Ann Nucl Med (2012) 26:744–751
DOI 10.1007/s12149-012-0637-9

ORIGINAL ARTICLE

Adjuvant thyroid remnant ablation in patients with differentiated thyroid carcinoma confined to the thyroid: a comparison of ablation success with different activities of radioiodine (I-131)

Marin Prpic · Nina Dabelic · Josip Stanicic · Tomislav Jukic · Milan Milosevic · Zvonko Kusic

Received: 11 January 2012 / Accepted: 12 July 2012 / Published online: 25 July 2012
© The Japanese Society of Nuclear Medicine 2012

Abstract
Objective To assess efficiency of various I-131 activities on thyroid remnant ablation in thyroid cancer patients. The significance of patients' characteristics, pathologic features and levels of Tg were analyzed.
Patients and methods This study included 259 consecutive differentiated thyroid cancer patients, with disease confined to the thyroid, treated with I-131 after total thyroidectomy. Patients were divided into the three groups: 80 patients receiving low [1110–1850 MBq (30–50 mCi)], 121 intermediate [2775 MBq (75 mCi)] and 58 high [3700 MBq (100 mCi)] postoperative I-131 activities. Six to eight months after the application of radioiodine, measurements of TSH, Tg, anti-Tg antibodies (in hypothyroid state) together with ultrasound exam and whole-body scintigraphy were performed.
Results The ablation was significantly more effective (after the first application) in patients receiving 100 mCi of I-131—89.7 % than in patients receiving lower activities ($P = 0.016$). There was no significant difference in ablation rate between the 30–50 mCi (77.5 %) and 75 mCi (70.2 %) groups. In the group receiving 30–50 mCi, patients with solitary tumors had significantly higher ablation rate ($P = 0.038$). In patients receiving 75 mCi ablation rates were higher among older patients ($P = 0.005$), with infiltration of the single lobe ($P = 0.005$), and with solitary tumor ($P = 0.012$). The rates of successful ablation after the second application of I-131 (after 12–16 months) amounted to 96, 97 and 96 % in the 30–50, 75 and 100 mCi groups, respectively. The activity of I-131 and age were independent factors for thyroid ablation failure after the first application of I-131 (model of binary logistic regression).
Conclusion The results of remnant ablation were satisfactory with all activities applied. Although after the first application of I-131 the activity of 100 mCi is significantly more effective in thyroid ablation than the administration of 30–50 mCi and 75 mCi, the ablation rates between all the three groups are similar (almost equal) after the second application. Thus, the activity to be administered may depend on patients' characteristics and a detailed consideration of the merits and demerits of each I-131 activity.

Keywords I-131 · Remnant ablation · Thyroid cancer · Predictive factors

Introduction

Thyroid cancer is relatively uncommon, but it is the most common malignancy of the endocrine system [1]. Differentiated thyroid carcinoma (DTC) accounts for about 85–95 % of all cancers of the thyroid gland. Postoperative thyroid remnant ablation performed with a wide variety of therapeutic activities of radioactive iodine (I-131) is indicated in numerous patients. According to the indications for the postoperative I-131 administration patients could be divided into three risk groups: the very low risk group in which there is no indication for the postoperative I-131 administration, the low-risk group in which the indication could be considered, and the high-risk group in which there is a clear indication for I-131 administration.

M. Prpic (✉) · N. Dabelic · J. Stanicic · T. Jukic · Z. Kusic
Department of Oncology and Nuclear Medicine, University Hospital Center "Sisters of Charity", Vinogradska cesta 29, 10 000 Zagreb, Croatia
e-mail: marin.prpic@inet.hr

M. Milosevic
School of Public Health "Andrija Štampar", School of Medicine, University of Zagreb, Zagreb, Croatia

The indications for radioiodine ablation in the low-risk group of patients are the subject of many debates [2–10]. The ablation benefit has not been yet confirmed with clear evidence in this group of patients. Also, there are different opinions about the optimal I-131 activity required for effective remnant ablation of the thyroid residue in this group of patients [11–19]. The empiric approach for administration of I-131, using activities in range from [1110 MBq (30 mCi)] to [3700 MBq (100 mCi)] is most commonly used in this group [20].

The remnant ablation is achieved when the remnant thyroid tissue is nondetectable with the most sensitive available methods. The successful radioiodine ablation is often defined as the lack of visible accumulation on subsequent whole-body scintigraphy (WBS) [5, 18, 21, 22]. Tumor marker thyroglobulin (Tg) can be used as an additional criterion in evaluation of ablation outcome [21, 22]. Successful ablation is followed by low or undetectable levels of Tg (<1–10 ng/mL). During the last few decades many prognostic scoring systems for differentiated thyroid carcinoma have been developed and different prognostic factors have been used to create various prognostic systems [23–27]. The guidelines of many international and national thyroid cancer societies are based on tumor node-metastasis system of staging [27].

The aim of this study was to assess efficiency of various I-131 activities on thyroid remnant ablation in patients with DTC. In addition, the significance of patients' characteristics, pathologic features and levels of Tg as possible predictive factors of effective radioiodine therapy were analyzed.

Patients and methods

Patients

This retrospective study includes 259 consecutive thyroid cancer patients who were treated with radioactive iodine and followed up in our medical center. All patients had total thyroidectomy. Diagnosis of the papillary or follicular thyroid cancer was confirmed by pathological analysis. Only patients with disease confined to thyroid without evidence of local or systemic spread of disease at the time of disease presentation were included in the study. The groups of patients were further standardized by age and gender.

Ablation of thyroid remnant tissue with various activities of I-131 was performed in all the patients in the study. First application of I-131 in patients occurred between 2004 and 2009 and the second application was administered in the cases of unsuccessful thyroid remnant ablation. Patients with infiltration of adjacent structures (T4), local (node positive), distant metastases and those with mixed variants of tumor (e.g. papillary–medullar type) were excluded from the study.

Based on clinical parameters (serum Tg level, ultrasonography exam, whole-body scintigraphy), patients were divided into three groups for the postoperative I-131 ablation: group receiving low [1110–1850 MBq (30–50 mCi)], intermediate [2775 MBq (75 mCi)] and high [3700 MBq (100 mCi)] activities of radioiodine. The second application of I-131, if needed, was in range from [1110 MBq (30 mCi)] to [3700 MBq (100 mCi)], and patients were not divided into three groups as after the first application.

Methods

All patients underwent total thyroidectomy. Four weeks after total thyroidectomy, levels of serum Tg, thyroid-stimulating hormone (TSH), and anti-Tg antibodies were measured. Stimulation of TSH was achieved by thyroid hormone withdrawal during the 4-week period. Elevation of TSH level ≥30 mU/L was marked as satisfactory for subsequent ablation. All patients underwent ultrasound exam of the cervical region and thyroid bed, and in some patients (with uncertain remnant size), preablative diagnostic radioiodine scintigraphy was performed to estimate the mass of the thyroid remnant with low diagnostic activities of I-131 [37–74 MBq (1–2 mCi)].

Empiric approach with application of various ablation activities of I-131 was used facilitating postoperative follow-up. Six to eight months after the application of radioiodine, repeated measurements of serum levels of TSH, Tg, anti-Tg antibodies (in hypothyroid state), together with ultrasound exam of the cervical region and the thyroid bed and WBS were performed. The outcome of ablation was assessed after the first and second application of radioiodine. Correlation between the ablation rates and possible predictive factors such as tumor size, gender, age, T-category, affection of lobe(s), number of foci (solitary or multifocal disease), and Tg levels were performed.

Successful ablation was defined as absence of remnant thyroid tissue (no visible accumulation) of I-131 in thyroid bed and in cervical region on WBS. Tg levels and ultrasound findings of the neck region were used as additional criteria, and the same had been compared with the WBS findings in estimation of mass of thyroid remnant. In patients with successful ablation, there was no indication for further radioiodine treatment. Elevated levels of serum Tg can be detected up to a year after the surgery but non-measurable postoperative levels of Tg (<0.1 ng/ml) imply an effective thyroid remnant ablation [28].

Patients with positive anti-Tg antibodies were excluded from evaluation of Tg, based on criteria that Tg findings are not considered reliable in cases of positive antithyroglobulin antibodies.

Thyroid remnant ablation effectiveness after the first and second application of I-131 has been compared in the groups with low, intermediate and high I-131 activities applied. Age, sex, tumor T-category, tumor multifocality and multilobularity, tumor size and levels of Tg were analyzed in each group as potential altering factors of radioiodine ablation success.

This study has been approved by a Clinical Ethics Committee of University Hospital Center and Medical Faculty Ethics Committee. The obtained data was used in concordance with current legislation.

Statistical methods

Kolmogorov–Smirnov test was used to show the distribution of values of certain variables. Furthermore, in order to determine differences in the values of variables between the certain groups, the independent t test and, one-way ANOVA and χ^2 test were used. Binary logistic regression was performed to assess the impact of a number of factors on the possibility of unsuccessful ablation after the first I-131 application. The model contained nine independent variables (age, gender, tumor size, tumor category, number of lobes affected, tumor multifocality, TSH levels, Tg antibodies and ablation activities groups). P value of less than 0.05 was considered statistically significant. The software SPSS for Windows version 17.02 (Chicago, IL) was used in the analysis.

Results

Out of 259 consecutive patients with differentiated thyroid cancer, there were 222 women, and 37 men (6:1 ratio). The median age was 50.88 years (range 21–81 years). There were no statistically significant differences in age, gender and TSH levels between the groups (Tables 1, 2). After the first application of I-131, the thyroid remnant ablation was significantly more effective in patients who received high activities of I-131 [3700 MBq (100 mCi)] 89.7 % than in patients receiving lower activities [1110–1850 MBq (30–50 mCi) or 2775 MBq (75 mCi)] 77.5 and 70.2 %, respectively ($P = 0.016$). No difference was observed in the efficiency of ablation after the second application of radioiodine between the three observed groups ($P = 0.230$). There was no significant difference between the first application of I-131 in patients receiving low [1110–1850 MBq (30–50 mCi)] and intermediate [2775 MBq (75 mCi)] activities in the terms of success of thyroid remnant ablation.

In the group receiving low activities of I-131 [1110–1850 MBq (30–50 mCi)], after first application of I-131, the patients with solitary tumors had significantly higher ablation rate, than patients with multifocal tumors (84.6 %:64.3 %; $P = 0.038$). After the second application, the above-mentioned difference was no longer significant. There were no differences between age, gender, T-category, lobe(s) affected, tumor size, or Tg level, in the patients with successful ablation and patients in whom ablation was not achieved (Table 3).

When it comes to the patients receiving intermediate activities of I-131 [2775 MBq (75 mCi)], the ablation rates were higher after the first application of I-131 among older patients (52.72 ± 12.96 years; 45.53 ± 11.37 years; $P = 0.005$), both in those with single lobe infiltration (74.8 vs. 44.4 %; $P = 0.005$), and those with solitary tumor (76.1 vs. 51.7 %; $P = 0.012$). The statistical differences disappeared after the second application of I-131. There were no statistically significant differences in gender, T-category, tumor size, and the Tg levels between the patients with successful ablation and the ones with unsuccessful ablation after the first and second application of I-131 (Table 4).

In patients receiving high ablation activities of I-131 [3700 MBq (100 mCi)], there were no statistically significant differences in any of the above-mentioned, observed characteristics, both in patients with successful ablation after the first and second application of I-131 and in patients in which ablation was not achieved. In all subgroups of patients receiving high ablation activities of I-131, high ablation rates were achieved after the first application of radioiodine, even in patients with tumor affection of both lobes (85.7 %) and multiple foci tumors (89.4 %) (Table 5).

The full binary regression model containing all predictors was statistically significant, $\chi 2$ test ($df = 10, N = 257$) $= 36.89$, $P < 0.001$, indicating that the model was able to distinguish between patients who have, and patients who do not have ablation failure after the first application of I-131. The model as a whole explained 20.1 % (Nagelkerke R squared) of the variance in ablation status and correctly classified 79 % of cases. As shown in Table 6, several of the independent variables made a unique statistically significant contribution to the model (age and ablation activities groups). Ablation activity group of 100 mCi has been chosen as a referent group due to previous univariate and bivariate analyses. The 30–50 mCi group compared to the referent group has 5.19 times more chance to have ablation failure after the first application, and 75 mCi group has even more chance on ablation failure compared to referent group (OR = 8.21) controlled for all other factors in the model.

Discussion

Radioactive iodine has been for a long time standard of care in the postoperative treatment of patients with

Table 1 Age and gender of patients, χ^2 test

Characteristics of patients	30–50 mCi ($N = 80$)	75 mCi ($N = 121$)	100 mCi ($N = 58$)	All groups ($N = 259$)	P value
Age at onset: mean ± SD*	51.45 ± 13.07	50.58 ± 12.89	50.72 ± 12.60	50.88 ± 12.84	0.891
Gender					
Male	10	17	10	37	0.731
Female	70	104	48	222	

* ANOVA

Table 2 TSH levels (before 1st application of I-131) and ablation success in patients, independent t test

Groups	30–50 mCi ($N = 80$) ($P = 0.505$)		75 mCi ($N = 121$) ($P = 0.585$)		100 mCi ($N = 58$) ($P = 0.057$)	
Ablation with 1st application of I-131	Yes ($N = 62$)	No ($N = 18$)	Yes ($N = 85$)	No ($N = 36$)	Yes ($N = 52$)	No ($N = 6$)
TSH level (mU/L)	88.32 ± 34.59	94.56 ± 35.39	82.38 ± 32.16	78.90 ± 31.84	73.97 ± 32.43	47.50 ± 21.30

Table 3 Comparison of predictive factors: group 30–50 mCi, χ^2 test

Possible predictive factors	Ablation with 1st application of I-131 ($N = 80$)			Ablation with 2nd application of I-131 ($N = 17$)		
	Yes, N (%)	No, N (%)	P value	Yes, N (%)	No, N (%)	P value
Age at onset (mean ± SD)*	52.37 ± 13.44	48.28 ± 11.52	0.245	49.00 ± 12.52	48.33 ± 7.23	0.931
Gender						
Male	6 (60.0)	4 (40.0)	0.157	4 (100)	–	0.290
Female	56 (80.0)	14 (20.0)		10 (76.9)	3 (23.1)	
Category						
T1	54 (78.3)	15 (21.7)	0.912	12 (85.7)	2 (14.3)	0.414
T2	5 (71.4)	2 (28.6)		1 (50.0)	1 (50.0)	
T3	3 (75.0)	1 (25.0)		1 (100)	–	
No. of lobes affected						
Single lobe	52 (80.0)	13 (20.0)	0.265	11 (91.7)	1 (8.3)	0.119
Both lobes	10 (66.7)	5 (33.3)		3 (60.0)	2 (40.0)	
Multifocal cancer						
Yes	18 (64.3)	10 (35.7)	0.038	8 (80.0)	2 (20.0)	0.761
No	44 (84.6)	8 (15.4)		6 (85.7)	1 (14.3)	
Tumor size (mm)						
<5	9 (90.0)	1 (10.0)	0.543	1 (100)	–	0.819
5–10	28 (73.7)	10 (26.3)		7 (77.8)	2 (22.2)	
>10	25 (78,1)	7 (21,9)		6 (85.7)	1 (14.3)	
Tg level						
Undetectable	6 (85.7)	1 (14.3)	0.926	1 (100)	–	0.382
≤2 ng/mL	15 (79.0)	4 (21.0)		3 (75.0)	1 (25.0)	
>2 ng/mL	26 (81.2)	6 (18.8)		6 (100)	–	

* Independent t test

differentiated thyroid carcinoma. The treatment benefit of radioiodine therapy has been confirmed in patients with high-risk disease [29, 30]. In patients with very low risk, the postoperative use of I-131 is not recommended, because of excellent disease outcome, even without the use of this therapeutic modality [31]. However, indications for I-131 application in low-risk group of patients are still debated. Besides the question of proper indication for I-131 ablation, opinions differ regarding the optimal amount of the therapeutic activity required for effective ablation of residual thyroid remnant tissue in this group of patients [7, 8, 10].

Table 4 Comparison of predictive factors: group 75 mCi, χ^2 test

Possible predictive factors	Ablation with 1st application of I-131 ($N = 121$)			Ablation with 2nd application of I-131 ($N = 35$)		
	Yes, *N* (%)	No, *N* (%)	*P* value	Yes, *N* (%)	No, *N* (%)	*P* value
Age at onset (mean ± SD)*	52.72 ± 12.96	45.53 ± 11.37	0.005	45.94 ± 11.80	36.33 ± 13.87	0.192
Gender						
Male	13 (76.5)	4 (23.5)	0.545	4 (100)	–	0.515
Female	72 (69.2)	32 (30.8)		28 (90.3)	3 (9.7)	
Category						
T1	75 (70.1)	32 (29.9)	0.940	28 (90.3)	3 (9.7)	0.809
T2	6 (75.0)	2 (25.0)		2 (100)	–	
T3	4 (66.7)	2 (33.3)		2 (100)	–	
No. of lobes affected						
Single lobe	77 (74.8)	26 (25.2)	0.009	24 (92.3)	2 (7.7)	0.752
Both lobes	8 (44.4)	10 (55.6)		8 (88.9)	1 (11.1)	
Multifocal cancer						
Yes	15 (51.7)	14 (48.3)	0.012	13 (92.9)	1 (7.1)	0.805
No	70 (76.1)	22 (23.9)		19 (90.5)	2 (9.5)	
Tumor size (mm)						
<5	18 (85.7)	3 (14.3)	0.222	2 (100)	–	0.772
5–10	35 (67.3)	17 (32.7)		15 (93.8)	1 (6.3)	
>10	31 (66.0)	16 (34.0)		15 (88.2)	2 (11.8)	
Tg level						
Undetectable	7 (58.3)	5 (41.7)	0.639	5 (100)	–	0.674
≤2 ng/mL	23 (69.7)	10 (30.3)		8 (88.9)	1 (11.1)	
>2 ng/mL	39 (72.2)	15 (27.8)		12 (85.7)	2 (14.3)	

* Independent *t* test

Various thyroid associations have published and updated guidelines for differentiated thyroid cancer management over the last few years [23, 32–35]. The recommendations are often graded according to the strength of evidence and based on different levels of evidence. In the absence of evidence of a stronger level, clinical decision is made upon low-level strength of evidence, that is, on the grounds of expert opinions and retrospective studies.

A meta-analysis performed by Hackshaw et al. [11], which included various retrospective studies, has not managed to determine which activities of I-131 to use in thyroid remnant ablation. As a result of this lack of consensus, the principal contribution of this research is to determine specific indications for application of distinct therapeutic activities of I-131 in patients with differentiated thyroid cancer.

Thyroid remnant ablation is usually performed with activities ranging from 1110 MBq (30 mCi) to 3700 MBq (100 mCi). In the determination of I-131 activity required for remnant ablation the three approaches are being used in clinical practice—empiric approach, dosimetric approach, and approach with measurement of radioactive dose in the blood and bone marrow of the patient [36, 37]. The optimal activity is usually determined empirically, using clinical factors, such as postoperative levels of Tg, ultrasonography exam, and in some cases postoperative whole-body scintigraphy. However, some centers use different methods (I-124 PET dosimetry). The I-124 PET-based dosimetry may facilitate whole-body and lesion dosimetry in specific situations (e.g. I-131 therapy in children or in patients with renal insufficiency), but it is not used as a routine procedure [38, 39].

Besides medical factors (patient characteristics, pathological characteristics of tumors, and type of surgical treatment), some non-medical factors play an important role in determination of proper I-131 ablation activity. In the absence of consensus on radioiodine ablation activities in low-risk patients, other factors such as, legislation regarding radiation protection, treatment and hospitalization costs, and radiation exposure of medical staff are of importance in determining treatment decision [40]. The costs of treatment and hospitalization are certainly not negligible factors in determining the amount of required activity. Patients treated with low therapeutic activities can often be treated at "outpatient" basis, thus incurring lower

Table 5 Comparison of predictive factors: group 100 mCi, χ^2 test

Possible predictive factors	Ablation with 1st application of I-131 ($N = 58$)			Ablation with 2nd application of I-131 ($N = 6$)		
	Yes, *N* (%)	No, *N* (%)	*P* value	Yes, *N* (%)	No, *N* (%)	*P* value
Age at onset: (mean ± SD)*	50.83 ± 13.11	49.83 ± 7.47	0.857	52.00 ± 8.12	45.50 ± 4.95	0.371
Gender						
Male	9 (90.0)	1 (10.0)	0.969	–	1 (100)	0.121
Female	43 (89.6)	5 (10.4)		4 (80.0)	1 (20.0)	
Category						
T1	20 (87.0)	3 (13.0)	0.571	1 (33.3)	2 (66.7)	0.083
T2	8 (100)	–		–	–	
T3	24 (88.9)	3 (10.3)		3 (100)	–	
No. of lobes affected						
Single lobe	46 (90.2)	5 (9.8)	0.715	4 (80.0)	1 (20.0)	0.121
Both lobes	6 (85.7)	1 (14.3)		–	1 (100)	
Multifocal cancer						
Yes	10 (89.4)	1 (10.6)	0.879	–	1 (100)	0.121
No	42 (90.9)	5 (9.1)		4 (80.0)	1 (20.0)	
Tumor size (mm)						
<5	4 (80.0)	1 (20.0)	0.745	–	1 (100)	0.153
5–10	17 (89.5)	2 (10.5)		1 (50.0)	1 (50.0)	
>10	31 (91.2)	3 (8.8)		3 (100)	–	
Tg level						
Undetectable	4 (100)	–	0.638	–	–	–
≤2 ng/mL	7 (100)	–		–	–	
>2 ng/mL	36 (92.3)	3 (7.7)		1 (33.3)	2 (66.6)	

* Independent *t* test

Table 6 Predictive factors of ablation failure after 1st application of I-131, binary logistic regression

Independent variables	*P*	OR	95 % CI	
			Lower	Upper
Age (years)	0.001	0.96	0.93	0.98
Female gender	0.746	0.86	0.34	2.18
Tumor size (mm)	0.179	0.97	0.92	1.02
T-category	0.191	1.51	0.81	2.82
No. of lobes affected	0.305	1.79	0.59	5.44
Multifocal cancer	0.189	1.88	0.73	4.79
TSH level (mU/L)	0.346	0.99	0.98	1.01
Tg antibodies	0.056	1.03	1.00	1.07
Ablation group: 100 mCi (ref)	0.005			
30–50 mCi	0.016	5.19	1.35	19.88
75 mCi	0.001	8.21	2.24	30.08

hospitalization costs. The costs of treatment with high activities are at least two to three folds higher (without hospitalization cost) than the costs of application of low activities. Therefore, the use of ablation activities in the lower therapeutic range is frequently observed in the clinical practice. Additional advantages of low therapeutic activities are reduced (radiation) exposure of medical personnel and less exposure of other body systems and tissues (outside the thyroid).

On the other hand, the advantage of treatment with high activities is a more effective ablation. However, no studies have reported thyroid remnant ablation effectiveness of 100 % yet, meaning that in some patients, thyroid remnant ablation cannot be achieved, even with multiple applications of I-131. Disadvantage of more aggressive treatment is a higher occurrence of side effects, which are more frequent in higher risk patients with multiple treatments, so the risk of side effects after one or two applications of I-131 is probably negligible [41, 42]. It is crucial to determine which therapeutic activity should be applied to specific risk group, because lower activities could result in an ineffective ablation, while avoiding higher activities reduces the cost of the therapy and staff exposure.

The results of remnant ablation of thyroid tissue were evaluated as satisfactory in the context of all activities applied, that is, the results obtained were in accordance with published studies [16, 17]. After the first application of I-131, the thyroid remnant ablation was significantly

more effective in patients when high activities of I-131 were applied (100 mCi; 90 %) than in the cases where lower activities were applied (30–50 or 75 mCi; 77, 70 %). However, there was no significant difference between the ablation with low and intermediate activities. After the first and second application (after 12–16 months) in majority of patients in all groups (96, 97, 96 %; low, intermediate, high activities, respectively), successful ablation of remnant thyroid tissue was achieved, and only in few patients thyroid remnant tissue persisted (4, 3, 4 %).

According to TNM classification, the thyroid tumors are divided into 4 categories (T1–4) and, within the said categories, the tumors may be recognized as solitary (single tumor focus) or multifocal (multiple tumor foci) [27]. After the first application of low and intermediate activities of I-131, we have observed the significantly higher ablation rates in patients with solitary tumors than in the patients with multifocal tumors ($P < 0.012$). On the other hand, in cases where high ablation activities were applied, there were no differences with regard to the ablation success. The differences in ablation rates observed in low and intermediate group of patients could be considered as the result of three principal factors: the different extent of operative procedures: total versus near-total thyroidectomy (various remnant volume), the difference in levels of TSH stimulation, and finally, the age of patients (various sensitivity to radiation damage).

In our series, all the patients underwent total thyroidectomy at "high volume centers". The values of the postoperative levels of Tg measured before ablation have been used in the assessment of thyroid remnant volume (patients with regional and distant metastases have been excluded from the study). In this regard, no significant difference in Tg levels has been observed between the patients with successful and unsuccessful ablation after the first application of I-131.

Higher levels of TSH in patients with equal thyroid remnant volume could lead to higher ablation rates due to higher I-131 uptake. After the first application of I-131, there were no differences regarding the TSH levels between the patients with successful and unsuccessful ablation within the observed groups, as confirmed by both independent t test (Table 2) and multivariate analysis (Table 6). When it comes to patients receiving intermediate activities, after the first application of I-131 more efficient ablation was observed in older patients (independent t test, $P = 0.005$). However, after performing a multivariate analysis, it turned out that the age is categorized as dependent variable in the model (OR = 0.96).

The ablation rates in patients receiving intermediate activities of I-131 (75 mCi) were unexpectedly low in comparison to the group of patients receiving low activities. The above-mentioned minor discrepancies may also be the result of a retrospective study design that could be source of potential bias or imprecision. However, there was no statistically significant difference in therapeutic result between the ablation rates in these two groups of patients (low vs. intermediate). On the other hand, ablation with 100 mCi I-131 was therapeutically significant.

It is necessary to determine the ablation activity on a "case to case" basis, because an individualized approach with tailored treatment leads to the optimal treatment outcome, followed by acceptable costs and radiation exposure risk. The thyroid remnant ablation was more effective, after the first application, in patients receiving 100 mCi. However, there were no differences between the ablation with low and intermediate activities. The ablation rates after the second application of I-131 did not differ among the three observed groups as well as the successful ablation of remnant thyroid tissue was achieved in most patients in all groups.

Conflict of interest No potential conflicts of interest were disclosed.

References

1. Biersack H-J, Grűnwald F, editors. Thyroid cancer. Berlin: Springer; 2005.
2. Mazzaferri E. A randomized trial of remnant ablation—in search of an impossible dream? J Clin Endocrinol Metab. 2004;89:3662–4.
3. Sawka AM, Thephamongkhol K, Brouwers M, Thabane L, Browman G, Gerstein HC. Clinical review 170: a systematic review and metaanalysis of the effectiveness of radioactive iodine remnant ablation for well-differentiated thyroid cancer. J Clin Endocrinol Metab. 2004;89:3668–76.
4. Robbins RJ, Schlumberger MJ. The evolving role of (131)I for the treatment of differentiated thyroid carcinoma. J Nucl Med. 2005;46(Suppl 1):28S–37S.
5. Rosario PW, Reis JS, Barroso AL, Rezende LL, Padrao EL, Fagundes TA. Efficacy of low and high 131I doses for thyroid remnant ablation in patients with differentiated thyroid carcinoma based on post-operative cervical uptake. Nucl Med Commun. 2004;25:1077–81.
6. Hay ID. Selective use of radioactive iodine in the postoperative management of patients with papillary and follicular thyroid carcinoma. J Surg Oncol. 2006;94:692–700.
7. Verburg FA, Dietlein M, Lassmann M, Luster M, Reiners C. Why radioiodine remnant ablation is right for most patients with differentiated thyroid carcinoma. Eur J Nucl Med Mol Imaging. 2009;36:343–6.
8. Rosario PW, Borges MA, Valadao MM, Vasconcelos FP, Rezende LL, Padrao EL, et al. Is adjuvant therapy useful in patients with papillary carcinoma smaller than 2 cm? Thyroid. 2007;17:1225–8.
9. Reiners C, Dietlein M, Luster M. Radio-iodine therapy in differentiated thyroid cancer: indications and procedures. Best Pract Res Clin Endocrinol Metab. 2008;22:989–1007.
10. Sawka AM, Rotstein L, Brierley JD, Tsang RW, Thabane L, Gafni A, et al. Regional differences in opinions on adjuvant radioactive iodine treatment of thyroid carcinoma within Canada and the United States. Thyroid. 2007;17:1235–42.
11. Hackshaw A, Harmer C, Mallick U, Haq M, Franklyn JA. 131I activity for remnant ablation in patients with differentiated

thyroid cancer: a systematic review. J Clin Endocrinol Metab. 2007;92:28–38.
12. Bal C, Padhy AK, Jana S, Pant GS, Basu AK. Prospective randomized clinical trial to evaluate the optimal dose of 131 I for remnant ablation in patients with differentiated thyroid carcinoma. Cancer. 1996;77:2574–80.
13. Bal CS, Kumar A, Pant GS. Radioiodine dose for remnant ablation in differentiated thyroid carcinoma: a randomized clinical trial in 509 patients. J Clin Endocrinol Metab. 2004;89:1666–73.
14. Johansen K, Woodhouse NJ, Odugbesan O. Comparison of 1073 MBq and 3700 MBq iodine-131 in postoperative ablation of residual thyroid tissue in patients with differentiated thyroid cancer. J Nucl Med. 1991;32:252–4.
15. Creutzig H. High or low dose radioiodine ablation of thyroid remnants? Eur J Nucl Med. 1987;12:500–2.
16. Maenpaa HO, Heikkonen J, Vaalavirta L, Tenhunen M, Joensuu H. Low vs. high radioiodine activity to ablate the thyroid after thyroidectomy for cancer: a randomized study. PLoS One. 2008;3(4):e1885.
17. Doi SA, Woodhouse NJ, Thalib L, Onitilo A. Ablation of the thyroid remnant and I-131 dose in differentiated thyroid cancer: a meta-analysis revisited. Clin Med Res. 2007;5:87–90.
18. Zidan J, Hefer E, Iosilevski G, Drumea K, Stein ME, Kuten A, et al. Efficacy of I131 ablation therapy using different doses as determined by postoperative thyroid scan uptake in patients with differentiated thyroid cancer. Int J Radiat Oncol Biol Phys. 2004;59:1330–6.
19. Lin JD, Kao PF, Chao TC. The effects of radioactive iodine in thyroid remnant ablation and treatment of well differentiated thyroid carcinoma. Br J Radiol. 1998;71:307–13.
20. Beierwaltes WH, Rabbani R, Dmuchowski C, Lloyd RV, Eyre P, Mallette S. An analysis of "ablation of thyroid remnants" with I-131 in 511 patients from 1947–1984: experience at University of Michigan. J Nucl Med. 1984;25:1287–93.
21. Verkooijen RB, Stokkel MP, Smit JW, Pauwels EK. Radioiodine-131 in differentiated thyroid cancer: a retrospective analysis of an uptake-related ablation strategy. Eur J Nucl Med Mol Imaging. 2004;31:499–506.
22. Silberstein EB. Comparison of outcomes after (123)I versus (131)I pre-ablation imaging before radioiodine ablation in differentiated thyroid carcinoma. J Nucl Med. 2007;48:1043–6.
23. Dutch Endocrine Society and Society of Nuclear Medicine. Nationwide Guideline Thyroid Carcinoma. 2008. http://oncoline.nl/index.php?pagina=/richtlijn/item/pagina.php%20h&richtlijn_id=554. Updated 2008, cited 6.9.2011.
24. Hay ID, Thompson GB, Grant CS, Bergstralh EJ, Dvorak CE, Gorman CA, et al. Papillary thyroid carcinoma managed at the Mayo Clinic during six decades (1940–1999): temporal trends in initial therapy and long-term outcome in 2444 consecutively treated patients. World J Surg. 2002;26:879–85.
25. Sherman SI, Brierley JD, Sperling M, Ain KB, Bigos ST, Cooper DS, et al. Prospective multicenter study of thyroid carcinoma treatment: initial analysis of staging and outcome. National Thyroid Cancer Treatment Cooperative Study Registry Group. Cancer. 1998;83:1012–21.
26. Wittekind C, Compton CC, Greene FL, Sobin LH. TNM residual tumor classification revisited. Cancer. 2002;94:2511–6.
27. Edge SB, Byrd DR, Compton CC, Fritz AG, Greene FL, Trotti A, editors. AJCC cancer staging manual. 7th ed. New York: Springer; 2010.
28. Francis Z, Schlumberger M. Serum thyroglobulin determination in thyroid cancer patients. Best Pract Res Clin Endocrinol Metab. 2008;22:1039–46.
29. Taylor T, Specker B, Robbins J, Sperling M, Ho M, Ain K, et al. Outcome after treatment of high-risk papillary and non-Hurthle-cell follicular thyroid carcinoma. Ann Intern Med. 1998;129:622–7.
30. Durante C, Haddy N, Baudin E, Leboulleux S, Hartl D, Travagli JP, et al. Long-term outcome of 444 patients with distant metastases from papillary and follicular thyroid carcinoma: benefits and limits of radioiodine therapy. J Clin Endocrinol Metab. 2006;91:2892–9.
31. Jonklaas J, Sarlis NJ, Litofsky D, Ain KB, Bigos ST, Brierley JD, et al. Outcomes of patients with differentiated thyroid carcinoma following initial therapy. Thyroid. 2006;16:1229–42.
32. Pacini F, Schlumberger M, Dralle H, Elisei R, Smit JW, Wiersinga W. European consensus for the management of patients with differentiated thyroid carcinoma of the follicular epithelium. Eur J Endocrinol. 2006;154:787–803.
33. BTA, RCP. British Thyroid Association Royal College of Physicians. Guidelines for the management of thyroid cancer 2007, 2nd edn.; 2007. http://www.british-thyroid-association.org. Updated 2007, cited 6.9.2011
34. Kusic Z, Jukic T, Dabelic N, Franceschi M. Croatian Thyroid Society guidelines for the management of patients with differentiated thyroid cancer. Lijec Vjesn. 2008;130:213–27.
35. Cooper DS, Doherty GM, Haugen BR, Kloos RT, Lee SL, Mandel SJ, et al. Revised American Thyroid Association management guidelines for patients with thyroid nodules and differentiated thyroid cancer. Thyroid. 2009;19:1167–214.
36. Kulkarni K, Van Nostrand D, Atkins F, Aiken M, Burman K, Wartofsky L. The relative frequency in which empiric dosages of radioiodine would potentially overtreat or undertreat patients who have metastatic well-differentiated thyroid cancer. Thyroid. 2006;16:1019–23.
37. Tuttle RM, Leboeuf R, Robbins RJ, Qualey R, Pentlow K, Larson SM, et al. Empiric radioactive iodine dosing regimens frequently exceed maximum tolerated activity levels in elderly patients with thyroid cancer. J Nucl Med. 2006;47:1587–91.
38. Sgouros G, Hobbs RF, Atkins FB, Van Nostrand D, Ladenson PW, Wahl RL. Three-dimensional radiobiological dosimetry (3D-RD) with 124I PET for 131I therapy of thyroid cancer. Eur J Nucl Med Mol Imaging. 2011;38(Suppl 1):S41–7.
39. Lassmann M, Reiners C, Luster M. Dosimetry and thyroid cancer: the individual dosage of radioiodine. Endocr Relat Cancer 2010 3;17(3): R161–72.
40. de Klerk JM. 131I therapy: inpatient or outpatient? J Nucl Med. 2000;41:1876–8.
41. Nakada K, Ishibashi T, Takei T, Hirata K, Shinohara K, Katoh S, et al. Does lemon candy decrease salivary gland damage after radioiodine therapy for thyroid cancer? J Nucl Med. 2005;46(2):261–6.
42. Van Nostrand D. The benefits and risks of I-131 therapy in patients with well-differentiated thyroid cancer. Thyroid. 2009;19(12):1381–91.