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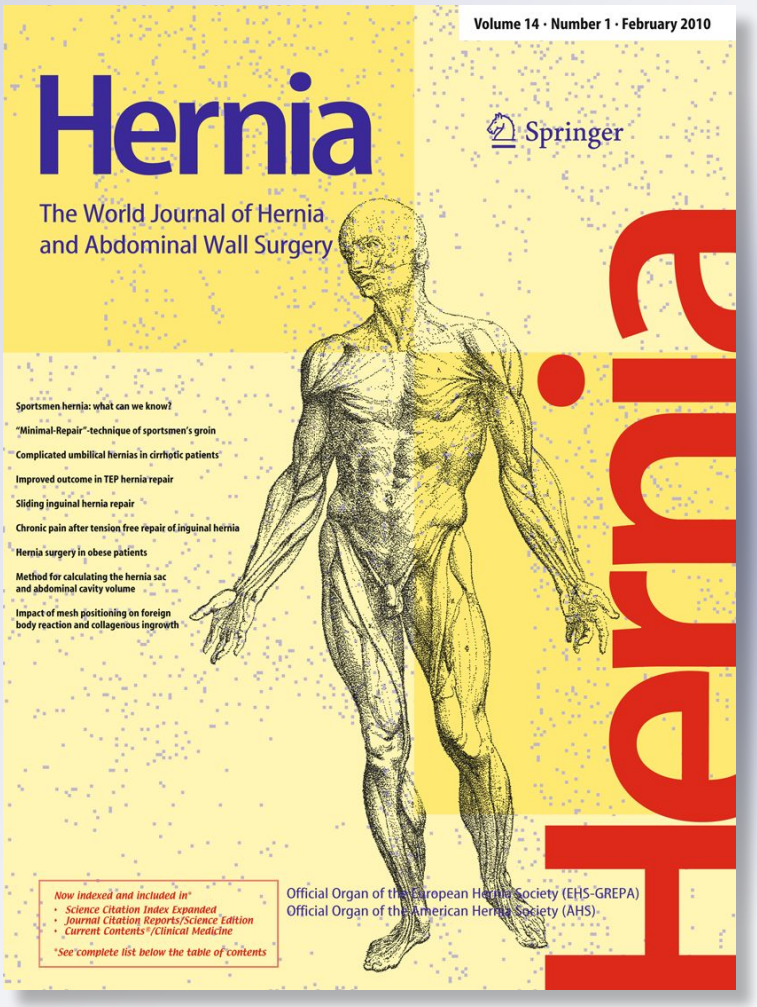

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ORIGINAL ARTICLE

Influence of inguinal hernia mesh repair on testicular flow and sperm autoimmunity

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Abstract
Background The incidence of infertility caused by the mesh inguinal hernia repair is not known. The aim of this study was to determine circulation and immunological testicular disorders after inguinal hernia mesh repair which can be related with infertility.
Methods From February 2010 to December 2010, 43 male patients who underwent inguinal hernia mesh repair were included in a prospective study. Testicular, capsular and intratesticular arterial flow dynamics were measured by Color Doppler ultrasound before the operation, in early and late postoperative period. The antisperm antibodies were analyzed before hernia repair and 5 months after.
Results The difference between patients who underwent laparoscopic (Group I) and anterior open tension-free hernia repair (Group II) in age, duration of symptoms and hernia characteristics were not significant. Statistically significant differences were found in peak-systolic and end-diastolic velocity in testicular and intratesticular arteries in Group II and in peak-systolic velocity on all levels in Group I. Only Group I had significant differences in resistive index of intratesticular arteries. All the values returned to basal in late postoperative period except testicular peak-systolic velocity in Group I which stayed in normal range. Wilcox matched pair test showed significant difference between preoperative and late postoperative measurements of the antisperm antibodies only in Group II, but it was within normal range in all cases.
Conclusions Inguinal hernia mesh repair do not have clinically significant influence on testicular flow and immunological response.

Keywords Inguinal hernia · Surgical mesh · Testicular flow · Antisperm antibodies · Color Doppler ultrasound

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Introduction

Inguinal hernia is a common medical problem affecting approximately 5–10 % of the population, and inguinal hernia repair is the most commonly performed general surgical operation [1]. Current surgical approaches to inguinal hernia repair are laparoscopic and open. Modern treatment of inguinal hernia mostly includes prosthetic mesh because of shorter hospital stay and lower recurrences [1, 2]. A fear for future fertility is a reason that mesh

hernia repair is not used as routine repair technique in young men. Infertility affects up to one in six couples of reproductive age [3]. Yavetz et al. found that among 8,500 patients attending the fertility clinic due to infertility, 565 men (6.65 %) reported an incidence of inguinal hernioplasty with or without subsequent atrophy of the testis. Semen quality of these patients was markedly reduced in comparison with that of fertile men [4]. A few experimental studies found that an inflammatory tissue response on mesh caused the functional obstruction of spermatic cord with spermatozoid repression and decreased the testicular perfusion over the time [5, 6]. Clinical studies of testicular flow after inguinal hernia repair showed several different outcomes. Even though some studies found no long adverse effect on testicular circulation and showed statistically nonsignificant difference between preoperative and postoperative spermiogram after mesh hernia repair, the infertility hypothesis of mesh repair is difficult to change [7, 8]. Recent published study by Hallen et al. [9] also does not support the hypothesis that hernia repair with mesh causes infertility at a significantly greater rate than those operated without mesh. The incidence of sperm autoimmunity in infertile couples is about 20 %. A conception rate in immunoinfertile couples with antibodies is 38 % lower than in a group without antibodies initially diagnosed with unexplained infertility [10]. Functional impairment due to antisperm antibodies (ASA) is more complex than decreasing the sperm concentration and the rate of progressive motility which is revealed by the spermiograms. Injury of the vas deferens, testicle ischemia and inflammatory reaction on mesh could be a possible reason for the sperm antigens intolerance. It is important that the antisperm antibodies can be detected before a histological damage to the testicle or if only one testis is damaged [11].

The aim of this study was to determine an influence of mesh inguinal hernia repair on testicular circulation and to detect an autoimmunological reaction as a possible reason for infertility.

Patients and methods

From February 2010 to December 2010, 43 male patients who underwent inguinal hernia mesh repair in the department of surgery, University Hospital Split, were included in a prospective study. Inclusion criteria were male sex and reducible hernia. Exclusion criteria were previous history of testicular trauma, operation or clinical detectable testicular disease, previous hernia repair, genitourinary infection or immunodeficiency. To perform this study, we obtained the approval of the Ethical Committee of Split University Hospital and each patient gave informed consent before inclusion in the study.

Mesh repairs of the inguinal hernia were performed via transabdominal preperitoneal laparoscopic approach—TAPP (Group I) or the anterior tension-free approach (Group II). All the procedures were performed by the same experienced surgical team.

General anesthesia was routinely used. During the procedure, all patients were placed in supine position with both arms tucked against their sides.

Anterior tension-free repair

After opening the aponeurosis of the external oblique muscle, the spermatic cord was mobilized. The indirect hernia sac was dissected and reduced or excised and sutured, whereas the direct sacs was inverted and imbricated. The posterior wall was covered by polypropylene mesh (Prolene, Ethicon, Norderstedt, Germany) with two vertical splits, and a round aperture was positioned around the spermatic cord and fixed with polyglactin 910 sutures (Vycril, Ethicon, Norderstedt, Germany).

Laparoscopic transabdominal preperitoneal approach

The patient was placed in Trendeleburg position (10°–20°) so that the viscera fall away from the inguinal areas. After the pneumoperitoneum was established, inguinal hernia was noted. Peritoneal defect or hernia was identified, and then the lateral umbilical ligament and inferior epigastric vessels were located. A peritoneal incision was made using an Ultracision (Ethicon Endo-Surgery, Cincinnati, OH, USA) at output level 5. The incision was extended from the lateral umbilical ligament to anterior iliac spine. Direct and small indirect hernia sacs were fully reduced. Larger indirect sacs were partially dissected and resected. The distal part of a large sac was left in situ. The anatomy was then defined and medially the dissection is carried to the symphysis pubis. A polypropylene mesh (Prolene, Ethicon, Norderstedt, Germany) was inserted via the 10 mm trocar into the abdominal cavity and deployed over the inguinal region. The mesh was attached to Cooper's ligament, around and lateral to the inferior epigastric vessels using tacks (Protac, Covidien, USA). The medial border of the mesh was adjacent to the symphysis pubis, and the upper part was placed at least 2–3 cm over the hernia defect and internal ring. The peritoneum was then reapproximated with the tacks.

Color Doppler ultrasound evaluation of the testicular blood flow was performed in all patients before the operation, in early postoperative period (between 24 and 48 h after the operation), and in late postoperative period (5 months after the operation). Testicular, capsular and intratesticular arterial flow dynamics were measured by a single experienced radiologist.

The patients were scanned in a supine position after 10 min of rest in a warm room using a ultrasound unit (Acuson X500, Siemens Medical Systems, Erlangen, Germany) with a 10-MHz linear array probe. The probe was gently placed directly on the scrotal skin, and the patient was asked to hold the penis suprapubically. Real-time scans were obtained in standard longitudinal and transverse plans to identify testicular blood flow on hernia side. After that, point spectral analysis was performed in the testicular artery 1 cm superior to the pole of the testicle, in the capsular artery and in the largest intratesticular vessel identified, in the middle and on both poles of the testicle. After testicular blood flow had been identified, the following parameters were evaluated: peak-systolic velocity (PSV), end-diastolic velocity (EDV), pulsative index (PI) and resistive index (RI) (Fig. 1).

Blood samples were drawn in all patients before hernia repair and 5 months after. The serum samples were immediately frozen and kept at a temperature of −70 °C until they were analyzed. The antisperm antibodies were analyzed by enzyme-linked immunoadsorbent assay (ELISA, Iason, Germany).

The data were analyzed using the nonparametric tests (Friedman, Wilcoxon, Mann–Whitney, χ^2 test; Statistica for Windows Release 7.0, Statsoft, Tulsa, Oklahoma, USA). All p values less than 0.05 were considered to indicate statistical significance.

Results

Forty-three male patients were initially recruited. Median age of patients was 62 years (range, 33–81 years). Mean duration of symptoms was 16 months (range, 2–108 months).

All patients described a sensation of a lump in their groin, but only 44 % reported pain in the groin of the affected side. Fifteen patients who underwent laparoscopic hernia repair (TAPP) were Group I, and the other 28 patients who had anterior open tension-free hernia repair were Group II. Both laparoscopic and conventional procedures were completed successfully for all patients without complication in either group during early and late postoperative periods. No significant differences between two groups were found regarding age ($p = 0.799$) hernia type ($p = 0.485$), hernia side ($p = 0.538$) and duration of symptoms ($p = 0.296$). Patients' characteristics and procedure statistics are reported in Table 1.

Both preoperative and postoperative antisperm antibodies (ASA) values were measured in only 27 patients. The basal and postoperative ASA values according to different type of operation are presented in Table 2.

There were no significant differences in basal ASA value between two groups ($p = 0.976$). The same was with postoperative ASA value ($p = 0.668$). A significant increase in antisperm antibody value after operation in Group II was found by average 36 % compared to basal value ($p = 0.004$), but in all cases the values of antisperm antibodies were within normal range (0–60 IU/ml).

Color Doppler ultrasound evaluation of the testicular blood flow was performed in all patients before the operation, in 42 patients on the second day after the operation and in 37 patients 5 months after the operation. In the statistical analysis, we included only patients who had all three measurements. No significant differences between the two groups were found in terms of Doppler flow parameters for the preoperative, early and late postoperative periods (Mann–Whitney test, $p > 0.05$).

Friedman analysis showed significant difference in RI only in intratesticular arteries in Group I ($p = 0.005$) with a significant increase between preoperative and early postoperative periods, returning to basal value in the late postoperative period (Fig. 2a).

Pulsative index (PI) showed significant differences only on intratesticular arteries in Group I ($p = 0.002$). The dynamic was the same as with RI, increasing between preoperative and early postoperative periods and returning to basal value in the late postoperative period (Fig. 2b).

On intratesticular artery level, a significant increase in PSV was found between basal and early postoperative periods in both groups, with a significant decrease and return to basal value in both groups (Friedman analysis; $p = 0.005$ for Group I and $p = 0.013$ for Group II).

On testicular and capsular artery level in Group I Friedman analysis showed a significant difference over time ($p = 0.032$; $p = 0.03$). Between early and late postoperative periods, PSV significantly decreased on both level. On the testicular artery, it became significantly lower (by 23 %) than before the operation.

Friedman analysis showed a significant difference in PSV only in the testicular artery in Group II ($p = 0.013$), with a significant increase between preoperative and early postoperative periods, returning to basal value in the late postoperative period (Fig. 2c).

Friedman analysis of variance showed significant difference in end-diastolic velocity (EDV) on testicular ($p = 0.013$) and intratesticular arteries ($p = 0.028$) in Group II**.** EDV showed a significant increase between preoperative and early postoperative periods, returning to basal value in the late postoperative period (Fig. 2d).

Discussion

After hernia repair, infertility can be related to the injury of vas deferens or the testicle. Injury of the testicle, which eventually leads to atrophy, is estimated to occur in about

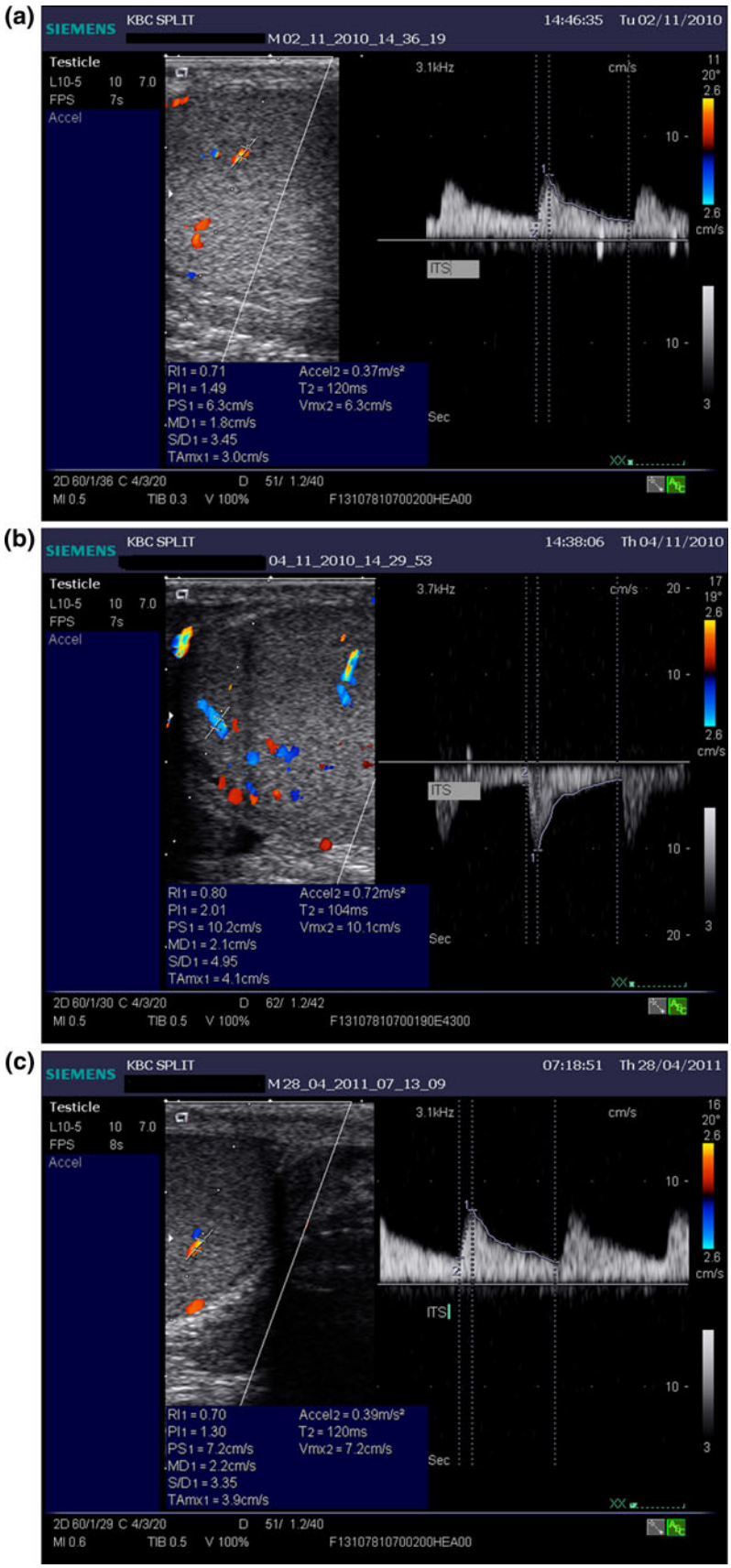

Fig. 1 Intratesticular flow measurements in a patient before operation (**a**), in early (**b**) and late postoperative period (**c**)

Table 1 Patients' characteristics and procedure statistics

	All patients	Group I	Group II	*p*
Patients (*n*)				
Unilateral	33 (77 %)	9 (60 %)	26 (87 %)	0.799[b]
Bilateral	10 (23 %)	6 (40 %)	4 (13 %)	
Age (years) median	62 (33–81)	61 (33–81)	60 (39–81)	
Hernia side (*n*, %)				
Right	28 (53 %)	10 (48 %)	18 (56 %)	0.538[a]
Left	25 (47 %)	11 (52 %)	14 (44 %)	
Nyhus hernia classification (*n*, %)				
Nyhus type II	14 (26 %)	7 (33 %)	7 (22 %)	0.485[a]
Nyhus type III (A)	6 (11 %)	3 (14 %)	3 (9 %)	
Nyhus type III (B)	33 (63 %)	11 (53 %)	22 (69 %)	
Duration of symptoms (months)	15.98 (2–108)	11.9 (2–30)	16.25 (2–108)	0.296[b]

[a] χ^2 test; [b] Mann–Whitney test

Table 2 Antisperm antibodies in basal and postoperative measurements [median (min–max), mean ± SD]

Procedures	Measurements	Median (min–max)	Mean ± SD	*p*[a]
Group I ($n = 10$)	Basal	14.4 (5.3–48)	22.8 ± 17.3	0.262
	After operation	27 (1.7–53.3)	26.5 ± 16.8	
Group II ($n = 17$)	Basal	20.4 (4.5–53)	22 ± 13.6	0.004
	After operation	27.8 (19.6–49.9)	29.5 ± 7.9	

[a] Wilcoxon test

0.5 % of the cases for primary hernia repairs but increases 10-fold to 5 % for recurrent repairs [12]. The main argument for no routine use of mesh in younger patients is to preserve fertility, which is ironical because the implantation of mesh decreases up to 3-folds the overall recurrence rate.

The incidence of vas deferens injury during inguinal hernia repair has been estimated at 0.3 % for adults and 0.8–2.0 % for children [13].

Both of these injuries can be a result of direct iatrogenic injury or delayed obstruction caused by scar tissue created as a result of inflammatory tissue response on mesh, which occurs as part of a normal healing process. Shin et al. [14] showed extensive fibrotic reaction with adhesions between the mesh and structures of the spermatic cord causing obstruction at the level of the inguinal canal in fourteen men with infertility after hernia repair with polypropylene mesh. In animals' studies, the histological examination of the spermatic cord revealed a foreign body reaction at the side of mesh implantation with a progress over time causing the spermatic cord remodeling with decreased spermatogenesis [5, 6].

Aydede et al. and Scull et al. in their studies showed statistically nonsignificant difference between preoperative and postoperative spermiogram after mesh hernia repair [7, 8]. It is possible that some unilateral obstruction was not detected either because it had no significant influence on spermiogram or the time between the operation and control spermiogram was not sufficient to detect the damage.

We measured the ASA instead of the spermiograms. The spermiograms revealed only sperm concentration and the rate of progressive motility. However, functional impairment due to ASA is more complex. The antisperm antibodies caused sperm agglutination, sperm cytotoxicity, poor penetration into cervical mucus and the impairment of acrosome reaction [15].

Also, the ASA can be detected before histological damage to the testicle has occurred. In addition, this immunological reaction can lead to the injury of both testicles [11]. The presence of ASA serum is highly accurate in predicting obstructive azoospermia, and it can obviate the need for testis biopsy [16].

A possible reason for sperm antigens intolerance after inguinal hernia repair could be injury of the vas deferens, testicle ischemia and inflammatory reaction [17, 18].

To the best of our knowledge in only three studies, the relation between inguinal hernia repair and ASA has been investigated. Matsuda et al. and Fribeerg et al. investigated ASA in infertile men who had previous hernia repair without mesh, and they found significant increase in ASA in these patients. Only patients with complication of hernia repair with consequential infertility were enrolled in these

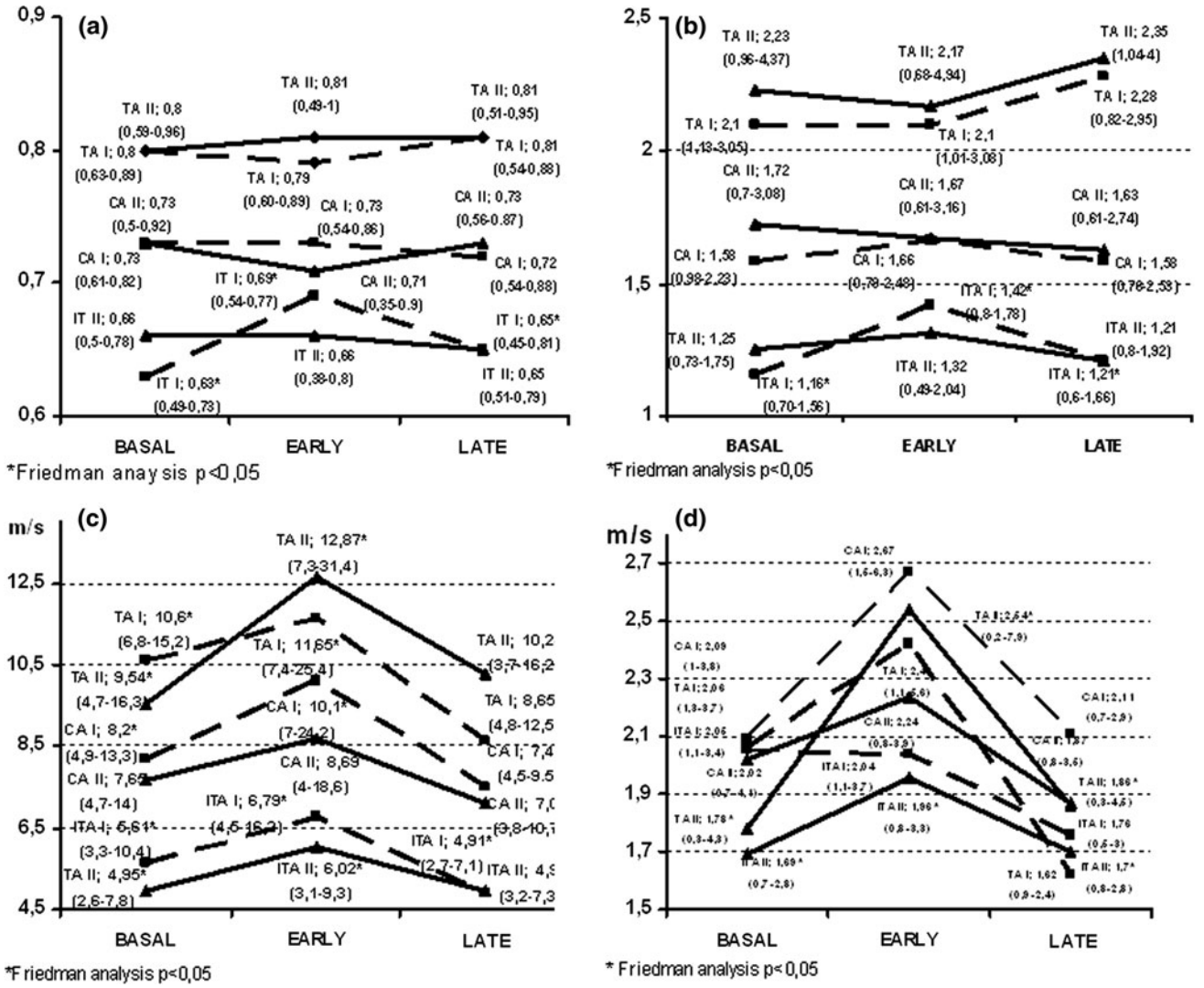

Fig. 2 Frideman analysis for **a** resistive index (RI), **b** pulsative index (PI), **c** peak-systolic velocity (PSV) and **d** end-diastolic velocity (EDV) of testicular, capsular and intratesticular artery measured in the preoperative, early and late postoperative periods. TA I (testicular artery Group I), CA I (capsular artery Group I), ITA I (intratesticular artery Group I), TA II (testicular artery Group II), CA II (capsular artery Group II), ITA II (intratesticular artery Group II)

studies [17, 19]. Kapral et al. measured serum ASA level before and after mesh hernia repair. They found a tendency of more frequent appearance of sperm antibodies after anterior open free tension method, but it was not significant. [20].

There are many commercially available ASA assays that either directly measure ASA bound to serum or indirectly measure ASA in solution, but the superior antibody detection assay does not exist. We chose ELISA because this method is both specific and quantitative and our hospital laboratory has a lot of experience with this technique. We based the time of postoperative ASA measurement on two facts: ASA production is not evident until 15–30 days after blood-testicle barrier is broken and the possibility of extrinsic compression leaving a scar ends within 3 months, that is, when the wound healing process after hernia repair is over [11].

Patients in Group II had a significant increase of average 36 % in the value of sperm antibodies after operation. It is important that in all cases before and after surgery the values of the ASA were within normal range (0–60 IU/ml) so the difference in ASA value was not clinically important. This postoperative increase in ASA value cannot be explained with injury of the vas deferens or testicle ischemia. A possible reason for postoperative increased ASA value can be inflammatory reaction to mesh with increased prevalence of B-cells on immunosuppressor T-cells, which would disturb the inhibition of autoimmune sperm response in distal genital ducts. A greater damage to tissue during anterior open approach can cause local hyperemia or edema, which can be connected with an increased ASA value in Group II. Edema of the surrounding tissue can also result in impaired venous drainage

of the testis, which is presumed in infertility connected with varicoceles [21]. In our patients, there was no significant correlation between change in testicular flow and the increase in ASA value.

In 33.3 % patients, the ASA value was decreased, which can be caused by functional obstruction of the spermatic cord with the hernia sac. Kapral et al. [20] also found that some preexisting sperm antibodies may frequently disappear after hernia repair.

There are only a few studies of testicular flow after laparoscopic hernia repair, comparing it with the anterior open technique [7, 22–24]. Different outcomes can partially be explained by different operation techniques or differences in periods of measurement, for example, only in acute or chronic phases.

In the study published by Ersin et al., it was found that laparoscopic technique has more significant influence on testicular flow, while Aydede et al. found a similar difference in testicular flow in both operation techniques [7, 22]. The laparoscopic technique had no influence on testicular flow in the early and the late postoperative period in the study of Leibl et al. [24]. Aydede et al. [7] also found no long-lasting adverse effects on testicular flow.

Instead of them, Beddy et al. showed a significant elevation in the resistive index (RI) in the hernia side compared with the normal side. This elevation in RI was reversed after hernia repair [23].

In our study, testicular flow was measured by linear array probe of 10 MHz which had better resolution than linear array probe of lower frequency used in other studies. Due to interdependence of flow within an arterial network, correct interpretation demands measurement on all levels. We therefore measured the flow in testicular, capsular and intratesticular arteries to avoid false normal results caused by partial measurement. Another reason for measurements of flow on intratesticular arteries is the fact that increased vascular resistance inside testicular tissue connected with spermatogenesis disturbance is of high clinical importance. Pingger et al. compared intratesticular RI with sperm counts and found a significantly greater RI in patients with pathological sperm counts. They suggested that the intratesticular RI can be a reliable indicator to identify subfertile men in routine clinical use [25].

We measured not only the PSV and EDV but also the resistive and pulsatile index because they have a strong correlation with vascular resistance and tissue perfusion.

We found a significant change in peak-systolic velocity on all three levels in Group I and on testicular and intratesticular arteries level in Group II. PSV increases between basal and early postoperative periods and returns to basal level in the late period on levels and in both groups except in the testicular artery in Group I. Testicular artery PSV in Group I became lower than before the operation but within normal range, so this decrease should not have clinical significance [26]. Possible explanation could be partial artery compression without significant stenosis because of normal PSV value with normal spectral wave. Besides, the outcome could have been biased due to the relatively small sample used. The most important outcome is the transitory change in the resistive and pulsatile index of intratesticular arteries in Group I. They both significantly increased between preoperative and early postoperative periods, returning to basal level in the late postoperative period. This means only a transitory decrease in testicular perfusion. The same results regarding intratesticular RI were shown by Ayede et al. [7], who also found increased vascular resistance in testicle in an early postoperative period with no long-lasting adverse effects on testicular perfusion. In our study as well as in Ersin et al., only the laparoscopic group had increased testicular vascular resistance in the early period, in contrast to Ayede et al., who found this in both, laparoscopic and conventional group [7, 22]. It was to expect that open hernia repair would cause greater testicular flow disturbance than the laparoscopic approach because of extensive dissection of the spermatic cord. Possible explanation for the increased vascular resistance of the intratesticular artery in the early postoperative period in the laparoscopic group can be the operation technique that places mesh directly above testicle vessels after peritoneum removal. This may lead to spasm of vascular vessels and transitory decreased testicular perfusion and is not connected with antisperm antibodies increase. Indeed, the significant increase in ASA value was not noticed in the laparoscopic group which had transitory increased vascular resistance.

Group II, however, did not show any significant change in the resistive and pulsatile index of intratesticular arteries.

End-diastolic velocity significantly increased only in Group II on testicular and intratesticular level between preoperative and early postoperative period, returning to basal value in the late postoperative period. This transitory change can be connected with postoperative edema or hyperemia, which should be greater after open hernia repair because of extensive tissue damage in comparison with the laparoscopic approach.

To the best of our knowledge, this is the first study to investigate testicular circulation and antisperm antibodies.

Conclusions

Mesh hernia repair caused only a transitory change in testicular perfusion without a long-lasting adverse effect on micro circulation. In addition, this change in testicular circulation had no effect on blood-testicle barrier which could lead to a significant immune reaction.

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