. No cancer recurrence occurred in the follow-up period.

Conclusion: ESD is a feasible strategy to manage superficial colorectal tumors. This study demonstrates favorable technical and short-term clinical outcome of colorectal ESD, but further studies are needed to confirm the long-term efficacy.

Disclosure of Interest: All authors have declared no conflicts of interest.
P1778 LONG-TERM OUTCOMES OF ENDOSCOPIC SUBMUCOSAL DISSECTION FOR EARLY CANCER AND HIGH GRADE DYSPLASIA IN COLORECTUM

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Introduction: Although endoscopic submucosal dissection (ESD) is a widely accepted treatment for colorectal neoplasm, little is known about large consecutive studies evaluating long-term outcomes of early cancer and high grade dysplasia. We aimed to assess the efficacy and safety of ESD for early cancer and high grade dysplasia in colorectum and evaluated the long-term outcomes, including local recurrence and metastasis.

Aims & Methods: We performed a retrospective analysis of data collected from 514 consecutive patients with 520 colorectal early cancer and high-grade dysplasia treated with ESD between January 2007 and December 2013. Histology and patient data were collected during an average follow-up time of more than 5 years to determine tumor stage and type, resection status, complications, tumor recurrence, and distant metastasis.

Results: The overall rates of en bloc resection, complete resection, R0 resection, major complications were 94.4%, 91.5%, 89.2% and 2.1%, respectively. Large tumors and snare-assisted ESD were independent factors of piecemeal resection. ESD of colorectal tumors increased the risk for complications. During the follow-up period, all patients remained free from metastasis. However, local recurrence occurred in 4 patients (0.8%); large tumors and piecemeal resection were risk factors.

Conclusion: ESD is effective and safe for resection of early cancer and high grade dysplasia in colorectum and long-term outcomes are favorable. ESD is indicated for the treatment of colorectal early cancer and high grade dysplasia to obtain curative resection and prevent the local recurrence.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1779 LOW UPTAKE OF PSYCHOLOGICAL THERAPIES AMONG PATIENTS WITH IRRITABLE BOWEL SYNDROME IN SECONDARY CARE

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Introduction: Patients with irritable bowel syndrome (IBS) often have co-existent mood disorder and psychological illness. Meta-analyses of randomised controlled trials consistently demonstrate that psychological therapies, such as cognitive behavioural therapy (CBT) and hypnotherapy, are effective treatments for IBS. In the UK the National Institute for Health and Care Excellence (NICE) recommends considering the use of these in patients with no response to pharmacological therapies, and for refractory symptoms.

Aims & Methods: We performed a cross-sectional survey to examine willingness of patients with IBS to engage with psychological therapies. We collected complete symptom data from consecutive, unselected referrals to secondary care seen in a specialist IBS clinic. All participants completed the validated Rome IV questionnaire for IBS, the IBS severity scoring system (IBS-SSS), the hospital anxiety and depression scale (HADS) to assess mood, and the patient health questionnaire-12 (PHQ-12) to examine somatof orm-type behaviour. They also provided their opinion on possible treatment options, and were asked to rate medical therapies, dietitian input, psychological therapies, including CBT and hypnotherapy, and an overview of the condition and/or reassurance in order of preference.

Results: Among 93 adults with confirmed IBS (74 (79.6%) female, mean age 36.0 years (range 16 to 77 years), 35 (37.7%) had high levels of anxiety, 22 (23.7%) had high levels of depression, and 23 (24.7%) had severe levels of somatof orm-type behaviour. Despite this, only 10 (10.8%) of 93 patients ranked psychological therapies as their first-choice treatment option. In total, 8.8% of patients with high levels of anxiety ranked psychological therapies as their first-choice treatment option, versus 13.2% without (P = 0.64), 9.5% of those with high levels of depression, versus 12.1% of those without (P = 0.91), and 17.4% of patients with severe somatoform behaviour, versus 9.2% of those without (P = 0.26). Those with severe symptoms according to the IBS-SSS were no more likely to select psychological therapies as their first-choice treatment option than those with milder or moderate symptoms (7.7% versus 21.7%, P = 0.10).

Conclusion: Despite high levels of psychological comorbidity and NICE recommendations, patients with IBS in a specialist clinic were generally reluctant to consider psychological therapies such as CBT or hypnotherapy. Those with anxiety, depression, somatof orm-type behaviour, or severe symptoms were no more willing to consider these therapies than those without.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1780 GUT SYMPTOMS AND TRANSIT DISTURBANCE IN PARKINSON’S DISEASE ARE PAN-ENTERIC BUT NOT UBQUITOUS: A WIRELESS MOTILITY CAPSULE STUDY

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Introduction: Symptoms of gastrointestinal dysfunction are among the most common non-motor complaints in Parkinson’s patients. These may involve muscles from the oropharynx to the anorectum, and the autonomic and enteric nervous systems are often involved, resulting in secondary bowel dysmotility.

Aims & Methods: The objectives of this study were to evaluate a technology measuring the spectrum of gut dysfunction, the Wireless Motility Capsule (WMC), in Parkinson’s disease. We also wanted to correlate transit measures with gastrointestinal symptoms. Fifteen PD patients and 7 controls (table1) were included. PD severity was scored with the modified Hoehn and Yahr (H&Y) staging scale. GI symptom burden was identified by Wexner constipation score and Gastrosparesis Cardinal Symptom Index (GCSI). Acidity, motility and transit data were obtained, as standard, by WMC. All medications affecting pH and motility, including L-dopa, were discontinued for 5 days before and for the duration of the WMC study. Were analyzed data about gastric emptying time (GET), small bowel transit time (SBTT), colonic transit time (CTT) and whole gut transit time(WGTT).

Results: One patient could not swallow the capsule, and of the 14 patients completing the study, 8 reported GI symptoms. Compared to non-symptomatic patients, those with GI symptoms showed significant delayed transit in the stomach, colon and whole gut (table 1). However, small bowel transit did not significantly differ. GI dysfunction was not correlated with H&Y score in this small study, used the risk lower constipation scores were correlated, suggesting a pan-enteric problem in symptomatic individuals. There was a significant correlation between the Wexner constipation score and CTT in all patients (p < 0.01) but not GCSI and GET (p > 0.10). The results of Wireless Motility Capsule did not differ between non-symptomatic PD and controls.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1781 OUTLET DYSFUNCTION IS PREVALENT IN SEVERE FUNCTIONAL BLOATING: PRELIMINARY REPORT FROM A MULTICENTER ITALIAN STUDY

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Introduction: Bloating and abdominal distension are common and bothersome symptoms and a frequent complaint of patients affected by functional gastrointestinal disorders (FGID). Recent studies demonstrated that an impairment in
the handling of gas is a relevant underlining mechanism in FGID patients with bowel gas accumulation who were grouped according to IBS and in patients with bloating. Aims & Methods: Our aim is to study the relationship between the defeation pattern, the severity of bloating and the abdominal girth measurements in FGID patients consulting for bloating as primary complain with/without visible abdominal distension. We designed a prospective, multi-center study of patients with severe abdominal bloating (VAS score ≥ 24 on a 100-mm scale) as primary complain with/without visible abdominal distension. Patients were recruited at 4 gastroenterology outpatient clinics in Italy. Combined dysfuncion tests included Rome III criteria. All patients were prescribed a lactose-free diet supplemented by dietary advice according to the NICE guidelines for two weeks. A belt around the abdomen at standardized sites provided assessment of abdominal girth measurements. During the 2-week run-in period, each patient completed a daily diary log including abdominal bloating and pain/discomfort scores (100-mm VAS), Bristol Stool Form and stool frequency. At randomization visit, all patients filled in a questionnaire on adequate relief of bloating on a Likert scale and a further abdominal bloating 100-mm VAS. An additional subset of patients at standardized sites provided assessment of abdominal girth two hours after a meal. All patients reporting insufficient adequate relief of abdominal bloating at the end of the run-in period underwent a standardized balloon expulsion test (BET) scored as either successful or failed. A straining questionnaire was also administered.

Results: 76 patients (66 female, 39.8 ± 12.2 mean age, 6 IBS-D, 6 IBS-M, 30 IBS-C, 9 IBS-U, 6 FC, 16 FB, 3 FD) completed the 2-week run-in period. A significant negative correlation was found between adequate relief and both bloating and abdominal girth changes (r = -0.53 and -0.52, p < 0.001, respectively). 53/76 (70%) patients reported inadequate relief (worse or no improvement). Among the non-responders the vast majority (68%) failed the BET. Multiple regression analysis showed that BET (successful or failed) and its dependent variable, was significantly related to bloating severity. No relationship was demonstrated for abdominal girth changes, FGID diagnosis and straining questionnaire.

Conclusion: In this prospective, multicenter trial simple diet advise was of benefit in approximately 30% of FGID patients consulting for severe bloating. In the non-responders outlet dysfunction was prevalent and correlated with subjective bloating perception. The study is ongoing, but our data may support bowel retaining as primary treatment option for functional bloating.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P1782 PATHOPHYSIOLOGY ASSESSMENT OF FECAL INCONTINENCE AND RISK FACTORS ASSOCIATED. RESULTS OF A TEN YEARS RETROSPECTIVE STUDY

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Introduction: Faecal Incontinence (FI) is a common and socially disabling condition, more prevalent among females over 50 years old. Detailed anatomical and physiological assessment of each patient is important to determine the correct cause of FI and selection the most appropriate therapy. Conventional and High Resolution (HR) Anorectal Manometry (ARM) is a useful tool to categorize anal and/or rectal dysfunction in addition to provide physiological assessment of both anal sphincters and rectum.

Aims & Methods: To evaluate symptoms and anorectal function of patients affected by FI, we included 358 patients with FI (77% female (F) and 23% men (M), mean age 63 range 22–92 year referring to the outpatient unit of Digestive Pathophysiology of S. Giovanni-Addolorata Hospital, Rome from January 2006 to December 2016. Clinical presentation (history, symptom profile and severity) and anorectal physiological evaluation (digital examination, manometry, rectal sensory testing, balloon evacuation test) were analyzed. The manometric parameters obtained with conventional and HR-ARM were: resting pressure, squeeze pressure, rectal compliance, rectal sensibility and the anorectal pattern during the defecatory maneuvers.

Results: 114 out of 358 patients (32%) reported both FI and difficulty evacuating stool and/or rectal urgency. Among these patients with coexistence UI (47%). Proctological surgery (n = 122, 34%), pelvic surgery (n = 77, 21%) and traumatic anal or vaginal history (n = 144, 40%) were statistically associated with FI (p < 0.05). Normal manometric parameters were found in 16 patients (4%). Manometric alterations observed were: internal anus sphincter (IAS) dysfunction: 228 (64%); isolated external anal sphincter (EAS) dysfunction: 274 (76%); combined sphincter dysfunction IAS and EAS: 198 (55%); isolated dysynergic defecation: 100 (28%); rectal hypersensibility: 130 (36%).

Conclusion: In our study, in accordance with the literature, we observed a female prevalence in FI. FI is significantly associated with previous proctological/pelvic surgery and traumatic anal/vaginal delivery. Furthermore, patients with FI referred difficulty evacuating stools, too. In fact in patients with dysynergic-type constipation, the FI may be confused with an encopresis. Finally we observed these prevalent manometric alterations: combined dysfunction IAS and EAS, and rectal hypersensibility. Manometric findings could help physicians to identify appropriated patients for a biofeedback therapy.

Disclosure of Interest: All authors have declared no conflicts of interest.
Patients who exhibited MAB (confirmed by SeHCAT test) were treated with HLA-DQ8 Haplotype (%) 14.1%(9/64) 6.3%(4/63)
HLA-DQ2 Haplotype (%) 23.8%(15/63) 31.7%(20/63), ingested less lactose than the "No-IBS" group (P = 0.024). Intake of other FODMAPs was similar in both groups (P = 0.346). Compared to the "No-IBS" group, individuals with IBS had a greater likelihood of depression (OR 1.5 (0.97-2.32); p = 0.05), anxiety (2.84(1.44-4.39), p < 0.001), recent life event stress (1.51(1.03-2.20); P = 0.03) or medical and/or surgical co-morbidity (OR 2.90(1.30-5.45), P < 0.001). The IBS group also had lower quality of life (FL-SF) and quality of life (SF-8).

Results: From 1999/2115 (94.7%) members of the community that completed psychiatric disease (HADS), life event stress (LES) and quality of life (SF-8).

Table 1 Continued

<table>
<thead>
<tr>
<th></th>
<th>Positive SeHCAT test</th>
<th>Negative SeHCAT test</th>
</tr>
</thead>
<tbody>
<tr>
<td>HLA-DQ2 Haplotype (%)</td>
<td>23.8% (15/63)</td>
<td>31.7% (20/63)</td>
</tr>
<tr>
<td>HLA-DQ8 Haplotype (%)</td>
<td>14.1% (9/64)</td>
<td>6.3% (4/63)</td>
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</tbody>
</table>

Conclusion: SeHCAT scanning must be considered as a diagnostic tool for the diagnosis of chronic diarrhoea, specially in those patients with long-standing diarrhoea.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
Bohn, L. "Nutrient intake in patients with IBS compared with the general population." Nutr Gastroenterol Motil 2013.
Bohn, L. "Diet low in FODMAPs reduces symptoms of IBS as well as traditional dietary advice: a randomized controlled trial." Gastroenterology 2015.
Van Oudenhove, L. "Depression and Somatization Are Associated With Increased Postprandial Symptoms in IBS Patients." Gastroenterology 2016.

Conclusion: FODMAP intake was similar in IBS and No-IBS groups in the community (lactose intake was lower in IBS subjects, likely due to avoidance of dairy products (Long 2017)). However, as expected, IBS patients in the community had a greater likelihood of psychiatric disease, life event stress and clinical co-morbidity. Joint effects analysis demonstrated that high FODMAP intake alone was not associated with abdominal symptoms; however, IBS was more common in those with a high FODMAP intake and concomitant psychosocial factors known to increase visceral sensitivity to digestive dysfunction (Zhu 2013). (ClinicalTrials: NCT0126597)

Disclosure of Interest: All authors have declared no conflicts of interest.

Table: Joint effects of psychiatric disease, life stress & total FODMAP intake on relative risk of IBS in community

<table>
<thead>
<tr>
<th></th>
<th>No IBS</th>
<th>IBS</th>
<th>No IBS</th>
<th>IBS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Psyche Disease</td>
<td></td>
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<tr>
<td>FODMAP Life Stress</td>
<td></td>
<td></td>
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<tr>
<td>IBS</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Physiological</td>
<td></td>
<td></td>
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<tr>
<td>IBS</td>
<td></td>
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</tbody>
</table>

"Adjusted variables: age, sex, marital status, education, job, income, smoking, drinking, and medical history.

P1784 INTAKE OF FERMENTABLE OLIGO-, DI- AND MONOSACCHARIDES AND POLYOLS (FODMAPS) INCREASES THE RISK OF IRRITABLE BOWEL SYNDROME (IBS) IN INDIVIDUALS EXPOSED TO PSYCHOSOCIAL STRESS IN THE COMMUNITY: RESULTS OF A LARGE, PROSPECTIVE, POPULATION-BASED STUDY


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Introduction: The cause of IBS is uncertain; however, food intolerance shares many features with this condition. Consumption of FODMAPs has been shown to induce IBS-type symptoms (Shepherd 2008) and clinical trials have shown that a low FODMAP diet can improve symptoms in this patient group (Halmos 2014). However, FODMAP intake is not higher in IBS than in health (Bohn 2015) and it is not proven that the outcome of low FODMAP diet is better than standard dietary advice in this condition (Bohn 2015). Recent, experimental research has shown that psychological factors are associated with increased postprandial symptoms in IBS patients (Zhu 2013, Van Oudenhove 2016). This study was designed to assess the relative importance of, and interaction between, psychiatric disease, social stress and diet in the aetiology of IBS in the general community.

Aims & Methods: This population based study tested the hypothesis that high FODMAP intake increases the risk of IBS more in individuals with psychiatric disease and/or life event stress than other members of the community.

Subjects aged 16–74 were randomly selected from five South-Chinese communities. All subjects completed questionnaires by face-to-face inquiry with investigators including demographic information, gastrointestinal symptoms (Rome III), dietary intake (food frequency chart validated in Chinese community), psychosocial (HADS), life event stress (LES) and quality of life (SF-8).

We included 772 patients with IBS (Rome III criteria) who attended a university hospital-based outpatient clinic specialized in functional GI disorders between 2005 and 2015. The patients underwent examinations to investigate o-roal transit time (OATT) and visceral sensitivity (rectal balloon distension and a lactulose challenge test), and they also completed questionnaires to assess anxiety and depression (HAD), overall IBS symptoms (IBS-SSS), bowel habits (BSF), quality of life (IBS-QOL), extraintestinal somatic symptoms (PHQ-12), sense of coherence (SOC), fatigue (MFI), GI-specific anxiety (VSI) and physical and sexual abuse.

Results: Based on validated HAD cut-off levels (≥8), anxiety and depression were present in 55% and 26% of the IBS patients, respectively. More women were anxious (p < 0.001), but for depression no gender differences were detected (p = 0.76). IBS patients with anxiety or depression were younger (p < 0.001, and more commonly reported sexual and/or physical abuse (p < 0.001) than IBS patients without anxiety or depression. The presence of anxiety or depression did not differ between IBS subgroups based on the predominant bowel habit (p = 0.41, p = 0.18). For an overview of comparisons of data from questionnaires and pathophysiological examinations, see table 1. Both the presence of anxiety and of depression were associated with reports of more severe GI and extraintestinal symptoms, GI-specific anxiety, fatigue, and lower sense of coherence. Regarding pathophysiological examinations, the findings were more inconsistent. OATT was similar between groups, as was stool form and frequency. Visceral sensitivity tended to be higher in patients with anxiety, and depressed patients reported more severe pain during the lactulose challenge
test. Quality of life (IBS-QOL) was reduced for all domains in patients with anxiety and depression (p = 0.001 for all comparisons).

Table 1: Characterization of IBS patients with anxiety or depression

<table>
<thead>
<tr>
<th>Variable</th>
<th>Anxiety</th>
<th>Median</th>
<th>P-value</th>
<th>Depression</th>
<th>Median</th>
<th>P-value</th>
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</thead>
<tbody>
<tr>
<td>IBS-SSS</td>
<td>No</td>
<td>283.33</td>
<td>&lt;0.001</td>
<td>No</td>
<td>298.30</td>
<td>&lt;0.001</td>
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<tr>
<td>VAS</td>
<td>No</td>
<td>35.52</td>
<td>&lt;0.001</td>
<td>No</td>
<td>39.56</td>
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</tr>
<tr>
<td>SOC</td>
<td>No</td>
<td>153.12</td>
<td>&lt;0.001</td>
<td>No</td>
<td>146.11</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PHQ-12</td>
<td>No</td>
<td>6.9</td>
<td>&lt;0.001</td>
<td>No</td>
<td>7.1</td>
<td>&lt;0.001</td>
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<tr>
<td>MFI</td>
<td>No</td>
<td>14.14</td>
<td>&lt;0.001</td>
<td>No</td>
<td>15.19</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>OATT (days)</td>
<td>No</td>
<td>1.34.1</td>
<td>0.67</td>
<td>No</td>
<td>1.14</td>
<td>0.52</td>
</tr>
<tr>
<td>Stool form (BSF)</td>
<td>No</td>
<td>4.4</td>
<td>0.93</td>
<td>No</td>
<td>4.0</td>
<td>0.49</td>
</tr>
<tr>
<td>Stool frequency ( stools/day)</td>
<td>No</td>
<td>1.7</td>
<td>0.53</td>
<td>No</td>
<td>1.7</td>
<td>0.36</td>
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<tr>
<td>Lactose challenge test, perceived pain (AUC)</td>
<td>No</td>
<td>776.833</td>
<td>0.06</td>
<td>No</td>
<td>705.170</td>
<td>0.01</td>
</tr>
<tr>
<td>Balloon distension, pain threshold (mmHg)</td>
<td>No</td>
<td>28</td>
<td>0.01</td>
<td>No</td>
<td>24</td>
<td>0.53</td>
</tr>
</tbody>
</table>

Conclusion: The presence of anxiety and depression seems to clearly potentiate the already substantial disease burden in IBS patients. However, the association with other pathophysiological findings is less distinct. This group of patients with complex and severe symptoms will benefit from a holistic management approach.

Disclosure of Interest: M. Simrén: Magnus Simrén has received unrestricted research grants from Danone and Ferring Pharmaceuticals, and served as a Consultant/Advisory Board member for AstraZeneca, Danone, Nestlé, Menarini, Almirall, Allergan, Albireo, Glycom and Shire, and as. All other authors have declared no conflicts of interest.

H. Törnblom: Hans Törnblom has served as Consultant/Advisory Board member for Almirall and Allergan as a speaker for Tillotts, Takeda, Shire and Almirall.

P1786 THE ASSOCIATION BETWEEN IRRITABLE BOWEL SYNDROME AND LACTOSE INTOLERANCE

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Introduction: Irritable bowel syndrome (IBS) and lactose intolerance may co-exist and readily cause diagnostic confusion due to similar symptomatology (1, 2).

Aims & Methods: This study aimed to examine the incidence of lactose intolerance in healthy controls and in subjects diagnosed with IBS based on Rome III criteria, as an effort to investigate the association between IBS and lactose intolerance. The patient population consisted of individuals between 18 and 80 years of age who attended between June-December 2013. Patients diagnosed with IBS based on Rome III criteria comprised the IBS group, and subtypes of IBS. Control subjects were healthy volunteers over 18 years of age with no IBS-like symptoms. All participants ingested 25 g of lactose dissolved in 250 ml of water based on Rome III criteria, as an effort to investigate the association between IBS and lactose intolerance.

Results: Of the total 200 participants, 100 (50%) were in IBS and 100 (50.0%) were in control group. There were 133 females (66.5%), and the mean age was 40.5 ± 12.3 years. Of the total 70 patients (35.0%) with lactose intolerance, 47 (47.0%) were in IBS and 23 (23.0%) were in control groups (p = 0.001). Symptoms related to IBS were more common in participants with lactose intolerance in both groups (p = 0.001, p = 0.001 respectively). A comparison of the two groups with regard to symptoms after lactose challenge test showed the presence of complaints in 35 (35.0%) patients in IBS group as compared to 24 (24.0%) subjects among controls (p = 0.092). The incidence of lactose intolerance in patients with IBS subtypes of diarrhea-predominant IBS, constipation-predominant IBS, mixed IBS, and unspecified IBS were 27 (57.4%), 7 (4.9%), 10 (21.3%) and 3 (6.4%), respectively, with no significant differences (p = 0.161, p = 0.124, p = 1.000, and p = 0.661 respectively).

Conclusion: A significantly increased frequency of lactose intolerance was found among IBS patients than in controls. In additional, symptoms associated with lactose intake occurred at a higher frequency in IBS patient, although the difference was insignificant.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P1788 THE PREVALENCE AND IMPACT OF OVERLAPPING ROME IV FUNCTIONAL GASTROINTESTINAL DYSFUNCTIONS ON SOMATISATION, QUALITY OF LIFE, AND HEALTHCARE UTILISATION: RESULTS FROM A THREE-COUNTRY GENERAL POPULATION STUDY

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Introduction: The population prevalence of Rome IV functional gastrointestinal disorders (FGIDs) and their cumulative effect on health impairment is unknown. We sought to address this issue.

Aims & Methods: An Internet-based health survey was completed by 5931 of 6300 general population adults from three speaking English-speaking countries (2100 each from US, Canada, and UK). The survey included questions on demographics, medication, surgical history, somatisation, quality of life, doctor-diagnosed organic GI disease, and criteria for the Rome IV FGIDs. Comparisons were made between those with Rome IV FGIDs on against non-GI and organic GI disease controls.

Results: The number of subjects having symptoms compatible with a FGID was 2083 (35%) compared to 3421 (57.7%) non-GI and 427 (7.2%) organic GI disease controls. The most frequently met diagnostic criteria for FGIDs was bowel disorders (n = 1665, 28.1%), followed by gastroduodenal (n = 627, 10.6%), anorectal (n = 440, 7.4%), oesophageal (n = 414, 7%), and gallbladder disorders (n = 10, 0.2%). On average, the 2083 individuals who met FGID criteria qualified for 1.5 FGID diagnoses, and 742 of them (36%) qualified for FGID diagnoses in more than one anatomic region. The presence of FGIDs in multiple regions was associated with increasing somatisation, worse mental and physical quality of life, greater use of medical therapies, and a higher prevalence of abdominal surgeries; all p < 0.001, see table. Notably, individuals with FGIDs in multiple regions had worse somatisation and quality of life scores than organ GI disease controls.

Conclusion: Roughly a third of the general adult population fulfills diagnostic criteria for a Rome IV FGIDs. As a third of this subgroup has FGIDs in multiple GI regions, this overlap is associated with increased health impairment. Study Support: The Rome Foundation

Disclosure of Interest: All authors have declared no conflicts of interest.

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P1789 WITHIN-PERSON CORRELATIONS BETWEEN GASTROINTESTINAL AND PSYCHOLOGICAL FEATURES OF THE IRRITABLE BOWEL SYNDROME

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Introduction: The prevalence and impact of overlapping Rome IV functional gastrointestinal disorders on somatisation, quality of life, and healthcare utilisation results from a three-country general population study.

Disclosure of Interest: All authors have declared no conflicts of interest.

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References

Number of subjects 3421 1341 493 166 83 427
Mean number of somatic symptoms 2.8 4.6 5.6 6.3 7.3 4.7
Mean PHQ-12 score 3.3 6 7.5 9.1 10.9 6.3
Mean SF8-MCS QOL 52.1 45.7 42.8 38.6 37.2 47.9
Mean SF8 PCS-QOL 51.9 47.4 44.1 40.2 38.6 43.8
GI-related medication (%) 35% 59% 74% 84% 93% 71%
Abdominal surgery (%) 19% 26% 31% 37% 54% 53%
IRRITABLE BOWEL SYNDROME WITH CONSTIPATION: IMPACT OF SYMPTOM SEVERITY ON HEALTH-RELATED QUALITY OF LIFE: A POST HOC ANALYSIS OF DATA FROM TWO PHASE 3 TRIALS OF LINACLOTIDE

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Introduction: Although correlations between features of irritable bowel syndrome (IBS) and health-related quality of life (HRQoL) have been reported, these were based on between-person rather than within-person variation. We investigated the longitudinal within-person correlations between features of IBS.

Aims & Methods: We used a longitudinal cohort of 276 IBS patients, who filled out questionnaires once annually over five years on the following features: gastrointestinal (GI) symptom severity (GSRS), quality of life (QOL), GI specific anxiety (VSI), general anxiety and depression (HADS), coping resources (CRI), and sense of coherence (KASAM). For each participant, scores were centered on their own mean, and within-person correlations were computed for all pairs of features.

Results: Aggregate within-person correlations are shown in figure 1. Within-person correlations were strong for the triad GI symptom severity, GI specific anxiety, and QOL (r ≥ 0.47 to 0.64). Another set of features was comprised of general anxiety, depression, coping resources, and sense of coherence (r ≥ 0.39 to 0.57). Within-person correlations between the two sets were weak (r ≤ 0.00 to 0.37). However, within-person correlations tended towards bimodal distributions across the population, especially for GI symptom severity and depression (r ~ 0.6 for half of participants, and r ~ 0.4 for the other half).

Conclusion: Here we show that, within individual IBS patients, GI symptom severity is strongly associated with GI specific anxiety and QOL, but not with four other psychological features. The presence of negative within-person correlations in some individuals may imply a lack of relation, but could also signal long-term causative processes.

DISCLOSURE OF INTEREST: J. Tack: Jan Tack has given Scientific advice to Abide Therapeutics, AlfaWassermann, Allergan, Christian Hansen, Danone, Genfit, Ironwood, Janssen, Kiowa Kirin, Menarini, Mylan, Novartis, Nutricia, Onco Pharma, Rhythm, Shionogi, Shire, SK Life Sciences, Takeda. H. Tornblom: Hans Tornblom has served as Consultant/Advisory Board member for Almirall and Allergan as a speaker for Tillotts, Takeda, Shire, and Nestle. L. Van Oudenhove: Lukas Van Oudenhove has received grant support from Almirall Therapeutics, AlfaWassermann, Danone, Genfit, Nestle, and Nestle and has given scientific advice to Grunenthal. M. Simren: Magnus Simren has received unrestricted research grants from Danone and Ferring Pharmaceuticals, and served as a Consultant/Advisory Board member for AstraZeneca, Danone, Nestle, Menarini, Allergan, Almirall, Albino, Glycom and Shire, and as a. All other authors have declared no conflicts of interest.

<table>
<thead>
<tr>
<th>Instrument</th>
<th>Sex</th>
<th>Age</th>
<th>GSS</th>
</tr>
</thead>
<tbody>
<tr>
<td>IBS-QOL</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total F</td>
<td>1595</td>
<td>1437</td>
<td>158</td>
</tr>
<tr>
<td>Total M</td>
<td>1511</td>
<td>1583</td>
<td>1503</td>
</tr>
<tr>
<td>&gt;65</td>
<td>1591</td>
<td>1437</td>
<td>158</td>
</tr>
<tr>
<td>&lt;65</td>
<td>1511</td>
<td>1583</td>
<td>1503</td>
</tr>
<tr>
<td>≥3</td>
<td>1437</td>
<td>1583</td>
<td>1503</td>
</tr>
<tr>
<td>&lt;3</td>
<td>304</td>
<td>304</td>
<td>304</td>
</tr>
</tbody>
</table>

Table P1791

Conclusion: Among this patient population, IBS-C patients with higher symptom severity reported greater impairments in HRQoL. These results indicate that symptom severity may be an important consideration for disease management and emphasise the need for IBS-C treatments that improve both symptom burden and quality of life.

DISCLOSURE OF INTEREST: A. Marciniak: Anne Marciniak is an employee of Allergan plc and shareholder in Pfizer, Amgen, and Allergan plc. Y. Mo: Yifan Mo is an employee of Allergan plc. J. M. Julia: Ma is an employee of Allergan plc. J. L. Abel: Jessica L. Abel is an employee of Allergan plc and shareholder in Allergan plc.

R.T. Carson: Robyn T. Carson is an employee of Allergan plc and shareholder in Allergan plc.

HEALTH CARE UTILIZATION FOR ROME IV IRRTABILE BOWEL SYNDROME: A THREE-COUNTRY SURVEY IN THE GENERAL POPULATION

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Introduction: No population-based studies have investigated the symptom burden and healthcare utilization associated with Rome IV defined irritable bowel syndrome (IBS).

Aims & Methods: The aim of the current study was to assess these variables in IBS subjects in the general population. An Internet survey was completed by 6300 individuals distributed equally between United States, United Kingdom and Canada. Equal sex, age and education distribution across the countries was ensured by use of quota-based sampling. The survey included questions on demographics, the Rome IV diagnostic questionnaire, the patient health questionnaire (PHQ-12), the 8-item Short Form (SF-8) quality of life (QOL) questionnaire, health care utilization and past gastrointestinal (GI) disease diagnoses by doctors. Respondents with an organic GI disease were excluded from the IBS population.

Results: From the 6300 individuals who completed the survey, 369 were excluded due to inconsistent responses, leaving 5931 (49.2% female; mean age 47.4 ± 17.1 years) to be included for analysis (1949 US, 1994 UK, 1988 Canada). 305 (5.1%) of those fulfilled Rome IV diagnostic criteria for IBS, after 36 individuals were excluded due to organic disease. Compared to the non-IBS population, the IBS population was younger (mean age 44.7 ± 14.5 years; p = 0.004) and predominantly female (66%; p < 0.001). Apart from reporting more frequent GI

point difference) subscales (Table). Patients with GSS ≥3 also had a lower EQ-5D index score compared to those with GSS <3 (0.67 vs 0.72) (Table). Women reported a slightly lower mean total IBS-QOL score compared to men, but had a notably lower score (14-point difference) on the body image subscale (Table). No difference in mean EQ-5D score was observed between sexes. IBS-QOL total and EQ-5D index scores were similar between patients aged <65 and ≥65 years, though the younger subgroup generally had lower scores on the IBS-QOL, including on the food avoidance and sexual subscales (Table).
symptoms, IBS subjects also reported more somatic symptoms; 103 (34%) had abdominal pain at least 3 times/week, 232 (76%) subjects reported sensation of bloating at least 3 times/month, and 232 (76%) scored ≥7 on PHQ-12, indicating high somatic symptom burden (p < 0.001 for all). They also had poorer self-rated overall health, more general body pain, and more health-related impairment of social activities (p < 0.001 for all). See table 1 for details. IBS subjects also reported more frequent visits to the doctor compared to the non-IBS population, both for non-GI and GI related problems. 232 (76%) reported seeing a doctor at least once/year for any health issue and 195 (63%) vs. 114 (38%) had seen a doctor for GI problems (p < 0.001 for all). IBS subjects also reported higher frequency of visits to gastroenterologists, gynaecologists and surgeons in secondary care; p < 0.001 for all. The use of medication for pain (both submitted and over the counter), GI related symptoms, depression and anxiety was increased amongst subjects with IBS, as was the rate of abdominal surgery (p < 0.001 for all), appendectomy excluded. See table 1 for details.

<table>
<thead>
<tr>
<th>GI symptoms</th>
<th>IBS, n = 570</th>
<th>Not IBS, n = 3590</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal pain</td>
<td>73 times/week</td>
<td>73 times/week</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Bloating</td>
<td>&gt;3 times a month</td>
<td>&gt;3 times a month</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Somatization PHQ-score 7 or above</td>
<td>323 (70%)</td>
<td>1243 (65%)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Quality Of Life

Overall estimation of health past 4 weeks (SF-8). Very poor/poor | 90 (29.5%) | 273 (4.9%) | <0.001 |
| Fair/good | Very good/excellent | 182 (59.7%) | 3026 (54.1%) | 0.124 |
| Bodily pain past 4 weeks | None/very mild | 35 (13.4%) | 3567 (63.8%) | <0.001 |
| Somatization | | 168 (55.1%) | 1707 (30.5%) | 0.034 |
| Limitation in social activities due to physical health or emotional problems past 4 weeks | 55 (17.4%) | 3084 (55.2%) | <0.001 |
| Not at all | Very little/somewhat | 144 (47.2%) | 2021 (36.2%) | 0.058 |

Conclusion: Individuals fulfilling the Rome IV criteria for IBS in the general population have increased GI and non-GI healthcare utilization in primary and secondary care, excess non-GI symptom burden and impaired QoL.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1794 ARTERIAL PH AND LACTATE HAVE SIGNIFICANT IMPACT ON THE OUTCOMES OF PATIENTS WITH ISCHAEMIC COLITIS

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Introduction: Ischaemic colitis (IC) encompasses a number of clinical entities resulting in insufficient blood supply to the colon. The incidence of adverse outcome in patients with IC remains high.

Aims & Methods: We conducted a multicenter retrospective cohort study including consecutive patients with IC diagnosed between January 2013 and December 2016, according to the Modified Brandt and Boley criteria (clinical, colonoscopy, pathology consistent with IC and negative culture). The following data were collected: age, sex, clinical symptoms (evidence of IC), organ failure, laboratory findings (hemoglobin, platelet number, leucocytes, C-reactive protein, creatinine, sodium, potassium, arterial pH and arterial lactate and LDH), endoscopic and CT findings, surgery and death. Logistic regression was used to study association with predictor variables: surgery and overall mortality.

Results: In this study, 349 patients were registered and 193 fulfilled the predefined criteria: 121 (62.7%) were females and mean age was 72-years-old (IQR: 23–94). At admission a total of 165 (85.5%) patients presented with hematochezia, 112 (58%) with abdominal pain, 82 (42.5%) with diarrhea, 27 (11.9%) with shock and 7 (3.6%) with occlusion. Twenty three (11%) required surgery. In-hospital, 30-day and overall follow-up mortality rates (up to 205 weeks) were 7.3%, 6.7% and 14%, respectively. On multivariate analysis, surgery was independently associated with shock (OR: 4.8; p = 0.011) intestinal occlusion (OR: 3.5; p = 0.046), and arterial lactate (OR: 1.3; p = 0.012). On univariate analysis, hemoglobin, hematocrit, C-reactive protein, LDH, the number of risk factors, arterial pH, and the need of red blood support were significantly (p < 0.05) associated with in-hospital and 30-day mortality. Creatinine was also associated with intra-hospital mortality. The variables that correlated independently in the multivariate analysis with in-hospital mortality were male gender (OR: 4.3; p = 0.03), and arterial pH (OR: 0.001; p = 0.036) and with 30-day mortality was the need of blood cell support (OR: 2.1; p = 0.008).

Conclusion: In our cohort of predominant elderly patients, arterial pH, shock and lactate were significantly associated with need of surgery. Arterial pH on admission was also independently associated with in-hospital mortality. Early identification of these factors can aid in the decision making in this context and select the best care level for each patient.

Disclosure of Interest: All authors have declared no conflicts of interest.
P1795 THE RISK PREDICTIVE VALUES OF ACG CLASSIFICATION IN A COHORT OF ISCHEMIC COLITIS—REFINING THE DEFINITION OF MILD DISEASE

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Introduction: Although most cases of colon ischemia (CI) are mild and self-limiting, when severe it implies high mortality rates. We aimed to evaluate the risk profile and validation of classification of disease severity proposed by American College of Gastroenterology (ACG) guidelines (2015), created to provide a management algorithm for these patients and select the level of care.

Aims & Methods: A retrospective multicenter study was conducted on adult patients with definite CI (clinical, colonoscopy, pathologic and culture criteria), between 2013 and 2016. Data was collected on clinical presentation, comorbidities, organ failure, management and outcome. Each case was classified according to ACG guidelines after assessment of the number of risk factors (gender, systolic blood pressure <90 mm Hg, heart rate >100 beats per min, abdominal pain without rectal bleeding, BUN > 20 mg/dl, Hgb < 12 g/dl, LDH > 350 U/l, serum sodium < 136 mEq/l, WBC > 15 x 109 /cmm). Patients were then classified as mild (0 risk factors (RF)), moderate (1–3 risk factors), and severe (more than 3 risk factors or any of the following: perianal signs, pneumatocele or portal venous gas, gangrene on colonoscopic examination and pan-colonic or isolated right-colon ischemia involvement on imaging by colonoscopy or computed tomography).

Results: 349 cases with the clinical diagnosis of IC were analyzed. 193 patients met the inclusion criteria of definitive diagnosis of CI (62.7% females; mean age 72 years ±13). ACG classification of mild, moderate and severe disease was attributed respectively to 21% of patients (0 intra-hospital deaths), 45% (2 deaths) and 34% (12 deaths). The number of ACG RF was: 40% with 0 RF, 8% with 1, 9% with 2, 15% with 3, 16% with 4, 8% with 5, 4% with 6 and 1% with 7. No patient with 0 or 1 RF died. Only 1 patient with 2 RF died. The remaining 13 deaths were verified with at least 3 RF. The univariate analysis revealed a statistical correlation between RF and intra-hospital or 30-day mortality as well as the need for surgery (mean = 4.06, sd = 1.85). ACG classification presented high predictive accuracy for in-hospital and 1-month mortality with a AUROC of 0.78 respectively. For a cutoff of 2 ACG RF, the sensitivity (SE) for death was 100%, specificity (SP) 52%, with a positive predictive value (PPV) of 14% and negative predictive value (NPV) of 100%. For 3 ACG RF the results were: SE 93%, SP 61%, PPV 16% and NPV 99%. 3 or more risk factors are associated with an increased mortality and 18.42 for 1-month mortality (CI 2.34–144).

Conclusion: No patient in this cohort with less than 2 ACG RF died, suggesting that the ACG classification as mild disease may include 0 and 1 risk factor without changing the prognosis. Short-term mortality risk increases significantly in patients with at least 3 ACG RF.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference


P1796 HOW COST AFFECTS THE TREATMENT CHOICE FOR IRREVERSIBLE BOWEL SYNDROME WITH DIARRHEA PATIENTS: A COST-EFFECTIVENESS ANALYSIS OF TRICYCLIC AGENTS AND RIFAXIMIN

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Introduction: Drug pricing and third party payer coverage exert a profound effect on access to prescription therapies in patients with irritable bowel syndrome with diarrhea (IBS-D). We performed a cost-effectiveness analysis to assess the trade-offs associated with treating IBS-D patients with a tricyclic agent (TCA) or rifaximin.

Aims & Methods: We constructed a decision analytic model evaluating three treatment strategies for IBS-D in the United States healthcare system: first-line therapy with TCA-only, first-line rifaximin followed by second-line TCA for nonresponders, and first-line TCA followed by second-line rifaximin for nonresponders. This model accounted for direct and indirect costs of therapy with TCA-only, first-line rifaximin followed by second-line TCA for nonresponders, and first-line TCA followed by second-line rifaximin for nonresponders.

Results: Based on the average acquisition cost of rifaximin (USD 29.78/pill), second-line rifaximin could be cost-effective from a societal perspective (Table 1). However, at contemporary WTP thresholds neither rifaximin strategy was cost-effective from a payer perspective despite greater effectiveness than TCA alone. Dependent on WTP, a 12-62% price reduction (USD $18.46-$26.34/pill) would enable the first-line TCA followed by second-line rifaximin to be more cost-effective than a TCA-only strategy (Table 1). An 84-88% price reduction (USD $3.53-$4.71/pill) would enable first-line rifaximin followed by second-line TCA to be more cost-effective than TCA-only, though first-line TCA followed by second-line rifaximin would remain the more cost-effective strategy. Our model was robust in tornado analysis and most influenced by rifaximin treatment interval. Sensitivity analysis on rifaximin retreatment interval suggests that current pricing may be based on longer retreatment intervals than those found in clinical literature (Fig 1a). Sensitivity analysis with a lower TCA responder rate could enable first-line rifaximin to be the preferred strategy, albeit at a reduced price (Fig 1b).

Conclusion: Rifaximin is an effective therapy for IBS but is less cost-effective than TCA as currently priced. We propose an evidence-based pricing strategy which would maximize the cost-effectiveness of rifaximin in IBS-D patients.

Disclosure of Interest: W.D. Chey: Dr. Chey is a consultant for Ironwood Pharmaceuticals and Allergan. All other authors have declared no conflicts of interest.

variable
Surgery group (N=18)
Conservative group (N=27)
P value
Age(year) 66 67 .688
Sex(M/F) 10/8 14/13 .807
Purpose of colonoscopy
Therapeutic 9 27 .000
Diagnostic 9 0
Location of perforation .002
Rectum 2 6
Sigmoid 14 7
Descending 0 1
Transverse 2 3
Ascending 0 10
Endoscopic clipping .007
Yes 8 23
No 10 4

P1797 PREDICTIVE FACTORS FOR BETTER OUTCOMES IN COLONOSCOPY-ASSOCIATED PERFORATION

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Introduction: Colonoscopy has been widely used for diagnostic and therapeutic purposes. Although the incidence is very low, perforation is one of the most serious complications. It is important to decide whether to try endoscopic clipping or to perform prompt surgical management.

Aims & Methods: We retrospectively reviewed charts of all patients who experienced colonoscopy-associated perforation in a single center between May 2009 and July 2015, and totally 45 patients were enrolled.

Table: The risk factors surgical treatment in colonoscopy-associated perforation

<table>
<thead>
<tr>
<th>Variable</th>
<th>Surgery group (N=18)</th>
<th>Conservative group (N=27)</th>
<th>P value</th>
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<tbody>
<tr>
<td>Age(year)</td>
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<td>67</td>
<td>.688</td>
</tr>
<tr>
<td>Sex(M/F)</td>
<td>10/8</td>
<td>14/13</td>
<td>.807</td>
</tr>
<tr>
<td>Purpose of colonoscopy</td>
<td>Therapeutic 9 27</td>
<td>Diagnostic 9 0</td>
<td>.000</td>
</tr>
<tr>
<td>Location of perforation</td>
<td>Rectum 2 6</td>
<td>Sigmoid 14 7</td>
<td>.002</td>
</tr>
<tr>
<td>Ascending</td>
<td>0 10</td>
<td>Endoscopic clipping 8 23</td>
<td>.007</td>
</tr>
<tr>
<td>No</td>
<td>10 4</td>
<td></td>
<td>.005</td>
</tr>
</tbody>
</table>

Results: Diagnostic cases in purpose, sigmoid colon in location and non-clipping status were significantly more common in surgery group than conservative group (Table). Endoscopic clipping was performed in 31 cases (immediate; 23, delayed; 8), and immediate clipping group had significantly lower rate of operation (p = 0.013) and better clinical outcome (duration of antibiotic: p = 0.006, hospital stay: p = 0.001). Among 18 surgical cases, 13 patients had primary closure and 5 patients had complex surgery (2; segmental resection, 3; Hartmann’s procedure). The early (<24hr) surgical management significantly decreased the possibility of complex surgery (p = 0.002), as well as had better clinical outcomes such as duration of antibiotic use, fasting time and length of hospital stay (p = 0.003, p = 0.001, p = 0.005, respectively). In therapeutic cases, all five perforated patients who had surgery within 1 day could be managed by simple primary closure, but all four patients who had surgery after 1 day required complex surgery.
Abstract No: P1796

**Table 1: Comparative cost-effectiveness of treatment approaches with and without rifaximin in irritable bowel syndrome with diarrhea (IBS-D)**

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Total cost (USD/yr)</th>
<th>Total effectiveness (QALY gained)</th>
<th>Incremental cost (USD)</th>
<th>Incremental effectiveness (QALY)</th>
<th>ICER (USD/QALY gain)</th>
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<tbody>
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<td>Societal perspective</td>
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<td>0.14</td>
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<tr>
<td>TCA only</td>
<td></td>
<td></td>
<td>$435</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rifaximin as first-line for IBS-D</td>
<td>$7,608</td>
<td>0.20</td>
<td>$2,263</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rifaximin as second-line for IBS-D</td>
<td>$4,783</td>
<td>0.02</td>
<td>$3,002</td>
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<td></td>
</tr>
<tr>
<td>Payer perspective</td>
<td>$728</td>
<td>0.04</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>TCA only</td>
<td></td>
<td></td>
<td>$728</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rifaximin as first-line for IBS-D</td>
<td>$4,177</td>
<td>0.20</td>
<td>$2,500</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rifaximin as second-line for IBS-D</td>
<td>$1,622</td>
<td>0.02</td>
<td>$1,000</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1 first-line rifaximin strategy was dominated (less effective and more expensive) than a second-line rifaximin strategy at all price points. ICER = incremental cost effectiveness ratio; QALY = quality adjusted life year; TCA = tricyclic antidepressant; IBS-D = irritable bowel syndrome with diarrhea; USD = US dollar.

Conclusion: In colonoscopy-associated perforation, immediate endoscopic clipping decreases the possibility of operation and shows better clinical outcomes, and early surgical approach decreases complex operation rate. Especially, early operation need be considered in diagnostic perforation regardless of endoscopic clipping.

Disclosure of Interest: All authors have declared no conflicts of interest.

**P1798** PATIENTS’ AND CLINICIANS’ VIEWS OF AND EXPERIENCE WITH A NOVEL CLINICAL PATHWAY FOR FUNCTIONAL GASTROINTESTINAL DISORDERS

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Introduction: Despite diagnostic criteria and effective management options for functional gastrointestinal disorders (FGID), confidence in managing these disorders in primary care is low, and long waiting lists for specialist care are common. New models which efficiently transfer specialist-held expertise to primary care practitioners is needed.

Aims & Methods: We aimed to explore and describe the patient and primary healthcare provider (PHCP) experience of a novel non-specialist-dependent algorithm-based approach to the diagnosis and management of FGID (ADAM-FGID). Consecutive patients triaged to the ‘routine waitlist’ of an Australian public hospital Gastroenterology Department over 2 years, with non-specific gastrointestinal symptoms (no alarms) were randomised to waitlist control or the algorithm (1:2). Algorithm patients were screened for organ disease with an alarms-based questionnaire and panel of routine blood/stool tests. When patients had clinical alarms or abnormal tests, data were reviewed by a gastroenterologist and, if appropriate, prompt gastroenterologist appointment offered. All others were classified using Rome III criteria. and received a letter explaining their FGID diagnosis and dietary/psychological management options. Waitlist control patients were not screened. All participants completed follow-up surveys at 6, 26 and 52 weeks. Referring doctors of the algorithm group were sent a feedback survey at study completion.

Results: 89 participants were screened (42 years [SD 14], 62% female). 35 had clinical alarming warranting gastroenterologist review and 45 were diagnosed with FGID (9 excluded). At 6 week follow up: 35/36 FGID respondents had read the diagnostic/management letter, and most (n=30) were satisfied with the information (96%, 8% partially satisfied). Few discussed it with their PHCP (n=13), yet most (n=28) commenced management (n=33 by 12 months). Dietary management options were preferred over psychological therapies (n=30 vs n=16) (p<0.001), as were do-it-yourself options above therapist consultation. 61% (n=22) of patients saw symptom improvement at 6 weeks, (18/21 at 12 months). 2 did not accept the diagnosis, and 3 consulted a specialist privately. 19/36 participants had no concerns at 6-week follow-up (19/21 at 12 months). Common concerns included symptom persistence (6-week n=10, 12-month n=10) and fear of missed pathology (6-week n=4, 12-month n=4). Most respondents (74%, 46/62) found the approach acceptable (FGID group: acceptable 12/36, moderately acceptable 10/36; Screen Fail Group: acceptable 20/26, moderately acceptable 4/26). Others expressed dissatisfaction with the healthcare system (n=4), diagnosis (n=3), screening questionnaire (n=1) and lack of improvement in symptoms (n=1). All responding PHCPs (23/30; 14 FGID group, 9 screen-fail group) found the approach acceptable (13 acceptable, 12 moderately acceptable).

Conclusion: An algorithm-based approach to the diagnosis and management of FGIDs, which does not rely on specialist input is feasible, acceptable and effective. A larger scale randomised controlled trial of this new clinical pathway for the diagnosis and management of FGIDs, in primary care is warranted.

Disclosure of Interest: P.R. Gibson; AbbVie, Ferring, Janssen, Ferring, Fresenius Kabi, Mylan Merck, Nestle Health Science, Danone, Allergan, Pfizer and Takeda. Research grants from AbbVie, Janssen, Falk Pharma, Danone and A2 Milk Company.

J.M. Andrews: JMA has served as a speaker, a consultant and/or an advisory board member for Abbott, Abbvie, Allergan, Celgene, Ferring, Takeda, MSD, Shire, Janssen, Hospira and Pfizer, and has received research funding from Abbott, Abbvie, Ferring, MSD, Shire, Janssen. All other authors have declared no conflicts of interest.

**P1799** ANNUAL FECAL IMMUNOLOGICAL TESTING IS LESS COSTLY THAN COLONOSCOPY EVERY 5 YEARS AND REDUCES MORTALITY IN FAMILIAL COLORECTAL CANCER SCREENING


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11 Servicio De Aparato Digestivo, Hospital Universitario Central de Asturias, Oviedo/Spain
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Introduction: Colonoscopy every 5 years, starting at the age of 40 years, is considered the first-choice screening strategy in first degree relatives (FDR) of patients with colorectal cancer CRC, as these individuals are considered at higher risk of developing CRC than average-risk individuals. However, this practice has a low adherence and remains opportunistic. Recently, it has been suggested that annual fecal immunochemical testing (FIT) might be a valid alternative to colonoscopy in this setting. However, there are scarce data regarding cost-effectiveness of these strategies from the perspective of healthcare services.

Aims & Methods: This study was aimed to compare the cost-effectiveness of annual FIT and colonoscopy every 5 years, to reduce CRC mortality, in FDR of patients with CRC. A Markov model was constructed to simulate the efficacy and cost of annual FIT (cut-off 10 μg Hgb/g feces) or colonoscopy every 5 years of
previously unscreened FDR, starting at age 40 years and ending at age 75. A 5-year gap between each strategy was assumed. The model was adjusted to the incidence of CRC in Spain and real prevalence of advanced adenoma and CRC in the familial-risk population (http://dx.doi.org/10.1371/journal.pmed.1002008.g001). The main outcomes were quality-life-year (QALY) gained compared to natural lifetime, lifetime burden of colonoscopy, lifetime burden of colonoscopy complications, and the incremental cost-effectiveness ratio (ICER). We applied a willingness-to-pay threshold of €25,000 per QALY gained. Data from a prospective EuroQol survey carried out on 920 Spanish patients at different disease stages were used for QALY measurement. Sensitivity analysis was performed to evaluate the robustness of the model.

Results: In a hypothetical cohort of 10,000 asymptomatic FDR, annual FIT and colonoscopy every 5 years were cost-effective over no screening. Taking no screening as the CER for annual FIT and colonoscopy every 5 years was 1989 and 4472 euros/QALY, respectively. Compared to no screening, annual FIT and colonoscopy every 5 years reduced CRC mortality by 59% and 81%, respectively. The annual FIT strategy saved 33% of colonoscopies and was associated with a number of colonoscopies reduced compared to colonoscopy every 5 years. The results were robust in sensitivity analyses.

Conclusion: Assuming a 50% adherence, annual FIT is less costly than colonoscopy every 5 years for CRC screening and reduces mortality in the familial-risk population. These data suggest that FDR of patients with CRC could be included in organized nationwide FIT-based screening programs.

Disclosure of Interest: All authors have declared no conflicts of interest.

References


P1800 COMBINATION OF FOBT AND FECAL CALPROTECTIN MAY BE USEFUL FOR REDUCING UNNECESSARY COLONOSCOPY IN SYMPTOMATIC PATIENTS

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Introduction: Faecal occult blood test (FOBT) is a non-invasive and easily performed test which has demonstrated to reduce CRC incidence and mortality in the populations. Fecal calprotectin (FCP) has good evidence for detecting inflammatory bowel disease but its value in CRC and adenoma detection in the symptomatic population is less well studied. Most patients with symptoms have benign pathology but in an effort to detect most cancer or pre-cancerous lesions, almost all patients undergo colonoscopy.

Aims & Methods: To evaluate and compare the diagnostic accuracy of the combination of FOBT plus FCP versus each test alone in symptomatic patients referred for diagnostic colonoscopy. A total of 171 patients who completed colonic investigations and returned stool samples, were prospectively recruited and included in the final analysis. FOBT was performed by SENTRY FIT 270 test (Sentinel Diagnostics, Milan, Italy) and FCP by the Elia Calprotectin immunoassay (Thermo Fisher Scientific, Waltham, United States). Reference cut-off levels for FOBT and FCP were 117 ng/ml for FOBT and 90 μg for FCP respectively. The diagnostic accuracy of FOBT and FCP were evaluated by a logistic regression model. CRC, advanced adenoma, IBD and angioidsplasia were considered as relevant pathology. Positive and negative predictive values, sensitivity and specificity were calculated. MedCalc software was used for the ROC curve analysis.

Results: 171 patients (42.7% female; median age 62 years, IQR: 51–68) had relevant colonic pathology. The most frequent indications for colonoscopy were previous episode of rectal bleeding in 71 (42%) patients, change of bowel habits in 28 (16%) and anaemia in 22 (13%). Diagnostic accuracy of FOBT, FCP and combination of both are summarized in table 1.

AuROC curves for relevant colonic pathology were 0.777 (95% CI: 0.708–0.837; P < 0.0001) for FOBT, 0.692 (95% CI: 0.617–0.760; P = 0.0005) for FCP and 0.848 (95% CI: 0.785–0.898; P < 0.0001) for combination of both tests respectively. Combination of both tests have a significant better diagnostic accuracy compared to either test alone (P = 0.043 vs FOBT and P = 0.002 vs FCP) with a higher NPV. No significant difference was observed between FOBT and FCP (P = 0.221).

Conclusion: Our model based on combination of FOBT and FCP has a better diagnostic accuracy performance compared to each test alone for the detection of relevant colonic pathology. Because of high NPV, performing FOBT and FCP in all patients before colonoscopy could be a feasible strategy in order to avoid unnecessary procedures.

Disclosure of Interest: A. Lanas: Angel Lanas is advisor to Sysmex Spain All other authors have declared no conflicts of interest.

References


J.R. Lightdale: Jenifer Lightdale did not receive any remuneration for participation in this research project. She has previously consulted for Medtronic and other medical device companies.
D. Whitaker: David Whitaker has consulted for Medtronic and Covidien. He did not receive any remuneration for participation in this research project.

Reference

P1802 PERFORMANCE OF THE MOTUS PURE-VU SYSTEM - A NOVEL DEVICE FOR ACHIEVING ADEQUATE BOWEL PREP IN POORLY PREPARED PATIENTS
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2Interventional Endoscopy Center, J. Medicinische Klinik Und Poliklinik, Universita¨t Erlangen-Nu¨rnberg, Mainz/Germany
3Gastroenterology & Hepatology, Erasmus Medical Center Rotterdam, Rotterdam/Netherlands

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Introduction: The success of colonoscopy depends on the quality of the bowel preparation, which is estimated to occur in as many as 25% of colonoscopy procedures. The MOTUS GI Pure-VuTM System (Tirat Carmel, Israel) is an FDA cleared device designed to improve visualization in an inadequately prepared colon by facilitating intra-procedural cleaning. Adverse events were reported. The Pure-Vu significantly increased the number of inappropriate polypectomy technique for polyps ranging 4 to 5 mm in diameter.

Aims & Methods: This study aims to evaluate the performance of the Pure-Vu System in colonoscopy with an inadequately prepared colon which may help to improve the overall quality of colonoscopy.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1803 THE EUROPEAN SOCIETY OF GASTROINTESTINAL ENDOSCOPY KEY PERFORMANCE MEASURES FOR COLONOSCOPY IN THE POLISH COLORECTAL CANCER SCREENING PROGRAM
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Contact E-mail Address: marek.bugajski@gmail.com

Introduction: Recently, the European Society of Gastrointestinal Endoscopy (ESGE) published guidelines on key performance measures for colonoscopy (1). We analyzed feasibility of monitoring these measures and whether the proposed standards were met in the Polish Colonoscopy Screening Program (PCSP).

Aims & Methods: We analyzed database records for 40,644 participants aged 55 to 64 years, who between 2014 and 2015, underwent screening colonoscopy in 24 centers of population-based PCSP. We used the ESGE guideline definitions to calculate values of all seven key performance measures. We compared key performance measures within the PCSP against proposed standards on the program and center level. Data on adequacy of bowel preparation was routinely assessed with the Boston Bowel Preparation Scale, whereas data on patient experience with the validated GastroNet questionnaire (2). Data on complication rates were collected from the National Health Fund database and Personal Identification Number Registry.

Results: Overall, on the program level, all minimum standards for colonoscopy key performance measures were met. Rate of adequate bowel preparation was 92.1% for the whole program, ranging 80.9–99.2% per individual center, with 7 centers (29.2%) not reaching minimum standard of 90% and 9 centers (37.5%) reaching the target standard of 95%. Cecal intubation rate was 97.4% (range 93.4–99.4%), with all centers reaching minimum standard of 90% and only one center not reaching target standard of 95%. Adenoma detection rate was 29.9% (range 19.1–39.1%), with 7 centers (29.2%) not reaching minimum standard of 25%. Appropriate polypectomy technique was applied in case of 90.9% (range 64.3–100%) with only 2 centers not reaching minimum standard of 80% and 48.2% of 4 to 5 mm polyps (range 0–100%) with only 6 centers reaching minimum standard of 80%. Target standard of 90% was reached in 15 centers for polyps 6 to 9 mm in diameter and only 2 centers for polyps 4 to 5 mm in diameter. For the whole program, 7-day hospitalization rate after screening colonoscopy was 0.3% (122 cases) and 30-day all-cause mortality was 0.02% (9 cases). GastroNet questionnaire coverage is assumed to be 100%, however the response rate was 65.3% (range 7.6%-81.8%), with painful colonoscopy rate of 19.2%. No minimum standard is set, however target standard of 90% of procedures with measured patient’s experience was not met. Appropriate post-polypectomy surveillance, based on the European guidelines, was proposed in 95.4% of cases (range 84.9-99.7%). Target standard of 95% was met in 15 centers, the minimum standard is not set.

Conclusion: Monitoring ESGE performance measures for colonoscopy is feasible in colonoscopy programmatic screening setting. 6 of 7 performance measures were easy to monitor with PCSP database, however monitoring complications needs further development to avoid extracting data from external registries. PCPS meets proposed minimum standards on program level, however some centers need additional interventions to meet the quality standards. Applying appropriate polypectomy technique for polyps ranging 4 to 5 mm in diameter.

Table: Most commonly reported adverse events by provider

<table>
<thead>
<tr>
<th>Rank</th>
<th>Most frequent</th>
<th>Anaesthesiologist</th>
<th>Sedation Nurse</th>
<th>Gastroenterologist</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Hypotension</td>
<td>Hypotension</td>
<td>Mild desaturation (short)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Bradycardia</td>
<td>Bradycardia</td>
<td>Bradycardia</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Tachycardia</td>
<td>Tachycardia</td>
<td>Tachycardia</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Mild desaturation (short)</td>
<td>Mild desaturation (short)</td>
<td>Hypotension</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Airway obstruction</td>
<td>Apnoea (short)</td>
<td>Mild desaturation (prolonged)</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>Mild desaturation (prolonged)</td>
<td>Hypertension</td>
<td>Severe desaturation</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>Apnoea (short)</td>
<td>Fainted sedation</td>
<td>Airway obstruction</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>Hypertension</td>
<td>Allergy</td>
<td>Prolonged apnoea</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>Prolonged apnoea</td>
<td>Airway obstruction</td>
<td>Apnoea (short)</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>Failed sedation</td>
<td>Allergy</td>
<td>Prolonged apnoea</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>Severe desaturation</td>
<td>Severe desaturation</td>
<td>Prolonged apnoea</td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>Cardiac arrest</td>
<td>Cardiovascular collapse</td>
<td>Seizure</td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>Cardiovascular collapse</td>
<td>Cardiac arrest</td>
<td>Seizure</td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>Seizure</td>
<td>Cardiovascular collapse</td>
<td>Seizure</td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>(Least Frequent)</td>
<td>Seizure</td>
<td>Cardiovascular collapse</td>
<td></td>
</tr>
</tbody>
</table>
is currently the biggest issue in PCSP and further training is needed to reach minimum standards for this performance indicator.

Disclosure of Interest: All authors have declared no conflicts of interest.

References


P1805 VALIDATION OF THE "FAILURE TO PROVIDE ADEQUATE RELIEF" (F-PAR) SCALE IN A SPECIALIST CLINIC SETTING

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Introduction: Treatment of chronic idiopathic constipation is somewhat empiric, but based on step-wise approach[1]. If first-line conservative treatment (lifestyle advice and laxatives) do not relieve symptoms sufficiently, secondary approaches but based on step-wise approach[1]. If first-line conservative treatment (lifestyle advice and laxatives) do not relieve symptoms sufficiently, secondary approaches

Results: Positive F-PAR items correlated to clinical assessment of relief

Table: Positive F-PAR items correlated to clinical assessment of relief

<table>
<thead>
<tr>
<th>Adequate relief (Clinical) n = 203</th>
<th>Inadequate relief (Clinical) n = 200</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bowel frequency inadequate</td>
<td>5</td>
</tr>
<tr>
<td>Strain most occasions</td>
<td>6</td>
</tr>
<tr>
<td>Stool hardness</td>
<td>3</td>
</tr>
<tr>
<td>Onset other symptom</td>
<td>2</td>
</tr>
<tr>
<td>Current therapy poor tolerable</td>
<td>8</td>
</tr>
<tr>
<td>0 FPAR replies</td>
<td>187</td>
</tr>
<tr>
<td>1 FPAR replies</td>
<td>10</td>
</tr>
<tr>
<td>2 FPAR replies</td>
<td>4</td>
</tr>
<tr>
<td>3 FPAR replies</td>
<td>2</td>
</tr>
<tr>
<td>4 FPAR replies</td>
<td>0</td>
</tr>
<tr>
<td>5 FPAR replies</td>
<td>0</td>
</tr>
</tbody>
</table>

Conclusion: Our findings showed that the F-PAR with only five questions can be considered sufficient to provide clinical evidence of treatment failure. The use of standardized process to investigate the efficacy of treatment may reduce the time and improve the quality of managing for the chronic constipation patients.

Disclosure of Interest: All authors have declared no conflicts of interest.

References


WEDNESDAY, NOVEMBER 01, 2017 09:00-14:00

OESOPHAGEAL, GASTRIC AND DUODENAL DISORDERS III - HALL 7...

P1806 ADHERENCE WITH TRANSMAL IRRIGATION USING THE NAVINA SYSTEM IS ASSOCIATED WITH PSYCHOLOGICAL TREATS EVEN WHEN THERE IS IMPAIRED HAND FUNCTION

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Introduction: Transanal irrigation has become a key therapeutic modality in managing patients with neurological diseases who experience constipation and/or faecal incontinence. Such neurogenic bowel dysfunction (NBD) complicates over three quarters of patients with spinal cord injury (SCI) and multiple sclerosis (MS). Approximately 60% of patients who start TAI continue with long-term treatment. A common cause of treatment cessation is impaired hand [1]. Training of the patient is a key aspect of TAI therapy and requires patients to be willing to manage their health themselves: self-efficacy.

Aims & Methods: We wished to study whether use of a novel TAI system, Navina™, which has an electronic pump component allows patients with impaired levels of hand function, to adhere to TAI therapy. We also wished to identify if there were physiological or psychological correlates of adherence. Twenty-eight consecutive patients (19 SCI and 9 MS; 17 male, mean age 42) were studied. All patients scored greater than 18 on the Cochin Hand Function questionnaire which was completed to assess anxiety/depression and locus of control respectively. Anorectal physiology (manometry, sensation and rectal compliance) was undertaken at baseline. Training in TAI was undertaken by the same experienced nurse, with weekly follow up until a stable regime was established. Adherence with therapy at 12 weeks was identified.

Results: At 12 weeks, 16/28 (57%) of patients were still using Navina TAI, similar proportions with SCI (11/19) and MS (5/9). There was no difference in baseline scores for HAD-anxiety (6.7 ± 3.9 vs 7.3 ± 2.9; p = 0.37) and HAD-depression (8.6 ± 3.9 vs 8.8 ± 4.2; p = 0.46) and were similar in both those who were and were not still using TAI (mean ± SD respectively). The Rotter score for non-adherers was significantly greater than adherers (14.2 ± 6.7 vs 10.6 ± 5.9 respectively; p = 0.008). There was no difference in any of the anorectal parameters between those who did or did not adhere with TAI.

Conclusion: Navina Smart TAI is an effective therapy in 57% of NBD patients with significant hand dysfunction. Anorectal physiology, anxiety and depression scores do not predict likelihood of treatment adherence. An external locus of control, reflecting a belief that health events occur because of outside forces (such as fate, chance, or powerful others), is associated with reduced treatment success. The results suggest that future studies of TAI should consider locus of control as an important potential predictor of outcome.

Disclosure of Interest: All authors have declared no conflicts of interest.

References


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Introduction: The microbiota inhabiting the gastrointestinal (GI) tract plays an essential role in gut health. Although mucosal biopsies are increasingly used for microbiota studies, these are subject to variations introduced through sampling technique and patient preparation. The impact of bowel preparation on the microbiota/associated microbiota (MAM) is of particular interest given it results in complete emptying of bowel contents via laxative ingestion. Although bowel preparation does not appear to induce long term changes to stool microbiota [1], it can induce short-term changes to the colonic MAM [2]. While improvements in clearance of the small intestine after bowel preparation have been reported [3], the impact on the upper GI microbiota is currently unknown. Given patients may undergo both upper GI endoscopy and colonoscopy consecutively, a subset of endoscopy patients will have consumed bowel preparation prior to their procedure, representing a potential bias in MAM analyses. Therefore, this study aimed to assess the impact of bowel preparation on the duodenal MAM.

Aims & Methods: Individuals undergoing upper GI endoscopy, with or without concurrent colonoscopy, were recruited consecutively with ethical approval. Individuals who underwent upper GI endoscopy following overnight fast (n = 58), or both upper endoscopy and colonoscopy following polyethylene glycol bowel preparation (n = 48). Participants were undergoing screening for iron deficiency anaemia or GI symptoms with no evidence of mucosal disease/inflammation (n = 58), or with diagnosed Crohn’s disease (n = 18). Duodenal biopsies were obtained and gDNA extracted. Amplicon libraries of the 16s rRNA gene were sequenced (Illumina MiSeq). Sequencing of reagent controls enabled exclusion of...
non-duodenal sequences. Bioinformatics and statistics were performed in QIIME and Calypso.

Results: A diverse microbiota was observed in duodenal mucosal samples from all subjects, following overnight fasting or bowel preparation. Overall the duodenal microbiota was dominated by the genus Streptococcus, followed by Prevotella, Veillonella and Neisseria. Microbial diversity within samples was not significantly different with and without bowel preparation (Chao1 metric). Principal coordinates analysis (weighted UniFrac) revealed substantial overlap between the two groups, and no significant clustering was observed (ADONIS) based on whether patients had undergone overnight fasting or bowel preparation. Similar findings were obtained when these analyses were repeated with exclusion of the Crohn’s disease population.

Conclusion: This study reveals a diverse duodenal MAM is retained following bowel preparation. The comparison of overnight fasting and bowel preparation indicates these differences in patient preparation do not substantially alter the duodenal MAM. Thus patients undergoing concurrent upper GI endoscopy and colonoscopy can be included in study cohorts investigating the upper GI MAM without risk of a substantial confounding effect.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P1808 PERFORMANCE OF GLASGOW-BLATCHFORD, ROCKALL, AND AIMS65 SCALES TO PREDICT OUTCOMES AND TO IDENTIFY THE LOW-RISK GROUP AFTER UPPER GI BLEEDING IN PATIENTS WITH CANCER

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Introduction: Upper gastrointestinal bleeding (UGIB) in patients with cancer presents a unique and difficult challenge as these patients are at higher risk for rebleeding and mortality.1 Currently available prognostic scoring systems for UGIB for the general population have produced variable accuracy in their validation studies.2 An effective method of stratification for cancer patients to identify the high-risk group for early hospital-based intervention and death could enhance the outcomes of this specific population.

Aims & Methods: The primary aim of this study was to compare the Glasgow-Blatchford scale (GBS), Rockall score (RS) and AIMS65 score for predicting ICU admission, blood transfusion, hemostatic therapy, rebleeding, and in-hospital mortality in cancer patients with UGIB. The secondary aim was to assess the above cited scales in correctly identifying low-risk patients that can be effectively managed as an outpatient. An IRB-approved, prospective study was conducted at the Cancer Institute of Sao Paulo, Brazil. Consecutive patients with known cancer admitted with UGIB were enrolled. Pre-endoscopic clinical parameters pertinent to the scoring systems, hemostasis techniques, and outcomes were collected into a prospective registry. Patients were followed for at least 30 days or until the day of discharge, whichever was longer. The low-risk group was defined as those without blood transfusion, hemostatic therapy (by endoscopy, radiotherapy, angiography or surgical intervention), rebleeding or mortality in 30 days. Multiple logistic regression with receiver operating characteristics analysis was done to assess the predictive ability of each scoring system for the above outcomes.

Results: From April 2015 to May 2016, 394 consecutive patient cases were screened, while 259 patients met the inclusion criteria. A total of 243 patients were considered for the final analysis, after excluding 16 patients due to missing data or lost to follow up (Table 1). Predicting outcomes: The AIMS65 score (area under curve [AUC] 0.85) was significantly better for predicting ICU admission than the GBS (AUC 0.79; p = 0.04), both the total and clinical RS (AUC 0.71 and 0.66; p < 0.001 for both). The GBS best predicted the need for blood transfusion (AUC 0.82, sensitivity 71% and specificity 80% for GBS ≥ 12) compared with the other prognostic scores. All scores performed poorly in predicting the need for hemostatic therapy and risk of rebleeding. The AIMS65 score best predicted in-hospital mortality (AUC 0.84) compared to the GBS (AUC 0.75; p = 0.004), both the total and clinical RS (AUC 0.70 and 0.69; p < 0.001 for both). Among patients with bleeding at EGD, there was no difference in 30-day mortality if the etiology of bleeding was tumoral or non-tumoral disease (38.1% vs 31.9%; p = 0.46). Identifying low-risk group: With GBS score of 0 as the cut-off value, its specificity was 100% with sensitivity of 5.8%. When GS ≤ 2, its specificity was maintained at 100%, while sensitivity was increased to 23.5%. This change increased the proportion of the patients from 1% to 5% without erroneously discharging high-risk patients. In comparison, when an AIMS65 value of 0 was chosen as definition for low-risk, this tool misclassified 20 patients who needed hospital interventions (specificity of 53% and sensitivity of 89.5%). Finally, head-to-head comparison between GBS vs. RS, and GBS vs. AIMS65 scoring system revealed GBS to be superior to both the clinical RS (p < 0.001) and AIMS65 (p = 0.001) in correctly identifying low-risk patients.

Table 1: Demographic and Clinical Characteristics

<table>
<thead>
<tr>
<th>Factor</th>
<th>Total (n = 243)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>60.6 ± 13.6</td>
</tr>
<tr>
<td>Female/Male</td>
<td>71 (29.2%)/172 (70.8%)</td>
</tr>
<tr>
<td>Outpatient/Inpatient</td>
<td>178 (73.3%)/65 (26.7%)</td>
</tr>
<tr>
<td>Cancer in the Upper GI Tract</td>
<td>74 (30.5%)</td>
</tr>
<tr>
<td>Cancer Stage: 1 or II</td>
<td>17 (7.0%)</td>
</tr>
<tr>
<td>III</td>
<td>48 (19.9%)</td>
</tr>
<tr>
<td>IV</td>
<td>177 (73.1%)</td>
</tr>
<tr>
<td>Hemoglobin</td>
<td>8.1 ± 2.9</td>
</tr>
<tr>
<td>Albumin</td>
<td>2.8 ± 0.75</td>
</tr>
<tr>
<td>Rebleeding</td>
<td>24 (9.9%)</td>
</tr>
<tr>
<td>RBC Transfusion</td>
<td>147 (60.5%)</td>
</tr>
<tr>
<td>ICU</td>
<td>107 (44.0%)</td>
</tr>
<tr>
<td>Hemostatic Therapy</td>
<td>104 (42.8%)</td>
</tr>
<tr>
<td>30-day Mortality</td>
<td>66 (27.2%)</td>
</tr>
<tr>
<td>Follow-up time (days)</td>
<td>30.0 [22.0,30.0]</td>
</tr>
<tr>
<td>Clinical Rockall</td>
<td>4.6 ± 1.2</td>
</tr>
<tr>
<td>Total Rockall</td>
<td>7.0 ± 2.0</td>
</tr>
<tr>
<td>AIMS65</td>
<td>1.7 ± 1.2</td>
</tr>
<tr>
<td>Glasgow-Blatchford</td>
<td>10.8 ± 4.2</td>
</tr>
</tbody>
</table>

Conclusion: The AIMS65 score was superior to other scoring systems in predicting in-hospital mortality and ICU admission in patients with cancer and UGIB, whereas the GBS was superior for predicting the need for blood transfusion. All scores performed poorly in prediction of hemostatic therapy and rebleeding. The GBS was superior in accurately identifying low-risk patients. Furthermore, the cut-off ≤2 in GBS score displays increased sensitivity without compromising specificity, effectively increasing the number of patients who can be safely managed as an outpatient.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P1809 THE EFFECTS OF ANTICOAGULANTS ON THE CLINICAL OUTCOME OF ENDOSCOPIC TREATMENT

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Introduction: Endoscopists are more frequently performing endoscopic resection (ER) in patients on antplatelet or anticoagulant therapy and nowadays patients have increasingly started taking direct oral anticoagulant (DOAC) therapies, including direct anti-Xa and thrombin inhibitors. Major guidelines recommend the cessation of anticoagulants before ER and heparin bridging therapy (HBT) for high thrombotic risk cases, although these are still controversial. A recent study has suggested that HBT may be associated with a higher post-endoscopic resection bleeding (PEB) rate in patients on anticoagulants.

Aims & Methods: This study aimed to evaluate the effect of anticoagulants on PEB rate. This was a retrospective study based on medical records from three centers. PEB was defined as bleeding that occurred 6h to 10days after ER, which required endoscopic hemostasis. We reviewed 108 gastric tumors including adenoma and early cancer in 97 patients on anticoagulant therapy who underwent endoscopic submucosal dissection (ESD) in our hospitals between June 2008 and February 2016. Further, we reviewed 69 colorectal polyps including adenoma and early cancer in 69 patients on anticoagulant therapy who underwent ER in our hospitals between October 2013 and September 2016. ER included polypectomy, endoscopic mucosal resection (EMR), and ESD. Patients were divided into two groups: those prescribed warfarin and patients prescribed DOAC. The management of antithrombotics was based on the Japanese Gastroenterological Endoscopy Society guidelines published in 2005 and 2012. The anticoagulants used during the study period were warfarin, dabigatran, rivaroxaban, apixaban, and edoxaban. Warfarin was discontinued 4–5 days before ER, whereas the others were stopped 24–48h prior to the procedure. For patients at a high thrombotic risk, intravenous unfractionated heparin was administered after ceasing anticoagulants.

Results: Warfarin and DOAC were prescribed to 73 (75%) and 24 (25%) patients, respectively. Apixaban was administered to 1 (1%), dabigatran to 12 (12%), rivaroxaban to 11 (11%) patients. There were no significant differences between the DOAC and warfarin groups in terms of clinical characteristics or

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PBET rate. Overall, 57 patients (78%) in the warfarin group underwent HBT, and 29 patients (43%) in the PBET group compared to the patients who did not undergo HBT in the warfarin group (36% vs. 0%, p < 0.05). Although there was no significant difference in the PBET rate between the group that did and did not undergo HBT in the DOAC group, the PBET rate was higher among rivaroxaban recipients (45% vs. 0%, p < 0.05). Multivariate analysis revealed that HB, rivaroxaban, and anticoagulants plus antiplatelet therapy were associated with PBET (P < 0.05). Warfarin and DOAC were prescribed to 72 (57%) and 54 (43%) patients, respectively. Dabigatran was administered to 16 (13%), rivaroxaban to 18 (14%), apixaban to 18 (14%), dabigatran to 2 (1.6%) patients. Patients underwent polypectomy (n = 50), EMR (n = 62), or ESD (n = 10). PBET occurred in 5 (4.0%) patients (one polypectomy and four EMRs). Among them, warfarin was prescribed to one patient (1.4%) who also underwent ESD. Aspirin and apixaban were prescribed to two patients (11%) each. PBET rate was higher in the DOAC group than in the warfarin group (7.4% vs. 1.4%).

Conclusion: Patients on HB, rivaroxaban, and anticoagulants plus antiplatelet therapy are at an increased PBET risk after ESD for gastric tumors. In patients who underwent ER for colorectal polyps, PBET was more common in DOAC than that in warfarin recipients. That was the difference between ER for colorectal polyps and ESD for gastric tumors. We suggested that the PBET rate differs among DOACs because each drug has its own blood concentration and metabolism. Most clinicians have a limited knowledge on PBET during DOAC therapy because these are relatively new drugs, and because PBET has a low prevalence. Therefore, comparative data on larger patient series are needed to address this issue.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P1811 CLINICAL FEATURES OF DELAYED BLEEDING AFTER ENDOSCOPIC SUBMUCOSAL DISSECTION FOR GASTRIC NEOPLASMS IN HIGH-RISK AND LOW-RISK PATIENTS
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Introduction: Antithrombotic drugs are administered to patients undergoing endoscopic treatment at high risk for thromboembolism. However, antithrombotic drugs have been also known as a cause of delayed bleeding associated with endoscopic treatment, including endoscopic submucosal dissection (ESD). We previously reported the clinical features of post-polypectomy bleeding associated with heparin bridge therapy (1), and then various risk factors of delayed bleeding after endoscopic treatment have been reported.

Aims & Methods: The aims of the present study are to investigate the risk factors of delayed bleeding after gastric ESD and to clarify the clinical features of delayed bleeding in high-risk and low-risk patients. Patients with heparin bridge therapy who underwent ESD for gastric neoplasms in Osaka General Medical Center between January 2009 and December 2016 were retrospectively investigated. Independent risk factors of delayed bleeding were analyzed by using a multivariate analysis by logistic regression model, and three predictors of delayed bleeding were selected. Patients were categorized into a high-risk group or low-risk group for bleeding, and the clinical features of post-procedural bleeding in each group were investigated.

Results: A total of 717 patients with 781 gastric neoplasms were identified. Mean age was 74.6, and 71.6% was male. With regard to comorbidity, the proportion of hypertension, diabetes, chronic liver disease, and hemodialysis was 50.2%, 19.2%, 7.7%, and 6.1%, respectively. Total 188 patients (6.8%) experienced delayed bleeding after gastric ESD. Hospital stay was significantly longer in bleeding cases than in non-bleeding cases (median hospital stay (range) 11 (3–20) vs. 9 (9–25), p<0.007). A univariate and multivariate analysis showed heparin bridge therapy, antiplatelet therapy, and hemodialysis as risk factors for delayed bleeding. Delayed bleeding occurred in each group.

Conclusion: Delayed high-risk patients with heparin bridge therapy, antiplatelet therapy, and hemodialysis should be carefully observed after gastric ESD while early hospital discharge is acceptable for bleeding low-risk patients.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

P1812 EFFICACY AND SAFETY OF FERRIC CARBOXYMALTOSE TREATMENT IN PATIENTS HOSPITALIZED FOR ACUTE GASTROINTESTINAL BLEEDING NOT ASSOCIATED WITH PORTAL HYPERTENSION
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Introduction: There are few studies of the efficacy of parenteral ferric carboxymaltose (FCM) treatment in acute gastrointestinal bleeding (GIB) of different origins. Few data are available on its use to treat anemia post-acute haemorrhage.

Aims & Methods: To determine the efficacy and safety of FCM treatment in patients with acute GIB not associated with portal hypertension. A retrospective descriptive 3-year-study of patients with acute GIB (anemia with evident bleeding and/or hemodynamic instability) treated with FCM as part of our hospital’s habitual clinical practice.

Results: Analysis of 84 patients admitted with acute GIB (69.0% male, mean age 68.0 years [SD 6.9]), with a Charlson index ≥3 in 67.1% of cases (≥5 in 31.6%). 15.5% had previously suffered acute GIB due to peptic ulcer. There were 86 hospital admissions for acute GIB; 93.8% were upper GIB (above the angle of Treitz). The most frequent clinical presentation was melena, in 76.7% of cases. 23.6% presented hemodynamic instability at admission. The mean Glasgow-Blatchford index score was 16.1 (SD 2.7) and the mean Rockall score post-endoscopy was 4.2 (SD 1.7). The most common causes of bleeding were: 36.0% duodenal ulcer, 29% gastric ulcer, 9.3% gastritis/erosions, and 7.3% angiodysplasia of the colon. The mean Hb at admission was 9.0 g/dL (SD 2.2)
P1814 NOVEL EUS-GUIDED TREATMENT OF GASTRIC VARICES WITH A LIQUID NON-ADHESIVE NEUROVASCULAR EMBOLIZATION AGENT
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Introduction: Endoscopic Injection of adhesive agents such as N-Butyl-2-Cyanoacrylate (NBC) is an accepted option for the management of gastric varices. Recently the combination of NBC and coils has been used with endoscopic ultrasound (EUS) assistance. Nevertheless adhesive properties of the polymer may cause blockage of instrumentation material and damage to endoscopes. Sometimes the ulcers, vascular wall necrosis, rebleeding and distal embolism. Ethylene-vinyl alcohol (EVOH) has been extensively used in interventional radiology to treat cerebral arteriovenous malformations and has the advantage of being radiopaque.

Aims & Methods: We aimed to demonstrate a novel gastric varices embolization therapy with EUS-guided injection of a composite non-adhesive endovascular liquid agent EVOH combined with Dimethylsulfoxide (DMSO) as a primer. Five cases of EUS-guided Injection under fluoroscopic vision with EVOH is described in 5 men and 2 women, aged 50–65 years with gastric fundus varices, portal hypertension, Child-B hepatic cirrhosis and previous episodes of bleeding. The endoscopy was advanced to the gastroesophageal junction. The selected gastric varix was punctured using a 22 Gauge needle. EVOH injected volume ranged between 1.5 and 3cc. Vascular flow promptly and obliteration was real time monitored by EUS. Ceftriaxone was intravenously administered during the procedure. Patients were discharged on the same day. The mean follow-up was 6 months.

Results: All patients presented mild epigastric pain during the first 12 hours effectively managed with oral analgesics. The obliteration of variceal flow was achieved in all patients in a single session. There were no new episodes of bleeding or complications related to the technique.

Conclusion: EUS-guided embolization of gastric varices with EVOH can be considered as an efficient alternative. The procedure promises effective advantages in terms of number of sessions required, local or systemic adverse events and endoscopic aspect of ulcer. A comparison of cases and cost evaluation against coils alone or combined with NBC are required.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P1815 PREDICTIVE FACTORS FOR IN-HOSPITAL MORTALITY IN PATIENTS WITH PEP TIC ULCER BLEEDING
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Introduction: Peptic ulcers are the most frequent cause of upper gastrointestinal bleeding. In different population based surveys regarding all-cause UGIB, mortality ranges between 3% and 14%.

Aims & Methods: The aim of this study was to assess in-hospital mortality in patients with peptic ulcer bleeding and to evaluate the risk factors associated with mortality. In this prospective study we enrolled all patients diagnosed with peptic ulcer bleeding in a tertiary medical center over a period of 24 months (January 2015- December 2016). Patients were divided into two groups - those who died and those who survived - and the following parameters were compared: age, signs of hemodynamic instability (hypotension, tachycardia), evidence of coagulopathy as defined by Charlson index, the number of cases and cost evaluation against coils alone or combined with NBC are required.

Results: The study included 431 patients. In-hospital mortality rate was 7.9%. The following differences have been observed by comparing patients who died and those who survived: age > 75 years 41.2% vs 23.4% (p = 0.036); hypotension 17.6% vs 2.3% (< 0.001); anemia 47.1% vs 21.4% (p = 0.001); one or more comorbidities 94.1% vs 63.5% (p = 0.001); high risk endoscopic stigmata 79.4% vs 62.2% (p = 0.070); multiple ulcers 41.2% vs 33.5% (p = 0.473); Rockall score ≥5 points 94.1% vs 46.9% (p < 0.001); Blatchford score ≥10 points 91.2% vs 66.2% (p = 0.005); hemoglobin < 9.5 g/dl 70.6% vs 41.1% (p = 0.002); INR ≥2.5 17.6% vs 5.8% (p = 0.022); creatinine ≥1.5 mg/dl 38.2% vs 10.8% (p = 0.001); rebleeding 20.6% vs 12.1% (p = 0.123); need for blood transfusion 82.4% vs 56.4% (p = 0.006); need for surgery 11.8% vs 3.5% (p = 0.063). In most cases (88.2%), the cause of death was other than hemorrhagic shock. Using multivariate analysis, three out of these factors were identified as representing independent factors significantly associated with in-hospital mortality: tachycardia (OR = 2.83, 95%CI:1.21–6.58, p = 0.016). Rockall score ≥ 5 (OR = 6.65, 95%CI:1.46–30.16, p = 0.014) and creatinine ≥1.5 mg/dl (OR = 1.25, 95%CI:1.25–7.73, p = 0.014).

Disclosure of Interest: All authors have declared no conflicts of interest.

References
P1816 ANAEMIA AND UPPER GI BLEEDING: A LOCAL EXPERIENCE

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Introduction: There has been significant research recently on the use of blood transfusions in upper GI bleeding (UGIB) [1] with recent evidence advocating a restrictive approach to blood transfusions as well as the use of iron therapy[2] for anemic patients. Our team conducted a local retrospective analysis of patients admitted with UGIB over a six month period and analysed the use of blood transfusions at our trust which consists of two District General Hospitals. Patient data over a period of up to 12 months post discharge was collected to monitor their anaemia.

Aims & Methods: Our aim was to monitor the appropriateness of transfusions in Upper GI Bleeding as well as monitoring the response to iron therapy following discharge. All inpatients that had an Upper GI endoscopy for UGIB were analysed.

Results: There were 148 patients, 81 male and 67 female. The mean age was 69.3, minimum 20 and maximum of 98. The average Hb on admission was 103.6 g/L (min = 32 g/L, max = 178 g/L). 78 out of 148 (52.7%) patients presenting with UGIB received a blood transfusion. The mean amount of blood received for those transfused was 3.7 units. 48 out of 78 (61.5%) of blood transfusions were given when Hb was below 70 g/L. 30 of 78 (38.5%) were transfused with Hb above 70 g/L. 80.7% of patients presenting with UGIB received a blood transfusion. The mean amount of blood received for those transfused above 70 g/L was 7.6 units.

Conclusion: The data obtained supports a restrictive transfusion policy (mortality rate of 13.5% vs 10.4%). 58.5% of patients who were anaemic on discharge did not receive any iron therapy. On follow up, there was a statistically significant rise in Hb level in the group discharged on iron (p = 0.005) follow- up versus those who did not receive it (n = 62). The anaemia readmission rates were similar for patients discharged on iron or not (91.5% vs 4 vs 9.7% vs 6)

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P1818 EFFECTS OF FAECAL MICROBIOTA TRANSPLANTATION ON NEUROGEN IN 3, MUSASHI 1 AND ENTEROENDOCRINE CELLS IN THE DUODENUM OF PATIENTS WITH IRRITABLE BOWEL SYNDROME

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Introduction: The interaction between gut microbiota and enterodendocrine cells alterations is believed to play an important role in the pathophysiology of irritable bowel syndrome (IBS). The densities of the duodenal enterodendocrine cells are abnormal in IBS patients, which appears to be caused by a reduced stem cell density and their differentiation into endocrine cells (1). Aims & Methods: The aim is to investigate the effects of faecal microbiota transplantation (FMT) on the differentiation of the stem cells into enterodendocrine cells as detected by neurogenin 3, the stem cells as detected by Musashi 1 and the enterodendocrine cells in the duodenum of patients with IBS. The study included 16 IBS patients according to Rome III criteria and four patients were excluded. The remaining patients (n = 12, 4 females and 8 males, age range 20–44 years) were divided according to the cause of IBS into PI-IBS patients (n = 6) and idiopathic IBS (n = 6) and received FMT donated from their relatives. The patients completed the IBS-symptom severity scoring system (IBS-SSS) before and 3 weeks after FMT. The patients underwent gastroscopies with biopsies taken from the descending part of the duodenum at baseline and 3 weeks after FMT. The biopsies were immunostained for neurogenin 3, Musashi 1 and all types of duodenal enterodendocrine cells, and quantified by computerized image analysis.

Results: The score of IBS symptoms as assessed by IBS-SSS was significantly reduced 3 weeks after (240.2 ± 33.6) compared to before (326.6 ± 22.3) receiving FMT, P = 0.0009. The scores of IBS-SSS before and 3 weeks after FMT for PN-IBS were 300.8 ± 27.8 and 210.2 ± 41, respectively (P = 0.025), and for idiopathic IBS are 352 ± 34 and 270.3 ± 54, respectively, (P = 0.034). The densities of neurogenin 3, Musashi 1 and enterodendocrine cells in the duodenum of IBS patients before and 3 weeks after receiving FMT are presented in Table 1.

Conclusion: Faecal microbiota transplantation improved the symptoms in IBS patients, both PI and idiopathic. This improvement was associated with a change in the enterodendocrine cell density. The changes in the enterodendocrine cell density does not appear to be caused by changes in the stem cells or their early progenitors, but rather by changes in the differentiation progeny as detected by changes in neurogenin 3.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P1817 THE RELATIONS AMONG SERUM GHELIN, MOTILIN, CIRCULATING ANTIMYENTERIC ANTIBODIES AND GASTRIC EMPTYING FUNCTION IN AUTONOMIC NERVOUS SYSTEM FUNCTION IN PATIENTS WITH AUTOIMMUNE GASTRITIS

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Introduction: Autoimmune gastritis (AGI) is an organ-specific autoimmune disease of the stomach marked by autoantibodies directed to hydrogen-potassium-ATPase and intrinsic factor. Gastric emptying of solids is delayed and autonomic nervous system function is decreased in patients with autoimmune gastritis. This may be a cause of symptoms and also there is a close relationship between autonomic nerve dysfunction and delayed gastric emptying. As ghrelin and motilin are putative regulators of gastric emptying and, some autoimmune gastritis patients may have delayed gastric emptying leading up to gastrointestinal symptoms.

Aims & Methods: The aims of this study were to: (i) compare serum levels of ghrelin and motilin in patients with delayed normal gastric emptying and (ii) investigate whether circulating antimyenteric antibodies, serum levels of ghrelin and motilin are related to autonomic nervous system function. Forty-one patients with AGI were included into this study. Autoimmune gastritis was diagnosed depending upon histopathological findings in gastric biopsy specimens. Non-invasive cardiovascular reflex tests were used in order to evaluate autonomic nervous system function. Sympathetic nerve function was evaluated with two tests: blood pressure response to standing and handgrip test. Parasympathetic nerve function was evaluated with three tests: valsalva manoeuvre, heart rate response to deep breathing (E/I ratio) and orthostatic blood pressure testing. Dysfunction was considered to exist if at least two tests were positive. Gastric emptying time was evaluated by a standard 2-hour scintigraphic test using a solid meal. A half-time of longer than 110 minutes was chosen in the present study to further investigate patients with delayed gastric emptying. Serum ghrelin and motilin levels were tested by ELISA and circulating antimyenteric antibodies were tested by IFA.

Results: Forty-one patients (27 women), mean age 56.61 ± 11.79 years with AGI were included into the study. Overall, 22 (53.6%) patients showed delayed GE and 19 patients showed normal GE (GET ≥); 241.19 ± 190 ± 90 mins, p = 0.001). Serum ghrelin and motilin levels of patients with delayed GE were significantly decreased compared to patients with normal GE, respectively (67.5 ± 8.81 vs 126.79 ± 25.81 pg/mL, p = 0.001 and 279.59 ± 111.12 vs 500.42 ± 155.95 pg/mL, p < 0.001). In all, 26 (63.4%) patients showed autonomic nervous system dysfunction and, 15 (36.5%) patients had normal autonomic nervous system test findings (total autonomic test score: 0.8 ± 0.25 vs 5.65 ± 1.74, p < 0.001). Serum ghrelin and motilin levels of patients with deranged autonomic nervous system function were significantly decreased compared to patients with normal autonomic nervous system function (67.5 ± 8.81 vs 28.46 ± 127.79 ± 28.06 pg/mL, p < 0.001 and 316.92 ± 160.47 vs 490.20 ± 141.02 pg/mL, p < 0.001). In a multivariate analysis, plasma motilin level was found as an independent factor that affected serum ghrelin level (r = 0.43, p = 0.019). However, serum ghrelin (r = 0.623, p < 0.001) and gastritis (r = 0.70, p < 0.001) levels were found as independent factors that affected plasma motilin level. We also investigated the presence of antimyenteric antibodies, however all the patients were negative by means of antimyenteric antibodies therefore, no further relationship was sought.

Conclusion: Mean fasting serum ghrelin and plasma motilin levels in autoimmune gastritis patients with delayed GE and deranged autonomic nerve function were significantly decreased. Nearly all patients in our study were affected by circulating antimyenteric antibodies. These decreased serum ghrelin and plasma motilin levels in patients with autoimmune gastritis suggest a potential role for ghrelin and motilin in explaining the finding of the delayed gastric emptying in autoimmune gastritis patients. We believe that these new observations supply more insight into the pathophysiology of autoimmune gastritis.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
P1819 THE EFFECT OF ESOPHAGEAL ACID EXPOSURE ON NMDA RECEPTOR SUBUNITs EXPRESSION AND D-SERINE IN PREFRONTAL CORTEX AND HIPPOCAMPUs

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Introduction: Neuronal plasticity has been reported to develop following nociceptive emotional experience in prefrontal cortex (PFC) and hippocampus. The N-methyl-D-aspartate receptor (NMDAR) and D-serine, the endogenous co-agonist of NMDAR1, may mediate the neural plasticity. However, whether the neural plasticity participates in the mechanism of esophageal visceral hypersensitivity is little known.

Aims & Methods: This study aims to investigate the expression of NMDAR and the alteration of D-serine after neonatal and adult esophageal acid exposure. All rats were exposed to esophageal acid or saline at postnatal days 7-15(P7-P15), and most rats underwent acute acid or saline exposure again at adult time (P60).All rats were randomly distributed to 5 groups, including P7S, P7H, P60S, P60H and P7S þ P60H (P7: postnatal 7–15 days; P60: adult at postnatal 60 days; P: 0.1 M HCl infusion; S: saline control). The tissue harvest was conducted at P60. We examined the expression of subunits of NMDAR (including NR1, NR2A, NR2B, and NR2B), and c-fos, and serum racemase in PFC, dorsal hippocampus(DH) and ventral hippocampus(VH). We also determined the D-serine and L-serine in PFC and hippocampus by LC-MS analysis. Statistical comparisons were performed by General Linear Model and one way ANOVA in SPSS.

Results: In PFC, compared with adult saline treatment (AS, including P7H þ P60H and P7S þ P60H group) and without adult treatment (A-, including P7S and P7H group), adult acid exposure (AHE) increased the expression of NR1 (P = 0.052, P = 0.298), NR2B (P = 0.035, P = 0.045), and serum racemase (P = 0.022, P = 0.017) significantly. In ventral hippocampus, compared with adult treatment absence, adult acid exposure caused increasing expression of NR2B (P = 0.012) and NR1 (P = 0.024) significantly. In PFC, the expression of c-fos in the P7S þ P60H group was obviously higher than that of other groups (P = 0.008). See Table1. In dorsal hippocampus, the expression of c-fos was also increased (P = 0.008, AS vs A-: P = 0.042, AH vs AS: P = 0.081) and L-serine(AH vs A-: P = 0.008) decreased in the AH and AS group, comparing with A- group.

The expression of serine Racemase and c-fos in VH

<table>
<thead>
<tr>
<th>Group (n = 8/group)</th>
<th>PFC Serine Racemase</th>
<th>VH c-fos</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>P value (mean ± SD)</td>
<td>P value (mean ± SD)</td>
</tr>
<tr>
<td>P7S</td>
<td>0.139 ± 0.131</td>
<td>0.035 ± 0.008</td>
</tr>
<tr>
<td></td>
<td>(vs P7S + P60H)</td>
<td>(vs P7S + P60H)</td>
</tr>
</tbody>
</table>

Conclusion: Acute esophageal acid exposure may increase the expression of NMDAR in PFC and ventral hippocampus. We also found that the first acid exposure at adult stage may enhance the expression of serine racemase in PFC and c-fos in ventral hippocampus, but this phenomenon may be absent in those rats having the experience of acid exposure in early life. Those long-term and transitional molecular alterations may mediate the development of acid exposure related esophageal visceral hypersensitivity.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1820 1.8. UPPER GI NERVE- GUT AND MOTILITY: TRANSMITTERS/SIGNALS/RECEPTORS/ENTERIC NERVOUS SYSTEM

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Disclosure of Interest: All authors have declared no conflicts of interest.

Abstract No: P1818

Table 1: Densities of stem cells and enterendocrine cells in the duodenum of total IBS group, PI-IBS and idiopathic IBS patients before and after receiving FMT

<table>
<thead>
<tr>
<th>Markers/Hormones</th>
<th>Immuneactive cells densities</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total IBS, before</td>
</tr>
<tr>
<td></td>
<td>before</td>
</tr>
<tr>
<td>Neurogenin 3</td>
<td>222.3 ± 13.8</td>
</tr>
<tr>
<td>Musashi 1</td>
<td>5.7 ± 0.4</td>
</tr>
<tr>
<td>Chromogranin A</td>
<td>370.3 ± 21</td>
</tr>
<tr>
<td>Serotonin</td>
<td>135.1 ± 14.7</td>
</tr>
<tr>
<td>Somatostatin</td>
<td>58.6 ± 4</td>
</tr>
<tr>
<td>Cholecystokinin</td>
<td>122.8 ± 6.7</td>
</tr>
<tr>
<td>Secretin</td>
<td>83.8 ± 4.9</td>
</tr>
<tr>
<td>Gastric inhibitory peptide</td>
<td>65.1 ± 3.8</td>
</tr>
</tbody>
</table>

Reference
To the best of our knowledge, our findings are the first to establish an association between SLC6A4 gene polymorphism and globus pharyngeus.

Aims & Methods: 84 patients diagnosed with globus according to Rome III and 160 healthy controls were genotyped for 5-HTTLPR polymorphism by PCR amplification and agarose gel electrophoresis. All globus patients were studied with single water swallow resolution manometry pre-therapy. Globus patients were randomized into paroxetine group; amitriptyline group for 6-week treatment, and were asked to complete the following questionnaires pre- and post-therapy: Glasgow Edinbrough Throat Scale (GETS), Pittsburgh Sleep Quality Index, Hamilton Rating Scale Anxiety/Depression. Treatment response was defined as a > 50% reduction in GETS scores.

Results: The significant difference was shown in globus performed S/S genotype with anxiety when compared to without (X2 = 14.579, P = 0.006). The S genotype showed a significant difference between high upper esophageal sphincter pressure (>104 mmHg) and non-high upper esophageal sphincter pressure patients (X2 = 14.433, P = 0.006). There was significant association between the S genotype and the response to antidepressants treatment, while patients with sleep disorders or depression had lower rates.

Conclusion: A significant association was observed between S/S genotype of SLC6A4 polymorphism and globus pharyngeus, suggesting that SLC6A4 is a potential candidate gene involved in the pathogenesis of globus pharyngeus.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P1821 DIAGNOSTIC YIELD OF PROVOCATIVE TESTS ON ESOPHAGAL HIGH RESOLUTION MANOMETRY (HRM)
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Introduction: Multiple rapid swallows (MRS) and rapid drink challenges (RDC) are provocative tests that can enhance the diagnostic value of esophageal HRM. The discriminatory characteristics of these provocative tests were evaluated in symptomatic patients referred for esophageal HRM.

Aims & Methods: Consecutive patients presenting for esophageal HRM were a 2-month prospective cohort where provocative testing with MRS and RDC in addition to the standard manometric protocol. Integrated relaxation pressure (>15 mmHg) identified outflow obstruction; those without outflow obstruction were further analyzed for imaging software tools (IRP, distal contractile integral, DCI; intrabolus pressure, IBP) for peristaltic reserve (MRS or RDC DCI > mean DCI from wet swallows), and obstruction (IBP > 30 mmHg during MRS or RDC). All patients completed symptom questionnaires addressing reflux symptoms (GERD-Q), dysphagia (Mayo Dysphagia Questionnaire, MDQ) and global symptom severity (GSS) on a 100 mm visual analog scale (VAS). Univariate and multivariate analyses were performed to evaluate overall yield (proportions with MRS/RDC findings not seen with the standard HRM protocol) and to assess association of presenting symptoms with results of MRS and RDC in patients without outflow obstruction.

Results: 149 patients (55±1.2yr, 68% F) fulfilled inclusion criteria and had no outflow obstruction on HRM. Of these, 91 (61%) had peristaltic reserve on MRS, 19 (12.6%) on RDC (p < 0.001), only 10 were concordant. Obstruction was noted in 16 (9.8% on MRS, 8 (4.9%) on RDC (p = 0.09), and 5 were concordant; of these, only 2 patients had panoesophageal compartmentalization of pressure, and only 1 had elevated IRP during provocative measures. Within ineffective esophageal motility, peristaltic reserve was noted in 59.3%. Within dysphagia presentations, obstruction was noted in 7.7%, and absent peristaltic reserve in 50%. Thus, the overall yield of MRS was 80.5%, and RDC 19.8% (p < 0.001). 131 patients had adequate questionnaire data. Findings on provocative tests did not predict presenting symptoms (GERD-Q or MDQ). Obstruction on RDC predicted higher GSS (odds ratio 5.56, 95% CI 1.04-29.72).

Conclusion: MRS identifies peristaltic reserve better than RDC and has higher sensitivity measured in THIN patients. The variation of findings between the databases likely results from differences in coding practice and marginally different population structures.

Disclosure of Interest: All authors have declared no conflicts of interest.

Prevalence of Achalasia in England in Two National Databases
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Introduction: Achalasia is an uncommon condition of failed lower oesophageal sphincter relaxation. Data regarding the incidence and prevalence are limited. The aim of this study was to provide accurate, contemporary epidemiological data utilising two national databases.

Aims & Methods: Hospital Episode Statistics (HES) includes demographic and diagnostic data for all English hospital admissions. The Health Improvement Network (THIN) database includes primary care records of 7% of the UK population, representative of national demographics. Both were searched for incident cases and THIN for prevalent cases of achalasia.

Results: There were 10,509 and 711 new achalasia subjects in HES and THIN respectively. The incidence per 100,000 person years in THIN was 1.99 (95% CI 1.87-2.11) and 1.53 (1.42-1.64) per 100,000 person years in THIN. The prevalence measured in THIN was 27.1 (25.4-28.9) per 100,000 population.

Table 1: Annual incidence and prevalence of achalasia

<table>
<thead>
<tr>
<th>Year</th>
<th>Incidence rate HES (per 100,000 population)</th>
<th>Incidence rate THIN (per 100,000 person years)</th>
<th>Prevalence THIN (per 100,000 population)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2006</td>
<td>1.733</td>
<td>1.62-1.85</td>
<td>1.08-1.81</td>
</tr>
<tr>
<td>2007</td>
<td>1.798</td>
<td>1.69-1.92</td>
<td>1.39-2.08</td>
</tr>
<tr>
<td>2008</td>
<td>1.798</td>
<td>1.68-1.91</td>
<td>1.21-1.96</td>
</tr>
<tr>
<td>2009</td>
<td>1.853</td>
<td>1.74-1.97</td>
<td>1.34-2.12</td>
</tr>
<tr>
<td>2010</td>
<td>2.015</td>
<td>1.90-2.14</td>
<td>1.31-2.09</td>
</tr>
<tr>
<td>2011</td>
<td>1.781</td>
<td>1.67-1.90</td>
<td>1.09-1.82</td>
</tr>
<tr>
<td>2012</td>
<td>2.032</td>
<td>1.91-2.16</td>
<td>1.20-1.96</td>
</tr>
<tr>
<td>2013</td>
<td>2.179</td>
<td>2.06-2.31</td>
<td>1.26-2.05</td>
</tr>
<tr>
<td>2014</td>
<td>2.241</td>
<td>2.29-2.56</td>
<td>1.12-1.91</td>
</tr>
<tr>
<td>2015</td>
<td>2.236</td>
<td>2.21-2.36</td>
<td>0.96-1.80</td>
</tr>
</tbody>
</table>

Conclusion: The incidence of oesophageal achalasia was approximately 15 to 20 per 1 million population. There were approximately 17,500 patients with achalasia in the UK in 2013. The incidence rate increased by 1.8% in 2015. The prevalence measured in THIN was 27.1 (25.4-28.9) per 100,000 population.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1823 ACHALASIA DESPITE NORMAL INTEGRATED RELAXATION PRESSURE WITH SMIL WATER SWALLOW S. Sanagappal1, M. Duffy1, A. V. Emmanuel2, A. Raeburn1, M. Banks3, R. Haider3, L. Lovat1, R. Swets3
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Introduction: Resistance to bolus flow across the lower oesophageal sphincter (LES) is a hallmark of achalasia. Presently the gold standard of diagnosis is by high-resolution manometry (HRM) demonstration of raised integrated relaxation pressure (IRP) following ten 5 mL water swallows; however, this does not rule out normal swallowing behavior. It has been demonstrated that the addition of adjunctive tests improves sensitivity of identifying relevant dysmotility. Such tests include multiple water swallows (MWS; 200 mL water drunk freely) and solid swallows. In addition, the timed barium esophagum (TBE) measures esophageal emptying. This study describes a cohort of patients who have been treated as having achalasia based on resistance to flow not exhibited with single water swallows.

Aims & Methods: Inclusion criteria were all patients between October 2014–2016 with normal mean and median IRP with 5 mL water swallows but considered to have achalasia due to resistance to flow demonstrated by pan-oesophageal pressure surpression (PEP) during MWS or solid swallows and/or a persistent column at 5 minutes during TBE. Outcome following treatment was based on the Eckardt symptom score (ES).

Disclosure of Interest: All authors have declared no conflicts of interest.
Results: 14 patients (9 male) fulfilled inclusion criteria. 7 were treatment-naive and 7 treatment-experienced (3 myotomy, 4 dilatation). Mean resting LES pressure was 14.6±4.7 mmHg. In all patients, and median IRP values for ten 5 mL water swallows were non-raised (mean 9.1±4.3 and 8.7±4.5 mmHg respectively). Of the 7 treatment-naive patients, 5 demonstrated PEP on MWS, 3 on solid swallows and 6 had a positive TBE at 5 minutes. In treatment-experience patients, 5 had PEP on MWS, 1 on solid swallows and all had a positive TBE. Of the 13 who had resistance to flow on TBE, 10 (77%) also had resistance on solid swallows and 6 had a positive TBE at 5 minutes. In treatment-experienced patients, Achalasia type III (n = 22), achalasia type IV (n = 17) and achalasia type V (n = 5) patients have (so far) undergone therapy based on these findings: one or more endoscopic myotomy and 7 pneumatic dilations. The median baseline ES was 7.5 (IQR: 5-8). The median ES at 3 minutes (range 3-15 months) following treatment was 1 (IQR 0-0.9; P < 0.001 cf. baseline). Similarly, there was significant improvement in TBE findings post-therapy (mean 5-minute column height 3.5±4.1 cm; P = 0.04 cf. baseline).

Conclusion: A normal IRP for water swallows does not preclude a diagnosis of achalasia. The addition of free drinking/solids during HRM or the TBE can identify pathology that might have been missed with standard 5 mL water swallows alone as normal, clinically relevant swallowing behavior is reproduced. Patients treated based on this algorithm exhibit excellent treatment outcomes, validating this approach. Further, the close correlation of HRM adjunctive testing with TBE supports its routine inclusion in clinical practice.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1824 200ML RAPID DRINK CHALLENGE DURING HIGH RESOLUTION MANOMETRY PREDICTS OESOPHAGOGASTRIC JUNCTION OBSTRUCTION IN DYSPHAGIA AND IS CORRELATED WITH SYMPTOM SEVERITY IN ACHALASIA

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Introduction: In patients with dysphagia, the identification of obstruction at the OGJ level determines the need for further endoscopic or surgical therapy. Timed barium esophagogram (TBO) is regularly used to detect impaired oesophageal emptying in dysphagia and achalasia. "Volume loading" the oesophagus with a 200ml rapid drink challenge (RDC) has recently been shown to help with the diagnosis of oesophageal motility disorders. We predict that this test can evaluate OGJ efficiency at HRM without the need for further TBO study. As such we hypothesised that RDC can predict pathological barium column at TBO, and associates with symptom severity in achalasia.

Aims & Methods: 39 patients with untreated dysphagia (mean age 55yr) were evaluated. All patients underwent HRM with standard protocol plus RDC, followed by TBO. In patients with achalasia, the Eckhardt score (ES) was calculated by reviewing HRM findings. Analysis of HRM followed the Chicago Classification v3 algorithm. A normal IRP for water swallows does not preclude a diagnosis of achalasia. The addition of free drinking/solids during HRM or the TBE can identify pathology that might have been missed with standard 5 mL water swallows alone as normal, clinically relevant swallowing behavior is reproduced. Patients treated based on this algorithm exhibit excellent treatment outcomes, validating this approach. Further, the close correlation of HRM adjunctive testing with TBE supports its routine inclusion in clinical practice.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1825 THE TIMED BARIUM ESOPHAGRAM SURFACE AREA CORRELATES WITH SYMPTOM IMPROVEMENT BETTER THAN COLUMN HEIGHT FOLLOWING TREATMENT IN ACHALASIA

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Introduction: The timed barium esophagram (TBE) is an objective measurement of esophageal (3 myotomy, 4 dilatation) used in the assessment of achalasia. Post-therapy resolution of the maximum height of the residual barium column has been found to correlate imperfectly with short-term symptomatic outcomes, but carries long-term prognostic implications. We hypothesise that the surface area (SA) of the barium column might be more accurate than height, firstly, by showing a more pronounced improvement in esophageal width that often occurs post-therapy, but also by correcting for artificially higher height values due to esophageal (longitudinal) contraction occurring during a single image. We aim to compare the correlation of TBE outcome measures of height and SA with symptom improvement post-therapy.

Aims & Methods: Inclusion criteria were achalasia patients who underwent therapy between August 2015-6 and had TBE and Eckardt score (ES) performed at baseline and 6 months post-treatment. With TBE upright single images were acquired at 1.2, and 5 minutes following ingestion of 100-200 mL of low-density barium sulfate. Barium height was measured between the gastro-esophageal junction and the superior extent of any residual barium column. After manually defining the column boundaries, software was used to calculate SA (AGFA IMPAX surface area tool (Figure)). Adequate symptom relief was defined as reduction in ES to ≤ 3. On TBE, metrics of adequate emptying evaluated were i) post-therapy column height < 5cm, ii) > 50% reduction in column height from pre to post-therapy and iii) > 50% reduction in column SA from pre to post-therapy. Associations between symptom improvement and TBE measures of emptying were assessed using Pearson's correlation (R). Paired t-tests compared TBE measures before and after therapy.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1826 NUTRIENTS ENHANCE BELCHING AND REDUCE INTESTINAL PROPULSION OF GASTRIC GAS IN HEALTHY VOLUNTEERS

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Introduction: During meal intake, large volumes of gas can be ingested together with nutrients, and patients with gas-related abdominal symptoms often refer symptom exacerbation by meals. Previous studies have shown that under fasting conditions gastric gas is rapidly eliminated from the stomach, either via gas belching or via belching. Nutrients have several effects on gastric and intestinal motor function that could modulate gas transport and symptoms.

Aims & Methods: We aimed to determine the effect of gastric nutrients on transport of gastric gas, and its relationship with abdominal symptoms. In 7 healthy volunteers without gastrointestinal symptoms (4 women and 3 men, age-range 21-25 yrs), a mixture of non-absorbable gases was infused into the stomach, 5 cm caudal to the lower margin of the LES, at 25 mL/min during 60 min (Total gas infused: 1500 mL). In each subject two gas infusion tests were performed on separate days, with simultaneous infusion of nutrients (Nutridrink 1.5 Kcal/ml, total 315 Kcal) or saline. Belching, by an esophageal multilumen impedance manometry catheter, rectal gas evacuation, via a rectal tube connected to a barostat, and epigastric and abdominal symptoms, by specific questionnaires (from 0–6), were continuously recorded from the start of gas infusion until 30min after gas infusion stopped. (Total recording time: 90 min).

Results: During saline infusion, participants evacuated via the rectum virtually all the infused gas (1631±87 ml), with exceptional belching (1.1±0.8 belches) and mild epigastric perception (score 1.7±0.6 at the end of infusion), that decreased during the 30 min following infusion stop (score 1.1±0.4; p = 0.051 vs infusion
PI827 MODIFICATIONS OF THE ECKARDT SCORE PARAMETERS AFTER PERORAL ENDOSCOPIC MYOTOMY

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Introduction: Peroral endoscopic myotomy (POEM) is a recently developed technique or the treatment of lower esophageal sphincter achalasia. POEM could be as efficient as surgical Heller myotomy, while associated with lower morbidity.

Currently, the Eckardt score is the clinical score that is the most widely used to assess the postoperative effect of the treatment of achalasia, clinical success being defined by a score below 4. However, POEM might not equally improve all four parameters of the Eckardt score.

Aims & Methods: All consecutive patients undergoing POEM for achalasia at our institution were performed by 3 operators with at least 6 months follow-up were prospectively included. Demographic, clinical, procedural, manometric and radiologic data were collected.

Results: Between March 2013 and July 2016, 62 POEM procedures were performed on 59 patients (Male/female 33/26; Median age ± SD – 54 ± 13, range (15–77)). Median (IQR) follow-up time was 8 (3–13) months. Achalasia was diagnosed for a median (IQR) of 24 (13–62) months, and 42% of the patients had a previously received treatment, by botulinum toxin injection (8%), pneumodilation (32%), or Heller myotomy (7%). Achalasia subtype were type I/II/III in 37%/47%/15% of cases. Median Eckardt score and integrated resting pressure varied from 2 (1–3) to 0 (0–1) and 1 (0–1) (p = 0.0001). Dysphagia score varied from 5 (3–7) to 3 (1–5) and 2 (0–3) (p = 0.0001), while regurgitations varied from 2 (1–3) to 0 (0–1) and 1 (0–3) (p = 0.0001), chest pain varied from 1 (0–2) to 0 (0–1) and 0 (0–1) (p = 0.0006), and weight loss from 2 (1–3) to 0 (0–0) and 0 (0–0) (p < 0.0001). At three months, median (range) drop of the integrated resting pressure varied from 16 (6–22) mmHg after 1-st procedure up visit, 86% of the patients still had clinical success, and 31% reported gastro-esophageal reflux symptoms.

Conclusion: Our results confirm the efficacy of the POEM as a first line or rescue treatment for a low complication rate. POEM is most effective on dysphagia and weight loss, while chest pain and regurgitations tend to persist after treatment.

Disclosure of Interest: All authors have declared no conflicts of interest.

PI828 SUBGROUP ANALYSES OF CLINICAL TRIALS ON A HERBAL MEDICINE IN FD, STW 5

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Introduction: Well-proven therapeutic options for the therapy of functional gastrointestinal diseases are rare and therefore gain high attention. One of these is STW 5 (Iberogast), for which more than five decades of therapeutic experience in gastrointestinal diseases are rare and therefore gain high attention. One of these is STW 5 (Iberogast), for which more than five decades of therapeutic experience in gastrointestinal diseases are rare and therefore gain high attention.

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Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

PI819 THE TREATMENT OF ACHALASIA IN PATIENTS WITH OESOPHAGEAL VARICES: AN INTERNATIONAL CASE SERIES

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Introduction: Achalasia is a chronic condition presenting with dysphagia, regurgitation, chest pain and/or weight loss. Management options include Heller’s myotomy, Botox, pneumatic dilatation and Per-Oral Endoscopic Myotomy (POEM). Treatments carry risks of bleeding and perforation. Concomitant portal hypertension with varices is very rare and achalasia treatment in this context has only been described in single case reports.

Aims & Methods: Experience from physicians/surgeons treating these disorders was sought through the International Manometry Working Group.

Results: 13 patients with portal hypertension from 6 international centres have been collected; mean age 61 ± 9 years. The median pre-therapy Eckardt score was 7 (IQR 6–9); 9/13 (69%) patients had a barium swallow and 12/13 (92%) had oesophageal physiology studies performed. There were 3 Type I, 6 Type II, 2 Type III achalasia and 2 with oesophago-gastric outflow obstruction. Varices had been identified endoscopically in 7 patients, radiologically in 5 and in 1 patient varices were first noted during surgical myotomy. 2 patients had grade 3 varices, 3 grade 2 and 3 had grade 1 varices (grading not provided for the rest). Cirrhosis was due to alcohol in 7 patients, non-alcoholic steatohepatitis in 3, cryptogenic in 2 and 1 had hepatitis C cirrhosis. 75% were Child-Pugh A and 25% were Child-Pugh B. Patients had diverse treatments for their achalasia. 4 were treated with Botox injections (1 with EU5, 4 had dilation alone, 3 received a POEM, another had POEM then dilation and 1 patient had Botox followed by Heller’s myotomy. 3 patients underwent variceal eradication in advance; all had banding first but in 2 patients superficial eradication was followed by a transjugular intrahepatic portosystemic shunt (TIPSS) before endoscopic dilation. All patients had symptomatic improvement with median Eckardt score post intervention = 1 (IQR 0–2) < 0.0001 compared to baseline. A matched group of 20 patients who underwent treatment for achalasia (all subtypes) but without varices had no complications of bleeding or perforation; however both patients who had TIPSS had transient hepatic decompensation.

Conclusion: This report 13 patients from international centres who have had interventions for achalasia on the background of oesophageal varices. None had bleeding complications despite only 3 having had variceal eradication. Symptom response mirrored those who undergo standard achalasia therapy,
PI830  THE NATURAL HISTORY OF ACHALASIA: EVIDENCE OF A CONTINUUM-THE PATTERN-EVOLUTIONARY STAGING THEORY
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Introduction: Esophageal achalasia is classified into three clinically relevant patterns at High Resolution Manometry (HRM) and according to Chicago Classification. Currently, it is unclear whether they represent distinct entities or are part of a disease continuum.

Aims & Methods: The aims of this study were: a) to test the hypothesis that the three manometric patterns represent different stages in the evolution of esophageal achalasia and b) to investigate whether manometric patterns change after Laparoscopic Heller-Dor (LHD). We evaluated the patients who had a diagnosis of achalasia and underwent LHD as first treatment from 1992 to May 2016. Symptoms were scored using a detailed questionnaire for dysphagia, food-regurgitation, and chest pain; barium swallow, endoscopy, and esophageal manometry (conventional or High Resolution technique) were performed, before and 6 months after surgical treatment. All conventional manometric tracings, before 2010, were reviewed and re-classified according to the manometric-pattern classification, whereas after 2010 the HRM data were prospectively collected.

Results: Five-hundred and eleven consecutive achalasia patients (M:F = 283:228) represented the study population. Based on their manometric findings, 231 patients (45.2%) were classified as having pattern I, 241 (47.2%) had pattern II, and 39 (7.6%) had pattern III. Demographic and clinical data showed that pattern III cases had a shorter duration of symptoms, a more incidence of chest pain, and a less dilated gullet (p < 0.001). Further, all patients with a sigmoid-shaped mega-esophagus (radiological grade IV) had pattern I achalasia. One patient with diagnosis of pattern III achalasia, who refused any treatment evolved to pattern II at a follow-up manometry performed for a progressive worsening dysphagia after 36 months. At a median follow-up of 30 months (IQR 12–56), the outcome of surgery was positive in 479 patients (91.7%).

The only predictor of final outcome was the preoperative manometric pattern (p < 0.001). All patients (42) whose surgical treatment failed underwent one or more endoscopic pneumatic dilations using Rigiflex balloons (30, 35 or 40 mm).

The overall success rate of the combined treatment (LHD plus endoscopic dilations where necessary) was 98%. All patients with pattern I preoperatively had the same pattern after LHD, whereas more than 50% of patients with pre-treatment pattern III had patterns I or II after surgery. There were no cases showing the opposite trend (Table 1). Five patients showed signs of a partial recovery of peristalsis (all patients had a pattern II before LHD).

Table 1: Changing manometric patterns after LHD. *5 patients had a recovery of peristalsis (all patients had a pattern II before LHD).

<table>
<thead>
<tr>
<th>Pattern 1</th>
<th>Pattern 2</th>
<th>Pattern 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pattern 1</td>
<td>159 (100%)</td>
<td>0</td>
</tr>
<tr>
<td>Pattern 2</td>
<td>65 (29.5%)</td>
<td>149 (67.7%)</td>
</tr>
<tr>
<td>Pattern 3</td>
<td>7 (24.1%)</td>
<td>8 (27.6%)</td>
</tr>
</tbody>
</table>

Conclusion: The data of this study strongly support the hypothesis/theory that the different manometric patterns of achalasia could represent different evolutionary stages of the disease - where pattern III is the earlier stage, pattern II an intermediate stage, and pattern I the end stage.

Disclosure of Interest: All authors have declared no conflicts of interest.

PI831  ROLE OF A SERUM BIOMARKERS PANEL (GASTROPEANES) IN NON-INVASIVE DIAGNOSIS OF UPPER GI DISEASE: DATA BY A PRIMARY CARE POPULATION OF NORTHEAST ITALY
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Introduction: The development of non-invasive methods to detect the presence of H. pylori, and to estimate the extent and severity of gastritis, have reduced the need for diagnostic endoscopy in asymptomatic individuals. However, it is not known whether the use of non-invasive diagnostic methods is effective in dyspepsia patients.

Aims & Methods: To use a non-invasive blood test with four stomach-specific biomarkers to assess the prevalence of different stomach conditions: gastroesophageal reflux disease (GERD), H. pylori (HP) infection, chronic atrophic gastritis (CAG), and the efficacy of proton pump inhibitor (PPI) therapy in a primary care population. A cohort of 2583 dyspeptic patients (male 36%, mean age 44.0 yrs, range 6-95) was selected in a primary care population and examined with a panel of biomarkers [Pepsinogen-I (PG-I) and -II (PG-II), anti-Helicobacter pylori (anti-Hp), and Hp IgG and Hp IgA] (Biohit, Finland). A standard questionnaire, including upper gastrointestinal symptoms and PPI use, was administered. Exclusion criteria were dysphagia, anemia, weight loss and vomiting. CAG patients underwent to endoscopy and histological examination.

Results: Healthy stomach was found in 21.2% patients. Prevalence of CAG increased with patient’s age in both sexes as well as the use of PPIs (p = 0.0001). Table 1 shows the serum biomarkers values divided according to five categories: healthy stomach (H), GER, HP, HP+CAG, and PPI therapy.

Conclusion: The combination of data on the levels of PG-I, PG-II, G17 and HP IgG allow to diagnose different pathological conditions such as HP- and non HP-related gastritis, the appropriateness of PPI administration, GERD and CAG, a precautionary condition.

Disclosure of Interest: All authors have declared no conflicts of interest.

PI832  SUSTAINED TREATMENT EFFECTS OF MENTHACARIN ON SYMPTOMS AND QUALITY OF LIFE IN PATIENTS WITH FUNCTIONAL DYSPEPSIA 8 WEEKS AFTER THE END OF A 4-WEEK PLACEBO-CONTROLLED TRIAL
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Introduction: Functional dyspepsia (FD) is one of the most common functional gastrointestinal disorders characterised by chronic or relapsing symptoms with no structural or biochemical abnormalities that can be identified in the routine clinical setting. Thus, treatment targets symptoms. Very little is known about prolonged treatment for more than 4 weeks. Fifty-four of them participated in the optional follow-up phase and received Menthacarin (34) or placebo (20) for further 8 weeks according to their original randomization. The results of these 54 patients are reported here.

Aims & Methods: The aim of the additional data analysis of a previous randomized placebo-controlled trial was to explore post-treatment effects that occurred after continuation of therapy after a 4-week randomised placebo controlled treatment with Menthacarin with regard to disease-specific symptoms and QoL in FD patients. After the 4-week randomised placebo-controlled treatment period, patients were allowed to continue the treatment. The treatment was given in a double-blind fashion and allocation of treatment followed the initial randomisation. 114 adult FD outpatients were initially treated and received twice a day one enteric-coated Menthacarin capsule or a matched placebo capsule for 4 weeks. Fifty-four of them participated in the optional follow-up phase and received Menthacarin (34) or placebo (20) for further 8 weeks according to their original randomization. The results of these 54 patients are presented here. Outcomes were assessed utilising the validated self-rating Nepean Dyspepsia Index (NDI). Intra-individual differences between baseline and week 4/week 12 for NDI sub-scores for pain (sum of the NDI items ‘pain or ache in upper abdomen’), ‘burping and flatus’ and ‘food-avoidance’ were calculated.

Results: Overall, there was a significant improvement in NDI pain score (p = 0.0001) and NDI symptom score (p = 0.0001) at week 12 compared to baseline (p = 0.0001). The 50% responder rate at week 12 is 57% (50% response rate at week 4). The NDI symptom score improved by 30% (p = 0.0001) at week 12.

Conclusion: Menthacarin was significantly effective for the treatment of functional dyspepsia for up to 8 weeks. Further studies are warranted to investigate the clinical relevance and cost-effectiveness of this approach.

Disclosure of Interest: None declared.

Abstract No: P1831
after 4 weeks of randomised double-blind, placebo-controlled therapy, the score had declined by 3.7 \pm 2.1 points during active therapy as compared to 5.4 \pm 2.1 points during placebo treatment (p = 0.003). For the 12-week therapy, the score had declined by 3.7 \pm 2.5 points and 1.3 \pm 2.6 for Menthacarin and placebo, respectively (p = 0.0014). Overall QoL improvement was better for active medication for 4 and 12 weeks as compared to placebo.

Conclusion: After 4 weeks of randomised double-blind, placebo-controlled treatment with either Menthacarin or placebo, patients who received active medication are more likely to opt for a continuation of therapy as compared to patients on placebo. The gain over placebo remained significant even after 12 weeks of treatment. Menthacarin is a proprietary combination of essential oils of specified quality from Menth\textsubscript{a} piperita L. (90 mg Peppermint oil WS\textsubscript{e} 1340) and Carum carvi (50 mg Caraway oil WS\textsubscript{e} 1520).

Disclosure of Interest: G.J. Holtmann: Financial support for research and lecture fees from Dr. Willmar Schwabe GmbH & Co. KG B. Stracke: Employee of Dr. Willmar Schwabe GmbH & Co. KG

P1833 IMPROVEMENT OF APPROPRIATENESS OF PROTON PUMP INHIBITOR (PPI)-THERAPY PRESCRIPTION WITH USE OF SEROLOGICAL MARKERS (GASTRANOPOL) IN A PRIMARY CARE POPULATION

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Introduction: The introduction of proton pump inhibitors (PPIs) into clinical practice has revolutionized the management of acid-related diseases. Studies in primary care and emergency settings suggest that PPIs are frequently inappropriately prescribed or used in clinical conditions with little benefit.

Aims & Methods: To evaluate the role of Gastropanol in relation to the appropriateness of PPI-therapy prescription. 2833 dyspeptic patients (male 36\%, mean age of 44.0 yrs, range 6-95) with no alarm symptom (i.e., dysphagia, anemia, weight loss and vomiting) from a primary care population were included in the study. For each patient a blood sample was collected for serum Pepsinogen I (PG-I) and II (PG-II), Gastrin 17 (G-17) and IgG HP (Biohit, Oyj, Finland); moreover, a clinical questionnaire searching for symptoms and presence of HP, and PPI therapy were filled out. We have evaluated the following serological profiles: HP infection, chronic atrophic gastritis (CAG), response to PPI therapy. The results obtained were used to evaluate the appropriateness of PPI-therapy prescription.

Results: 1015/2583 (39.3\%) received PPI therapy up to three months before serum sampling and were included in the study. Among 1015 patients under PPI therapy, 294 (29.0\%) received half-dose PPIs, 709 (69.8\%) full-dose PPIs and 12 (1.2\%) an exceeding-dose PPIs. Patients under PPIs therapy (3.7\%) showed a serological status compatible with body CAG (the definitive diagnosis was confirmed histologically). 68 (6.7\%) presented HP infection. Table 1 shows the values of PG-I and G-17 values according to the response to PPI therapy.

Conclusion: An appropriate prescription of PPI should be preceded by the assessment of gastric functional status. In particular, patients with HP infection should be eradicated before PPI therapy, while CAG patients should not receive PPI therapy because they are no responders. Patients who do not respond to PPI therapy should be further investigated (compliance, diagnosis).

Disclosure of Interest: All authors have declared no conflicts of interest.

Abstract No: P1833

<table>
<thead>
<tr>
<th>N</th>
<th>Therapy</th>
<th>Half PPI n,%</th>
<th>Full PPI n,%</th>
<th>Excess PPI n,%</th>
<th>Gastric Function status</th>
<th>Gastric Functional status</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>1015</td>
<td>294</td>
<td>709</td>
<td>12</td>
<td>PG-I (ug/L) means+/−/DS</td>
<td>PG-I (umol/L) means+/−/DS</td>
</tr>
<tr>
<td>Good response G17 &gt; 7</td>
<td>351</td>
<td>83 (23.6)</td>
<td>279 (73.8)</td>
<td>9 (2.6)</td>
<td>194.5+/−/121.1</td>
<td>22.1+/−/17.9</td>
</tr>
<tr>
<td>Low response G17 1−7</td>
<td>421</td>
<td>141 (33.5)</td>
<td>279 (66.3)</td>
<td>1 (0.2)</td>
<td>127.1+/−/8.3</td>
<td>3.1+/−/1.76</td>
</tr>
<tr>
<td>No response G17 &lt; 1</td>
<td>205</td>
<td>64 (31.2)</td>
<td>140 (68.3)</td>
<td>1 (0.5)</td>
<td>91.7+/−/40.9</td>
<td>0.38+/−/0.28</td>
</tr>
<tr>
<td>CAG</td>
<td>38</td>
<td>6 (15.8)</td>
<td>31 (83.3)</td>
<td>1 (2.6)</td>
<td>16.6+/−/14.8</td>
<td>70.3+/−/55.2</td>
</tr>
</tbody>
</table>

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Introduction: Gastric acid secretion is believed to decrease in the aging stomach, but the number of elderly patients on proton pump inhibitor (PPI) therapy is...
increasing. Pepsinogen I (PG1) <30μg/L, PG1/PGII <3 and gastrin-17 (G17) >10μmol/L are non-invasive serological markers to surrogate to evaluate gastric function, with a negative predictive value for chronic atrophic gastritis (CAG) of 96%.

**Aims & Methods:** Aim of the study was to evaluate gastric function by means of serology (PG1, PGII, G17 and IgG-antibodies against Helicobacter pylori) in very elderly patients, including centenarians. A total of 379 patients were prospectively enrolled (M=126, F=253, mean age=83.6±6.7, range 70-106). They were divided in four groups: 132 subjects with an age between 70 and 79 years (first group), 107 subjects between 80 and 89 (second group), 76 subjects between 90 and 99 (third group) and 25 subjects between 100 and 106 (fourth group). Demographics and drug intake, particularly the PPI intake, were collected. For all patients, serological markers were determined in fasting blood. PPI was determined by using Gastropanel® (Biohit Oy, Finland; normal values: PG1: 30-120μg/L; PG2: 2-15μg/L; PG1/PGII ratio: >3; G17: 1-9μmol/L; H.p.-IgG: <30 EU).

**Results:** In the first group (age 70-79), 18.2% of the subjects showed H. pylori infection (PG1 >80μg/L, IgG against H.p. >50 EU), 22.7% had CAG (PGI <30μg/L and PG1/PGII <3) and 53.8% were under PPI therapy. 16.9% of the patients on PPI therapy had CAG. In the second group (age 80-89), 32.9% of the patients showed H. pylori infection, 8.9% had CAG and 48.6% were under PPI therapy, 8.5% of the patients on PPI therapy had CAG. In the third group (age 90-99), 22.4% of the patients showed H. pylori infection, 10.5% had CAG and 48.7% were under PPI therapy. 8.1% of the patients on PPI therapy had CAG. In the fourth group (age 100-106), 46.0% of the patients showed H. pylori infection, 16.0% had CAG and 72.0% were under PPI therapy. 16.7% of the patients on PPI therapy had CAG.

**Conclusion:** Acid secretion is preserved in most of the elderly and very elderly subjects, even in centenarians. Serological markers may be useful to identify patients affected by CAG in which the administration of PPI is inappropriate, especially in the elderly.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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**P1836 THE PSYCHOLOGICAL CHARACTERISTICS OF REFUX HYPERSENSITIVITY-A PILOT STUDY BASED ON SCL-90 QUESTIONNAIRE AND 24 HOUR PH-IMPEDEANCE MONITORING**

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**Introduction:** Reflux hypersensitivity (RHV) was lately defined as a functional heartburn in patients with a negative response to either on the different technology (3-D VS two-dimensional) or in the new contractile parameters (i.e.: DCI and DL) introduced by the two HRM systems. This is particularly relevant in the evaluation of the LES resting pressure and abdominal length may rely on the different technology (3-D VS linear transducers) or on the different algorithms and threshold used. The latter may probably also apply to the differences found with the two systems in the duration of the esophageal contractions and in the new contractile parameters (i.e.: DCI and DL) introduced by the Chicago Classification. This study emphasizes the need for a careful validation of any new semisolid manometric system. The acquisition of new sets of normal values, to be used to compare the data measured in patients, is therefore mandatory. The results of our study may represent the reference normal values for other esophageal laboratories that are using the HRM systems and devices we tested here.

**Disclosure of Interest:** All authors have declared no conflicts of interest.
With PPI-REE before and after a course of PPI therapy

**Introduction:**

Information on the effect of PPIs in improving high resolution manometry (HRM) documented that patients with PPI-REE present frequently motility abnormalities, mostly weak peristalsis and hypotension. Eosinophilic esophagitis (EoE) is a condition characterized by symptoms of esophageal dysfunction associated with eosinophilic infiltration in the esophageal wall. EoE is mainly found in children, however, recent studies document that EoE is also prevalent in adults. The prevalence of EoE has increased in recent years, and this increase is likely due to a combination of factors, including increased awareness of the disease, improved diagnostic techniques, and more accurate reporting of symptoms. The disease is characterized by dysfunction in the distal esophagus, which is presented by esophageal dysfunction and histologically characterized by predominance of eosinophilic infiltration. The presentation of esophageal symptoms directly linked to esophageal infiltration (93%), bolus impaction (68%) and chest pain (25%) were diagnosed with PPI-REE had higher median EGJ resting pressure [baseline 11 (1–34) vs. post-PPI therapy, 9 (1–25) mmHg, p<0.001].

**Results:**

Eighty-two patients [23M:5F; mean age 33] reporting dysphagia (93%), bolus impaction (68%) and chest pain (25%) were included in this study. After a course of PPI therapy, patients with symptomatic suggestive of EoE underwent upper endoscopy to assess the presence of at least 15 eos/hpf on esophageal biopsies at mid/proximal esophagus and, therefore, treated with twice-daily PPIs for at least 8 weeks. Therefore, patients repeated upper endoscopy and PPI-REE was identified in case of less than 15 eos/hpf and a 50% decrease from baseline. Patients with PPI-REE underwent HRM at the time of the diagnosis (off-PPI) and after the course of PPIs (on-PPI). Pathologies with achalasia and absent peristalsis were excluded (Chicago Classification v.3).

**Conclusion:**

Eosinophilic esophagitis is a chronic immune disease of the esophagus characterized by predominance of eosinophilic infiltration. In inducing motor dysfunction and related symptoms. Disclosed of interest: All authors have declared no conflicts of interest.

**References**


**Disclosure of Interest:** All authors have declared no conflicts of interest.

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**P1838 PROTON PUMP INHIBITOR THERAPY IMPROVES ESOPHAGEAL SYMPTOMS BY RESTORING A NORMAL ESOPHAGEAL PERISTALSIS IN PATIENTS WITH PROTON PUMP INHIBITOR-RESPONSE ESOPHAGEAL EOSINOPHILIA**

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**Introduction:**

Proton Pump Inhibition response esophageal eosinophilia (PPI-REE) is a condition characterized by symptoms of esophageal dysfunction in the setting of eosinophilic inflammation on esophageal biopsies responding to a course of 8 weeks of PPI therapy. Recent data collected by using esophageal high resolution manometry (HRM) documented that patients with PPI-REE present frequently motility abnormalities, mostly weak peristalsis and hypotension. Eosinophilic esophagitis (EoE) is a condition characterized by symptoms of esophageal dysfunction in association with eosinophilic infiltration of esophageal wall. EoE is mainly found in children, however, recent studies document that EoE is also prevalent in adults. The prevalence of EoE has increased in recent years, and this increase is likely due to a combination of factors, including increased awareness of the disease, improved diagnostic techniques, and more accurate reporting of symptoms. The disease is characterized by dysfunction in the distal esophagus, which is presented by esophageal dysfunction and histologically characterized by predominance of eosinophilic infiltration. In inducing motor dysfunction and related symptoms. Disclosed of interest: All authors have declared no conflicts of interest.

**Disclosure of Interest:**


**Disclosure of Interest:** All authors have declared no conflicts of interest.

**References**

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**P1840 IG4 EXPRESSION IS ELEVATED IN PATIENTS WITH EOSINOPHILIC ESOPHAGITIS COMPARED TO PATIENTS WITH GASTROESOPHAGEAL REFUX DISEASE**

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**Introduction:**

Eosinophilic Esophagitis (EoE) is a chronic immune disease of the esophagus characterized by predominance of eosinophilic infiltration. EoE is mainly found in patients with atopic conditions. However, recently an association with IgG4 but not with IgE has been reported. Gastroesophageal reflux disease (GERD) is the most important differential diagnosis of EoE. In this study we measured systemic serum IgG4 and IgE levels of EoE patients before and after a topic steroid therapy, correlated them to esophageal IgG4-positive plasma cells and compared them to GERD patients.

**Disclosure of Interest:**


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A794
Aims & Methods: Serum levels of IgG4 and IgE of 19 EoE patients were measured before and after eight weeks of therapy with budesonide (1 mg twice a day).
Biopsies were taken from the esophagus before and after therapy for histological
and immunhistochemical evaluation. 14 patients with GERD without histological proof of eosinophilic granulocyte infiltration were taken a as control group.
Serum levels of IgG4 and IgE of 19 EoE patients were measured before and after
eight weeks of therapy with budesonide (1 mg twice a day). Biopsies were taken
from the esophagus before and after therapy for histological and immunhistochemical evaluation. 14 patients with GERD without histological proof of eosinophilic granulocyte infiltration were taken a as control group.
Results: Serum IgG4 levels of EoE patients were significantly higher than in
GERD patients (mean: 121.0 mg/dL vs. 71.2 mg/dL, p ¼ 0.034). In contrast, no
significant difference of IgE levels in EoE and GERD patients was observed. In
EoE patients, the number of eosinophilic granulocytes in histology was decreased
at a significant level after topic steroid therapy (mean: 51.9 eosinophiles/high
power field (hpf) vs. 6.4 eosinophiles/hpf p 5 0.001). After therapy lower levels
of IgG4-serum-levels could be measured (mean: 121.0 mg/dL vs. 104.2 mg/dL
p ¼ 0.019), whereas IgE levels did not show a significant difference.The esophageal biopsies of EoE patients showed a high number of IgG4-positive plasma
cells (mean expression of 27.4 IgG4-positive plasma cells of 46.4 stromal plasma
cells/hpf).
Conclusion: EoE patients show higher systemic IgG4- but not IgE-serum levels
compared to GERD-patients. These elevated levels normalize under effective
topic steroid therapy. Additionally high local expression of IgG4- positive
plasma cells can be seen in EoE patients. These findings might be further evidence for a possible IgG4-association of EoE.
Disclosure of Interest: All authors have declared no conflicts of interest.

P1841 SYSTEMATIC REVIEW: HEALTH-RELATED QUALITY OF
LIFE IN CHILDREN AND ADULTS WITH EOSINOPHILIC
ESOPHAGITIS: MEASURE INSTRUMENTS AND DETERMINANT
FACTORS
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Introduction: Measurement of Health-related quality of life (HRQoL) with generic or specific intruments has been increasingly used in patients suffering from
EoE to support both research and clinical care. Generic instruments aim at
measuring the overall HRQoL of patients across several conditions, being
useful to compare HRQoL across different disease states and for evaluating
health economics outcomes. Disease-specific instruments assess domains specific
to a given disease and are considered more sensitive to changes in the patient’s
health state. An up-to-date systematic review will provide a useful resource for
researchers and EoE specialists to ensure they can select an appropriate HRQoL
measure for patients in their practice in order to identify correctable factors
determining an impaired perception and to improve treatment outcomes.
Aims & Methods: We aim to systematically review the current HRQoL measures
for patients with EoE and to appraise their measurement properties using a
robust evaluation methodology checklist. We also sought to identify diseasespecific determinant factors for HRQoL in children and adults with EoE, and
the effect of investigations and interventions for EoE on HRQoL. A search
strategy was designed to identify and retrieve all documents dealing with the
relationship between HRQoL and EoE in children and adults. This systematic
literature search was performed in 5 major databases (PubMed, EMBASE,
Scopus, PsycInfo and Web of Science) for the period up to March 2017. The
measure properties of each specific EoE instrument identified and their performance properties were assessed using the quality properties checklist proposed by
Terwee et al. Levels of the HRQoL measure establishment or use in literature: we
used Cohen’s criteria. Cohort studies, case series and case reports were evaluated
for the risk of bias with the aid of the Joanna Briggs Institute critical appraisal
checklist. A descriptive summary with data tables was produced to summarize
the literature. Quantitative pooling of data was not meaningful so a narrative
synthesis of the data was undertaken.
Results: Of the 596 references identified, data was collected from 34 studies
including a total of 1,842 individual patients. Three disease-specific HRQoL
measures in EoE covering different aspects of patients’ lives and developed in
English were scored positive regarding measurement properties. Respectively, the
PedsQL inventory (including parent and child report forms) and the Peds-QoLä
EoE module were the generic and specific instruments respectively used in children, while the SF-36 and EoE-QoL-A were the most used questionnaires in
adults. EoE significantly impairs HRQoL of affected children and adolescents,
which manifests in the normal development of their daily activities, their physical
health and their mental status, with parents generally underestimating the impact
of the disease regarding children declared HRQoL. Regarding determinant factors, age was not associated with HRQoL. Number and severity of symptoms
negatively correlated with child-reported and Parent proxy-reported PedsQL
score and family impact score. Disease duration was identified as a risk factor
for a low SF-36 score. EoE impacts on a number of domains including frustration, embarrassment or fear about the disease outcomes. No significant differences in the overall QoL score were found in adult patients managed with dietary
or pharmacological therapy, with specific treatment modalities having a negligible influence on overall EoE-specific QoL. Symptoms scores determined exerted
an increased impact on swallowing anxiety and emotional impact subscales.
Female gender negatively influenced QoL scores. Disease activity, as expressed
by endoscopic findings, were also significant determinants of QoL. A higher
educational level was also found to be a strong determinant for a worse QoL.

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Emotional impact was the only dimension with a significantly worse score in
patients under dietary restrictions.
Conclusion: HRQoL is a relevant outcome that should be considered in clinical
practice and research of EoE. Further validation studies in several languages and
populations are required to support the use of disease-specific HRQoL measures.
Disclosure of Interest: All authors have declared no conflicts of interest.

P1842 TREATMENT SATISFACTION OF ADULT EOSINOPHILIC
ESOPHAGITIS PATIENTS
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Introduction: Available treatment options for adult EoE patients include drugs
(proton-pump inhibitors [PPI], swallowed topical corticosteroids [STC]), food
elimination diets, and esophageal dilation. Knowledge about patients’ view
regarding the different therapeutic options is very limited.
Aims & Methods: We aimed to systematically assess adult EoE patients’ satisfaction with different EoE-specific treatment modalities. We first created a questionnaire that included items that queried general demographic characteristics (7
items), EoE-specific patient history and presence of atopic disease (8 items), past
and present EoE-specific therapy (9 items), concomitant medication use (7 items),
important considerations for choice of therapy (2 items), as well as treatment
satisfaction with various therapies recalled over a period of 12 months (assessed
using the validated ‘‘Treatment Satisfaction Questionnaire for Medication’’
[TSQM], 52 items). The TSQM consists of 14 items falling into 4 scales: effectiveness (3 items), side effects (5 items), convenience (3 items), and overall satisfaction (3 items). The score for each TSQM scale ranges from 0 (dissatisfied) to
100 (satisfied). In analogy with other conditions, a score above 66.6 and 83.3
identifies patients that are ‘satisfied‘ and ‘very satisfied’ with therapy, respectively. The psychologist-guided focus groups with adult EoE patients were conducted to inform the content and the structure of the questionnaire and ensure
that patient understand the items, instructions, and response options. The questionnaire was sent to 148 patients in Switzerland. Data were double-entered by
two researchers into an EpiData database (version 3.1, the EpiData Association,
Odense, Denmark). Dataset was then imported into Stata (version 13, College
Station, Texas, USA) for analysis.
Results: Patient response rate was 73.5% (108/147). Mean patient age at inclusion was 46.3  15.9 years, 85/108 (78.8%) of patients were male, and mean
disease duration (from the time of diagnosis to the time of enrollment) was
6.8  5.1 years. In the last 12 months, 11.1%, 48.1%, 10.2%, and 28.7% of
patients reported to have suffered from symptoms of asthma, rhinoconjunctivitis,
eczema, and food allergy, respectively. In the last 12 months, 25.0%, 3.7%,
77.8%, 1.9%, 19.4%, and 13.0% were treated with PPI, STC in the form of a
syrup, STC in the form of a powder, STC in a form of a spray, diet, and
esophageal dilation, respectively (37.0% patients received more than one treatment; 7.4% of patients did not receive any treatment). Patients identified the
following considerations as important for the choice of therapy: the effect of the
treatment on the symptoms (88.9%), the effect of treatment on esophageal
inflammation (75.9%), possible side effects (69.4%), ease of therapy use
(58.3%), recommendation of the physician (50.0%), and compatibility of therapy
with lifestyle (46.3%). When asked about single most important criterion for the
choice of therapy, 48.5%, 33.7%, 11.9%, 3.0% and 2.0% of patients chose the
effect of treatment on symptoms AND esophageal inflammation, the effect of the
treatment on the symptoms, the effect of treatment on esophageal inflammation,
compatibility of therapy with lifestyle, possible side effect, and recommendation
of the physician, respectively, as deciding factor. The TSQM scales scores as well
as average TSQM values for patients on PPI, STC, and diet are shown in Table 1.
Conclusion: Adult EoE patients consider both effect of medication on symptoms
as well as inflammation as most important criteria, when choosing EoE therapy.
EoE patients appear to be ‘satisfied’ with PPI, STC, and dietary therapy and
‘very satisfied’ with STC, if the therapy is taken twice daily.
Disclosure of Interest: All authors have declared no conflicts of interest.

P1843 SYSTEMATIC ANALYSIS OF SUBEPITHELIAL
EOSINOPHIL COUNTS INCREASES DIAGNOSTIC YIELD IN
ADULTS WITH EOSINOPHILIC ESOPHAGITIS
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Introduction: For technical reasons, the histologic characterization of eosinophilic (EoE)-specific alterations is almost exclusively based on those found in the esophageal epithelium, whereas little is known about subepithelial abnormalities.

Aims & Methods: In this study, we aimed to systematically assess the nature of subepithelial histologic alterations, analyze their relationship with epithelial histologic findings, endoscopic features, and symptoms, and evaluate the diagnostic impact of subepithelial eosinophil counts in patients with an epithelial eosinophil count of <15/hpf. We prospectively included in this cohort study adult EoE patients who underwent assessment of clinical, endoscopic, and histologic disease activity using scores.

Results: We included 200 EoE patients (mean age 43.5 ± 15.7 years, 74% males) with a median peak count of 36 intraepithelial eosinophils/hpf (IQR 14–84). The following histologic features were identified in the subepithelial layer: eosinophil infiltration (median peak count of 20 eosinophils/hpf [IQR 10–51]), eosinophil degranulation (43%), fibrosis (82%), and lymphoid follicles (56%). Peak intraepithelial eosinophil counts were higher, identical, and lower when compared to the subepithelial layer in 62.5%, 7%, and 30.5% of patients, respectively. Subepithelial histologic activity correlated with epithelial histologic activity (rho 0.331, p < 0.001), endoscopic severity (rho 0.208, p = 0.003), and symptom severity (rho 0.179, p = 0.011). Forty percent (21/52) of patients with <15 intraepithelial eosinophils/hpf had subepithelial peak counts of <15/hpf.

Conclusion: In one third of patients subepithelial peak eosinophil counts are higher than epithelial eosinophil counts. Systematic assessment of subepithelial eosinophil counts can aid in diagnosing EoE in additional 40% of patients with epithelial eosinophils <15/hpf.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1844 GASTROESOPHAGEAL REFUX DISEASE PATIENTS REFUXATE TYPE INFLUENCE ON MACROPHAGE PHENOTYPE

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Aims & Methods: To systematically assess the nature of refluxate pH on macrophage phenotype we recruited 68 patients with different forms of gastroesophageal reflux disease (GERD), endoscopic findings, and symptoms, and evaluated the diagnostic impact of refluxate pH on macrophage phenotype. Pooled analysis of patients refluxate type influence on macrophage phenotype showed the prevalence of M1 phenotype in groups: 2.49 ± 0.15 (II) vs 1.29 ± 0.12 (III) (p < 0.05). Th2 cytokine macrophage production increased with increasing pH, and most significantly changed in II (0.84 ± 0.13 pg/mL in group I vs 27.7 ± 8.65 pg/mL in group III [p < 0.05]). The expression of surface M1/M2 macrophage CD markers significantly varied depending on the acidity of refluxate. Mild-alkaline pH (III group) resulted in increasing expression of M2 markers CD163/CD206, respectively performed by flow cytometry (Beckman Coulter FC500).

Results: Analysis of cytokine macrophage production revealed the prevalence of Th1 and Th1/Th2 bivalent (IL-17, IL-6) cytokines as compared to Th2. The most significant changes due to the influence of refluxate pH were observed in Th1 cytokine IL-8, TNFα and TNFβ. Increasing of pH resulted in 2 times-fold and 3.5 times-fold fall of these cytokines production respectively (p < 0.05). Th2 cytokine macrophage production increased with increasing pH, and most significantly changed in II (0.84 ± 0.13 pg/mL in group I vs 27.7 ± 8.65 pg/mL in group III [p < 0.05]). The expression of surface M1/M2 macrophage CD markers significantly varied depending on the acidity of refluxate. Mild-alkaline pH (III group) resulted in increasing expression of M2 markers CD163/CD206, respectively performed by flow cytometry (Beckman Coulter FC500).

Conclusion: Pooled analysis of GERD patients refluxate type influence on macrophage phenotype showed the prevalence of M1 phenotype in groups: 2.49 ± 0.15 (II) vs 1.29 ± 0.12 (III) (p < 0.05). Th2 cytokine macrophage production increased with increasing pH, and most significantly changed in II (0.84 ± 0.13 pg/mL in group I vs 27.7 ± 8.65 pg/mL in group III [p < 0.05]). The expression of surface M1/M2 macrophage CD markers significantly varied depending on the acidity of refluxate. Mild-alkaline pH (III group) resulted in increasing expression of M2 markers CD163/CD206 as compared to M1–CD80/CD25, but changing M1/M2 index of CD163/CD206 to CD80/CD25 in definite trend of increasing expression of CD1 M2 markers and increased production of Th2 cytokines as compared to the other refluxate types. Analysis of MDM phenotype showed the prevalence of M1 phenotype regardless of refluxate pH.

Disclosure of Interest: All authors have declared no conflicts of interest.

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Introduction: The pathophysiology of heartburn perception in gastro-esophageal reflux disease (GERD) remains unclear. The degree of reflux-induced epithelial change seldom predicts symptom severity, as evidenced by the greater symptom burden seen in non-erosive reflux disease (NERD) compared to patients with Barrett’s esophagus (BE). Existing models of acid hypersensitivity are inadequate to explain this discordance.

Aims & Methods: To test the hypothesis that differences in peripheral esophageal nerve fiber distribution may be relevant, we studied the distribution of mucosal nerve fibers in patients with NERD and BE and compared the results with that of healthy subjects. 13 patients with NERD undergoing reflux testing and 16 patients with BE undergoing endoscopic surveillance were prospectively recruited. Biopsies were obtained from the proximal and distal esophageal mucosa. Contact E-mail Address: sylvia@qmul.ac.uk

Table 1: TSQM scales scores for PPI, STC (in powder form), and other diets in adult EoE patients.

<table>
<thead>
<tr>
<th>TSQM scales</th>
<th>PPI (n = 27; median treatment duration 6 years [3–9])</th>
<th>STC (n = 54; median treatment duration 5 years [2–6])</th>
<th>STC only (n = 17; once daily; median treatment duration 5 years [3–6])</th>
<th>STC only (n = 22; twice daily; median treatment duration 3.5 years [1–6])</th>
<th>Diet (n = 21; median treatment duration 2 years [1–4.5])</th>
</tr>
</thead>
<tbody>
<tr>
<td>Effectiveness</td>
<td>66.7 [38.9–77.8] 100</td>
<td>83.3 [66.7–94.4] 100</td>
<td>83.3 [66.7–94.4] 100</td>
<td>83.3 [66.7–94.4] 100</td>
<td>77.8 [61.1–94.4] 100</td>
</tr>
<tr>
<td>Side-effects</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>Convenienence</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>Overall satisfaction</td>
<td>94.4 [72.8–92.3] 100</td>
<td>94.4 [72.8–92.3] 100</td>
<td>94.4 [72.8–92.3] 100</td>
<td>94.4 [72.8–92.3] 100</td>
<td>94.4 [72.8–92.3] 100</td>
</tr>
</tbody>
</table>

The location of oesophageal mucosal afferent nerves is more superficial in patients with NERD than in healthy volunteers and patients with Barrett’s oesophagus.

Abstract No: T1842

Table 1: TSQM scales scores for PPI, STC (in powder form), and other diets in adult EoE patients.
Disclosure of Interest: P. Woodland: Research grant Reckitt Benckiser (Hull UK). D. Sifrim: research grant Sandhill Scientific (Denver USA) research grant Reckitt Benckiser (Hull UK)
All other authors have declared no conflicts of interest.

P1847 BELeching PATTERNS IN PATIENTS WITH ISOLATED PATHOLOGICAL UPRIGHT REFLUX AND PATHOLOGICAL BIPOZATIONAL REFLUX
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Introduction: Belching is a commonly occurring symptom in patients with gastroesophageal reflux disease (GERD). Belching may reflect reflux. It is unknown whether GERD patients with isolated pathological upright reflux (UP) have belching patterns that are different from GERD patients with pathological bipositional reflux (BIP).
Aims & Methods: Aim of this study was to therefore examine the belching patterns of UP reflux patients as compared with BIP reflux patients. We included 50 consecutive patients with pathological reflux and typical symptoms who underwent 24-h pH-impedance monitoring at the Maastricht University Medical Centre from 2015 to 2017. Patients referred for excessive belching were excluded.
A group of 25 UP reflux patients (10 male, mean age 52.9 years (range 22–77)) and 25 BIP reflux patients (11 male, mean age 47.9 years (range 18–77)) were enrolled. All 24-h pH-impedance tracings were analysed manually. We classified belches according to: a) physiological mechanism: supragastric vs. gastric; and b) their temporal relationship with a liquid reflux episode: isolated belch, preceding or during a liquid reflux episode. Symptoms-assocation analysis was performed to assess a relationship between reported symptoms and reflux episodes.
Results: BIP patients showed higher acid reflux time (17.8 ± 2.4% vs. 7.3 ± 0.6%, p < 0.001) and higher number of total reflux episodes (121 ± 9 vs. 97 ± 8, p = 0.05) than UP patients. Notably, both the proportion of reflux episodes with belches of any type and the proportion of belches preceding liquid reflux were higher in UP patients than in BIP patients (51.7 ± 3.6% vs. 32.1 ± 3.7%, p < 0.001 and 27.3 ± 3.1% vs. 17.8 ± 2.9%, p = 0.03, respectively). No difference was found in the proportion of both supragastric and gastric belches between groups. During 24-h pH-impedance monitoring UP patients reported more symptoms (21.6 ± 6 vs. 12.4 ± 3, p = 0.16) and had more positive symptoms with belches (60.2 ± 7.1% vs. 39.0 ± 6.6%, p = 0.03) than BIP patients. Of the total number of belches that were detected using 24-h pH-impedance, more belches were symptomatic in UP patients than in BIP patients (24.8 ± 6.4% vs. 11.1 ± 3.2%, p = 0.06).
Conclusion: In our study, GERD patients with isolated pathological upright reflux had more often (symptomatic) belches than GERD patients with pathological bipositional reflux. Therefore, examination of belching patterns can assist diagnostic and therapeutic strategic planning in GERD patients who are refractory to medical therapy.
Disclosure of Interest: All authors have declared no conflicts of interest.

P1848 TREATMENT WITH PROTON PUMP INHIBITORS (PPI) DOES NOT REDUCE ACIDIC LARYNGOPHARYNGEAL REFLUX (LPR) DESPITE REDUCING DISTAL ACIDIC GASTROESOPHAGEAL REFLUX AND IMPROVING SYMPTOMS IN PATIENTS WITH LPR
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Introduction: PPI improve LPR symptoms in many patients. It is implicitly assumed that this effect is due to reduction of acidic LPR by PPI. Here we tested this assumption. We evaluated LPR and distal gastroesophageal reflux by using simultaneous pH/impedance monitoring in laryngopharyngeal segment and in distal esophagus before and after PPI treatment.
Aims & Methods: Patients referred for suspected LPR were screened and those with positive reflux finding score (RFS) > 7, determined by ENT physician) and/or positive reflux symptom index (RSI > 13) and at least one acidic LPR episode during 24-h pH-impedance study were enrolled. The RSI, RFS and dual pH/impedance study of LPR and distal reflux were done both before and after 3 months therapy with PPI twice a day. Appropriate distance between pH sensors was chosen based on manometrically determined LES and UES so that the proximal pH sensor was positioned 1 cm above UES and distal sensor was positioned 4–6 cm above LES. By definition each LPR event was preceded by reflux detection in the distal esophagus.
Results: 18 patients (11M/7F, 51 ± 10yrs) completed the study. In this group the PPI treatment substantially improved the symptoms of LPR. Reflux finding score (RFS) was decreased by 40% from 9/1 ± 5/1 ± 1 (P < 0.01). The number of distal acidic reflux episodes was reduced from 17 ± 2 to 3 ± 1 (P < 0.01). Surprisingly, acidic LPR was not decreased by PPI treatment. The number of LPR with pH < 5.0 was 2 ± 0.5 vs. 3 ± 1, P = NS, and the number of LPR episodes with pH < 4.0 was 0.7 ± 0.1 vs. 0.6 ± 0.2, P = NS. Surprisingly, the number of acidic LPR episodes with pH = 5.0–6.0 was even increased (14 ± 2 vs. 21 ± 3, P < 0.05) leading to an increase in the overall number of LPR episodes by approximately 50% from 16 ± 2 to 24 ± 3 (p < 0.05). PPI treatment did not decrease laryngopharyngeal time the pH with a normal oesophageal index (RSI) did not decrease laryngopharyngeal reflux (LPR = NS).
Conclusion: Proton pump inhibitor treatment does not reduce acidic laryngopharyngeal reflux despite substantially improving symptoms in patients with objectively established LPR. This suggests that PPI treatment influences some aspects of pathogenesis of LPR symptoms that are not readily detected by laryngopharyngeal pH/impedance monitoring.
Disclosure of Interest: All authors have declared no conflicts of interest.

References
The aim of the study was to evaluate the effect of the menthol infusion into the esophagus on the esophageal peristalsis and lower esophageal sphincter pressure in healthy volunteers. High-resolution manometry and the parameters of esophageal pressure topography were used to quantitatively evaluate the certain components of esophageal motility. 13 healthy volunteers with at least 30 days without PPI treatment were used to quantitatively assess the impact of menthol on the esophageal peristalsis and LES tone.

Aims & Methods: The effect of the menthol infusion into the esophagus on the esophageal peristalsis and lower esophageal sphincter pressure in healthy volunteers. High-resolution manometry and the parameters of esophageal pressure topography were used to quantitatively evaluate the certain components of esophageal motility. 13 healthy volunteers without esophageal sphincter were enrolled. High-resolution manometry with a thin silicon tube attached was placed transanally so that the distal end of the tube was 5 cm above the LES. After a 5 min. adaptation period the measurement was performed in the supine position according to the protocol as follows: recording 10 min. after 10 ml of 5 ml and 3 ml water swallows of 10 and 15 ml and after that a 20 min. infusion challenge with 3 mM menthol 8 ml/min. was carried out and subsequently the water swallows in order described above were repeated. HRM tracings were manually analyzed using ManoScan software and parameters used in the Chicago classification (v3.0) were evaluated. Integrated relaxation pressure (IRP), nadir LES pressure and distal contractile integral (DCI) values from 5 ml, 10 ml and 15 ml swallows were obtained. These were compared before and after the menthol infusion. Paired test was used for statistical analysis.

Results: None of the subjects had any motility disorder defined by the Chicago Classification v3.0. Few volunteers reported only mild cold sensation during infusion presumed to be of the esophageal origin. The nadir LES pressure before and after menthol infusion was 7.5±0.8 mmHg vs. 7.3±0.7 mmHg, respectively (p > 0.7). IRP of 5 ml swallows was 2.8±0.6 mmHg vs. 2.1±0.5 mmHg showed significance (p = 0.01). However, difference of IRP of 10 ml and 15 ml swallows was not significant (p > 0.1, p > 0.5, respectively). Averaged IRP of 10 ml swallow [5±1.8 vs. 6.3, respectively, p = NS], for the distal swallows 814±2.1 vs. 116.2 mmHg before and after menthol infusion, respectively (p > 0.5). We found no difference in DCI in 10 ml and 15 ml swallows before and after menthol infusion. Menthol seemed to have had only a marginal insignificant effect on IRP and DCI in rapid swallow flow.

Conclusion: We quantified the effect of menthol on the esophageal function and LES pressure in healthy volunteers using high resolution manometry. The analysis of HRM tracings revealed that menthol has no effect on particular parameters of the esophageal peristalsis and esophageal motility.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

P1850 ANALYSIS OF THE RELATIONSHIP BETWEEN GLOBUS PERCEPTION AND ACIDIC LARYNGOPHARYNGEAL REFLUX BY DUAL PHARYNGEAL AND ESOPHAGEAL 24-HOUR pH/IMPEDANCE MONITORING
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Introduction: Globus is considered to be related to the gastroesophageal reflux disease/laryngopharyngeal reflux (LPR). However, a substantial part of subjective and self-perception of globus sensation which is impossible to measure objectively makes this symptom difficult to study. Visceral hypersensitivity and/or altered functional state of the afferent nerve endings in the hypopharynx resulting from reflux have been suggested responsible for the development of globus. We hypothesized differences in the reflux burden and esophageal/pharyngeal symptoms between the patients with LPR symptoms with globus compared to the patients with LPR symptoms without globus.

Aims & Methods: Patients referred for suspected LPR were screened and those with positive reflux symptom index (RSI > 15) and at least one acidic LPR episode during 24 h pH/impedance study were enrolled. We recruited patients that were at least 30 days without PPI treatment. Appropriate distance between pH sensors was chosen based on manometrically determined LES and UES so that the proximal pH sensor was positioned 1 cm above UES and distal sensor was positioned 4-6 cm above LES. For each LPR event we determined the maximal difference of pH on the pH index determined between globus positive (tick 4–5 in the RSI) and globus negative (tick 0–1 in the RSI).

Results: 19 (13M/6F) completed the study. The number of globus positive and negative patients was 11 and 8, respectively. There were no major differences between groups. Disregarding these differences there was a significant difference between the globus positive and negative group (25±2 vs. 21±2, respectively, p = NS). As for the reflux in distal esophagus, we observed no difference in the acid exposure time between the globus positive and negative patients (11.1%, respectively, p = NS). We therefore assumed differences in the results from the hypopharyngeal pH sensor. However, the number of LPR events with pH drop to <5.5 showed no significant difference between the globus positive and negative patients, either for the number of events (92±5.6 vs. 86±4.2, respectively, p = NS) or for the pharyngeal acid exposure time (45±14 vs. 88±4.2, respectively, p = NS). We speculated that more acidic LPR events (pH drop to <5.5) might be of greater relevance. However, no significant difference was found between the globus positive and negative patients either in terms of the number of these LPR events (10±2 vs. 1±1, respectively, p = NS), or the pharyngeal acid exposure time (16±6.9 vs. 42±3.6, respectively, p = NS).

Conclusion: We found no significant difference in the reflux burden in the distal esophagus/hypopharynx between the groups of symptomatic LPR patients with and without globus using 24h dual channel pH/impedance. Other factors, e.g. visceral hypersensitivity might play a role in the development of globus symptoms, even in patients with objectively established LPR.

Disclosure of Interest: All authors have declared no conflicts of interest.
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P1852 HIGH RESOLUTION MANOMETRY SHOULD BE CONSIDERED THE BEST TEST TO DIAGNOSE SLIDING HIATAL Hernia
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Introduction: Sliding hiatal hernia (HH) is a frequent diagnosis during upper endoscopy (UE) in patients with GERD-related symptoms. Recently, high resolution manometry (HRM) allowed an accurate evaluation of the esophago-gastric junction (EGJ) and its sub-types (Chicago Classification V3.0; CCv3). Few data are available comparing the diagnostic accuracy of HRM and UE to detect HH.

Aims & Methods: The aim of this study was to compare the prevalence of HH obtained with UE and HRM and to determine the role of this finding by diagnosing gastroesophageal reflux disease (GERD) on the basis of impedance and pH (MII-pH) monitoring. We enrolled consecutive patients with heartburn and HH diagnosed with UE. After UE, all patients underwent HRM and MII-pH to investigate GERD. All tests were performed previous a 20-day wash-out from antireflux therapy. GERD was diagnosed in patients with gastroesophageal reflux symptoms with GERD and those with functional heartburn (FH), classified by means of upper GI endoscopy and impedance-pH (MII-pH) monitoring off-medication. We also aimed to develop a predictive model for distinguishing FH from GERD by using the prevalence of these HRM features. Consecutive patients with heartburn and/or regurgitation and a recent endoscopic assessment were enrolled. All patients underwent HRM to assess the EGJ and 10 single water swallows to evaluate esophageal peristalsis and EEJ function and their motility pattern were measured. Moreover, all patients underwent MII-pH off-therapy. We measured the esophageal acid exposure time (AET), mean of total impeded reflux events and symptom-reflux association analysis using both symptom association probability (SAP) and symptom association index (SI).

Results: Overall, 68 patients (39 F/29 M, median age 42.3 years) underwent HRM and MII-pH. HRM findings stratified according to MII-pH positivity for GERD are provided in Table 1. At univariate analysis, statistical differences were found in EGI pressure, EGJ-CI, mean DCI and MRS DCI/mean DCI ratio between GERD and FH. Based on logistic regression analysis and according to Hosner’s purposeful selection of covariates, a predictive model based on HRM variables was built by logistic regression analysis. The model was tested for discriminative performance by computing the area under ROC curve (AUROC), and calibration was assessed by Hosmer-Lemeshow goodness-of-fit test. The bootstrap resampling method was used to evaluate the internal validity of the model and to correct for over-fitting.

Results: Overall, 68 patients (39 F/29 M, median age 42.3 years) underwent HRM and MII-pH. HRM findings stratified according to MII-pH positivity for GERD are provided in Table 1. At univariate analysis, statistical differences were found in EGI pressure, EGJ-CI, mean DCI and MRS DCI/mean DCI ratio between GERD and FH. Based on logistic regression analysis and according to Hosner’s purposeful selection of covariates, a predictive model based on HRM variables was developed a predictive model which ultimately encompassed in HRM variables, a HRM mean DCI/mean DCI ratio (OR 1.614, 95% CI 0.993–2.895) and EGJ-CI (OR 0.952, 95% CI 0.913–0.985). The model had a fair discriminative performance (AUROC: 0.798, 95% CI 0.650–0.894) between MII-pH positivity and negativity for GERD and was well calibrated according the Hosmer-Lemeshow goodness-of-fit test (p = 0.769). The internal validation of the model by bootstrap method showed AUROC = 0.797. Considering that the predicted cut-off of the predicted probability of MII-pH for GERD which maximized sensitivity and specificity (i.e. 67.4%), sensitivity and specificity of the predictive model in predicting GERD against FH were 80.8% and 76.2%, respectively.

Table 1

<table>
<thead>
<tr>
<th>HRM variable</th>
<th>GERD group (n = 47)</th>
<th>No GERD group (n = 21)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>EGI resting pressure, mmHg (median, IQR)</td>
<td>17.6 (16.9)</td>
<td>22.7 (19.1)</td>
<td>0.028</td>
</tr>
<tr>
<td>Peak DCI, mmHg * cm * sec (median, IQR)</td>
<td>991 (1887)</td>
<td>1632 (2160)</td>
<td>0.018</td>
</tr>
<tr>
<td>Mean DCI, mmHg * cm * sec (median, IQR)</td>
<td>590 (1299.5)</td>
<td>1191 (1166)</td>
<td>0.004</td>
</tr>
<tr>
<td>DCI MRS, mmHg * cm * sec (median, IQR)</td>
<td>1039 (1983)</td>
<td>842 (1764)</td>
<td>0.465</td>
</tr>
<tr>
<td>DCI MRS/mean DCI, mmHg * cm * sec (median, IQR)</td>
<td>1.723 (2.299)</td>
<td>1.131 (2.122)</td>
<td>0.002</td>
</tr>
<tr>
<td>EGJ CI, mmHg * cm * sec (median, IQR)</td>
<td>7 (18)</td>
<td>22 (17.6)</td>
<td>0.004</td>
</tr>
<tr>
<td>EGJ morphology (type I vs. type II, n (%))</td>
<td>14 (29.8)</td>
<td>3 (14.3)</td>
<td>0.232</td>
</tr>
</tbody>
</table>

Conclusion: Our data indicate that HRM can be useful in detecting GERD, with our predictive model allowing a high level of suspicion for reflux disease. In particular the role of the EGJ-CI in GERD pathophysiology has been
P1854 GORD PATIENTS ARE FREQUENTLY DISSATISFIED ON LONG-TERM PPI THERAPY: EXPLORING THE REASON(S) AND MANAGEMENT IN ROUTINE CLINICAL CARE (LOPA II STUDY)

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Introduction: Randomized controlled trials report about 30% of GORD patients complain of bothersome remaining symptoms (heartburn, regurgitation) despite PPI. The LOPA (Lost Patients) I Study of 333 GORD patients seen in general practice revealed 46% of patients experienced heartburn or regurgitation symptoms at least twice per week despite PPI. A total of 20% were dissatisfied with their treatment. Few patients had received specific GORD diagnostics or recommended other options (<10%).

Aims & Methods: The LOPA II study is a prospective, multicenter, observational study conducted in 17 general practice clinics. Patients with chronic GORD, taking PPI therapy for at least 1 year, and not satisfied with their treatment were asked to complete a questionnaire. Patients were asked the duration of their PPI therapy, satisfaction with their current condition, frequency of symptoms in the last week, whether they had previously received diagnostic evaluation or surgical consult related to GORD, whether they plan to consult a reflux specialist for further diagnostics, and reasons for dissatisfaction with their current medication treatment. “Lost Patients” were defined as those with a satisfaction score of 0 or 2 on a 5-point Likert scale (1: very dissatisfied; 2: dissatisfied; 5: very satisfied).

Results: 510 consecutive patient responses were collected within one year. Patients suffered from GORD an average of 9.6 years and prescribed PPI therapy for an average duration of 7.9 years. 70% were dissatisfied or very dissatisfied with their PPI therapy (satisfaction score of 1 or 2). 83% reported heartburn or regurgitation at least 2 days in the prior week (53% 4-7 days). 49% reported using additional medication other than their prescribed PPI at least 2 days per week (34% 4-7 days). In patients dissatisfied on PPI, most cited insufficient symptom control (78%). Reasons for dissatisfaction included: 31% cited concerns with long-term use of drugs and 27% the need for daily medication. 92% of patients had an upper endoscopy, 12% had a prior pH-meter, 7% manometry, and 9% received prior surgical consult for GORD. Of patients who never received diagnostic evaluations, 48% were not aware of any surgical anti-reflux methods, 25% were concerned about possible complications, 18% felt their condition is not serious enough, 6% were recommended against anti-reflux procedures by their doctor.

Conclusion: Chronic GORD patients who are dissatisfied with their PPI therapy are rarely offered specialized GORD diagnostic procedures or treatment alternatives. Half of the patients took medication in addition to PPI to control their symptoms. In addition to persistent symptoms, concerns of long-term PPI use and burden of daily medication play a role in patient dissatisfaction with PPI therapy.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1855 PREVALENCE AND PATHOPHYSIOLOGY OF GASTROESOPHAGEAL REFUX DISEASE IN PATIENTS WITH AUTOIMMUNE GASTRITIS

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Introduction: Autoimmune gastritis (AIG) is characterized by corpus-predominant atrophy with consequent hypo-acchlorhydria. In AIG patients dyspepsia is frequent but acid reflux symptoms are uncommon, with few data available regarding gastroesophageal reflux disease (GERD) in AIG.

Aims & Methods: Our study was aimed to define the prevalence of reflux symptoms in AIG patients, to evaluate the serological, histological and clinical differences in AIG patients with or without reflux symptoms and to investigate the pathophysiology behind these symptoms. One hundred and fifty AIG outpatients were evaluated and 87 were included in the study: 29 AIG patients with reflux symptoms (AIG-R) and 58 without (controls), selected with similar age and gender distribution. AIG-R underwent a pH-impedance (pH/I) and high resolution manometry (HRM). Serum biomarkers, EGDS, histology and anamnestic data were evaluated in both groups. Statistics was performed as indicated.

Results: AIG-R were 19% overall and 28% of them showed endoscopic esophageal lesions, with more frequent hiatal hernia than in controls (p < 0.02). pH/I diagnosis acid reflux, esophageal hypersensitivity and a normal pattern in 7%, 28% and 66% patients, respectively. The number of non-acid reflux (NAR) was higher when compared with acid ones (p < 0.0001), moreover NAR and NAR proximal extension were associated with endoscopic lesions (p < 0.03 and p < 0.05, respectively). HRM revealed normal pattern in 62% of patients, minor peristaltic disorders in 24%, and outflow obstruction in 14%. According to the new Rome IV criteria, 55% of patients presented “functional esophageal disorders” (Rome IV-IN). No differences were detected in serological marker and clinical presentation. AIG-R presented lower antrum gastritis (p < 0.07) and a trend towards lower corpus gastritis (p = 0.07) when compared with controls. The two patient with acid GERD were an OLGA 0 with mild gastrin increase and an OLGA I with short segment Barrett’s esophagus. Lower OLGA stages, lower corpus atrophy (p < 0.02) and more frequent response to PPI (p < 0.05) were associated with Rome IV-OUT status.

Conclusion: AIG-R patients are not uncommon despite the hypo-acchlorhydria. Acid reflux is rare in AIG, while motility and “functional” disorders are frequent. Lower corpus atrophy and OLGA stage in Rome IV-OUT patients, with an at least partly preserved secretion, is likely related to the presence of symptoms. Treatment should consider use of proton pump inhibitor drugs only in specific patients.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1856 DIET IS MORE EFFECTIVE THAN ANTACIDS IN RELIEVING REFUX SYMPTOMS IN MILD GORD

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Introduction: Gastroesophageal reflux disease (GERD) is a common disorder commonly overlapping with several functional or allergic/immunological disorders, whose symptoms are related to food intake. Awareness of health care costs and potential side effects of long-term acid suppression has increased the attention in non-pharmacologic treatment for alleviating reflux symptoms.

Aims & Methods: The aim of our prospective study was to evaluate the non-inferiority of a controlled diet compared to antacid compounds in relieving reflux symptoms in patients suffering from mild GERD. We considered 500 consecutive patients referred to the Division of Allergy and Clinical Immunology of Azienda IST IRCCS San Martino of Genova for gastrointestinal symptoms associated to food intake. Patients with a clinical and instrumental diagnosis of food allergy, food intolerance, Irritable Bowel Syndrome (IBS) and Small intestinal Bacterial Overgrowth (SIBO) were excluded. Patients with a diagnosis of GERD based on clinical history represented our study population. Basal metabolic rate and calories needs of patients was assessed by means of Harry-Benedict equation corrected for their physical activity. Patients were asked to take antacids for one month. Subsequently patients discontinued medication consumption and followed an elimination diet of food commonly associated to eliciting reflux symptoms, based on their calories need. Efficacy of the two treatments was evaluated by means of a validated symptomatic questionnaire (RDQ administered at baseline, after antacids course (1 month) and after diet (1 month). A treatment was considered effective if a 50% improvement in the symptom score was recorded.

Results: After investigations 261 patients out of 500 (52.2%) were excluded because of IBS (146), celiac disease (6), nickel allergy (25), lactose intolerance (60), SIBO (10), and allergy to other foods (20). The remaining 239 patients were diagnosed as affected by mild GERD (median age 47; BMI 24; 123F/107M; no erosive reflux disease) and were included in our interventional prospective study. All patients, antacids treatment was effective in 198 cases (75.3%). Symptoms relief was reported by 220 patients (92.1%) after diet based on calories need. No differences were noted between responders and non responders in terms of BMI, age and gender. Diet was more effective than antacids treatment in relieving reflux symptoms in mild GERD (p = 0.01)

Conclusion: A structured diet regimen, tailored on the metabolic need of the patients, appears more effective than antacids alone in relieving reflux symptoms in patients with mild GERD. Further controlled studies are mandatory to confirm these preliminary data.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1857 INTERIM RESULTS OF A PROSPECTIVE MULTICENTER REGISTRY OF LOWER OESOPHAGEAL SPHINCTER STIMULATION FOR GORD: THE LESS-GORD REGISTRY

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Disclosure of Interest: All authors have declared no conflicts of interest.

A799
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Introduction: Safety and efficacy of electrical stimulation of the lower oesophageal sphincter (LOS) using the EndoStim® LOS Stimulation System (Nijmegen, The Netherlands) has been demonstrated in clinical trials up to >5 years. Data on outcomes in routine clinical practice is growing.

Aims & Methods: An ongoing, prospective international multicenter web-based registry, collecting data in patients with refractory GERD symptoms, treated with ES-LOS in clinical practice. Data is collected at baseline and at routine follow-ups for 5 years. Demographics, adverse events, GORD symptoms, GORD related quality of life (GORD-HRQL) scores, use of proton pump inhibitors (PPI), and physiological data (oesophageal pH,manometry) are collected when available.

Results: 180 patients at sites in Europe and Latin America have been enrolled. Follow-up data up to 2 years is available. Median (IQR) age at the time of implant was 51 (41–60), 57% were male. All patients were taking prescription PPI at baseline. At their last follow-up between 6 and 24 months post op, 70% (84/121) were completely off PPI (p < 0.001). Median (IQR) composite GORD-HRQL score improved from 23 (17–29) preoperatively to 8 (4–15) at 6 months, 7 (2–12) at 12 months, and 5 (4–15) at 24 months (p < 0.001 at all time points, n = 154, 121, 66, 33 at baseline, M6, M12, M24, respectively). Oesophageal pH testing post-op was performed by a few sites either as standard of care or in particular situations. Median (IQR) 24-hour oesophageal acid exposure improved from 8.2% (4.6–18.4) at baseline to 4.7% (1.4–14.5) at 6 months (p = 0.26) and 3.6% (1.0–5.8) at 12 months (p = 0.04) at 12 months, 39, 10 at baseline, M6, M12, respectively). The proportion of patients with moderate to severe regurgitation decreased from 64% at baseline to 22.5% after 6 and 13.4% after 12 months. Extra-oesophageal symptoms (recurrent cough, pneumonitis, shortness of breath) and sleep disturbances also decreased substantially. Overall, dysphagia and gas were less common at 12 months than preoperatively. Four serious adverse events were reported in one patient. One myocardial infarction related sudden death at 11-month post-op, not related to the device or procedure; 1 event of asymptomatic electrode erosion into the oesophagus detected during routine endoscopy and the device safely removed during laparoscopic fundoplication; and 2 events of gastroparesis in 1 patient requiring hospitalization, possibly related to the device, were reported.

Conclusion: ES-LOS is safe and effective in treating patients with refractory GERD symptoms despite PPI in routine clinical practice. ES-LOS should be considered as a treatment option for these difficult to treat patients.

Disclosure of Interest: J. Labenz: Consulting fees - EndoStim BV
All other authors have declared no conflicts of interest.

Disclosure of Interest: A. Bapaye: Speaker- Boston scientific corporation, Cook medical, Taewoong medical
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P1681 LONG-TERM RESULTS OF RADIOFREQUENCY ABLATION (RFA) IN PATIENTS WITH BARRETT'S ESOPHAGUS RELATED NEOPLASIA

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Introduction: Radiofrequency ablation (RFA) with or without endoscopic resection (ER) is an established endoscopic treatment of early Barrett’s esophagus (BE) related neoplasia (BORN). After successful treatment, follow-up is still required as recurrences may occur. The aim of this prospective single-center case series was to assess the long-term efficacy of endoscopic treatment (RFA with or without ER) for BORN. Main outcomes were complete remission of neoplasia (CR-N) and intestinal metaplasia (CR-IM) and recurrence of IM (R-IM) and neoplasia (R-N).

Aims & Methods: A total of 99 consecutive patients with BORN have been treated with RFA and/or ER in our center (media 64 years, range 22–91), 57 patients (57.5%) had no prior therapy and 42 patients completed the treatment and were included into this analysis. The patients had been followed up during 296 patient-years (mean 3.4 years, range 0.5–6). Thirty-three patients were diagnosed with adenocarcinoma (38%), 24 patients with high-grade dysplasia (28%) and 30 patients with low-grade dysplasia (34%). Prior to RFA, ER for visible lesions was performed in 57 patients (66%). Mean length of the Barrett’s esophagus (BE) was 4.6 cm (range 1–13 cm). After treatment, the patients have undergone regular endoscopic surveillance with multiple biopsies. Recurrence of complete remission of IM (CR-IM) and complete remission of neoplasia (CR-N) were attained in 54 patients (54.3%, 65.1%; 95% CI 54.3–74.5) and 82 patients (98.8%; 95% CI 92.8–99.9), respectively. All patients who did not achieve CR-IM had macroscopic normal neo-Z-line without visible abnormality. The only one patient who macroscopic eradication of BE was not achieved due to giant hiatal hernia and who was referred for anti-reflux surgery. During the follow-up, 18 patients (13.3%, 18/134 pts) experienced a recurrence of IM and 3.8% (3/79 pts) had a recurrence of neoplasia (LGD 2x, HGD 1x). We did not encounter any patient with a subsquamous neoplasia. All recurrences occurred at the level of neo-Z-line and 6 patients with recurrent IM had also macroscopic recurrence of BE. A total of 13 patients underwent endoscopic retreatment: 7x probe-based re-RFA, 5x escape argon plasma coagulation (APC) and 1x ER. After retreatment, we achieved 100% CR-N and 54% (7/13 pts) CR-IM. Treatment-related adverse events occurred in 22 patients (25%): 12x chest pain and 10x stricture. Two patients with a stricture had to undergo surgical resection - first patient due to perforation during balloon dilatation of a post-RFA stricture, the second because of refractory post-RFA stricture after 20 sessions of dilatation.

Conclusion: RFA combined with ER for patients with BORN achieves a high success rate of CR-N with durable results. Recurrence of IM occurs in approxi- mately one-third of patients and supports continuous endoscopic surveillance even after complete eradication. Nonetheless, the majority of recurrent IM occurs within a normally appearing neo-Z-line with questionable clinical relevance.

Disclosure of Interest: All authors have declared no conflicts of interest.

References


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Introduction: Barrett’s Esophagus (BE) is a premalignant condition, in which prolonged gastroesophageal reflux results in intestinal metaplasia, leading to an annual risk of adenocarcinoma 0.12%/year1. The current standard of treatment is Endoscopic Resection (ER) of visible nodular lesions and Radiofrequency Ablation (RFA) that Barrett’s, which has a success rate of 92%2. For refractory cases, wide field ER, cryotherapy and other methods are used, but may have higher adverse events. We hypothesize that thicker Barrett’s tissue is less likely to respond to RFA and have developed methods to precisely measure mucosal thickness with Volumetric Laser Endomicroscopy (VLE). These methods may facilitate future studies, correlating tissue thickness with response to therapy and prediction of optimal treatment.

Aims & Methods: We performed a nested cohort study from the U.S. VLE Registry (which comprises 1000 patients) of patients with BE, who had a baseline VLE scan, followed by RFA ablation and had at least one follow up exam. We excluded patients who had any ablative therapy prior to baseline VLE. The primary outcome was the percentage reduction of Prague length after the first treatment. Secondary outcomes were: 1. complete remission of intestinal metaplasia (CRIM) during 12 months after baseline procedure, 2. complete remission of dysplasia (CRD) during 12 months after baseline procedure, and 3. number of RFA treatments necessary for complete response of intestinal metaplasia.

Results: We included 92 patients with BE (at least COM1), who had a baseline VLE scan, followed by RFA, and had no prior ablative therapy. These patients were divided into three patient groups: without prior EMR and treated with only RFA (n = 53, mean Prague length(M) = 5.396, SEM = 0.520), with prior EMR treated with combined EMR and RFA at baseline(n = 3, mean Prague length(M) = 6.67, SEM = 1.67), with prior EMR and RFA at baseline (n = 19, mean Prague length (M) = 3.816, SEM = 0.616). After determination of gastro-esophageal junction (GEJ) location on VLE, we measured mucosal thickness in 8 segments at 0.5 cm intervals from GEJ to the top of the Barrett’s tissue. The mean amount of selected cross sections in the scan for the first 40 patients was 6.33 (SEM = 0.50, n = 40). The measurements of thickness, using the subjective and objective protocol in one patient is shown in Table 1.

Conclusion: We developed an algorithm, that automatically adjusts raw VLE images in order to recognize superficial layers of the esophageal wall and measure the thickness of these different layers in Barrett’s tissue. We performed both subjective and objective methods for thickness calculation. This is the first step to the production of a biomarker for the prediction of treatment response in patients with Barrett’s Esophagus. Further research is needed to demonstrate whether one of these two measurement protocols can predict the response to RFA and ER.

Disclosure of Interest: G. Tearney; Tearney G is the co-inventor of the VLE scan; he contributed VLE expertise to be able to do the measurements. The measurements itself were done by Iris Levink.

S. Schlachter; Schlachter, S is an employee at Ninepoint Medical and manages the data of the Ninepoint registry. Schlachter, S had no influence on the outcome of the measurements. The measurements were done by Levink, I.

All other authors have declared no conflicts of interest.

References


Abstract No: P1862

Table 1: The measurements of Barrett’s thickness in one patient, using the two different measurement protocols.

<table>
<thead>
<tr>
<th>Pt.</th>
<th>Age (years)</th>
<th>SEX</th>
<th>BMI</th>
<th>Highest grade prior biopsy</th>
<th>Prior Treatment</th>
<th>Prague Length, circumferential and maximum extend in cm</th>
<th>Thickness subjective measured, pixels [SEM, number of measurements]</th>
<th>Thickness objective measured, pixels [SEM, number of measurements]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>85</td>
<td>Male</td>
<td>25.8</td>
<td>High grade dysplasia</td>
<td>None</td>
<td>C16M16</td>
<td>317.38 [9.96, 65]</td>
<td>286.85 [8.96, 65]</td>
</tr>
</tbody>
</table>
SEVEN-YEAR PROSPECTIVE FOLLOW-UP RESULTS OF RADIOFREQUENCY ABLATION FOR BARRETT’S ESOPHAGUS WITH HIGH-GRADE DYSPLASIA AND EARLY CANCER

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Introduction: Radiofrequency ablation (RFA) of Barrett’s oesophagus (BE), with or without prior endoscopic resection (ER) of focal lesions, results in complete eradication of intestinal metaplasia (CE-IM) and complete eradication of neoplastic tissue in 96–100%, respectively.

Aims & Methods: The aim of this study was to assess if the excellent results after successful RFA for BE with high-grade dysplasia (HGD) or early cancer (EC) are sustained on the long term. We screened all patients treated with RFA, and EC were excluded. Patients were included if they were previously enrolled in 5 consecutive cohort studies in a tertiary referral center in the Netherlands. All patients who had reached endoscopic and histologically confirmed NE neo-SCJ and CE-IM after RFA were included for evaluation of long-term follow-up (FU). Primary outcome: recurrence of HGD/EC; recurrence of endoscopically visible Barrett’s mucosa. Secondary outcomes: Buried Barrett’s glands; IM in biopsies obtained distal to a normal appearing neo squamos-columnar junction (neo-SCJ); need for retreatment; sustained CE-IM and neo-SCJ at last FU.

Results: 68 patients were included (55 men, median 64 yrs, median BE C5M6). In 53/68 patients ER was performed (worst pathology: low-grade dysplasia (LGD)).

Conclusion: With 7-years of follow-up, this study presents the longest published follow-up data on RFA for BE with HGD/EC to date. Our long-term outcomes show that after successful RFA recurrence of HGD/EC is rare (3%). Recurrence of endoscopically visible BE was found in 32% of patients, however it was confined to small islands or tongues <1 cm in the vast majority of patients.

Table 1: A 14-point based questionnaire which was used to check the understanding amongst patients with Barrett’s Oesophagus (BE–Barrett’s Oesophagus; OAC–Oesophageal adenocarcinoma; PPI–Proton pump inhibitor).

<table>
<thead>
<tr>
<th>Question</th>
<th>Yes (%)</th>
<th>No (%)</th>
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<tbody>
<tr>
<td>1. Did you receive a letter or see someone in clinic to discuss your diagnosis and plans for future follow-up?</td>
<td>32 (31)</td>
<td>72 (69)</td>
</tr>
<tr>
<td>2. If yes, did you understand this?</td>
<td>15 (47)</td>
<td>17 (53)</td>
</tr>
<tr>
<td>3. Broadly speaking, do you understand what BE is?</td>
<td>43 (41)</td>
<td>61 (59)</td>
</tr>
<tr>
<td>4. Do you understand that chronic acid reflux into the lower oesophagus is the most likely cause of BE?</td>
<td>50 (48)</td>
<td>54 (52)</td>
</tr>
<tr>
<td>5. Are you on a regular PPI?</td>
<td>96 (92)</td>
<td>8 (8)</td>
</tr>
<tr>
<td>6. Do you know what the overall risk of progression to cancer is?</td>
<td>46 (44)</td>
<td>58 (56)</td>
</tr>
<tr>
<td>7. Are you of the term ‘dysplasia’ and how this helps to stratify your condition and interval length for surveillance endoscopy?</td>
<td>6 (6)</td>
<td>98 (94)</td>
</tr>
<tr>
<td>8. Do you understand what the rationale for endoscopic surveillance in BE is?</td>
<td>4 (57)</td>
<td>3 (43)</td>
</tr>
<tr>
<td>9. Have you ever been told if you have a short or long segment of BE and the importance of this?</td>
<td>36 (35)</td>
<td>68 (65)</td>
</tr>
<tr>
<td>10. Are you aware of any treatment options for BE?</td>
<td>7 (7)</td>
<td>97 (93)</td>
</tr>
<tr>
<td>11. Do you yes, do you know when this indicated?</td>
<td>4 (57)</td>
<td>3 (43)</td>
</tr>
<tr>
<td>12. Does or has anyone in your family suffered with BE or OAC?</td>
<td>36 (35)</td>
<td>68 (65)</td>
</tr>
<tr>
<td>13. Do you feel or have you ever felt anxious about your diagnosis of BE?</td>
<td>53 (51)</td>
<td>51 (49)</td>
</tr>
<tr>
<td>14. Do you think it would be useful for your understanding or reduce your anxiety if you either sat down with someone in clinic or spoke to someone over the phone regarding your BE?</td>
<td>82 (79)</td>
<td>22 (21)</td>
</tr>
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</table>

Conclusion: We have demonstrated that patients with BE have a relatively poor understanding of their diagnosis and the treatment options that are available to them. Further efforts need to be made to address this and help empower a group of patients who are understandably anxious about their diagnosis.

Disclosure of Interest: All authors have declared no conflicts of interest.

BARRETT’S ESOPHAGUS IS ASSOCIATED WITH TOTAL SERUM ADIPONECTIN IN WOMEN, BUT NOT WITH OTHER INFLAMMATORY OR METABOLIC MARKERS

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Introduction: Data on the association between inflammatory and metabolic biomarkers and Barrett’s oesophagus (BE) are scant and conflicting.

Aims & Methods: We aimed to study the association between circulating inflammatory biomarkers (interleukin-6 [IL-6], high-resolution C-reactive protein [hsCRP], intra-cellular adhesion molecule [ICAM], tumor necrosis factor receptor-2 [TNF-R2]) and metabolic biomarkers (leptin, adiponectin, C-peptide, insulin-like growth factor 1 [IGF-1], and insulin-like grow factor binding proteins -1, -2 and -3 [IGFBP1, -2 and -3]) with BE. This was a case-control study, nested within two female-only prospective cohort studies (Nurses’ Health Study 1 and 2) and one male-only prospective cohort (Health Professional Follow-up Study). Participants of provided biennial detailed information on demographic, lifestyle, dietary and medical factors, including endoscopy use. Overall, 80,437 participants enrolled in these cohorts provided a prediagnostic blood specimen between 1989 and 1995. Among these participants, through 2012, we identified 283 cases of BE (163 females and 120 males). Two study physicians, blinded to biomarkers results, reviewed the medical records of patients reporting BE. We matched BE cases to controls in a ratio of 1:2 by sex and year of birth. A total of 1044 controls were identified.

Results: In women, plasma adiponectin was significantly associated with BE (p-value = 0.01). When compared to the lowest quintile (Q1), the tetra latent odds ratio (OR) for the highest quintile (Q5) of adiponectin was 0.39 (95%CI 0.17, 0.88). This association was not materially altered after further adjustment
Conclusion: There was little evidence that pre-diagnostic inflammatory or metabolic biomarkers are associated with risk of BE. Only adiponectin was associated with a decreased risk of BE in women but not in men. These findings may serve to inform future clinical risk assessment for BE and shed light on potential mechanisms of its pathogenesis.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1866 OUTCOMES OF TREATMENT OF PATIENTS WITH EARLY-STAGE ADENOCARCINOMA OF THE ESOPHAGUS WITH INCipient SUBMUCOSAL INVASION, RETROSPECTIVE ANALYSIS OF 19 CASES FROM A TERTIARY REFERRAL CENTER IN THE UK

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Introduction: Endoscopic mucosal resection (EMR) is an established diagnostic and treatment tool in the management of Barrett’s oesophagus (BO) with early neoplasia, but not enough data exists regarding the use on the patients, in whom the EMR’s histologic assessment identifies early-stage adenocarcinoma of the oesophagus with incipient submucosal invasion (pT1b smI).

Aims & Methods: We have conducted a retrospective analysis using our electronic database for endoscopic procedures for patients with BE, who underwent EMR from October 2010 to December 2016. We investigated the size of the EMRs, the complication rates of the EMRs, the histological features and the resection margins of the EMR specimens and also the outcomes with the mortality.

Results: A total of 99 patients underwent 134 EMR procedures, and the histology identified early adenocarcinoma with incipient invasion of the submucosa in 25 patients. 23 (92%) were male, the mean age at the EMR was 71 years (SD: 8.1). In all 25 EMR 9 (36%) patients had a single piece, 7 (28%) patients had a 2 piece, 7 (28%) patients 3 piece and 4 (16%) patients 4 piece EMR. The median length of the circumferential and maximum extent of the BO segments were 2 and 5 cm respectively (interquartile range (IQR) 2-4). We observed 6 (24%) intra-procedural bleedings and 2 (8%) patient needed admissions with post procedural bleeding and 1 (4%) of them required transfusion. Stricture was endoscopically detectable but not causing any symptoms in 1 (4%) patient and another patient (4%) had slight dysphagia post EMR, but did not need dilatation. Histology showed lymphovascular invasion in 6 (28%) patients and vascular invasion in 1 (4%) patient. Of all 25 early adenocarcinomas 7 (28%) were reported as poorly differentiated, 11 (44%) as moderately differentiated and 3 (12%) as well differentiated. In 4 (16%) cases differentiation was not reported. All resection margins were reported as being clear from dysplasia or cancer. There were 2 (8%) cases, radial resection margins were reported with dysplasia in 3 (12%) cases and with cancer in 15 (60%) cases, but this included the multiple piece EMRs. The deep margin was reported as being clear in 18 (72%) cases, with dysplasia in 1 (4%) case and with cancer in 6 (24%) cases. There were 5 (20%) patients with carcinoma on the radial and/or deep margin of the EMR specimen, of these patients 9 (60%) had oesophagectomy and in the histologic assessment of these specimens, lymph node involvement was observed in 2 cases (22.2% of all oesophagectomies and 9.5% of all surviving and currently cancer-free patients). There was no residual cancer in 3 (33.3%) of the surgical specimens. Radical radio-chemotherapy was given in 1 (6.7%) patient and 3 (33.3%) patients did not have radical treatment for clinical reasons. There were 10 (40%) patients without cancer invasion of the EMR resection margins, of these 4 (40%) had oesophagectomy and 1 (10%) radical radio-chemotherapy. The histologic assessment of these surgical specimens showed residual cancer in 3 (30%) cases and high-grade dysplasia in 1 (10%) case. Of the 25 patients 5 (20%) met the criteria and had radio frequency ablation of the residual Barrett’s oesophagus. Of the 13 (52%) patients who had oesophagectomy 1 (7.7%) patient died of the deterioration precipitated by the oesophagectomy, and sadly in this case the oesophagectomy specimen did not show residual cancer. Of the 12 (48%) patients who did not have oesophagectomy 3 (25%) died since their EMR, 1 (8.3%) of cardiac arrest, 1 (8.3%) of chronic obstructive pulmonary disease and 1 (8.3%) of advanced oesophageal cancer, 18 months after the EMR, and the 9 (75%) surviving patient are all cancer free on follow up investigations, one after radical chemoradiotherapy. The median survival of all 21 (84%) patients currently alive is 25 months (range: 2-68 months; SD: 22.2).

Conclusion: This retrospective analysis we have found that the clinical outcomes are very difficult to predict for patients with early adenocarcinoma and incipient invasion of the submucosa. Clinical decision making remains very challenging and has to be individualised for all patient, until further in depth studies gives us more useful prognostic factors.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1867 THE USE OF ENDOCYSTOSCOPY FOR THE EARLY DETECTION OF ESOPHAGEAL NEOPLASMS

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Results: From July 2015 to March 2017, forty-four patients were included in the study. Seventeen of the forty-four (38.6%) patients had histological confirmed cancer of the esophagus. There were sixteen patients who had normal finding and nine patients with epithasia. The positive predictive value for malignancy (ECA 4 and 5) was 89.5%; the negative predictive value was 100%. Sensitivity was 100% and specificity was 92.6%. Similar findings were noted with IPCL on magnifying NBI. The positive predictive value for malignancy (IPCL 4 and 5) was 100%; the negative predictive value was 99.7%. Sensitivity and specificity were also similar at 100% and specificity 92.6% respectively. To compare the diagnostic accuracy of endocystoscopy and magnifying NBI, the McNemar test was performed. The McNemar chi-squared statistic is NaN, meaning that the two tests have the same diagnostic accuracy.

Conclusion: Endocystoscopy had a high positive predictive value and sensitivity for esophageal malignancy. Its diagnostic accuracy was comparable to magnifying NBI. It may be helpful as an adjunct for better characterization of esophageal lesions. However, further studies on interobserver variability is required.

Introduction: Early detection of esophageal cancers can significantly reduce the mortality. The incorporation of endocystoscopy incorporating the endocystoscopy function into a magnifying endoscope has been designed. Previously, Inoue et al have published a pilot trial on evaluating the use of this endocystoscopy in various types of benign and malignant pathology. We aimed to evaluate clinicopathological findings and outcome.

Aims & Methods: All consecutive patients who had esophagogastroduodenoscopy (EGD) arranged for screening of the esophagus during the period July 2015 to March 2017 were included in the study. EGD with narrow band imaging and endocystoscopy were performed in these patients. During the procedure, the esophageal mucosa was stained with 0.5% methylene blue and then with crystal violet. The endocystoscopic findings were graded from 1 to 5 according to the Inoue’s ECA classification. The esophageal mucosa was also evaluated with narrow band imaging (NBI) and the findings were classified according to the Intrapapillary capillary loop (IPCL) pattern classification. These findings were compared against the gold standard of histopathological diagnosis which was based on the Lauren classification.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

P1868 CLINICAL OUTCOMES OF ENDOCYSTOSCOPIC RESECTION FOR ACHALASIA-ASSOCIATED SUPERFICIAL ESOPHAGEAL CANCER


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Introduction: Esophageal achalasia is considered to be a high-risk factor for superficial esophageal cancer. But there are few reports of endoscopic resection for this cancer, and the outcome is unclear. In our hospital, we have performed over 1300 Per-Oral Endoscopic Myotomy procedures for esophageal achalasia and related esophageal abnormalities. In this process, we diagnosed 10 superficial esophageal cancers in patients with achalasia. We performed endoscopic resection for all cases and report relatively long-term outcome.

Aims & Methods: We aimed to evaluate clinicopathological findings and outcomes of endoscopic resection for 10 achalasia-associated superficial esophageal cancer. This is a case series study at our hospital. Between August 2010 and February 2017, 10 achalasia patients with superficial esophageal cancer underwent endoscopic resection. We performed in all cases upper gastrointestinal endoscopy using narrow’s solution and narrow band imaging. We included all patients that had early cancers that were eligible for endoscopic resection in this series. At 2 and 12 months after treatment, we performed follow-up endoscopy in all cases. After this, we performed long-term endoscopic follow-up every year. In the case that the tumor invasion depth is to the muscularis mucosae(MM) on histopathology, we performed endoscopic follow-up every 6 months and CT scan.

Results: There were 6 men and 4 women and their average age was 61.7 years. 8 patients were diagnosed with lesions before POEM. We performed endoscopic submucosal dissection (ESD/EMR;9/1) in all cases after POEM. None of the patients had a severe adverse event. The mean tumor diameter was 30mm (range: 5-80mm). The pathological diagnosis was 8 SCC, 2 high grade intraepithelial neoplasia. Out of the SCC cases, 7 were found with superficial lesion with depth of Tis-EP to T1a-LPM, and 1 with depth of T1a-MM, without lymphatic invasion(0) or venous invasion(0). Follow-up surveillance mean term was 32 months (range: 1–
only patient who had venous involvement was 92 years old, and followed up without an additional therapy. 6. Local recurrent rate was 0%. 7. LNM rate of EP and SEP was 0% and 5.7% (2/35), respectively. One of two patients who had LNM was a 76-year-old male. He had SEP SCC without lymph duct involve- ment. A cervical LNM was diagnosed 6 months after ESD. Lymph node dissec- tion (LND) and chemoradiotherapy (CRT) was performed for the patient. The patient died of other disease without recurrence of pharyngeal SCC. The other patient also had a cervical LNM and treated by lymph node dissection + CRT. The patient is alive without recurrence for 10 years after ESD. 8. Prognosis No patient died of pharyngeal SCC after ESD.

Conclusion: ESD is a safe and useful treatment for superficial pharyngeal SCC. However, surveillance of LNM is important for the patients who had SEP SCC.

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Introduction: While definitive chemoradiotherapy (CRT) showed high efficacy for patients with high-risk early esophageal cancer (EEC), approximately 40% of patients develop local failure, resulting in poor long-term survival. However, there is no definitive biomarker which is useful to predict survival outcome after CRT for ESCC. Several studies have investigated the correlation of expression of CD24, cytokeratin 4 (CK4), or podoplanin (PDPN) with prognosis of various malignant tumors who underwent surgical resection. However, it remains unclear whether the expression of these proteins can predict the outcome of CRT for patients with EEC.

Aims & Methods: The aim of this study was to clarify the predictive values of expression of CD24, CK4, and PDPN for ESCC patients who received CRT. Among patients with ESCC who received CRT or curative esophagectomy with extended lymph node dissection (OPE) as an initial treatment between 2005 and 2015 at our institution, cohorts were selected based on the following criteria: clinical stage II, III (UICC-TNM classification 6th edition), age of 75 years old or younger, ECOG Performance Status 0–1, and no prior or concurrent other cancers. The method of immunohistochemistry (IHC) was utilized to examine the protein expression of CD24, CK4, and PDPN in pretreatment biopsy specimens of ESCC. The cut-off values for CD24, CK4, and PDPN expression were used hazard ratio for overall survival (OS). The prognostic factor of CD24, CK4, and PDPN expression were statistically analyzed. OS was calculated from the date of CRT or OPE to the date of death or last follow-up, using the Kaplan-Meier method. The survival predictors identified by univariate analysis was assessed by multivariate analysis using a Cox’s proportional hazards model.

Results: 148 ESCC patients (CRT group, n = 83; OPE group, n = 65) were analyzed. In the CRT group, 40 patients had stage II and 43 patients had stage III, and the 5-year OS was 52%. In the OPE group, 32 patients had stage II and 33 patients had stage III, and the 5-year OS was 66%. By univariate analysis, there were significant variables for OS in differences between CRT and OPE group. The cut off value for CD24, CK4, and PDPN expression were 20%, 10%, and 20%, respectively. While the expression equal to the cut off value or more was defined as strong, the expression less than the cut off value was defined as weak. The frequency of strong protein expression was 50% for CD24, 12% for CK4, 65% for PDPN, respectively. In the CRT group, the OS of patients with strong CD24 expression was significantly better than that of patients with weak CD24 expression (p = 0.015; strong/weak 5-year OS: 65%/43%). On the other hand, CD24 and strong CD24 expression was poorer OS comparing with patients with weak expression in the OPE group, however there was no significant difference (p = 0.286; strong/weak 5-year OS: 57%/74%). Strong CD24 expression was significantly different between CRT group and OPE group (p = 0.046), however there was no significant difference between CRT and OPE group in patients with weak CD24 expression (p = 0.009). There were also no significant differences of the OS based on expression of CK4 or PDPN between the CRT and OPE group, respectively. Multivariable analysis showed the strong CD24 expression in the CRT group (p = 0.012; HR = 2.787; 95% CI: 1.253–6.200) as an independent variable for favorable outcome.

Conclusion: CD24 expression was significantly associated with the survival outcome in EEC patients when used in combination with CRT. Furthermore, weak CD24 expression might be a useful predictive biomarker of poor outcome for CRT in EEC patients.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P1874 DIAGNOSTIC ACCURACY OF ENDOSCOPIC ULTRASONOGRAPHY FOR ESOPHAGEAL SUBMUCOSAL GLAND DUCT INVOLVEMENT ACCOMPANYED BY EARLY ESOPHAGEAL CANCER
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Introduction: Normally, resided within the submucosal layer of esophagus, each esophageal submucosal gland will culminate in a single duct. The esophageal submucosal gland ducts (ESMGDs) can traverse the subepithelial connective tissue and muscularis mucosa, and deliver the acinar secretions to the esophageal lumen. However, the clinicopathological features of the esophageal submucosal gland duct involvement accompanied by early esophageal cancer (ESMUDG) and its precursor lesion have not been comprehensively evaluated so far, and the series study focusing on endoscopic features of this lesion has not been reported widely. While since the 1990s, the esophageal lesions presumed to originate from ESMGDs had been described constantly in various case reports. Currently, in addition to the gold standard of histopathology, almost no useful modality could be applied to this lesion. In our study, we considered that the ESMUDG had a correlation with early esophageal cancer, and we noted that the ESMUDG had special features under the endoscopic ultrasonography (EUS). The typical ultrasonic images of EUS could help diagnose ESMUDG.

Aims & Methods: In order to investigate the clinical value of EUS for diagnosing ESMUDG accompanied by early esophageal cancer, which were suggested by conventional endoscopy or endoscopic ultrasonography (EUS). We included consecutive patients with early esophageal cancer diagnosed in the Endoscopy Center at the Affiliated Drum Tower Hospital, Nanjing, China from September 2009 to November 2016. The clinical data of 519 patients were included in this study, and all of them had already underwent EUS combined Endoscopic Submucosal Dissection(ESED). The EUS preoperative diagnosis were compared with the results of postoperative pathology from ESD.

Results: According to the pathological results, all patients (371 males and 148 females, with a mean age of 67.5±4.5 years) had been diagnosed with early esophageal cancer with different invasive depth. Out of 519 patients, about 478 patients were not found ESMUDG by both examinations. Besides, postoperative pathology confirmed that 40 patients were identified with ESMUDG, 34 patients of which were completely consistent with the preoperative diagnosis of EUS. Approximately 98.7% (512/519) of ESMUDG were diagnosed exactly by EUS. Another six cases were estimated as false negative inaccurately, including two squamous cell carcinoma and four high-grade intraepithelial neoplasia. One case was diagnosed as ESMUDG in EUS, but confirmed not by pathology. Therefore, the EUS values for sensitivity and specificity for the diagnosis of ESMUDG were 85.0% (34/40) and 99.8% (478/478) respectively. Furthermore, the positive predictive value was 97.1% (34/35), and the negative predictive value was 98.8% (478/480).

Conclusion: The esophageal submucosal gland duct involvement is a kind of lesion performed as a hypoechoic sonographic pattern located in the thickened mucosa. EUS has a satisfactory diagnostic accuracy for ESMUDG as well as a high positive predictive value.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1873 ENDOSCOPIC TREATMENT OF PATIENTS WITH HIGH-RISK EARLY ESOPHAGEAL CANCER
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Introduction: Endoscopic treatment is a standard therapeutic approach for patients with Tla early esophageal cancer (EEC). In patients with ‘high-risk’ Tla EEC, the treatment of choice is endoscopic mucosal resection (EMR), whereas for patients with Tla early esophageal cancer (EEC), and in patients with any submucosal (sm) invasion (Tlb), surgery is recommended as a standard of care. However, recent data suggest, that endoscopic treatment might be curative in selected patients with ‘high-risk’ EEC. Aims & Methods: The aim of this study was to assess outcomes of endoscopic treatment in patients with ‘high-risk’ EEC. ‘High-risk’ cancer was defined as any cancer with sm invasion or mucosal cancer with at least one of the following: poor differentiation (G3/G4), invasion to blood (A+) or lymphatic vessels (L+) and high tumor cell dissociation (TC3D). The main outcome measurement was tumor-free survival. A single-center, retrospective analysis of prospectively collected data. Patients with EEC underwent endoscopic resection (ER) or endoscopic submucosal dissection (ESD). Based on histopathological staging, patients with ‘high-risk’ features underwent endoscopic submucosal dissection (ESD). Based on histopathological staging, patients with ‘high-risk’ features continued in endoscopic treatment consisting of further sessions of ER and/or radiofrequency ablation if necessary. The patients have been followed up for a median of 39 months (range 2–156).

Results: Of the total of 56 patients with ‘high-risk’ EEC underwent endoscopic treatment: 21 patients (41%) had Tla cancer with ‘high-risk’ features and 35 patients (59%) had Tlb cancer with sm invasion (sm1: 15; sm2: 9, sm3: 11); 45 patients had adenocarcinoma (EAC), 11 patients had squamous carcinoma (SCC); 19 (34.5%) were referred for surgery and 37 patients were referred for endoscopic treatment. Complete local remission (CLR) of neoplasia was achieved in 35/37 patients (95%). Two patients without CLR continued endoscopic therapy with palliative intent. Tumor generalization occurred in 2 patients (one of them achieved CLR) 24 months after endoscopic treatment (both patients had sm3 invasion, A+, L+ and these patients are undergoing oncological treatment. All remaining patients with CLR (n = 33) have experienced neither local relapse nor generalization. One patient had to undergo surgery due to esophageal related perforation. Tumor-free survival was 89% (CI 79–99%) in patients treated endoscopically and endoscopic related mortality was 0% (0/37). Among 19 patients who were referred for esophagectomy, one patient presented with tumor generalization revealed during the operation. The remaining 18 patients underwent esophageography; local residue of malignancy was present in 5/18 patients (28%). Lymph node (LN) metastases have not been detected in any patient among the 337 examined LNs. Surgery related mortality was 6% (1/18).

Conclusion: Endoscopic treatment provides long-term remission or cure in a considerable number of patients with ‘high-risk’ EEC and it may thus represent a valid alternative to surgery. Brodening of indications for radical endoscopic treatment of early EEC should be reconsidered.

Disclosure of Interest: All authors have declared no conflicts of interest.
PRETREATMENT NEUTROPHIL TO LYMPHOCYTE RATIO IS NOT A PREDICTOR OF RESPONSE TO NEOADJUVANT THERAPY IN ESOPHAGEAL CANCER

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Introduction: Preoperative Neutrophil to Lymphocyte Ratio (NLR) has been proposed as a prognostic marker in several solid tumors (Templeton 2014). A retrospective prospective study of 60 patients showed the prognostic relevance of NLR as a predictor of response in esophageal cancer patients treated with chemoradiotherapy. The aim of this study is to assess the NLR prognostic strength in a retrospective series of two high-volume centers.

Aims & Methods: A retrospective review of two prospective esophageal cancer database was conducted. Neutrophil to lymphocyte ratio was defined as the prochemoradiotherapy serum neutrophil count divided by lymphocyte count. We dichotomized the NLR data using as cut-off values 2.5 and 3 respectively. Univariable logistic regressions were performed to determine the effect of NLR on response after neoadjuvant treatment. Survival curves were constructed with Kaplan Meier method and compared with the long rank test.

Results: We included of 280 patients. The analysis of NLR as predictor of pathologic complete response (pCR) showed a OR of 0.963 (95% CI 0.531–1.746, p = 0.991) and 1.161 (95% CI 0.647–2.081, p = 0.617) considering as cut-off values 2.5 and 3 respectively. In our large series, NLR did not result as a predictive marker neither in terms of Overall Survival nor in terms of Disease Free Survival (p = 0.997 and p = 0.672 respectively).

Conclusion: Our results did not confirm NLR as a significant marker of pCR. Moreover, the survival analysis did not reveal significant differences using NLR as a preoperative predictive marker. The heterogeneity of treatments, the complexity of the disease, the absence of a validated and pre-defined NLR cut-off value in the available literature are the main limits to our analysis. Further studies are needed to assess the clinical relevance of NLR as a predictive marker of response to neoadjuvant treatment.

Disclosure of Interest: All authors have declared no conflicts of interest.

References


ACCELERATION OF HEALING OF PREEXISTING GASTRIC ULCERS BY CARBON MONOXIDE RELEASING MOLECULE -2 (CORM-2), INVOLVEMENT OF HEME OXYGENASE, OXIDATIVE STRESS AND PROINFLAMMATORY MECHANISMS

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Introduction: Carbon monoxide (CO) is produced endogenously in the body as a by-product of heme degradation via activity of the enzyme heme oxygenase (HO-1). This gaseous mediator with multidirectional biological activity exerts anti-inflammatory, anti-fibrogenic, and immunomodulatory properties. The newly discovered class of compounds, named CO-releasing molecules (CORMs), is capable of releasing CO gaseous molecule that can be useful as pharmacological tool to assess the pathobiological role of CO under experimental conditions. CORM-2 was implicated in gastrointestinal protection against formation of acute gastric lesions but the contribution of CO to the mechanism of ulcer healing has not been fully elucidated.

Aims & Methods: We determined the effect of daily treatment with vehicle or CORM-2, on healing of preexisting gastric ulcers induced by serosal application of acetic acid (ulcer area = 28 mm²) in rats. Our second goal was to examine the mechanism of CO released from its donor by the determination of the CORM-2-induced alterations in gastric blood flow (GBF) at ulcer margin, the parameters of oxidative stress and the gastric mucosal expression of pro-inflammatory and anti-inflammatory factors. Groups of seventy rats with gastric ulcers (A-D) received daily treatment with A) vehicle (saline), B) CORM-2 in doses from 1 up to 10 mg/kg i.g., C) the HO-1 inhibitor, hemin (5 mg/kg i.p.), D) the HO-1 activity inhibitor, zinc protoporphyrin IX (ZnPPIX) (5 mg/kg i.p.). After 9 days of treatment, the ulcer area was measured by planimetry, the gastric blood flow (GBF) at ulcer margin was determined by Laser Doppler technique, plasma TNF-α and IL-1β levels were analyzed by ELISA and TNF-α, HO-1, HO-2, COX-1, COX-2, iNOS, eNOS mRNAs were analyzed by RT-PCR and Western blot. Gastric mucosal samples were collected for the assessment of MPO activity, level of reduced glutathione (GSH) and lipid peroxidation products (MDA + 4HNE) by spectrophotometric method.

Results: Treatment with CORM-2 significantly reduced the area of gastric ulcers and significantly raised GBF at ulcer margin. The dose accelerating ulcer healing up to 10 mg/kg (CORM-2) received daily treatment with A) vehicle (saline), B) CORM-2 in doses from 1 up to 10 mg/kg i.g., C) the HO-1 inhibitor, hemin (5 mg/kg i.p.), D) the HO-1 activity inhibitor, zinc protoporphyrin IX (ZnPPIX) (5 mg/kg i.p.). After 9 days of treatment, the ulcer area was measured by planimetry, the gastric blood flow (GBF) at ulcer margin was determined by Laser Doppler technique, plasma TNF-α and IL-1β levels were analyzed by ELISA and TNF-α, HO-1, HO-2, COX-1, COX-2, iNOS, eNOS mRNAs were analyzed by RT-PCR and Western blot. Gastric mucosal samples were collected for the assessment of MPO activity, level of reduced glutathione (GSH) and lipid peroxidation products (MDA + 4HNE) by spectrophotometric method.

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Results: Treatment with CORM-2 significantly reduced the area of gastric ulcers and significantly raised GBF at ulcer margin. The dose accelerating ulcer healing up to 10 mg/kg (CORM-2) received daily treatment with A) vehicle (saline), B) CORM-2 in doses from 1 up to 10 mg/kg i.g., C) the HO-1 inhibitor, hemin (5 mg/kg i.p.), D) the HO-1 activity inhibitor, zinc protoporphyrin IX (ZnPPIX) (5 mg/kg i.p.). After 9 days of treatment, the ulcer area was measured by planimetry, the gastric blood flow (GBF) at ulcer margin was determined by Laser Doppler technique, plasma TNF-α and IL-1β levels were analyzed by ELISA and TNF-α, HO-1, HO-2, COX-1, COX-2, iNOS, eNOS mRNAs were analyzed by RT-PCR and Western blot. Gastric mucosal samples were collected for the assessment of MPO activity, level of reduced glutathione (GSH) and lipid peroxidation products (MDA + 4HNE) by spectrophotometric method.
CORM-2 was accompanied by a significant decrease in plasma levels of IL-1β and TNF-α when comparing to vehicle-control group. The expression of IL-1β, TNF-α, COX-2 and iNOS mRNA was strongly upregulated in vehicle-treated gastric mucosa but expression of these factors was significantly attenuated in CORM-treated animals. The increased mucosal expression of mRNA for HO-1 but not HO-2 was detected in vehicle control group and these effects were ameliorated by treatment with CORM-2. The gastric mucosal MPO activity and thermocanal content of MDA + 4HNE in gastric mucosa were elevated in vehicle-control group and these effects were significantly inhibited by CORM-2. Consumption of CORM is donor CORM’s specific property that decreases the levels of pre-existing gastric ulcerations by the mechanism involving an increase in gastric microcirculation at ulcer margin, the inhibition of inflammatory response as manifested by the attenuation of enhancing synthesis of the proinflammatory markers IL-1β, TNF-α, COX-2 and iNOS as well as by antioxidant properties of CORM-2 releasing CO limiting lipid peroxidation.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1878 PROTON PUMP INHIBITORS INAPPROPRIATE USE IN PATIENTS ADMITTED IN A TERTIARY HOSPITAL AND IN THE COMMUNITY

Introduction: There is evidence of proton pump inhibitors (PPIs) misuse in the community and in the hospitals causing significant direct and indirect costs burden for the health care system.

Aims & Methods: We aimed to evaluate the frequency of inappropriate PPIs administration in hospitalized patients, to measure the direct in-hospital costs of PPI misuse and to calculate the number of patients exposed to the risk of upper gastrointestinal (UGI) complications due to medication underuse. This was a prospective, cross-sectional, prescription-indication drug-utilization, chart-review study in hospitalized patients with follow-up until discharge, in a tertiary hospital in Athens, Greece. We recorded data of all patients admitted (intensive care, cardiac, psychiatric, obstetrics and day clinic admission were excluded) during three consecutive on-call days of the hospital in March 2017 regarding PPIs utilization before admission, during hospitalization and on discharge. Patient’s data was collected for patients prescribed PPIs overuse and the number of patients at risk of UGI complications due to PPIs underuse for 1 year period, using a simulation model.

Results: We included data from 470 patients aged 67 ± 19 yrs; 32.5% were pre-scheduled admission, 65.9% during hospitalization and 72.8% at discharge. PPIs overutilization was detected in 15.7%, 41.3% and 12.6% of the patients before, during and after the admission, while medications underutilization was detected in 10.2%, 8.1% and 9.5% of them, respectively. Adverse drug reaction and orthostatic hypotension was associated with the highest unadjusted ORs (1.68 [95% CI 1.63–1.72] and 1.68 [1.59–1.78]) for PPIs misuse, 80% of the 193 over treated patients received PPIs iv (80% of them od, 20% bid) while the rest were treated with PPIs per os (80% of them od, 10% bid) during hospitalization. This accounts for 140 PPI iv and 344 PPI per os doses inappropriately given during the observation period. Taking into account in our simulation model that there are 90 on-call days of our hospital’s activity, the cost of each PPI iv dose is 3.435 and 0.235 euros for iv and per os preparations and assuming a similar to that of our sample case distribution for the next 12 months, we calculated the direct hospital costs burden of inappropriate PPIs use at 154940 euros per year. Using the same model, 1200 patients would be at risk of UGI complications annually, due to under prescription of PPIs at discharge.

Conclusion: Hospitalization does not represent an opportunity for optimization of PPIs utilization. On the contrary, the frequency of PPIs inappropriate use during hospitalization is higher than that of outpatient admission, causing significant direct costs for the hospital and exposing patients to the risks of UGI complications.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1890 ENDOSCOPIC RESECTION OF ADVANCED AMPULLARY ADENOMAS: A SINGLE-CENTER 14-YEAR RETROSPECTIVE COHORT STUDY

Aim: To assess the technical success, complications and recurrence of endoscopic resection for treating patients with ampullary adenomas with intraductal extension (AIE), and patients with lateral spreading adenomas (LSA). Between January 2002 and November 2016, all patients were identified by using ENDOBASE and we provided a search in our local PALGA database. We included patients with a histological diagnosis of adenoma. Endoscopic resection was performed by 5 experienced endoscopists. Endoscopic success was described as complete excision of the adenoma, irrespective of the number of attempts, and in the absence of recurrence. All patients underwent endoscopic follow-up. Early and late complications were registered.

Methods: The aim of our study was to evaluate the technical success, complications and recurrence of endoscopic resection for treating patients with ampullary adenomas with intraductal extension (AIE), and patients with lateral spreading adenomas (LSA). Between January 2002 and November 2016, all patients were identified by using ENDOBASE and we provided a search in our local PALGA database. We included patients with a histological diagnosis of adenoma. Endoscopic resection was performed by 5 experienced endoscopists. Endoscopic success was defined as complete excision of the adenoma, irrespective of the number of attempts, and in the absence of recurrence. All patients underwent endoscopic follow-up. Early and late complications were registered.

Results: We included 84 patients, 56 patients (67%) had an adenoma confined to the ampulla (ACA), 17 patients (20%) had a LSA and 11 patients (13%) were treated for adenomas that demonstrated growth pattern with intraductal extension. Fifty-five percent of the patients were men and the median age was 65.4 years (range 32–89). The median lesion size was 24.6 mm (range 0–80). The median follow-up duration was 31.1 months (range 0–129) for ACA, 23.1 months (range 0–127) for LSA and 11.9 months (range 0–37) for IAE (P = 0.039). Complications occurred in 26 patients (30.9%), of which hemorrhage was most seen in 17.9%, followed by perforation in 5.9% of the patients. Complications were equally divided over these three groups (P = 0.775). The mean follow-up duration was 31.1 months (range 0–129) for ACA, 23.1 months (range 0–127) for LSA and 11.9 months (range 0–37) for IAE (P = 0.036). Endoscopic resection was curative in 87.5% of patients with a localized adenoma, 82.3% in patients with a lateral spreading adenoma and in only 9.1% of patients with an intraductal extended tumor (P < 0.000). Recurrence occurred in 9 patients (10.7%), 5 of them had a localized adenoma, 3 patients with a lateral spreading adenoma and 1 patient with an intraductal extended adenoma (P = 0.875).

Conclusion: Endoscopic ampullactomy is a safe and successful treatment in patients with an adenoma with or without a lateral spreading growth pattern. In contrast, an intraductal extended adenoma endoscopic success rates are significantly lower.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference


P1879 CONTINUOUS INCREASE IN PREVALENCE OF FUNDIC GLAND POLYPS WITH THE LENGTH OF PROTON PUMP INHIBITORS USE. IS THERE ANY CLINICAL CONSEQUENCE?

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Introduction: Proton pump inhibitor (PPI) usage is associated with an increased risk of development of fundic gland polyps (FGP). The trend of change in the prevalence with increasing length of PPI exposure over 5 years is not known. Theoretical risk of FGP seems to be very low for clinical consequence in management.

Aims & Methods: To evaluate the relationship between the length of PPI use and risk of fundic gland polyps. Prospective cohort study in patients referred for upper gastrointestinal endoscopy between years 2015–2016 was performed. The length of PPI use was ascertained from direct patient interview and confirmed from medical records. The prevalence of FGP in history not continuing at the time of endoscopy was also queried. FGP were determined both endoscopically and histologically. Odds ratios for subsequent intervals of length of PPI use were calculated. Clinically relevant complications—dysplasia and bleeding from large polyps were recorded.

Results: During study period 1525 patients (mean age 59.2 years, 53% male) were included. Only 612 (40%) of patients had no history of any PPI use. Fundic gland polyps were identified in 170 patients (11%) and only 13 of them (7.6%) were without PPI use. The prevalence of FGP in subgroup of patients according to the length of PPI use was: 10.6% of 161 patients using PPI less than 1 year, 9.4% of 405 (1–4 years of PPI), 25.2% of 230 (5–9 years of PPI), 35.1% of 94 (10–15 years of PPI) and 47.8% of 23 patients using PPI more than 15 years. The approximate odds ratios were 57.6 (2.6–11.4), 4.8 (95% CI 8.5 (CI 8.3–29.0), 24.9 (CI 12.4–49.5) and 42.2 (CI 15.7–113.1) respectively, all with statistical significance (p < 0.001). Only 1 case of low grade dysplasia within FGP was observed in the patient with familiar adenomatous polyposis. Polyps larger than 15 mm with signs of bleeding determined as a case of sidereopenic anemia were diagnosed in 6 patients.

Conclusion: The prevalence of FGP is permanently growing during prolonged use of PPI. Complex source of informations regarding history of PPI use identified quite low proportion of patient with FGP and without prior PPI use. Rather rare complications like bleeding from FGP might be clinically significant in increasing number of long term PPI users. The requirement of repetitive endoscopies and therapeutic interventions may burden gastroenterologists and sources.

Disclosure of Interest: All authors have declared no conflicts of interest.

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FACTORS ASSOCIATED WITH TECHNICAL DIFFICULTY OF ENDOSCOPIC SUBMUCOSAL DISSECTION FOR EARLY GASTRIC CANCER WHICH MET EXPANDED INDICATION CRITERIA; POST HOC ANALYSIS USING DATA OF MULTIPLE INSTITUTIONAL PROSPECTIVE CONCLUSIVE TRIAL (JCGOG0607)

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Introduction: There are few reports about the technical difficulty of gastric endoscopic submucosal dissection (ESD) which were investigated through the prospective trial.

Aims & Methods: The aim of this study was to evaluate the factors associated with the technical difficulty of ESD for early gastric cancer (GC) which met expanded indication criteria using data from JCGOG0607. The major inclusion criteria of JCGOG0607 was as follows: 1) histopathologically proven intestinal-type adenocarcinoma; 2) cT1aN0M0; 3) lesion without finding of ulcer (UL negative) and 4) age 20-75. ESD were performed by certified endoscopists or under the supervision of certified endoscopists. 162 cases (55%) had the studied 100 cases or more. The difficult case was defined that ESD took 120 minutes (min) or longer, and/or developed perforation during procedure. Multivariate analysis was performed to investigate the clinical factors associated with technical difficulty of ESD.

Results: Between June 2007 and Oct. 2010, a total of 470 patients (pts) (male/female: 385/85, median age 65y-o (range: 40–75)) were enrolled from 29 institutions. The difficult case was defined that ESD took 120 minutes (min) or longer, and/or developed perforation during procedure. Multivariate analysis was performed to investigate the clinical factors associated with technical difficulty of ESD.

Operation time, min 76.7
Suture time, sec 296.7

Reference

Comparison of clinical characteristics and therapeutic outcomes between STER and EFTR

STER (n = 15) EFTR (n = 28) P
No. of clips for suture 5.8 ± 1.4 7.6 ± 1.6 0.001
Complications, % 6.7% (1/15) 14.3% (4/28) 0.643
En bloc resection, % 6.7% (1/15) 3.6% (1/28) 1.000
GIST/Liomomyoma/Schwannoma 11/4.0 25/2.1 0.173
Length of stay, d 6.1 ± 1.5 6.2 ± 2.0 0.856
Cost, USD 3260.0 ± 618.3 3237.5 ± 615.8 0.906
Follow-up time, mon 12.1 ± 12.2 22.8 ± 18.4 0.052

Conclusion: The treatment efficacy between submucosal tunneling endoscopic resection and endoscopic full-thickness resection for treating gastric fundus submucosal tumors was comparable, but submucosal tunneling endoscopic resection offers advantages over endoscopic full-thickness resection in terms of shorter surgery time and smaller number of clips needed to close the gastric wall defect.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P1884 COMPARISON OF THE DIAGNOSTIC YIELDS OF ENDOSCOPIC ULTRASOUND-GUIDED FINE NEEDLE ASPIRATION FOR DUODENAL AND GASTRIC SUBEPITHELIAL LESIONS
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Introduction: The progress of diagnosis and treatment for gastrointestinal subepithelial lesions (SELs) have been remarkable by the wide use of Endoscopic Ultrasound-Guided Fine Needle Aspiration (EUS-FNA) and the development of Laparoscopy and Endoscopic Cooperative Surgery. EUS-FNA is used widely for SELs that occur in the digestive tract. There are many reports on gastric SELs, but there are no studies on a large group of patients focusing on duodenal SELs.

Aims & Methods: The aim of this study was to investigate the usefulness and safety of EUS-FNA for duodenal SELs, comparing them with gastric SELs. Cross-sectional study was conducted using 41 patients who underwent EUS-FNA at tertiary medical center in Tokyo between April, 2012 and February, 2017. We divided into 2 groups: 6 patients with duodenal SELs (group D) and 35 patients with gastric SELs (group G). Tumor location was not significantly different between the two groups. Median specimen was the same in both groups with no significant difference: 43 mm and 15 mm, respectively. The en bloc resection rates (96.3% and 97.8%) and the curative resection rates (82.5% and 84.6%) were not significantly different. The perforation rates were not statistically different (2.44% and 3.21%). However, the postoperative bleeding rate (5.28% vs. 2.72%: p = 0.05), postoperative delirium (2.0% vs. 0.25%; p = 0.009) and pneumonia (2.0% vs. 0.25%; p = 0.009) were significantly higher in the elderly group (30.9% vs. 17.0%: p < 0.0001.). Comorbidities were significantly higher in the elderly group including heart disease (24.8% vs. 10.5%: p < 0.0001), lung disease (13.6% vs. 7.4%: p = 0.002) and diabetes (13.3% vs. 1.0%; p = 0.009). Tumor location was not significantly different between the two groups.

Conclusion: Endoscopic ultrasound-guided fine needle aspiration biopsy of submucosal lesions including duodenal SELs can be applicable in elderly patients, and our results are expected to be useful in EUS-FNA study for duodenal SELs.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P1885 SHORT-TERM OUTCOME OF ENDOSCOPIC SUBMUCOSAL DISSECTION FOR EARLY GASTRIC CANCER IN ELDERLY PATIENTS AND LONG-TERM OUTCOME AFTER NON-CURATIVE RESECTION
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Introduction: Endoscopic submucosal dissection (ESD) is widely used as a standard treatment for superficial tumors in the GI tract and its safety has been established. Opportunities for elderly patients to undergo ESD for early gastric cancer is increasing due to the continued improvement in life expectancy. However, short-term and long-term outcome of ESD for elderly patients is still uncertain because of the high incidence of comorbidities and possible increased risk of complications related to ESD in this population.

Aims & Methods: Therefore, we investigated the safety, efficacy and short-term outcome of gastric ESD for patients over 80 years old. Additionally, we evaluated the long-term outcome of non-curative resections according to both age groups. 1056 lesions in 886 patients treated with ESD between January 2011 and December 2015 in our hospital were retrospectively reviewed. They were classified into two groups; elderly group > 80 years old (346 lesions in 201 patients) and non-elderly group > 79 years old and younger (810 lesions in 685 patients). The patient demographics, lesion characteristics, short-term ESD outcome, complications (perforation, postoperative bleeding, postoperative delirium, pneumonia), were compared and we considered the safety, efficacy and short-term outcome of non-curative ESD, cases performed between 2011 and 2013 were assessed.

Results: The median age was 83 years old (range: 80–92) in the elderly group and 67 years old (range: 36–78) in the younger group. The ratio of female patients was significantly higher in the elderly group (30.9% vs. 17.0%: p < 0.0001). Comorbidities were significantly higher in the elderly group including heart disease (24.8% vs. 10.5%: p < 0.0001), lung disease (13.6% vs. 7.4%: p = 0.002) and diabetes (13.3% vs. 1.0%; p = 0.009). Tumor location was not significantly different between the two groups.

Conclusion: Concerning the long-term outcome of non-curative ESD, cases performed between 2011 and 2013 were assessed.

Disclosure of Interest: All authors have declared no conflicts of interest.
published guidelines regarding appropriate surveillance of patients with GIC and how to safely and efficiently perform and interpret follow-up biopsies. GIC is associated with a varying risk of progression to GC, and a genetic predisposition is a major risk factor. The goal of this study is to evaluate the risk of progression of GIC in family history GC and 887 (81.4%) did not have. Genotype of TGFB1 was obtained from surgery, endoscopic submucosal dissection (ESD), endoscopy, histology and outcomes were reviewed.

**Results:** 160 patients (including those with Barrett’s oesophagus, GIC and family history of gastric cancer) were enrolled on the surveillance programme. 42 patients with GIC were identified–20 females (47.6%) and 22 males (52.3%). The mean age at which GIC was first diagnosed was 60.6 years (range from 7.9 to 71.5 years). 15/42 patients (35.7%) had a co-existent Barrett’s oesophagus and Helicobacter pylori was identified in 6/42 (14.3%). The follow-up period ranged from 0.5 to 17.3 years. 27 patients had repeat gastroscopies following initial diagnosis. 15 patients are still awaiting a repeat gastroscopy. A large degree of variability in the number and frequency of follow-up gastroscopies was observed. The average interval of follow-up gastroscopies was 3.3 years per person. 14/27 patients (51.8%) had no evidence of GIC on most recent gastroscopy, 7/27 patients (26%) had repeat findings of persistent focal GIC, 5/27 patients (18.5%) progressed to extensive GIC. No cases of dysplasia were recorded but 1 patient (3.7%) developed gastric cancer.

**Conclusion:** This study suggests a low apparent risk of progression of gastric intestinal metaplasia in a small western cohort. Further studies may be necessary to address if the applicability of published surveillance guidelines can be generalised to regions with low gastric cancer prevalence.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**References**


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P1888 GASTRIC ADENOCARCINOMA AND PROXIMAL POLYPOSY OF THE STOMACH. A GENETIC STUDY OF A NEWLY DIAGNOSED FAMILY

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**Introduction:** Gastric adenocarcinoma and proximal polyposis of the stomach (GAPPS) has to be described recently only in a few families worldwide (only one in Europe till now). Three different point mutations in promoter 1B of the APC gene were identified as causol (c.191T>C, c.192A>G, and c.195A>C). We diagnosed GAPPS in the second Czech white family (not related to that one published previously–ref. 1).

**Aims & Methods:** We diagnosed GAPPS across 3 generations in a new Czech white family. A genetic analysis of the family was performed.

**Results:** The Proband (a 43-year-old male) was endoscopically regularly surveyed from his 34 years of age because of fundic-gland polyposis with predominant involvement of the gastric fundus and body (with relative sparing of the lesser curve) and microcytic anemia. Polyposis slowly progressed with the intestinal differentiated low-grade dysplasia in polypyctomy specimens 10 years after the diagnosis. As the GAPPS criteria were fulfilled (ref. 2), he and his family underwent genetic testing and bi-directional Sanger sequencing of promoter 1B revealed a point mutation (c.–191T>C). The same type of mutation was described in his father (63 years old), sister (41 years old), nephew (son of his sister, 6 years old), uncle (father’s brother, 51 years old) and 2 cousins (uncle’s daughters, 23 and 27 years old), all have been asymptomatic. No gastric cancer in the family history was mentioned. The Proband underwent preventive total gastrectomy, histology of the surgical specimen confirmed severe involvement of gastric body with fundic gland polyps, low-grade and focal high-grade dysplasia. The microcytic anemia improved rapidly after surgery. The rest of family is scheduled for gastroscopy. The fundic-gland polyposis of similar distribution (with significantly lower number of polyps, without any dysplastic changes) was recently diagnosed in the 23-year-old cousin.

**Conclusion:** The second European family with GAPPS is presented. The recently described mutations in promoter 1B of the APC gene does not automatically mean a faster progression of the disease as suggested earlier. GAPPS can be presented with various phenotypes with a different course of disease, the prevalence can be higher than previously reported. Acknowledgement: The study was supported by the Research Project PROGRES Q40–15.

**Disclosure of Interest:** All authors have declared no conflicts of interest.
P1889 ENDOSCOPIC TREATMENT FOR LATERAL SPREADING SUPERFICIAL ESOPHAGEAL SQUAMOUS CELL CARCINOMA
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Introduction: ESD is the one of the options of treatment even for lateral spreading (size is over 5 cm) esophageal squamous cell carcinoma (ESCC). Endoscopic diagnosis is developed by magnified endoscopy, however accuracy of diagnosis for lateral spreading ESCC is not high. Some patients have to undergo additional treatment because tumor is invaded to submucosal layer or lymphvascular invasion. On the other hand, wide resection by ESD could cause the delay of additional treatment because of the treatment for esophageal stricture after ESD. Thus, treatment strategy for lateral spreading ESCC has to include additional treatment after ESD. Aim of this study is to evaluate our treatment strategy for lateral spreading superficial ESCC.

Aims & Methods: From January 2010 to December 2014, 49 cases of lateral spreading superficial ESCC were resected by surgery or ESD. Diagnosis, treatment methods and outcomes are evaluated. Our indications for additional treatment after ESD are the cases of over pT1b (SM2) or lymphvascular invasion. Results: In 49 cases of lateral spreading superficial ESCC, 32 cases were treated by ESD and 17 case were treated by surgery. All lesions of 32 cases are completely resected by ESD. Average size of tumor treated by ESD is 59.4mm(50-88mm). Accuracy of estimated depth of invasion by endoscopy for ESD cases was 65.7%. Four of 32 cases of ESD underwent additional therapy (3 for surgery and 1 for CRT) because of pT1b (SM2) or lymphvascular invasion, and one case has lymph-node metastasis. Rate of stricture after ESD was 20.0% for sub-circumferential ESD and 77.3% for circumferential ESD instead of steroid injection. Average time and duration for control of esophageal stricture by Baloon Bougie is 13.5 times and 18 weeks. In 17 surgical cases, all cases are treated by thoracoscopic esophagectomy. Average size of tumor treated by surgery is 76.5 mm (50-130 mm). Accuracy of estimated depth of invasion by endoscopy for EUS combined diagnosis was 97.1% (34/35), and the negative predictive value was 98.8% (478/484).

Conclusion: The esophageal submucosal gland duct involvement is a kind of endoscopic performed diagnosis pattern located in the thickened mucosa. EUS has a satisfactory diagnostic accuracy for ESCMID as well as good sensitivity and specificity.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1890 Diagnostic Accuracy of Endoscopic Ultrasonography for Esophageal Submucosal Gland Duct Involvement Accompanied by Early Esophageal Cancer R. Y. Jie, L. Ying

Disclosuer of Interest: All authors have declared no conflicts of interest.

References
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Introduction: miRNAs are a group of small non-coding RNAs that dysregulate in various types of cancers [1–3]. They play a pivotal role in several pathological processes. Growing evidence show that miRNAs can act as either tumour oncogenes or suppressors in different types of cancers. Previous studies revealed that miR-211-5p could suppress melanoma proliferation, migration, and invasion [4]. Aims & Methods: We aimed to investigate and characterize the biological roles of miR-211 in the development of gastric cancer. The expression level of miR-211-5p was measured in paired primary gastric cancer with corresponding adjacent nontumoral gastric mucosa by RT-PCR. Furthermore, we investigate the biological role of miR-211-5p in proliferation, apoptosis, migration of gastric cancer cell lines in vitro. Results: The expression levels of miR-211-5p were significantly decreased in gastric cancer and low expression of miR-211-5p correlates with poor prognosis in gastric cancer patients. Ectopic expression of miR-211-5p suppressed proliferation, migration and induced apoptosis in gastric cancer cell lines in vitro. Bioinformatics and quantitative analysis revealed that FoxC1 might be a target of miR-211-5p. Downregulation of FoxC1 inhibited proliferation and migration of gastric cancer cells and Overexpression of FoxC1 partly abrogated the inhibitory effects of miR-211-5p on gastric cancer cell proliferation and motility. Conclusion: We confirm that miR-211-5p acted as a tumour suppressor by targeting FoxC1 in gastric cancer and miR-211-5p might be a potential target for the treatment of gastric cancer.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
associated, in our series, with a higher incidence of residual/recurrent adenoma, when compared to sporadic adenomas. These results are similar to those reported in the literature. Residual and recurrent duodenal adenomas were successfully retreated by EMR in all of them but one. Mortality related to NASDA was absent in our series after a median follow-up of 59 months (range 1–147). The incidence of interventional radiologists and surgeons with experience in retroperitoneal surgery. In our experience colorectal adenomas was correlated to NASDA (33.3%), colonoscopy is considered part of the pre-EMR assessment when NASDA is diagnosed. A recall system and patient’s compliance to endoscopic follow-up are mandatory to detect recurrences and their prompt treatment.

Disclosure of Interest: G. Costamagna: Grant/research support from Olympus Japan Member of advisory committees or review panels for Cook, Inc., Boston Scientific Corporation, Chang Medical, Inc., Speaker and teacher for Boston Scientific, Corp. and Given Imaging.

All authors have declared no conflicts of interest.

References
ACh on T (nicotinic receptor agonist, increased the number and size of T, while hexamethonium, a selective muscarinic receptor agonist, increased the number and size of T as compared to control conditions (p<0.001).

Results: ACh at concentrations of 0.1 and 1 μM significantly increased the number and size of T as compared to control conditions (p<0.001). Bathemonium, a selective muscarinic receptor agonist, increased the number and size of T, while hexamethonium, a nicotinic receptor agonist, significantly inhibited the stimulatory effect of ACh on T (p<0.001 as compared to ACh-stimulated cells). Interestingly, L-NAME, significantly inhibited the effects of ACh on the number of T. Conversely, SNP, at 1 and 10 μM, increased the number and size of T. Finally, ACh induced the expression of CSC markers (CD44, ALDH and EMT markers (Snail, ZEB1 and Vimentin)) on gastric cancer cells.

Conclusion: This study shows that ACh induces CSC properties of gastric cancer cells through type via activation of muscarinic and nicotinic pathways. It also shows that ACh effects are, at least in part, mediated by nitric oxide pathway. These results suggest that ENS may be a new actor in gastric carcinogenesis.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

Aims & Methods: In this study, we investigated whether activation of gGlu-HMRG fluorescence detects a wild-type of H. pylori (WT) and a ggt gene disrupted mutant of H. pylori (ggt mutant). In addition, we investigated whether activation of gGlu-HMRG fluorescence was suppressed in H. pylori culture solution which was co-incubated with an inhibitor of GGT (GGsTop). Furthermore, we applied gGlu-HMRG to biopsy specimens which were taken from antrum and corpus of stomach in H. pylori positive patients (n = 13) and H. pylori negative patients (n = 14). We then observed the increase of fluorescence intensity over time (1 min, 5 min, 10 min, 15 min). Fluorescence intensity was quantified by Image J2 software (National Institutes of Health, Rockville, Maryland).2

Results: Activation of gGlu-HMRG fluorescence was detected in WT strain, but was not in ggt mutant strain. Activation of gGlu-HMRG fluorescence was inhibited by GGsTop. There was significant difference of the increase of fluorescence intensity between H. pylori positive and negative both in antrum corpus of stomach (antrum p = 0.0008, corpus p = 0.047).

Conclusion: GGT-activated fluorescent probe can be useful for H. pylori infection diagnosis.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P1903 SEROLOGICAL CHANGES AFTER EQUIVOCAL HELICOBACTER PYLORI-SEROLOGY TEST FINDINGS DEPEND ON THE GASTRIC SECRETING ABILITY

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Introduction: The serum anti-Helicobacter pylori (H. pylori) IgG and serum pepsinogen (PG) assays are widely used for gastric cancer screening. An equivocal serology test finding indicates IgG titre between the positive and negative test findings.

Aims & Methods: The study aim was to evaluate the long-term, follow-up result after an equivocal test finding on the serum anti-H. pylori IgG assay. Koreans above 18 years-old with an equivocal serum anti-H. pylori IgG assay finding were included. Subjects were excluded if they did not undergo H. pylori serology test, serum PG assay, and upper gastrointestinal (UGI) endoscopy on the same day at our center. Annual test findings were followed up using the same methods.

Results: Of the 7,178 subjects who underwent the serum assays and UGI endoscopy on the same day, 274 (3.8%) subjects showed an equivocal H. pylori serology test finding. Of the 98 followed-up subjects, 58 (59.2%) showed sero-positive finding at the mean follow-up period of 30.6±12.4 months. Subjects with seroconversion showed a higher initial serum PG I (p = 0.023) and PG II (p = 0.036) levels than the subjects without seroconversion.

Conclusion: An equivocal H. pylori serology test finding is not rare (3.8%) in Korean adults, and 60% of the equivocal subjects show seroconversion within 3 years. Higher seroconversion rates in the subjects with high PG I and PG II levels suggest that intact gastric secreting ability play a role for the survival of H. pylori. Therefore, equivocal subjects with increased serum PG levels should be considered as a potential seropositive subjects.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
tives of patients with pernicious anemia. Gastroenterology 1982;83:204–209.
P1905  SERUM PEPSONOGEN II AS A NON-INVASIVE MARKER FOR DIAGNOSIS OF HELICOBACTER PYLORI INFECTION: A PROSPECTIVE STUDY IN A COHORT OF Dyspeptic PATIENTS

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Introduction: The diagnosis of Helicobacter pylori (H.p.) infection is currently made by means of non-invasive (Urea Breath Test or HpSA) or invasive (gastric biopsy or culture) methods. Serological assessment of H.p. infection by using levels of IgG is not recommended. Pepsinogen II (PGII) is validated in the literature as a non-invasive marker of gastric inflammation. Aim of the study was to assess in a population of dyspeptic patients the clinical availability of PGII determination in singling out subjects infected by H.p. in comparison with non-infected ones.

Aims & Methods: A cohort of 880 consecutive dyspeptic patients (F 439; mean age 55.5 yrs; range 29.83-93 yrs) were enrolled in the study. Exclusion criteria: previous surgery, previous H.p. eradication therapy, concomitant PPI. In all patients the diagnosis of H.p. infection was made by means of upper GI endoscopy and at least one of these two methods: UBT, HpSA. All patients underwent blood sample for determination of serum levels of PGII (Biobit Oyj; Finland; normal values: 2-15 μg/l). In a group of 670 pts a course of antibiotics (triple, concomitant or sequential therapy) to cure H.p. infection was performed and PGII levels were assessed at baseline (T0) and after two months (T1) from the end of the antibiotic therapy. The search for the most appropriate cut-off of PGII in diagnosis of H.p. infection was assessed by using the ROC curve method.

Results: 430 out of 660 dyspeptic patients (F 245;mean age 52.3 yrs; range 32-69 yrs) showed an H.p-related gastritis (group1) in comparison with 430 (F 261; mean age 57.3 yrs; range 38-74 yrs) resulted negative for H.p infection (group 2). The mean value of PGII in group 1 was 20.9±6.1 opposite to 7.2±1.7 in group 2; p<0.0001. 415 out of 670 patients treated with antibiotics schedules were cured from H.p infection, opposite with 255 non-eradicated ones. In the group of cured patients, the PGII values at T0 were 16.5 in comparison with 8.6 at T1; p<0.001. The cut-off for PGII in the diagnosis of H.p infection, by comparing the 430 H.p positive pts and the 430 negative ones with method of ROC curve identified the mean value of 10.6 μg/l, youden index J=0.997.

Conclusion: serum PGII levels seem able to perform diagnosis of H.p infection in dyspeptic patients, as well as the efficacy of antibiotics treatment for H.p eradi- cation, being 10.6 μg/l the best cut-off in singling out infected from non-infected subjects.

Disclosure of Interest: All authors have declared no conflicts of interest.

Abstract No: P1903. Table: Different characteristics of the subjects with an equivocal H. pylori test finding according to the repeated H. pylori serology test findings

<table>
<thead>
<tr>
<th>Variables</th>
<th>Seropositive finding on the follow-up test (n=38)</th>
<th>Seronegative or equivocal finding on the follow-up test (n=40)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years-old)</td>
<td>52.1 ± 9.8</td>
<td>54.0 ± 11.2</td>
<td>0.386</td>
</tr>
<tr>
<td>Gender (male)</td>
<td>43 (74.1%)</td>
<td>23 (57.5%)</td>
<td>0.084</td>
</tr>
<tr>
<td>Follow-up period (months)</td>
<td>32.1 ± 13.0</td>
<td>28.6 ± 11.3</td>
<td>0.165</td>
</tr>
<tr>
<td>Past H. pylori eradication</td>
<td>6 (10.3%)</td>
<td>10 (25.0%)</td>
<td>0.054</td>
</tr>
<tr>
<td>Initial serum pepsinogen I (ng/ml)</td>
<td>61.2 ± 32.0</td>
<td>48.5 ± 15.6</td>
<td>0.023</td>
</tr>
<tr>
<td>Initial serum pepsinogen II (ng/ml)</td>
<td>12.3 ± 8.8</td>
<td>9.3 ± 5.5</td>
<td>0.036</td>
</tr>
<tr>
<td>Initial serum pepsinogen I/II ratio</td>
<td>5.5 ± 1.5</td>
<td>5.5 ± 1.4</td>
<td>0.985</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>24.6 ± 3.4</td>
<td>23.8 ± 2.6</td>
<td>0.231</td>
</tr>
<tr>
<td>Cigarette smoking</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current smoker Past smoker Non-smoker</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alcohol drinking (Heavy drinkers* Social drinker Non-drinker</td>
<td>1.0 (1.2%)</td>
<td>16 (27.6%)</td>
<td>4 (41.4%)</td>
</tr>
<tr>
<td>Upper gastrointestinal symptom</td>
<td>18 (31.0%)</td>
<td>10 (25.0%)</td>
<td>0.516</td>
</tr>
<tr>
<td>Recent intake of drugs</td>
<td>14 (24.1%)</td>
<td>8 (20.0%)</td>
<td>0.629</td>
</tr>
<tr>
<td>Comorbidity Hypertension Diabetes mellitus Others</td>
<td>17 (29.3%)</td>
<td>13 (32.5%)</td>
<td>0.736 0.816 0.979</td>
</tr>
</tbody>
</table>

Statistically significant values are highlighted in bold. Continuous variables are shown as mean value ± standard deviation using the Student’s t-test. Categorical variables are shown in frequency (%) using the Chi-square test or Fisher’s exact test. *Critical for heavy drinking was ≥15 drinks/week for men and ≥8 drinks/week for women. Social drinker was defined as those who drink alcohol, but less than heavy drinkers.
P1906 CAN THE UREA BREATHE TEST PREDICT HELICOBACTER PYLORI ERADICATION?

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Introduction: The Urea Breath Test (UBT) is considered the gold standard non-invasive test for detection of Helicobacter pylori infection in Ireland. In Ireland, eradication rates for standard clarithromycin-based triple therapy have fallen below the 80% deemed acceptable for a given treatment. With this in mind, it is important to optimise management of H. pylori infection. It has been suggested that the DOB value is reflective of the amount of bacteria present in the stomach and could predict whether the infection is eradicated.

Aims & Methods: The aim of this study was to determine whether there is an association between DOB and eradication of H. pylori infection in an Irish cohort. Treatment naïve adult patients undergoing UBT were included. Patients were deemed to be H. pylori positive if a Delta Over Baseline (DOB) value of > 10% was obtained. Positive patients were categorised into low (< 16%), intermediate (16-35%) and high (> 35%) DOB groups. A random subset of positive patients was given clarithromycin-based triple therapy for 7 days. A follow-up breath test was performed at 8 weeks post-treatment to confirm eradication of H. pylori in all patients. The three DOB groups were compared with respect to age, gender and eradication rates.

Results: Out of 860 of UBT’s assessed (mean age 43.3 ± 15.2 years, 39% male), 289 (33.6%) were positive (mean age 43.1 ± 14.9 years, 41.9% male). Of the total positive patients, 91 (31.5%) returned for a follow-up UBT to confirm eradication of H. pylori. When patients were categorised into low, intermediate and high UBT groups, there was no significant difference in age and gender between the groups (p = 0.06 for age, p = 0.3 for gender). Eradication rates in the low, intermediate and high UBT groups were 70.5%, 63.0% and 50.0% respectively (p = 0.3). Patients were then categorised according to eradication status. When eradication was successful, the average DOB value was significantly lower than the DOB value compared to unsuccessful (p = 0.03, 95% CI 0.69 to 17.5). 46 (50.5%) patients were patients categorised for triple therapy for 7 days. When this subset of positive patients was categorised into low, intermediate and high UBT groups, eradication rates were 76.2%, 75% and 70% respectively. When these rates were compared to respective rates in those whose treatment was not known, no difference was observed. The subset was also categorised according to eradication status. When eradication was successful, the average DOB value was lower, at 22.0 ± 30.2% compared to 29.8% when eradication was unsuccessful (p = 0.03, 95% CI 0.69 to 17.5). Similarly, when these DOB values were compared to respective values in whose treatment was not known, no difference was observed.

Conclusion: As the DOB value increases in the UBT, the eradication rate of H. pylori decreases, regardless of treatment regimen. When categorised according to eradication status, the DOB value was significantly lower when eradication was successful (20.6% vs 29.8%, p = 0.03). The DOB value could be a useful value in stratifying patients with H. pylori infection; especially as histology and antimicrobial resistance information is unavailable in patients undergoing non-invasive testing for H. pylori infection.

Disclose of Interest: All authors have declared no conflicts of interest.

P1908 COMPARISON OF THE EFFICACY BETWEEN BISMUTH AND ALTERNATING RIFAXIMIN ON SECOND-LINE QUADRUPEL THERAPY REGIMEN OF HELICOBACTER PYLORI ERADICATION

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Introduction: Bismuth is a heavy metal which has antimicrobial activity through its inhibition of bacterial metabolism. Rifaximin has been confirmed as 92.7% (789/851, PPS) as the strongest HP eradication therapy in Japan. The aim of this study was to determine whether there is an association between DOB and eradication of H. pylori infection in an Irish cohort. Treatment naïve adult patients undergoing UBT were included. Patients were deemed to be H. pylori positive if a Delta Over Baseline (DOB) value of > 10% was obtained. Positive patients were categorised into low (< 16%), intermediate (16-35%) and high (> 35%) DOB groups. A random subset of positive patients was given clarithromycin-based triple therapy for 7 days. A follow-up breath test was performed at 8 weeks post-treatment to confirm eradication of H. pylori in all patients. The three DOB groups were compared with respect to age, gender and eradication rates.

Results: Out of 860 of UBT’s assessed (mean age 43.3 ± 15.2 years, 39% male), 289 (33.6%) were positive (mean age 43.1 ± 14.9 years, 41.9% male). Of the total positive patients, 91 (31.5%) returned for a follow-up UBT to confirm eradication of H. pylori. When patients were categorised into low, intermediate and high UBT groups, there was no significant difference in age and gender between the groups (p = 0.06 for age, p = 0.3 for gender). Eradication rates in the low, intermediate and high UBT groups were 70.5%, 63.0% and 50.0% respectively (p = 0.3). Patients were then categorised according to eradication status. When eradication was successful, the average DOB value was significantly lower than the DOB value compared to unsuccessful (p = 0.03, 95% CI 0.69 to 17.5). 46 (50.5%) patients were patients categorised for triple therapy for 7 days. When this subset of positive patients was categorised into low, intermediate and high UBT groups, eradication rates were 76.2%, 75% and 70% respectively. When these rates were compared to respective rates in those whose treatment was not known, no difference was observed. The subset was also categorised according to eradication status. When eradication was successful, the average DOB value was lower, at 22.0 ± 30.2% compared to 29.8% when eradication was unsuccessful (p = 0.03, 95% CI 0.69 to 17.5). Similarly, when these DOB values were compared to respective values in whose treatment was not known, no difference was observed.

Conclusion: As the DOB value increases in the UBT, the eradication rate of H. pylori decreases, regardless of treatment regimen. When categorised according to eradication status, the DOB value was significantly lower when eradication was successful (20.6 % vs 29.8%, p = 0.03). The DOB value could be a useful value in stratifying patients with H. pylori infection; especially as histology and antimicrobial resistance information is unavailable in patients undergoing non-invasive testing for H. pylori infection.

Disclose of Interest: All authors have declared no conflicts of interest.

P1909 COMPARISON OF 10-DAY STANDARD TRIPLE THERAPY AND LEVOFLOXACIN BASED THERAPY FOR HELICOBACTER PYLORI ERADICATION: RANDOMIZED CONTROLLED TRIAL

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Introduction: Standard triple therapy (STT) has been widely used in Helicobacter pylori infection, but eradication rate is decreasing because of clarithromycin resistance. Recently, Levofloxacin-based therapy (LBT) has been evaluated to overcome the low eradication rate of standard triple therapy and reported eradication rate over 80%.

Aims & Methods: We compared the efficacy and safety of STT group and LBT group for Koreans. Between April 2014 and April 2016, 49 patients in the STT group (amoxicillin 1g bid, clarithromycin 500mg bid and esomeprazole 20mg bid for 10 days) and 48 in the LBT group(levofloxacin 500mg bid, amoxicillin 1g bid, PPI Rabeprazole (RPZ) b.i.d. for 7 days. The judgement of success or failure on eradication was done with UBT breath test on 3 months later after eradication therapy to avoid false negative results.

Results: Success rate of VAC 800 showed significantly high (416/428 = 97.2%, PPS) than VAC 400 (373/423 = 88.2%, PPS) (p < 0.001). The average eradication rate of VAC regimens was 92.7% (789/851, PPS). On the other hand, success rate of RAC 800 showed high (190/245 = 77.6%, PPS) rather than RAC 400 (140/198 = 70.7%, PPS) (p = 0.125). The average success rate of RAC regimens was 74.5% (330/443, PPS). The average success rate of VAC regimens was significantly higher than the average success rate of RAC regimens (330/443 = 74.5%) (p < 0.001). These results suggest that using high dose CAM with VPZ (P-CAB) plus AMX regimen might be the strongest H. pylori eradication triple therapy regimen to overcome CAM resistance.

Conclusion: High-dose CAM with Vonoprazan (P-CAB) plus AMX triple therapy regimen is the strongest H. pylori eradication therapy even if CAM resistance. We will be able to expect significantly high success rate (more than 97%) on HP 1st eradication therapy.
TREATING HELICOBACTER PYLORI INFECTION
WILL TAILORING THERAPY FIRST TIME EVERCOME INCREASING FAILURE OF STANDARD TRIPLE THERAPY?

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Introduction: In Ireland, Helicobacter pylori infection has become increasingly resistant to commonly used antibiotics, such as clarithromycin. Concurrently, eradication rates for standard clarithromycin-based triple therapy have fallen below the 80% deemed acceptable for a given treatment. Aims & Methods: To compare eradication rates of standard clarithromycin-based triple therapy with that of tailored therapy based on antimicrobial susceptibility as a first-line treatment for H. pylori infection. Treatment-naïve adult patients undergoing endoscopy were prospectively recruited. Biopsies from H. pylori-positive patients (assessed by CLO test) were processed for sensitivity testing by E-testing and genotyping by the GenoType HelicoDR assay (Hain). Results: To date 889 patients have undergone endoscopy and 186 (21%) were H. pylori positive. Infected patients were significantly younger (mean age 53 vs 49 years, p = 0.002) and tended to be male (43% vs 55%, p = 0.02). Of 186 H. pylori-positive patients, 112 (60%) were treatment naïve. Culture of H. pylori was successful in 75% (64/112) of samples and primary clarithromycin resistance was 47% (30/64) by E-test. Genotypic resistance data was available for 93% (92/99) of samples. The eradication efficacy of tailored therapy by intention-to-treat analysis was higher at 74% (40/54) compared to 67% (n = 30.45) for standard therapy (p = 0.5). The eradication efficacy for per-protocol analysis was also higher, at 82% (40/49) for tailored versus 70% (30/43) for standard therapy (p = 0.2). Patients in each arm were further categorised by clarithromycin resistance status, phenotypically by E-test and genotypically by the GenoType HelicoDR assay. Of note, in clarithromycin resistant patients, tailored therapy achieved a better eradication rate per protocol analysis than standard triple therapy (83% vs 57% per protocol, p = 0.09).

Conclusion: In those who are sensitive to clarithromycin, standard clarithromycin-based triple therapy achieves an acceptable eradication rate of approximately 81%. However, a high primary clarithromycin resistance rate of 24% was observed in this study (47%). In those who are resistant to clarithromycin, prescribing a regimen based antibiotic susceptibilities increases eradication rates to 83%, compared to those treated with standard triple therapy (57%, p = 0.09).

Disclosure of Interest: All authors have declared no conflicts of interest.
A. Benkirane1

the PPI side effect was 14.7% in the PPI group, 10.0% in the VPZ group and 19.1% in the MBM group, and there was no significant difference between 3 groups. Conclusions: This study shows that Concomitant therapy led to statistically significant higher eradication rates over sequential therapy. Both therapies showed excellent compliance and an acceptable safety profile. The use of quadruple therapy in this setting is not recommended; however, a combination scheme should be the adopted for first-line H. pylori eradication in Morocco.

Disclosure of Interest: All authors have declared no conflicts of interest.

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Disclosure of Interest: All authors have declared no conflicts of interest.

P1916 PROSPECTIVE COMPARATIVE STUDY OF TWO FIRST-LINE REGIMENS FOR HELICOBACTER PYLORI ERADICATION: 14-DAYS NON-BISMUTH QUADRUPLICATE OPTIMIZED CONCOMITANT THERAPY VERSUS 10-DAYS BISMUTH-CONTAINING QUADRUPLICATE THERAPY USING A TWO-ARM DESIGN


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Introduction: The Maastricht V/Florence Consensus Report recommends bismuth quadruple or non-bismuth concomitant therapies as first-line treatments for H. pylori infection, in areas where clarithromycin resistance is high (>15%). Head-to-head studies between both therapies are needed.

Aims & Methods: We aimed to compare compliance, efficacy and adverse effects of two first-line H. pylori eradication therapies in a high clarithromycin resistance
area, and in clinical practice. A prospective study was performed in a Spanish center recruiting consecutive naive adult patients, candidates to H. pylori eradication. Omeprazole 40mg, Clarithromycin 500mg, Amoxicillin 1g and Metronidazole 500mg, all drugs b.i.d, for 14 days (OCAM); or Omeprazole 20mg b.i.d and 3-in-1 capsule with Bismuth 140mg + Tetracycline 125mg + Metronidazole 125mg, 3 capsules q.i.d, for 10 days (3–1-OBMT) were prescribed according to physician criteria. Compliance was assessed by striking the consumed doses in a patient filled template, and adverse effects using a specific questionnaire with a 1–3 intensity scale. Efficacy was determined by 13C-urea breath test. A descriptive study and analysis of efficacy by intention to treat (ITT) were performed. Cases with poor therapeutic compliance (<80%) or no available data were excluded in per-protocol (PP) analysis. Chi2, Student’s t, and Mann-Whitney U tests with significance level p < 0.05 were applied. The primary endpoint was approved by the Ethics Committee.

**Results:** 216 patients (63.43% women; mean age 51.33 year 18–94 years-) were included. OCAM were prescribed in 103 and 3–1-OBMT in 113. No differences in sex, age and functional dyspepsia as indication to eradicate were observed between groups. Main indications for treatment were functional dyspepsia (39.35%), gastroduodenal ulcer (19.44%) and non-investigated dyspepsia (13.89%). Compliance was <80% in 11 patients and unknown in 7. The efficacy outcome was unavailable in 9 subjects. Compliance >80% was obtained in 91% with OCAM and in 93.53% with 3–1-OBMT (p = 0.064). The ITT rates were 82.52% vs 85.84% (p = 0.63), and PP 89.47% vs 96.04% (p = 0.13), for OCAM and 3–1-OBMT respectively. The outcomes of adverse effects (frequency, number, duration and intensity) are shown in the Table.

**Conclusion:** H. pylori infection management at primary care level is inappropriate with 30% on PCP compared to GS group (57.1% vs 81.1%; p < 0.0001) and eradication rates (78% vs 57.1%; p < 0.0001). The introduction of a specific counselling to PCP has significantly improved these outcomes. These data should encourage the implementation of interventional strategies in order to reduce the actual increase in antibiotic resistance.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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**Reference**


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**Conclusion:** Hp infection management at primary care level is inappropriate with 30% on PCP compared to GS group (57.1% vs 81.1%; p < 0.0001) and eradication rates (78% vs 57.1%; p < 0.0001). The introduction of a specific counselling to PCP has significantly improved these outcomes. These data should encourage the implementation of interventional strategies in order to reduce the actual increase in antibiotic resistance.

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**Disclosure of Interest:** All authors have declared no conflicts of interest.

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**Reference**

**P1919 PREVALENCE OF CELIAC DISEASE AMONG RELATIVES OF CD PATIENTS IN ALGERIA**

**Introduction:** Celiac disease (CD) is an important health problem worldwide. It is characterized by a high prevalence (1%), non-specific morbidity, long-term complications and epidemiological progression. However, mass screening is not recommended. Currently, the strategy of 'Targeted screening,' defined as screening of high-risk groups, is widely practiced and recommended by learned Societies, in first-degree relatives of CD patients. In the world, targeted screening studies related to CD showed prevalence ranging from 4.2 to 42.5%. 

**Aims & Methods:** The main aim of our study is to determine the prevalence of CD in the first degree relatives in Algerian population. This was a descriptive-transversal study with prospective recruiting. This is a screening of first-degree relatives of patients known and treated for CD. Relatives are screened by using antitransglutaminase (tTG) antibodies in the serum. Upper digestive endoscopy and duodenal biopsy are performed in all sero-positive relatives and graded as per Marsh modified by Oberhuber classification to confirm the diagnosis. 546 first degree relatives of 107 families are included in our study.

**Results:** Among the 546 first-degree relatives, we have 18.5% of parents, 57.5% of siblings and 24% of children (8% sons and 16% daughters). The main parameter for the prevalence of CD among first-degree relatives is 8.1% with Confident Interval (CI) at 95% [5.8–10.4]. The prevalence of CD in first-degree relatives with positive serology and positive duodenal biopsy is 7.3% with CI at 95% [5.2–9.4]. The average age of screening cases is 31.8 years with CI at 95% [27.2 to 36.4] and extremes of [3–71] years. The mean duration of symptoms before diagnosis is 3.4 years, with CI at 95% [2.8 to 4.0] years. Among the 44 new cases detected by targeted screening, few cases [5 cases, 1.5 cases, Marsh IIIa, 27 cases Marsh IIIb and 3 cases Marsh IIIc. 44 patients are screened with CD: they are divided as follows: 9% Parents (4 mothers), 11% of children (son 3 and 5 girls) and 72% of siblings (brothers and sisters 23). The average age of screening cases is 31.8 years with CI at 95% [27.2 to 36.4]. The prevalence of CD in first-degree relatives is 8.1% with CI at 95% [5.8–10.4]. Our investigation supports the idea that the development of an extensive screening approach is needed to promote early diagnosis and prevent complications of CD in first-degree relatives. 

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**Conclusion:** The present work entitled “Prevalence of celiac disease in relatives” is the first screening study of CD in the first-degree relatives carried out in Algeria. Among the 546 first-degree relatives, it is shown that 44 patients present positive serology which corresponds to the prevalence of CD in first degree relatives of 8.1% with CI at 95% [5.8–10.4]. Our investigation supports the idea that the development of an extensive screening approach is needed to promote early diagnosis and prevent complications of CD in first-degree relatives.

**Reference**

NICE Quality Standards (QS134) for Coeliac Disease (October 2016) NICE guidelines NG20 (September 2015)
0.05

P1924 CIRCULATING EXTRACELLULAR VESICLES, A NOVEL MECHANISM OF ENDOCRINE CELLULAR CROSS-TALK, ARE INCREASED IN NEWLY DIAGNOSED CELIAC DISEASE PATIENTS


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Introduction: Extracellular vesicles (EVs) have been recently hypothesized to represent a major peripheral mechanism of cellular cross-talk. EVs carry surface receptors and proteins characteristic of their cells of origin and shuttle molecules (proteins, RNAs, microRNAs) potentially controlling physiological and pathological systemic processes. Recent studies have demonstrated an increased number of circulating EVs in a variety of conditions characterized by multi-organ impairment and/or damage such as insulin-resistance, atherosclerosis and obesity. Celiac disease (CD) is an immune-mediated inflammatory enteropathy, culprit by gluten ingestion in genetically susceptible individuals. It is frequently associated with a variety of systemic conditions both autoimmune and potentially immune-mediated in nature.

Aims & Methods: The aim of this study was to assess and characterize patterns of circulating EVs in newly diagnosed CD patients. We enrolled consecutive adult anti-ITG positive, biopsy proven CD patients. Circulating EVs were identified and quantified on whole blood samples by a no-lyse/no-wash method, combined with EVs volumetric count (FACSVerse, BD), based on a novel six-colour flow cytometry panel, in order to identify and enumerate both the whole EV compartment and different EV subpopulations. Data are expressed as mean ± SD and statistical differences were evaluated by means of T-test.

Results: We evaluated 12 CD patients (mean age 42.9 ± 19.1 vs. 40.8 ± 15.9 years, F:M = 4:1) at diagnosis and 12 age- and sex-matched healthy controls. Histology was considered positive for lesions of grade ≥B1 according to the Corazzi-Villanacci classification. Mean anti-ITG levels at diagnosis were 6.9 ± 3.1 times U/L. Mean number of total circulating EVs was significantly higher in CD than in controls (5985 ± 72482 vs 14383 ± 10018 EV/microL, p = 0.035). Subgroup analysis showed that EpCAM + EVs, of epithelial origin, and CD41 + platelet-derived EVs were not significantly different between CD and controls (894 ± 1004 vs. 548 ± 1237 and 3052 ± 1563 vs. 1734 ± 1810 respectively, p > 0.05). On the contrary, CD45 + EVs, of leucocyte origin, showed a significantly higher number in CD patients vs. controls (460 ± 492 vs. 119 ± 50 p = 0.026).

Abstract No: P1923

Data on levels of ROS and oxidative damage biomarkers in sera of naïve patients (N-CD), coeliac patients on a gluten-free diet (GFD) including responders (CD-GFD) or non-responders (NRCD) to treatment.
P1925 COELIAC DISEASE AND REPRODUCTIVE DISORDERS: IS THERE ANY CORRELATION

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Introduction: The coeliac disease is an autoimmune enteropathy induced by the intake of gluten-containing foods (Corn, barley, rye), that occurs in people who are genetically predisposed primarily affecting the small intestine inducing atrophic lesions, which are regressive with a gluten-free diet. The classic form is actually a minority of patients. The extradigestive forms are currently the most found, with varied manifestations including reproductive disorders. The aim of our study is to evaluate the frequency of these disorders in the coeliac disease and their evolution under gluten-free diet.

Aims & Methods: It's a single-center, retrospective and descriptive study including 241 patients with coeliac disease enrolled within period of 17 years from 1995 to 2016 in the department of Gastroenterology « Medecine C » in Ibn Sina University Hospital.

Results: About 241 patients suffering from coeliac disease, 58 patients presented reproductive disorders, either 28.9%. Recruiting 53 women and 5 men, with a sex ratio M/F of 10.6:1. The mean age was 32.25 years ranging from 13 to 59 years old. The diagnosis of coeliac disease was based on: Histology (severe or partial Villous atrophy with intraepithelial lymphocytosis exceeding 30%), the antientomysial antibodies and/or antitransglutaminase antibodies positive. The reproductive disorders were never isolated but always associated with digestive or extradigestive signs at the time of the diagnosis of coeliac disease. These disorders were in our study: Amenorrhea in 11 cases (19%), secondary amenorrhea in 13 cases (22.4%), Metrorrhagia in 12 cases (20.6%), absence of development of secondary sexual characters in 8 cases (12.5%), spontaneous abortion in 7 cases (10.9%), menometrorrhagia in 4 cases (13.8%), primary sterility in 5 cases (8.6%), precocious menopause in 6 cases (10.3%), premature labour and/or IUGR in 3 cases (5%), primary amenorrhea in 2 cases (3.4%), and intrauterine Fetal death IUFD in one case (1.7%). All our patients benefited from a gluten-free diet. 15 patients were excluded from the study, 2 patients died, and 12 patients were lost to follow-up. Of the remaining patients stayed, the evolution of the reproductive disorders under gluten-free diet was good in 26 cases (90%), with normalization of the cycles in 15 cases. The cycle was returned in 6 cases, development of secondary sexual characters in 2 cases, fertility was returned in one case. A patient developed her cycle after primary amenorrhea, and one case was delivered a baby in term after a repeated premature deliveries. The evolution was good in 3 cases as regard missed abortion four years after the gluten-free diet in 1 patient, and amenorrhea continued in 2 cases.

Conclusion: Reproductive disorders related to the coeliac disease were frequent and variable. In our study, these disorders well responded to the gluten-free diet in 90% of cases, and these disorders were reversible under gluten-free diet.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1926 SEVERITY OF MUCOSAL DAMAGE AND TISSUE TRANSGLUTAMINASE ANTIBODY LEVELS CORRELATE WELL IN ADULT CELIAC DISEASE IRRESPECTIVE OF CLINICAL FEATURES

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Introduction: Celiac disease (CD) is a chronic imune-mediated enteropathy that occurs in genetically predisposed individuals. The clinical phenotypes ranges from classical gastrointestinal manifestations to only atypical signs, thus making the clinical diagnosis a challenge. The aim of our study was to investigate the relationship between duodenal histology, specific antibody levels and clinical presentation in adult CD Romanian patients.

Aims & Methods: The study group included 81 adult patients with a female: male ratio of 3:1. Hemoglobin levels were evaluated and anemia was diagnosed in 61.7% patients with anemia and Marsh 3b lesions (P = 0.001) and IgA anti-gladiol antibodies (IgA-AGA) levels (61.83 ± 69.41 u/mL vs 77.15 ± 71.02 u/mL, P = 0.001) correlated with intestinal villous atrophy (Marsh 3b and 3c) in CD patients by Spearman rank correlation. Among symptoms, abdominal distention and diarrhea were associated with abnormal histology. Hemoglobin levels were evaluated and anemia was diagnosed in 61.7% patients with anemia with patients with elevated IgA-AGA levels (r = 0.516, P = 0.004), IgA-AGA (r = -0.301, P = 0.006) and Marsh 3b-c lesions (P = 0.004). Among biological markers included in the statistical analysis, low iron levels (cut off 30 mg/dl), hypocholesterolemia and low protein levels were associated with Marsh 3b lesions (P = 0.008) and elevated IgA-AGA titers (r = -0.384, P = 0.001). Coeliac disease (CD) IgA-AGA and AGA levels correlate with duodenal villous atrophy in adult CD patients. An IgA-AGA titer >160 was nearly always associated with severe CD histopathology. GI and non-GI symptoms are not reliable predictors of CD.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1927 ASSOCIATION OF CELIAC DISEASE AND PATENT FORAMEN OVALE

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Introduction: Celiac disease is an immunologically-mediated enteropathy that triggered by the intake of gluten-containing foods in genetically predisposed individuals. It causes intestinal and extraintestinal manifestations. Extraintestinal findings are observed in many systems. The prevalence of extraintestinal findings in CD patients is controversial. Reports have shown that extraintestinal manifestations are more common in pediatric patients [1]. There is also no data in the literature regarding the association of patent foramen ovale (PFO) and celiac disease, which is 10–25% common in the general population. We performed an echocardiography study to determine the frequency of accompanying cardiac findings in our patients with celiac disease. In this article, we aimed to share the frequency of the PFO detected in celiac patients with high results.

Aims & Methods: Between May-June 2015, 65 patients who applied to the gastroenterology clinic of Derince Education and Research Hospital and followed up with celiac disease were identified. The sociodemographic characteristics, celiac disease diagnosis duration, symptoms and complaints, accompanying diseases, drug use histories, hemogram and biochemical parameters of these patients were recorded. The patients underwent saline contrast transthoracic echocardiography in the cardiology clinic. Patients' data were recorded. The obtained data were evaluated with appropriate statistical methods.

Results: Sixty-five celiac patients were included in the study. 21 (32.3%) male and 44 (67.7%) female. The mean age of our patients was 41.3 ± 14.1 years. PFO was detected in 39 (60%) of the patients. There was no difference in the incidence of PFO in between male and female patients. (61.9% and 59.1%, respectively, p=0.829). Compared with the frequency of PFO in the general population, the incidence of PFO in celiac patients was higher (25% and 60% respectively).

Conclusion: As a result, the incidence of PFO is more prevalent in celiac patients than in the general population. For this reason, the evaluation and treatment of this cardiac atrial septal defect in clinical follow-up of patients, are required. In addition, the high incidence of PFO in celiac patients suggests that celiac disease is a factor affecting the development of patients from intratuber period. Because our patients did not undergo transesophageal echocardiography, this rate may be less than real exist. For this reason, further evaluation is required with a wider patient group and by transesophageal echocardiography.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1928 USEFULNESS OF BULB BIOSPY SAMPLES IN CELIAC DISEASE DIAGNOSIS IN ADULTS

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Introduction: Currently available celiac disease (CD) guidelines recommend sampling of both the bulb and distal duodenum for diagnostics. This has been reinforced by the recent data on ultra-short CD [1]. However, it has been previously shown in pediatric CD that bulb specimens are frequently of poor quality [2-4]. The aim of this study was to assess the usefulness of bulb biopsy samples in the clinical follow-up of celiac patients also, and it can lead to false-positive diagnoses [2]. Our aim was to address the same issue in adult CD, using the same validated morphometric methods [3].

Aims & Methods: We prospectively recruited cases of clinically recommended upper GI endoscopy; all patients also had signs and symptoms of CD and were checked for CD serology (serum tissue transglutaminase 2 antibodies and endomyosal antibodies) and biopsy sampled according with current
recommendations. Paraffin embedded biopsy samples were assessed for villous height (VH) and crypt depth (CD) and VH:CD ratio. The corresponding frozen duodenal samples were assessed for duodenal IgA deposits targeting transglutaminase 2 (TG2-IgA), density of CD3 (cut-off 37 cells/mm epithelium) and γδ T cell receptor bearing intraepithelial lymphocytes (IELs) (cut-off 4.3 cells/mm epithelium). The study was approved by the Local Ethical Committee.

**Results:** Altogether 41 patients, mean age 45.4±14.6 years, 61% female, were recruited. Among these, 21 were finally diagnosed as adult CD (mean TG 156 U/l, CD:50% and crypt hyperplastic mucosal lesion in distal duodenum) and the rest 20 were non-CD controls (serum negative and normal on distal duodenal biopsy). All patients were on a gluten-containing diet. Quality of bulk biopsy samples was unsatisfactory and unreadable in 67% of CD cases and 50% of controls, even after reorientations and reittings. All CD patients had, when measurable, VH:CD < 2 in the anatomical abundant (value 0.31, range 0.02-0.61). On the other hand also non-CD controls had a crypt hyperplastic diseased bulk mucosa in 80% of patients (average VH:CD 1.63, range 0.7–4.1), but the injury was not that severe compared to CD (p = 0.0006). The inflation was significantly higher in CD compared to controls (CD3 81.87 vs. 34.05, p < 0.01; γδ IELs 29.12 vs. 6.44, p < 0.01). Bulk IgA deposits were positive in all CD patients and were able to discriminate CD cases from disease controls.

**Conclusion:** As reported in previous, bulk biopsy samples in adults are frequently of poor quality and not reliable for accurate histological measurements. Also, interpretation of results from bulk samples should be done with caution, as non-CD patients may have mild injury in the bulk lining and could be misinterpreted as positive. Assessment of bulk TG2-IgA subepithelial is a powerful tool to confirm CD.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**References**


**Disclosure of Interest:** All authors have declared no conflicts of interest.

**References**

bleeding rate with or without treatment, the rate of anaemia exacerbation (hemoglobin ≤2.0 g/dL), 5 year overall survival rate (OS), and 5 year disease specific survival rate (DSS). Occult OGBD was defined as recurrent or persistent iron deficiency anaemia with or without a positive faecal occult blood test and no bleeding findings by esophagogastroduodenoscopy and colonoscopy. Results: The positive CE findings rate was 44% (157/357) and the detection rate of bleeding source lesions was 27% (95/357). All of the treated recurrent bleeding source lesions (Group A) were as follows: angioectasia 61 patients (Yamano-Yamamoto classification Type 1a 37 patients, Type Ib 24 patients), non-specific ulcer 22 patients, metastatic abdominal/rectal-anti-inflammatory drug-induced ulcer. In patients, hemangiomata 5 patients, Crohn’s disease 3 patients, primary cancer 2 patients, metastatic cancer 2 patients, gastrointestinal stromal tumour 2 patients, malignant lymphoma 2 patients, others 3 patients. Lesions that were not recognized as bleeding source without treatment (Group B) were as follows: angioectasia 25 patients (Type 1a without oozing 25 patients), erythema 31 patients, others 3 patients. There were no patients with overt bleeding in Group B. Although 6 patients (10%) had anaemia exacerbation in Group B, 1 patient (Type 1a) that was not a bleeding source lesion. OS in both Group A and Group B was 90%. DSS in Group A was 99% and in Group B was 100%. One patient in Group A died of a primary small-bowel cancer.

Conclusion: Long-term outcomes with occult OGBD patients were good except malignant tumor, because overt bleeding and/or anaemia exacerbation did not occur within the follow-up period. Thus, occult OGBD patients without bleeding source lesions, including Type 1a angioectasia without oozing, and erythema, are unnecessary to follow-up with CE in occult OGBD patients.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1932 A PILOT STUDY EXPLORING THE VALUE OF FAEAL IMMUNOCHEMICAL TEST (FIT) WHEN INVESTIGATING ANAEMIA OR OCCULT GASTROINTESTINAL BLEEDING WITH SMALL BOWEL CAPSULE ENDOSCOPY

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Introduction: Small bowel capsule endoscopy (SBCE) is a very useful method of investigating iron-deficient anaemia, or occult gastrointestinal (GI) bleeding. It can identify causes of anaemia or bleeding, such as angiodysplasia, small bowel Crohn’s disease, polyps, lymphoma, and malignant lesions. There is however a need to improve the diagnostic yield, particularly where resources and access to capsule endoscopy are restricted. Faecal immunochromestic test (FIT) has an established role, in investigating large bowel bleeding, and is incorporated into a number of bowel cancer screening programmes.

Aims & Methods: The aim of our study was to investigate whether FIT could help predict likelihood of small bowel bleeding or other significant pathology at time of small bowel capsule endoscopy. This was a prospective pilot study, performed at our centre from September 2016-April 2017. Indications for enrolment were patients referred for SBCE with the indication of anaemia or occult GI bleeding. Baseline patient characteristics were obtained including age, gender, history of recent GI disease, transfusion requirements and use of anti-platelet/anti-coagulants. Patient haemoglobin (Hb) level was checked on the day of capsule endoscopy where possible. Patients were asked to return one completed FIT for further analysis. A cut of 50 ng/ml was chosen as this is the standard cut-off used, in the Irish National Bowel Cancer Screening programme.

Results: A total of 40 patients were enrolled, mean age 55.4 years (range 18–77), 64% were female. A total of 27.6% of patients were on anti-platelet agents or anti-coagulants. 34% of patients had a blood transfusion within the last year. Mean Hb for the cohort was 12.8 g/dL (range 7.8–15.9 g/dL). The average FIT reading was 459 ng/ml (range 0–4246 ng/ml). 30% of patients had a FIT level >50 ng/ml. 46% of patients, had positive findings at SBCE. 9/12 (75%) of patients with a FIT level >50 ng/ml had positive findings at capsule endoscopy compared to 5/28 (17.8%) for FIT ≤50 ng/ml, p value = 0.002. 95% C.I. 0.29–0.86 O.R. 0.16. These included 4/12 (33%) new cases of Crohns, 3/12 (25%) angiodysplasia, 3/12 (33%) non-BD enteritis, 1/12 (16.7%) small bowel tuberculosis and 1/12 (16.7%) malena, with no clear source. In addition there was a good correlation between FIT and Haemoglobin levels. 60% of patients with FIT >50 ng/ml were anaemic (Hb <11.5 g/dL), compared to 17% with FIT <50 ng/ml, p value = 0.02 95% C.I. 0.09–0.76 O.R. 0.14. Combining Hb and FIT levels, was also informative and predictive of small bowel pathology. 83% of patients, who were anaemic and had a FIT >50 ng/ml had clinically significant findings at SBCE compared to 21% pick up rate in patients with normal Hb and FIT levels, p value = 0.05 95% C.I. 0.22–1.03 O.R. 0.05. Overall the sensitivity for a FIT >50 ng/ml for detecting small bowel pathology was 83% with a specificity of 92%, giving a positive predictive value of 83.3% (95% C.I. 56.9%-95%). Plateletpleatelet use was not predictive of a positive FIT, as 16.7% of patients with a FIT >50 ng/ml were on anti-platelet agents, compared to 83.3% who weren’t.

Conclusion: FIT is useful at predicting clinically significant small bowel pathology at the time of capsule endoscopy. It may help better identify and prioritise patients who would best benefit from referral.

Disclosure of Interest: All authors have declared no conflicts of interest.
Conclusion: VCE detected small bowel lesions in 71% of our cohort. There is a high prevalence of PHE in patients with decompensated cirrhosis. Vascular lesions are the most common finding in the small bowel of this population.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P1934 MULTICENTER PROSPECTIVE CASE-CROSSOVER STUDY ON THE ASSOCIATION BETWEEN OVERT SMALL-BOWEL BLEEDING AND DRUGS USING CAPSULE ENDOSCOPY

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Introduction: Small-bowel capsule endoscopy (SBCE) have been useful in managing obscure gastrointestinal bleeding. We previously reported that the use of oxicams and diclofenac was associated with an increased risk of nonsteroidal anti-inflammatory drug (NSAID)-induced small-bowel injury (Aliment Pharmacol Ther 2014). However, the etiology and temporal development of drug-associated small-bowel bleeding (SBB) have not been well characterized.

Aims & Methods: The aim of this study is to determine the risk of drugs associated with overt SBB using a case-crossover design. The Japanese Association for Capsule Endoscopy developed a prospectively recorded database of outpatients and inpatients that underwent SBE at 18 medical centers in Japan, and for Capsule Endoscopy developed a prospectively recorded database of outpatients and inpatients who underwent SBCE at 18 medical centers in Japan, and to evaluate long-term outcomes and drug exposure in patients undergoing VCE for OGIB.

Results: Of 1052 patients with OGIB (male/female: 678/374, age of onset: 64±26, 455 with SBB (male/female: 291/164, age of onset: 66±20), 313 patients were on 134 drugs which could be identified 24 weeks before overt SBB were analyzed. ORs (95%CI) of enteric-coated aspirin, clopidogrel, and loxoprofen were identified as risk factors causing overt SBB during a relatively short period after administration.

Conclusion: Enteric-coated aspirin, clopidogrel, and loxoprofen were identified as risk factors causing overt SBB during a relatively short period after administration. Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

P1935 META-ANALYSIS REVEALS SIMILAR REBLEEDING RATES AMONG EASTERN AND WESTERN POPULATIONS UP TO FIVE YEARS AFTER INDEX VIDEO CAPSULE ENDOSCOPY

EXAMINATION FOR OBSCURE GASTROINTESTINAL BLEEDING

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Introduction: Video capsule endoscopy (VCE) is the first-line diagnostic modality for obscure gastrointestinal bleeding (OGIB) investigation and different re-bleeding rates have been published among Western and Eastern studies.

Aims & Methods: Aim of this meta-analysis was to examine the differences in re-bleeding rates in patients with OGIB after index VCE, as measured in Western and Eastern studies. A comprehensive literature search in MEDLINE was conducted to identify all studies examining re-bleeding rate after VCE for OGIB. Meta-analysis assessed the pooled proportion of re-bleeding events after VCE for OGIB according to study’s origin (Western vs. Eastern) as the primary end point. Potential heterogeneity and publication bias were detected using Egger’s test and Begg’s test. Funnel plot asymmetry was analyzed by using the trim-and-fill method. Heterogeneity was measured using the I² statistic and publication bias risk was examined with Funnel plots inspection.

Results: Thirty-eight (14 Eastern and 24 Western) studies were included in the analysis with 5197 patients followed from 6 to 52 months. We detected significant heterogeneity with no evidence for publication bias in the meta-analyzed studies. While the overall, pooled rate of re-bleeding after VCE was 25(21–29)%, I² = 93%, similar re-bleeding rates were detected among Eastern and Western populations [22(16–28)%, I² = 71% vs. 25(21–29)%, I² = 95%]. The re-bleeding rate after positive compared to negative VCE index examination was higher [1.89(1.00–3.34), I² = 72%] in Eastern population studies, while a similar difference was not detected in the Western studies [1.46(0.72–2.94), I² = 88%]. When only studies with short-term follow-up were analyzed, the OR of re-bleeding after positive vs. negative VCE was 1.23(0.81–1.88), I² = 77% and 1.93(0.90–4.13), I² = 71% in Western and Eastern studies, respectively. For studies with long-term follow-up, no significant difference in the OR of re-bleeding after positive vs. negative index VCEs was detected either in the East [2.03(0.86–4.29), I² = 71%] or in the West [7.01(1.37–37), I² = 99%].

Conclusion: Our analysis shows that patients undergoing VCE for OGIB have similar re-bleeding rates in the East and in the West, regardless of the length of the follow-up. An increased re-bleeding risk after positive vs. negative index VCE was noted only in studies originating from the East.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1936 LONG-TERM OUTCOMES AFTER NEGATIVE DOUBLE-BALLOON ENTEROSCOPY FOR SUSPECTED OVERT SMALL BOWEL BLEEDING (OBSCURE-OVERT GASTROINTESTINAL BLEEDING)

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Introduction: There are very few reports about long-term outcomes in patients undergoing negative balloon assisted enteroscopy for suspected overt small bowel bleeding (obscure-overt gastrointestinal bleeding). Aims & Methods: The aim of this study is to evaluate long-term outcomes and risk factors of re-bleeding after negative double balloon enteroscopy (DBE) for suspected overt small bowel bleeding. We investigated 297 patients undergoing DBE for suspected overt small bowel bleeding between December 2004 and April 2016 at Sendai Kosei Hospital. Prospectively collected data were reviewed, and 83 patients (27.9%) showed negative results in the first antegrade and/or retrograde DBE. For these patients, letter and telephone interviews were conducted in April 2017. As a result, a cohort of 64 patients could be followed. The primary outcome measurement is overt rebleeding and necessity for clinical assessment after negative DBE.

Results: The rebleeding was observed in 19 of 64 patients (29.7%) with 76 months follow-up period. The mean period during the first DBE and the first rebleeding episode was 11.6 months (2day–48months). Three patients showed rebleeding after more than three years of the first DBE. At the time of rebleeding, emergent endoscopy including DBE (within less than 48 hours) and/or contrast-enhanced computed tomography (CECT) was performed in all patients. The bleeding source was identified in 17 of 19 patients (89.4%). The bleeding source were duodenum (n = 8), jejunoileum (n = 7) and colon (n = 2), respectively. One
patient died due to uncontrollable duodenal bleeding. Blood transfusion before the first DBE was associated with rebleeding (odds ratio 22.5, p = 0.0005), but total endoscopy rate, use of capsule endoscopy, use of anti-thrombotic agents and use of NSAIDs were not associated with rebleeding.

Conclusion: Rebleeding after negative DBE for suspected overt small bowel bleeding is lethal. Blood transfusion before the first DBE may predict rebleeding. Emergent endoscopy including DBE and concomitant CECT use could help in the diagnosis on re-bleeding.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
3 was superior to CapsoCam SV-1 (27 min. vs. 40 min, p = 0.01). 95% of the physicians were satisfied with each capsule system and evaluation software. The acceptance rate of the patients to retrieve the CapsoCam SV-1 was high. Adverse events/SAEs were 17.9%/1.3% with CapsoCam SV-1 and 16%/0% with PillCam SB 3. Re-bleeding rate was 28.75% within 3 months.

**Conclusion:** Both capsules allow high-quality imaging of the small bowel. CapsoCam SV-1 detected more lesions, however, relevant bleeding sources were visualized by both capsules. Physician’s satisfaction was high with both capsule systems and evaluation software. Patient’s acceptance with CapsoCam SV-1 was unexpectedly high. SAEs were 0% with PillCam SB 3 and 1.3% with CapsoCam SV-1.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**P1940 VALIDATION OF A SCORE CHART TO PREDICT THE RISK OF CHRONIC MESENTERIC ISCHEMIA: A DISTRIMINATIVE AND USEFUL TOOL IN CLINICAL DECISION-MAKING**

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**Introduction:** Chronic mesenteric ischemia (CMI) is the result of insufficient mucosal perfusion of the gastrointestinal tract, mostly caused by atherosclerotic stenosis of the mesenteric arteries. Other causes of CMI are vasculitis, median arcuate ligament syndrome or non-occlusive ischemia (NOI) due to decreased cardiac output or hypo-oxygenation. The diagnosis of CMI remains challenging as chronic abdominal pain is common and mesenteric artery stenoses are frequently observed in the general population but not necessarily related. Harki et al.(1) designed a score chart to predict the risk of CMI based on a cohort of CMI suspected patients. This score chart consists of patient characteristics (female 1 pt, weight loss 1 pt, cardio-vascular disease 1 pt) and radiologic evaluation (50–70% celiac artery (CA) stenosis 1 pt, >70% CA stenosis 4 pts, 50–70% superior mesenteric artery (SMA) stenosis 1 pt and >70% SMA stenosis 3 pts). A total score of 0–2 pts predicts an absolute risk of CMI of 0–21%, 3–6 pts a 22–91%, 7–9 pts a risk of 91–95% and ≥10 pts a risk of >95%. We aimed to validate this prediction model in a prospective large multicenter patient cohort.

**Aims & Methods:** Patients suspected of CMI referred to two Dutch specialized CMI centers were included consecutively from January 2006 to August 2016. After diagnostic work-up of medical history taking, mesenteric CT-angiography or MR-angiography, and a mucosal ischemia test (visible light spectroscopy or tonometry), all patients were discussed in an expert based consensus diagnosis. All patients with a CMI consensus diagnosis were planned for treatment (revascularization or sclerotherapy or medication for NOMI). A definitive diagnosis of CMI was made if successful treatment resulted in durable symptom relief. The score chart to predict the risk of CMI was computed for each patient.

**Results:** A total of 246 patients were included and consensus diagnosis of CMI was made in 108 (44%) patients, which resulted in 96 (39%) patients with a definitive diagnosis of CMI after a positive response therapy. A definitive diagnosis of CMI, leading to an expert based consensus diagnosis. Patients with CMI, 107 (43.3%) patients were included were classified according to the score chart. The definitive ability of the score chart was strong (C-Statistic 0.87).

**Conclusion:** The score chart for CMI based on patient characteristics and anatomy is a reliable tool to discriminate the risk of CMI and useful for clinical decision-making, for example to adopt a wait-and-see policy in patients with a low risk and immediate vascular intervention in patients with high risk of CMI.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**Reference**

**P1941 LONG-TERM SYMPTOM RELIEF AFTER REVASCULARIZATION IN PATIENTS WITH SINGLE ARTERY CHRONIC MESENTERIC ISCHEMIA**

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**Introduction:** Isolated stenosis of the celiac artery (CA) or the superior mesenteric artery (SMA) is frequently detected in patients with abdominal complaints. These patients may suffer from chronic mesenteric ischemia (CMI) causing nonspecific abdominal complaints as postprandial pain, nausea or diarrhea. However, the exact role of single artery mesenteric ischemia is a topic of continuous clinical debate and reports on the effectiveness of single mesenteric artery revascularization are scarce. We evaluated the long-term clinical success rates for single CA or SMA revascularization in patients with gastrointestinal symptoms and confirmed mesocoeal ischemia.

**Aims & Methods:** Data were collected from all 97 consecutive patients with gastrointestinal symptoms and a single mesenteric artery stenosis referred to the outpatient clinic of our tertiary care institution for analysis of CMI between January 2006 and October 2010. All patients underwent a standardized diagnostic work-up for CMI at baseline consisting of medical history taking and physical examination, imaging of the gastrointestinal arteries with either CT- or MR-angiography and/or conventional catheter angiography, and a functional test for detecting mucosal ischemia using either tonometry or visible light spectroscopy. All cases were discussed in a multidisciplinary meeting attended by a vascular surgeon, interventional radiologist and gastroenterologist, all specialized in CMI, leading to an expert based consensus diagnosis. Patients with consensus diagnosis of CMI underwent surgical or endovascular revascularization. The primary outcome was clinical response to revascularization, defined as relief of presenting symptoms as experienced by the patient.

**Results:** Consensus diagnosis of CMI was obtained in 62/97 patients and all consensus patients were revascularized. Isolated CA stenosis was present in 55/ 62 patients (89%) (31 vascular disease; 24 median arcuate ligament syndrome, MALS) and isolated atherosclerotic SMA stenosis in 7 patients. After a mean follow-up of 5.5 ± 3.0 years, 42/62 patients (68%) experienced sustained symptom relief. Responders to revascularization had a BMI increase during follow-up in contrast to the non-responders (+0.43 ± 2.5 versus −1.06 ± 2.4 kg/m², p = 0.033). Response to revascularization was not related to lesion localization (CA 67% versus SMA 71%, p = 0.825) or lesion etiology (MALS 63% versus vascular disease 71%, p = 0.483). See table.

**Conclusion:** The score chart for CMI based on patient characteristics and anatomy is a reliable tool to discriminate the risk of CMI and useful for clinical decision-making, for example to adopt a wait-and-see policy in patients with a low risk and immediate vascular intervention in patients with high risk of CMI.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**Reference**
We aimed to review various digestive manifestations of vasculitis for diagnosis. The other difficulty remains the interference of digestive side and granulomatosis is broad and can affect any segment of the digestive tract.

**Conclusion:** Revascularization of the CA or SMA provides long-term symptom relief in 68% of patients with chronic gastrointestinal symptoms and confirmed mucosal ischemia due to single mesenteric artery stenosis. This provides the opportunity to help patients with otherwise unexplained, refractory abdominal complaints.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**P1942 UNDERUTILIZATION OF ENDOSCOPIC ARGON PLASMA COAGULATION FOR TREATMENT OF BLEEDING GASTROINTESTINAL ANGIODYSPLASIAS: AN INTERNATIONAL MULTICENTRE COHORT STUDY**

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**Introduction:** Endoscopic argon plasma coagulation (APC) is the first-line treatment in patients with iron deficiency anaemia or overt bleeding resulting from gastrointestinal angiodysplasias. In the minority of patients active bleeding angiodysplasias are seen during endoscopy, but in contrast non-bleeding angiodysplasias can be an incidental finding. This can make the decision whether to treat endoscopically detected angiodysplasias with APC difficult.

**Aims & Methods:** The aim of this study is to investigate the need for repeat endoscopies with APC in patients with angiodysplasias who were left untreated during the index endoscopy. We initiated an international, multicentre cohort study to collect clinical, laboratory and endoscopic data from angiodysplasia patients. Cases were identified through a systematic search in endoscopy reports from 2010–2015 with follow-up until July 2016. Inclusion criteria was endoscopic detection of angiodysplasia in the context of overt bleeding or iron deficiency anaemia. Exclusion criteria were other vascular anomalies and angiodysplasias as incidental finding.

The primary outcome was repeat endoscopy with APC.

**Results:** A total of 197 patients with proven angiodysplasia as cause for anaemia or bleeding were included (mean age 68 years, 58% male). Median follow-up was 37 months (range 18–57). In 52% of the cases (n = 103) APC treatment for bleeding angiodysplasia(s) was performed at the index endoscopy. Repeat endoscopy with APC was necessary in 17 patients (18%) in whom angiodysplasias were detected but left untreated during the index endoscopy. Median time between index and repeat endoscopy was 21 weeks. A total of 48 patients (51%) who received a purely diagnostic index endoscopy were in need of other treatment modalities (e.g. iron supplementation, blood transfusion, stop anti-coagulants). Anaemia and/or overt bleeding resolved spontaneously in 24 patients (26%).

**Conclusion:** A substantial proportion of patients with clinical symptomatic angiodysplasia bleeding do not receive APC at the index endoscopy and continue to be dependent on iron supplementation, blood transfusion or undergo repeat endoscopy with APC.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**P1943 DIGESTIVE INVOLVEMENT IN SYSTEMIC DISEASES: A UNIVERSITY HOSPITAL EXPERIENCE**

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**Introduction:** Digestive manifestations in systemic diseases including vasculitis and granulomatosis is broad and can affect any segment of the digestive tract and related organs. The clinical symptoms are not specific and it can be challenging for diagnosis. The other difficulty remains the interfereance of digestive side effects of medication used

**Aims & Methods:** We aimed to review various digestive manifestations of systemic diseases. This was a retrospective study from Feb 2009 to Sep 2016 in internal medicine and gastroenterology departments. The exclusion criteria was incomplete data considering the diagnosis of the systemic disease.

**Results:** We included 39 patients. Thirty-two were females (82.1%) and the mean age was 43.6 ± 11.3 years. The mean BMI before surgery was 21.6 ± 4.5 kg/m2. There was a significant decrease in BMI after surgery and, on average, the mean total body weight loss was 34% and the mean excess BMI loss was 90%. Before
bariatric surgery, 52.3% of patients had VDD and 36.8% had VDI. After surgery, the number of VDD increased to 71.1% (p = 0.0079). The mean levels of 25(OH)D decreased significantly from 19.8 ng/mL before surgery to 16.6 ng/mL after surgery (p < 0.05). There was no correlation between the amount of weight loss and the changes in the levels of 25(OH)D in our study.

**Conclusion:** There is a high prevalence of vitamin D deficiency in obese patients eligible for bariatric surgery. The level of deficiency tends to increase after RYGB. This population of patients should, therefore, be offered an adequate level of vitamin D supplementation, especially after the procedure.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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**Disclosure of Interest:** M. Galvao Neto: I declare that I have received personal fees from FRACYTL LABS, GI WINDOWS, APOLO ENDO SURGERY, GI DYNAMICS, ETHICON ENDO SURGERY, not related to the present study.

All other authors have declared no conflicts of interest.

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**Disclosure of Interest:** M. Galvao Neto: I declare that I have received personal fees from FRACYTL LABS, GI WINDOWS, APOLO ENDO SURGERY, GI DYNAMICS, ETHICON ENDO SURGERY, not related to the present study. All other authors have declared no conflicts of interest.
According to A. Scudero Sanches, 71.1% of patients experience nausea and 57.9% most common side effects after IGB implant.

**Introduction:**

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Endoscopic treatment of obesity and overweight with intragastric balloon (IGB), is a safe and effective option. Nausea and vomiting are the most common side effects after IGB implant. According to A. Scudero Sanches, 71.1% of patients experience nausea and 57.9% most common side effects after IGB implant.

**Aims & Methods:**

Evaluation of Frequency of vomiting and number of patients requiring intravenous hydration (HEV) after gastric balloon placement. This was a retrospective analysis of medical records of 340 obese and overweight patients requiring intravenous hydration to quell nausea and vomiting during the first day of the accessory use.

**Results:**

There were 340 patients treated with intragastric balloon between 2015 and 2016. The present study showed 74.41% vomiting until the third day after placement of the IGB, and it is in accordance with literature. Those 252 patients who had vomiting, 67.58% presents frequency of 0 to 5 times per day and 32.42% of the group 5 to 7.48% of the patients required intravenous hydration and there were no early explant.

**Conclusion:**


All other authors have declared no conflicts of interest.

**Disclosure of Interest:** M. Galvao Neto: Apollo endosurgery consultant.
Disclosure of Interest: M. Galvao Neto: I received personal fees from FRACTYL Ltd, Grants/other from GI WINDOWS, personal fees from APOLLO ENDO SURGERY, personal fees from GI DYNAMICS, personal fees from ETHICON ENDO SURGERY, outside the submitted work. All other authors have declared no conflicts of interest.

P1951 FRUCTO-OligoSACCHARIDE EXACERBATES STRESS-INDUCED VISCERAL HYPERALGESIA AND GUT INFLAMMATION IN A MURINE MODEL
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Introduction: Many factors contribute to the development of irritable bowel syndrome (IBS) including the altered visceral perception, intestinal low-grade inflammation and psychosocial factors. Recent research has revealed a relationship between intake of FODMAPS (Fermentable, Oligo, Lacto, and Poly) and abdominal complaints. A diet low in FODMAPs can reduce symptoms in patients with IBS but mechanisms were poorly understood.

Aims & Methods: We aim to explore the role of FODMAPs in triggering IBS symptoms by investigating visceral sensitivity, intestinal inflammation and short chain fatty acid (SCFA) in stress induced IBS mice model. Fructo-oligosaccharide (FOS) as one of the most frequently exposed FODMAPs in daily life was used in this study. Intestinal mucosa of mice were subjected to water avoidance stress (WAS condition; 1 h/day for 10 days) or sham stress (basal condition; 1 h/day for 10 days) with an oral gavage of saline or saline solution containing FOS (8 g/kg) for 2 weeks. Then visceral sensitivity was measured by abdominal withdrawal reflex (AWR) in response to colorectal distension (CRD) and histologic analyses were used to evaluate mucosal inflammation. Immunohistochemistry, reverse transcription, and scanning were used to estimate mucosal mast cell level, levels of cytokines (IL-6, IL-23, TNF-α, IL-10, IL-1β) and SCFA, respectively.

Results: Visceral hypersensitivity and intestinal inflammation aggravated by certain FODMAPs in stress induced IBS mice model. Fructo-oligosaccharide (FOS) administration reduced visceral sensitivity, intestinal inflammation and short chain fatty acid (SCFA) in stress induced IBS mice model. Fructo-oligosaccharide (FOS) administered mice compared with saline-administered mice. In WAS condition, increased visceral sensitivity and mucosal mast cell (12.3 ± 2.61 vs. 8.33 ± 3.55, P < 0.01) were observed in FOS-administered mice compared with saline-administered mice. In WAS condition, cytokine expression were mediated by FOS with increased IL-23 (3.17 ± 2.11-fold, P < 0.05) in ileum and IL-1β (2.45 ± 1.55-fold, P < 0.05) in colon compared with saline. In addition, the average concentrations of acetate (2.48 ± 0.62 vs. 1.04 ± 0.10, P < 0.01), propionate (0.48 ± 0.09 vs. 0.33 ± 0.00, P < 0.01), and butyrate (0.19 ± 0.03 vs. 0.21 ± 0.03, P < 0.05) and total SCFA (3.61 ± 0.89 vs. 1.79 ± 0.17, P < 0.01) significantly increased in FOS-administered mice compared with saline-administered mice in WAS condition. In basal condition, no difference of visceral sensitivity, intestinal inflammation and SCFA were observed between mice treated with FOS or saline.

Conclusion: Oral gavage of FOS leads to both an increase in visceral sensitivity and gut inflammation in stress induced IBS mice. These effects are linked with the production of SCFA in the gut which involved in the regulation of sensitivity and intestinal immune activation. These findings support the hypothesis that visceral hypersensitivity and intestinal inflammation aggravated by certain FODMAPs may be responsible for IBS symptom generation, and indicate an alternative mechanism of the efficacy of the low-FODMAP diet for IBS patients.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P1952 GENOMIC ANALYSIS OF THE MULTISPECIES PROBiotic PRODUCT VSL#3
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Introduction: Several formulations consisting of live lactic acid bacteria, including bifidobacteria, are marketed as probiotic products. However, these products are currently poorly understood in their effect in human beings. Fructooligosaccharides (FOS) are fermentation by probiotic bacteria, generating short chain fatty acids and providing prebiotic potential probiotic functions. Full sets of genes for the production of metabolites and bioactivities were identified in the VSL#3 product specification and showed the 8 strains of this multispecies probiotics. A number of studies have shown the potential probiotic functions. Many factors contribute to the development of irritable bowel syndrome (IBS) including the altered visceral perception, intestinal low-grade inflammation and psychosocial factors. Recent research has revealed a relationship between intake of FODMAPS (Fermentable, Oligo, Lacto, and Poly) and abdominal complaints. A diet low in FODMAPs can reduce symptoms in patients with IBS but mechanisms were poorly understood.

Aims & Methods: We aim to explore the role of FODMAPs in triggering IBS symptoms by investigating visceral sensitivity, intestinal inflammation and short chain fatty acid (SCFA) in stress induced IBS mice model. Fructo-oligosaccharide (FOS) administration reduced visceral sensitivity, intestinal inflammation and short chain fatty acid (SCFA) in stress induced IBS mice model. Fructo-oligosaccharide (FOS) administered mice compared with saline-administered mice. In WAS condition, increased visceral sensitivity and mucosal mast cell (12.3 ± 2.61 vs. 8.33 ± 3.55, P < 0.01) were observed in FOS-administered mice compared with saline-administered mice. In WAS condition, cytokine expression were mediated by FOS with increased IL-23 (3.17 ± 2.11-fold, P < 0.05) in ileum and IL-1β (2.45 ± 1.55-fold, P < 0.05) in colon compared with saline. In addition, the average concentrations of acetate (2.48 ± 0.62 vs. 1.04 ± 0.10, P < 0.01), propionate (0.48 ± 0.09 vs. 0.33 ± 0.00, P < 0.01), and butyrate (0.19 ± 0.03 vs. 0.21 ± 0.03, P < 0.05) and total SCFA (3.61 ± 0.89 vs. 1.79 ± 0.17, P < 0.01) significantly increased in FOS-administered mice compared with saline-administered mice in WAS condition. In basal condition, no difference of visceral sensitivity, intestinal inflammation and SCFA were observed between mice treated with FOS or saline.

Conclusion: Oral gavage of FOS leads to both an increase in visceral sensitivity and gut inflammation in stress induced IBS mice. These effects are linked with the production of SCFA in the gut which involved in the regulation of sensitivity and intestinal immune activation. These findings support the hypothesis that visceral hypersensitivity and intestinal inflammation aggravated by certain FODMAPs may be responsible for IBS symptom generation, and indicate an alternative mechanism of the efficacy of the low-FODMAP diet for IBS patients.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

P1953 RAISING PUBLIC AWARENESS OF GASTROINTESTINAL DISEASES: AN INNOVATIVE STRATEGY FOR A NATIONAL CAMPAIGN
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Introduction: Disease prevention and public awareness are fundamental to reduce morbidity, mortality and health-related costs. Extensive research led to identification of causes of gastrointestinal (GI) diseases, nevertheless it is still difficult to get population involved. The goals of our pilot campaign are: (a) to raise awareness about GI diseases, risk factors, signs, symptoms, in order to convince people to change behavior and to prompt them with concerns to visit doctors as early as possible; (b) facilitate communication between healthcare providers and population; (c) to determine the knowledge of health personnel about the appropriate diagnostic investigations. Any information we can share may also benefit patients and their families, in recognition of the many people who suffer with the pain and discomfort caused by GI disorders.

Aims & Methods: We organized population-based events, out of health facilities during which: (a) giant inflatable anatomical models of GI organs that can be visited inside, were installed; (b) educational panels and brochures were set and exhibited both inside and outside the models; (c) videos illustrating endoscopy exams and histopathology examinations were projected and discussed; (d) clinical cases, also mimicking patient encounter, were simulated.

Results: We started an innovative strategy focused on the keywords: multidisciplinary team, scientific rigor but simple words, people attraction, inducing communication, in Parma and neighbouring Cities. Specialists in Gastroenterology, Anatomic Pathology, Radiology, Surgery, Biochemistry, Nutrition, together with pre- and post-graduate Students, discussed various aspects of the disease, in a friendly and informationally engaging way. Municipal and civil society were also involved to ensure organizational efficiency. The most discussed topics regarded dyspepsia, gastritis, helicobacter pylori infection, gastroesophageal reflux disease, alcohol abuse, cirrhosis, hepatitis, intestinal bowel disease, inflammatory bowel disease, IBS, Crohn disease, food allergy and intolerance, optimal nutrition in health and disease. The event performed in the main square of Parma lasted two full consecutive days and was attended by about 3,000 people, most of which also filled a questionnaire. A total of 120 ultrasound examinations were performed. In neighbouring Cities the events were organized for one day; as a consequence, the number of participants was lower in proportion, but very satisfactory.
Conclusion: The events were educational and enjoyable for all age groups. The interactive approach and the environment out of health-care centres facilitated population to feel comfortable and eager to learn, as well as clinical cases simulation provided a valuable entertaining experience. This strategy of raising public awareness of GI diseases seems promising, we are refining the model for a national campaign.

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P1958 OPTIMAL NUTRITIONAL ROUTE FOLLOWING TOTAL GASTRECTOMY: A SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

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Introduction: Total gastrectomy can profoundly influence patients’ nutritional status and recovery, and controversy surrounds the various nutritional options available post-operatively, namely total parenteral nutrition (TPN), or enteral nutrition (EN) either via the nasojejunal (NJ) or feeding jejunostomy (JEJ). The aim of this review was to determine the optimal nutritional route after total gastrectomy for cancer.

Aims & Methods: PubMed, MEDLINE and the Cochrane Library (January 1985 to January 2017) were systematically searched for randomized controlled trials comparing various nutritional routes after total gastrectomy. The primary outcome measure was overall morbidity. The secondary outcome was time to morbidity.

Results: Six studies involving 353 patients (median age 62 years, 217 males, 170 TPN, 96 NJ, 87 JEJ) who underwent total gastrectomy were analysed. Overall morbidity was significantly greater in patients after TPN compared with EN (OR 1.95, 95% CI 1.16–3.28, p = 0.02). Time to morbidity was measured after 16 hrs. of food and 24 hrs. of water deprivation. Weight of faeces for 16 hrs. and transit time with charcoal were measured. Data was expressed as mean standard deviation, comparison between groups was done with two-way ANOVA.

Results:

- VAD increased body weight significantly (p < 0.05) during feeding period irrespective of fat content of the diet. Fat content and VAD had no effect on 1 hr food intake after food deprivation. HFD decreased water intake (p < 0.05), VAD blunted this effect (p < 0.05). Both HFD and VAD decreased faces weight significantly (p = 0.0001 and p < 0.05 respectively) but there was no change in intestinal transit. HFD impaired short-term memory (p < 0.02), whereas VAD compromised spatial learning (p < 0.04). HFD rats were more anxious in OFT (p < 0.01).

Conclusion: HFD-induced alterations in memory and anxiety were not affected by VAD but VAD blunted effect of HFD on water intake and faces weight, suggesting that their operating mechanisms are different. VAD by itself impaired spatial memory that requires further investigation.

Disclosure of Interest: All authors have declared no conflicts of interest.

P1959 TAUROLIDINE PREVENTS CATHERETER-MEDATED BLOODSTREAM INFECTIONS IN PATIENTS ON HOME PARENTERAL NUTRITION–A RANDOMIZED CONTROLLED TRIAL

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Introduction: Patients on home parenteral nutrition (HPN) are exposed to a lifetime risk of catheter-related bloodstream infections (CRBSI), which threaten catheter and patient survival. Both taurodine 2% and saline 0.9% solution are used as catheter lock solutions (CLS) to prevent CRBSI. The optimal agent however, remains unclear. We hypothesized that taurodine as CLS is superior to saline in preventing CRBSI in HPN patients.

Aims & Methods: We hypothesized that taurodine 2% as CLS is superior to saline 0.9% in preventing CRBSI in HPN patients. This multicenter double blinded trial randomly assigned HPN patients to use either the CLS taurodine 2% or saline 0.9% for one year. Primary outcome was the number of CRBSI/1000 catheter days. Secondary outcomes included time to CRBSI or catheter removal due to CRBSI, number of catheter removals due to CRBSI, exit-site infections, catheter occlusions, and (serious) adverse events.

Results: Of 105 randomized patients enrolled as modified intention-to-treat population. With taurodine, 5 CRBSI occurred during 15318 catheter days. In the saline arm CRBSI occurred over 12493 catheter days. CRBSI/1000 catheter days were 3.33±4.44 in the taurodine and saline groups, respectively. Relative risk, 0.23; 95% CI, 0.07 to 0.63; P = 0.002. The cumulative proportion of CRBSI-free patients after one year was 88% in the taurodine group and 49% in the saline group (P = 0.002). The number of catheter removals due to CRBSI was two (4%) in the taurodine group and eight (16%) in the saline arm (P = 0.049). The cumulative proportion of patients without a catheter removal due to CRBSI was higher in the taurodine group (P = 0.025). Exit-site infection and catheter occlusion rates were similar in both groups. Except for occurrence of CRBSI (P = 0.002), there was no difference in (serious) adverse events between groups. Drug-related adverse events were rare and generally mild to moderate.

Conclusion: Taurodine 2% decreased the risk for CRBSI by more than four times in HPN patients compared to saline 0.9%. Given its favorable safety profile and lack of evidence for altering microbial susceptibility, taurodine lock solution therefore seems a key strategy to prevent CRBSI.

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P1960 REPAIR OF DAMAGED CENTRAL VENOUS CATHETERS SUBSTANTIALLY ALONGS DEVICED SURVIVAL IN PATIENTS ON HOME PARENTERAL NUTRITION

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Introduction: Patients with severe intestinal failure depend on life-long home parenteral nutrition (HPN) support. Repeated central venous catheter (CVC) loss due to complications, including mechanical damage, compromises vascular access. It remains unclear whether repair of damaged CVCs is an effective strategy to extend catheter life, avoid surgical replacement and maintain vascular access.

Aims & Methods: The objective of this study was to characterize patients who underwent catheter repair and to evaluate effects on catheter survival and describe complications. This study concerns a retrospective analysis of all catheter repairs that were performed in HPN patients in the Radboud University Medical Center between January 2000 and May 2017. Primary endpoint was the difference in catheter survival in the presence or absence of catheter repair. To this end, a non-parametric survival analysis was performed. Secondary outcomes included localization of catheter damage and frequency of repair-related complications within 1 month after catheter repair.

Results: A total of 50 repairs in 38 CVCs of 32 HPN patients were included in the analysis. 16 CVCs (32%) were damaged at the distal end, near the screw thread of the catheter, 25 CVCs (50%) at the junction between the rigid and flexible part of the catheter, and 9 CVCs (18%) at the flexible part of the catheter. The mean time to catheter repair after placement was 2.2 years (95% CI = 1.55–2.89). The mean catheter survival after repair was extended by 1.4 years to 3.36 years (95% CI = 2.69–4.46; p = 0.01). No repair-related complications occurred within 1 month after catheter repair.

Conclusion: Repair of damaged CVCs significantly extends catheter life in HPN patients with previous vascular access. Catheter repair is a safe procedure.

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P1961 LONG-TERM CLINICAL OUTCOMES OF PATIENTS ON HOME PARENTERAL NUTRITION USING TAUROLIDINE CATHETER LOCKS

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Introduction: Catheter-related complications (CRCs) in home parenteral nutrition (HPN) patients are a threat to both catheter and patient survival. Taurine 2%, an antimicrobial catheter lock solution (CLS), is an effective agent in the prevention of catheter-related bloodstream infections (CRBSI).

Aims & Methods: The aim of this retrospective study was to evaluate long-term clinical outcomes of our HPN patient cohort that uses the CLS taurolidine. Between 2008 and 2016, all adult HPN patients requiring a central venous catheter (CVC) were included. CRBSI rates/1000 catheter days were described. Kaplan-Meier analysis was used to determine the time until a first CRC. Cox proportional hazard analysis was performed to identify risk factors for a first CRC.

Results: In 221 HPN patients, 658 CVCs (418 Hickmans, 172 PACs, and 28 non-tunneled CVCs) were inserted, comprising 261252 catheter days. Median survival for Hickmans, PACs and non-tunneled catheters was 175 (43–544), 310 (61–827) and 14 (7–19) days, respectively. During years eight follow-up, 176 CRBSI occurred and 50 catheter-related occasions (CRO). CRBSI and CRO rates/1000 catheter days were 0.74 and 0.34, respectively. In 47% and 32% of patients, at least one CRBSI or CRO occurred, respectively. Median time to a first CRBSI or CRO was 246 (54–817) and 215 catheter days (5–2070). Numerically, but not statistically, a lower CRBSI or CRO rate was associated with tauroline (RR 0.32). Twenty patients reported adverse events (5 grade 1, 13 grade 2 and 2 grade 3) or CRO was 246 (54–817) and 215 catheter days (5–2070). Numerically, but not statistically, a lower CRBSI or CRO rate was associated with tauroline (RR 0.32).

Conclusion: The study describes the largest cohort of HPN patients to date on long-term taurolidine 2% as CLS. Overall, CRC incidence rates were low when compared with the literature. We found no evidence for a decreased effect of taurolidine over time.

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P1962 INTESTINAL DYSBIOSIS IN PATIENTS WITH SHORT BOWEL SYNDROME DEPENDENT ON TOTAL PARENTERAL NUTRITION IS REFLECTED BY ALTERED METABOLOME IN FAECES

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Introduction: Patients with short bowel syndrome (SBS) exhibit substantial disturbances in gut microbiota composition, which implicates significant alterations of intestinal metabolism.

Aims & Methods: The aim of this study was to perform genetic and metabolomic analysis of stool samples collected from SBS patients totally dependent on parenteral nutrition (TPN). We compare the stool samples from 8 healthy individuals and 8 patients with SBS dependent on TPN. Faecal microbiota composition was assessed by sequencing of variable V4 and V3 regions of 16S rRNA gene using Illumina MiSeq TM platform. Library preparation, template and template sequencing was performed according to manufacturer’s protocol. Obtained data were filtered by quality and length and processed for alpha and beta diversity analyses using QIIME software package. SCFA profile was measured using solid phase microextraction (SPME) coupled to gas chromatography and high resolution mass spectrometry employing time of flight mass analyser (Pegasus GC-HRT; LECO, USA). D-lactate content was determined using Megazyme kit.

Results: Weighted Unfmac analysis revealed significant differences between control and TPN subjects. In healthy controls, most abundant phylum was Firmicutes (64.2±7.5%), followed by Bacteroidetes (22.5±9.1%) and Actinobacteria (8.9±4.5%). Proteobacteria were found in one control sample. In TPN group, Firmicutes represented 64.6±29% of microbiota but Bacteroidetes were absent and Actinobacteria significantly reduced (1.6±4%). Proteobacteria were found in all samples (23.6±15%). The most abundant metabolites in control stool samples were short - chain fatty acids (SCFA): acetate, propionate and butyrate. In the TPN group, lactate predominated significantly, while SCFA were absent in the intestinal content of these patients.

Conclusion: Long-term dependency on total parenteral nutrition results in dysbiosis of the intestine residuum characterized by extinction of Bacteroidetes and appearance of Proteobacteria. This metabolic change was reflected by the changes in the composition of prevailing metabolites in stool.

Disclosure of Interest: All authors have declared no conflicts of interest.

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P1963 COMPARING RISKS OF ADVERSE EVENTS ASSOCIATED WITH PERCUTANEOUS ENDOSCOPIC GASTROSTOMY (PEG) PLACEMENT BETWEEN THE MODIFIED INTRODUCER TECHNIQUE AND THE OVERTUBE ASSISTED PULL TECHNIQUE

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Introduction: Techniques of percutaneous endoscopic gastrostomy (PEG) placement can be divided into two techniques, the pull technique or the introducer technique. Although the introduction of the pull technique has improved procedural safety for the gastrostomy placement, the pull technique, in which the PEG catheter is delivered through the oral cavity and the hypopharynx, inevitably contaminates the peristomal site. A series of studies directly comparing the newly developed modified introducer technique using a blunt cannula compared with the conventional pull technique demonstrated that the modified introducer technique was more preferable regarding procedure related adverse events. Meanwhile, use of an overtube while guiding the catheter into the stomach is expected to reduce the occurrence of the bacterial implantation. It is still unclear if the modified introducer technique or the overtube assisted pull technique would reduce risks of adverse events.

Aims & Methods: In this study, we retrospectively investigated risks of adverse events associated with the modified introducer technique and the overtube assisted pull method. Outcomes of patients who underwent the PEG placement from Jan 2013 to Oct 2016 at Jikei University Hospital were analyzed. The following data were collected from clinical records: age, gender, technique of PEG, reasons for PEG, lab tests and prognostic nutritional index (PNI).

Results: During the study period, 236 PEG placements were done in 234 patients. The average age was 69.3 ± 12.5. The modified introducer technique was applied in 167 procedures (70.8%) and the overtube assisted technique was applied in 69 procedures (29.2%). The nutritional index (PNI) of the PEG was placed aiming for a target PNI > 30.2%. Twenty patients reported adverse events (5 grade 1, 13 grade 2 and 2 grade 3) which were possibly related to the use of taudoline.

Conclusion: This study describes the largest cohort of HPN patients to date on long-term taurolidine 2% as CLS. Overall, CRC incidence rates were low when compared with the literature. We found no evidence for a decreased effect of taurolidine over time.

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patients required blood transfusion for the peristomal bleeding. In a univariate analysis, age, the rate of aspiration pneumonia as the reason for the PEG placement were higher in patients encountering adverse events (p < 0.05) (table 1). Also, serum platelet level, serum albumin and the rate of nutrition supports for cancer as the reason of the PEG placement was lower in patients encountering adverse events (p < 0.05). In a multivariate analysis, lower serum platelet level was solely recognized as a relevant predictive factor for adverse events (p < 0.05). The types of the technique used were not relevant to risks of adverse events.

Clinical backgrounds of patients with and without adverse events.

<table>
<thead>
<tr>
<th></th>
<th>with adverse events (n = 19)</th>
<th>without adverse events (n = 217)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean ± SD)</td>
<td>77.4 ± 7.9</td>
<td>68.6 ± 12.6</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>Sex (male/female)</td>
<td>13/6</td>
<td>162/55</td>
<td>n.s.</td>
</tr>
<tr>
<td>Technique for PEG (introducer/pull)</td>
<td>13/6</td>
<td>154/63</td>
<td>n.s.</td>
</tr>
<tr>
<td>Reasons for PEG (cancer/cerebrovascular accident/aspiration pneumonia/others)</td>
<td>5/5/6/3</td>
<td>127/46/26/18</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>Lab tests (mean ± SD)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ChE (U/L)</td>
<td>184.9 ± 60.8</td>
<td>214.9 ± 78.9</td>
<td>n.s.</td>
</tr>
</tbody>
</table>

Conclusion: There was no significant difference in overall risks of adverse events between the modified introducer technique group and the overtube assisted pull technique group. However, the modified introducer technique may be associated with higher risks of severer adverse events. Especially, special care should be taken in patients with lower serum platelet level.

Disclosure of Interest: All authors have declared no conflicts of interest.

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