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Analysis of malignancy predictors for follicular thyroid tumors

Analiza prediktora maligniteta folikulskih tumora štitaste žlezde

Goran V. Zorić*, Marina M. Nikolić-Djurović†‡, Ivan R. Paunović*†, Aleksandar D. Diklić*†, Zoran M. Bukumirić†§, Nikola A. Slijepčević*†, Katarina M. Taušanović*†, Božidar A. Odalović*, Milan D. Jovanović*, Vladan R. Živaljević*†

Clinical Centre of Serbia, *Centre for Endocrine Surgery, ‡Clinic for Endocrinology, Diabetes and Metabolic Diseases, Belgrade, Serbia; University of Belgrade, †Faculty of Medicine, §Institute for Medical Statistics and Informatics, Belgrade, Serbia

Abstract

Background/Aim. Establishing a preoperative diagnosis of thyroid follicular tumors is difficult due to the fact that the cell morphology of adenomas and carcinomas are similar and that capsular and vascular invasion cannot be determined by cytology. We analyzed predictive factors of follicular carcinoma in order to enable a surgeon to indicate operative treatment and to perform an adequate operation for each patient with a follicular neoplasm. **Methods.** In this retrospective study, we analyzed medical records of all patients with follicular thyroid tumors operated at an endocrine surgery unit of a tertiary referral academic hospital, between 2008 and 2012. A total of 263 operated patients were included and divided into follicular adenomas (n = 97) and follicular carcinomas (n = 166) based on the histopathology results. The most important demographic and clinical characteristics were analyzed by univariate and multivariate logistic regression analysis. **Results.** In adenoma group (19 males, 78 females) age range was 19–79, mean age 50. In carcinoma group (35 males, 131 females) age range was 15–78, mean age 48. Univariate analysis showed that thyroglobulin concentration ≥ 500 ng/mL, tumor diameter < 30 mm, presence of more than one thyroid nodule and an afunctional/hypofunctional nodule were significantly more frequent in follicular carcinoma than in follicular adenoma. Independent predictive factors of malignancy were: elevated preoperative thyroglobulin concentration (≥ 500 ng/mL) and presence of more than one nodule. Based on our results we formed a nomogram, a two-dimensional diagram designed to enable estimation of preoperative probability of malignancy. **Conclusion.** Elevated preoperative thyroglobulin concentration, ≥ 500 ng/mL, and the presence of more than one nodule are independent predictors of malignancy for follicular thyroid carcinomas.

Key words:
thyroid neoplasms; diagnosis; diagnosis, differential; thyroidectomy; thyroglobulin; nomograms.

Apstrakt

Uvod/Cilj. Prema raspoloživim dijagnostičkim metodama nije moguće preoperativno razlikovati benigne od malignih folikulskih tumora štitaste žlezde, a najčešće ni intraoperativno zbog veoma slične ćelijske morfologije folikulskih adenoma i folikulskih karcinoma i nemogućnosti citološkog dokaza invazije kapsule ili krvnih sudova karakteristične za folikulske karcinome. U ovoj studiji, istraživali su se mogući prediktivni faktori maligniteta kod bolesnika s folikulskim karcinomom štitaste žlezde koji bi omogućili ispravnu selekciju bolesnika za hirurško lečenje, a potom i izvođenje adekvatnog tipa operacije kod bolesnika s folikulskom tireoidnom neoplazmom. **Metode.** Ovom retrospektivnom studijom su obuhvaćeni svi bolesnici operisani zbog postojanja folikulskog tumora štitaste žlezde u tercijarnoj univerzitetskoj zdravstvenoj ustanovi endokrine hirurgije, tokom petogodišnjeg perioda (2008–2012). U istraživanje su bila uključena 263 operisana bolesnika. Na osnovu definitivnog histopatološkog nalaza ispitanici su bili podeljeni u dve grupe: folikulske adenome (n = 97) i folikulske karcinome (n = 166). Najvažnije demografske i kliničke karakteristike operisanih bolesnika analizirane su univarijantnom i multivarijantnom logističkom regresionom analizom. **Rezultati.** U grupi bolesnika operisanih zbog folikulskog adenoma (19 osoba muškog i 78 ženskog pola) starosna dob je iznosila 19–79 godina s prosečnom starošću od 50 godina. U grupi bolesnika operisanih zbog folikulskog karcinoma (35 muških, 131 ženska osoba) starosna dob je bila u rasponu 15–78 godina, a prosečna starost 48 godina. Univarijantnom analizom pokazano je da se koncentracija tireoglobulina ≥ 500 ng/mL, promer tumora < 30 mm, prisustvo više od jednog

Correspondence to: Goran Zorić, Centre for Endocrine Surgery, Clinical Centre of Serbia, Koste Todorovića 8, 11 000 Belgrade, Serbia. E-mail: goranvanjazoric@gmail.com

tireoidnog čvora i nalaz afunkcijskog/hipofunkcijskog čvora značajno češće nalaze kod folikulskog karcinoma u odnosu na folikulski adenom. Nezavisni prediktivni faktori maligniteta bili su povišena preoperativna koncentracija tireoglobulina (≥ 500 ng/mL) i prisustvo više od jednog čvora. Ovi rezultati su, u cilju primene u praksi, prikazani i nomogramom, dvodimenzionalnim dijagramom dizajniranim da omogući približno preoperativno grafičko izračunavanje verovatnoće postojanja maligniteta. **Zaključak.** Povišena preoperativna koncentracija tireoglobulina, ≥ 500 ng/mL, i prisustvo više od jednog čvora su nezavisni prediktori maligniteta folikulskih karcinoma štitaste žlezde.

Ključne reči:
tireoidna žlezda, neoplazme; dijagnoza; dijagnoza, diferencijalna; tireoidektomija; tireoglobulin; nomogrami.

Introduction

Primary thyroid malignancies, according to their cell origin are divided into two groups: larger, from follicular cells (papillary, follicular, oxyphilic and anaplastic carcinoma – more than 90%) and smaller, which originate from C-cells (medullary carcinoma, less than 10%).

The aim of the modern medicine is to know the nature of the tumor preoperatively or at least intraoperatively. The best tests to predict malignancy and the need for surgery in patients with thyroid nodules are fine-needle aspiration biopsy (FNAB) and measurement of serum calcitonin for medullary cancer. The reported accuracy of FNAB ranges from 70–90%. It is useful in the diagnostics of goiter, some benign thyroid tumors (like colloid adenoma or cysts), papillary and anaplastic carcinoma; but it is not reliable in distinguishing benign from malignant follicular and Hurthle-cell neoplasms.

Follicular adenoma and follicular carcinoma give the same cytological diagnosis – follicular lesion that includes both, benign follicular tumors (adenomas) and malignant (follicular carcinomas and follicular variant of papillary cancer). The role of the intraoperative frozen-section examination is controversial for those two types of thyroid tumor, too.

Consequently, it is difficult to establish a correct preoperative diagnosis for follicular tumors because of a very similar benign and malignant cytological morphology and because of the fact that capsular and vascular invasion cannot be verified by cytological examination [1]. Up to 70% of these patients with a diagnosis of follicular lesion undergo surgery for benign disease with risk of surgical complications. The need for a thyroidectomy completion increases the risk of complications and the costs [2, 3].

Malignant follicular neoplasms include follicular carcinoma and the follicular variant of papillary carcinoma. Follicular carcinoma is rare, but the follicular variant of papillary cancer is more often present on histopathology findings thus it has a bigger differential diagnostic and clinical importance.

In this study, we looked for possible predictive factors of malignant follicular neoplasms in order to enable a surgeon to indicate operative treatment and to perform an adequate operation for each patient with a follicular neoplasm.

Methods

In this retrospective study, we analyzed medical records of all patients with follicular tumors of the thyroid operated at an endocrine surgery unit of a tertiary referral academic hospital, in a five-year period (2008–2012). The study was approved by the Ethic Committee of the tertiary referral university hospital. A total of 263 patients were included and divided, on the basis of definite histopathology, into two groups: 1) follicular adenomas (97 patients) and 2) follicular carcinomas and follicular variant of papillary cancer (166 patients – 11 follicular carcinomas and 155 patients with follicular variant of papillary cancer). The most important demographic and clinical characteristics were analyzed (n = 34) including gender (male/female), age (≤ 50/> 50 years), smoking (smokers/nonsmokers), duration of disease (> 60/≤ 60 months), type of operation, tumor diameter (< 30/≥ 30 mm), type of nodule (dominant, non-dominant/solitary), multifocality of the tumor (yes/no), microcalcifications (yes/no), echostructure (iso-, hyper-, heteroechoic/hypoechoic), vascularization of nodule (irregular/regular), scintigraphy (afunctional and hypofunctional/functional and hyperfunctional), thyroid functional status (hypothyroid, euthyroid, hyperthyroid), level of serum thyroglobulin (≥ 500/< 500 ng/mL), anti-thyreoglobulin (Tg) antibodies (increased/normal), anti-thyroperoxidase (TPO) antibodies (increased/normal), coexisting benign thyroid diseases (yes/no), coexisting Hashimoto thyroiditis (yes/no), coexisting Graves' disease (yes/no), coexisting multinodular goiter (yes/no), coexisting thyroid adenoma (yes/no), coexisting malign thyroid diseases (yes/no), coexisting oxyphilic carcinoma (yes/no), coexisting papillary carcinoma (yes/no), coexisting micropapillary carcinoma (yes/no), coexisting malignant tumors of other organs (yes/no), presence of arterial hypertension (yes/no), diabetes mellitus (yes/no), ABO, Rh, presence of benign (yes/no) and malignant (yes/no) family thyroid diseases and other malignant family diseases (yes/no). Dichotomy of continuing variables was made on the base of data distribution and referral literature value.

The Cox regression model was used in statistical data processing. All the variables were tested by univariate logistic regression analysis and those with $p < 0.05$ were included in the multivariate logistic regression analysis to test for independence in the prediction of malignancy with a 95% confidence interval (CI) for the odds ratio (OR). A p value < 0.05 was considered as statistically significant. Based on our results we formed a nomogram, a two-dimensional diagram designed to enable calculation of preoperative probability of malignancy. The software package SPSS 12.0 for windows was used for all statistical analyses.

Results

Over the study period, there were 263 patients who underwent surgical treatment: 97 (36.9%) with benign histology of follicular adenoma and 166 (63.1%) with malignant

histology of follicular carcinoma (n = 11) or follicular variant of papillary carcinoma (n = 155). Results are presented in Tables 1 to 3.

Table 1
Demographic and clinical characteristics of all patients

Characteristics	Adenoma	Carcinoma
	n (%)	n (%)
Gender		
male	19 (19.6)	35 (21.1)
female	78 (80.4)	131 (78.9)
Age (years)		
≤ 30	12 (12.4)	21 (12.7)
31–40	15 (15.5)	37 (22.3)
41–50	18 (18.6)	36 (21.7)
51–60	26 (26.8)	41 (24.7)
61–70	21 (21.6)	20 (12.0)
≥ 71	5 (5.2)	11 (6.6)
Smoking		
smokers	24 (32.4)	45 (36.6)
former smokers	15 (20.3)	18 (14.6)
nonsmokers	35 (47.3)	60 (48.8)
Disease duration (months)		
≤ 11.9	13 (13.8)	35 (22.3)
12–35.9	19 (20.2)	27 (17.2)
36–59.9	15 (16.0)	27 (17.2)
60–119.9	21 (22.3)	26 (16.6)
120–239.9	16 (17.0)	28 (17.8)
Thyroid functional status		
hypothyroidism	4 (4.1)	8 (4.8)
euthyroidism	85 (87.6)	147 (89.1)
hyperthyroidism	8 (8.2)	10 (6.1)
Thyroglobulin (ng/mL)		
≥ 500	3 (5.4)	19 (17.1)
< 500	53 (94.6)	92 (82.9)
Anti-Tg antibodies		
increased	8 (18.6)	22 (21.4)
normal	35 (81.4)	81 (78.6)
Anti-TPO antibodies		
increased	10 (24.4)	23 (26.4)
normal	31 (75.6)	64 (73.6)
Type of operation		
hemithyroidectomy	44 (45.4)	46 (27.7)
lobectomy with partial resection	0 (0.0)	5 (3.0)
near-total thyroidectomy	5 (5.2)	11 (6.6)
thyroidectomy with/without dissection.	48 (49.5)	104 (62.7)

Anti-TPO antibodies – antithyroperoxidase antibodies; Anti-Tg antibodies – anti-thyroglobulin antibodies.

In the adenoma group (19 males, 78 females) age ranged from 19 to 79 with a mean age of 50 years. In the carcinoma group (35 males, 131 females) age ranged from 15–78 with a mean age of 48 years. The mean tumor diameter in the adenoma group was 37.5 mm (median 36, range 12–150 mm) and 33.4 mm (median 30, range 3–90 mm) in the carcinoma group. The mean preoperative level of thyroglobulin in the adenoma group was 226.6 ng/mL, and 320.3 ng/mL in the carcinoma group.

Table 2
Tumor characteristics in all patients

Characteristics	Adenoma	Carcinoma
	n (%)	n (%)
Tumor diameter (mm)		
< 30	43 (44.3)	98 (59.0)
≥ 30	54 (55.7)	68 (41.0)
Type of nodule		
solitary	56 (57.7)	71 (43.0)
dominant	35 (36.1)	65 (39.4)
non-dominant	6 (6.2)	29 (17.6)
Multifocal tumor		
no (unifocal)	94 (97.9)	112 (67.9)
two tumors	0 (0.0)	34 (20.6)
three tumors	2 (2.1)	19 (11.5)
Microcalcifications		
yes	13 (14.4)	32 (20.1)
no	77 (85.6)	127 (79.9)
Ehostructure		
isoechoic	10 (14.7)	14 (12.7)
hyperechoic	7 (10.3)	6 (5.5)
hypoechoic	19 (27.9)	38 (34.5)
heteroechoic	32 (47.1)	52 (47.3)
Nodule vascularisation		
regular	39 (84.8)	65 (75.6)
irregular	7 (15.2)	21 (24.4)
Scintigraphy		
afunctional	29 (50.9)	56 (71.8)
hypofunctional	15 (26.3)	18 (23.1)
functional	3 (5.3)	0 (0.0)
hyperfunctional	10 (17.5)	4 (5.1)

Patients in the carcinoma group significantly more often had more than one nodule ($p = 0.012$) below 30 mm in diameter ($p = 0.021$), afunctional on scintigraphy ($p < 0.01$), serum thyroglobulin level ≥ 500 ng/mL ($p = 0.045$) and coexisting thyroid adenomas ($p < 0.01$).

Coexisting malignant thyroid diseases ($p < 0.01$), thyroid micropapillary ($p = 0.027$) and papillary carcinomas ($p < 0.01$) were significantly more frequent in the group of adenomas.

There were no significant differences between these two groups regarding gender, age, smoking, disease duration, consistence of nodule, microcalcifications, echostructure, nodule vascularization, thyroid functional status, levels of anti-Tg and anti-TPO antibodies, coexisting benign thyroid diseases (Hashimoto thyroiditis, Graves' disease, nodular and multinodular goiter), coexisting oxyphilic carcinoma and malignant tumors of other organs, arterial hypertension, diabetes mellitus, ABO, Rh, benign and malignant family thyroid diseases and other malignant diseases in family.

All variables that can be preoperatively determined were included in the univariate regression analysis. Results are presented in Table 4.

Univariate analysis showed that thyroglobulin concentration greater or equal than 500 ng/mL, tumor diameter < 30 mm, presence of more than one thyroid nodule and an afunctional/hypofunctional nodule on scintigraphy were significantly more frequent in patients with follicular carcinoma compared to patients with follicular adenoma.

Table 3
Coexisting thyroid and other diseases in all patients

Coexisting diseases	Adenoma	Carcinoma
	n (%)	n (%)
Benign thyroid diseases		
yes	56 (57.7)	115 (69.3)
no	41 (42.3)	51 (30.7)
Hashimoto thyreoiditis		
yes	16 (16.5)	18 (10.8)
no	81 (83.5)	148 (89.2)
Graves disease		
yes	0 (0.0)	4 (2.4)
no	97 (100.0)	162 (97.6)
Nodular/multinodular goiter		
yes	38 (39.2)	49 (29.5)
no	59 (60.8)	117 (70.5)
Thyroid adenoma		
yes	2 (2.1)	44 (26.5)
no	95 (97.9)	122 (73.5)
Malign thyroid diseases		
yes	25 (25.8)	10 (6.0)
no	72 (74.2)	156 (94.0)
Oxyphilic carcinoma		
yes	2 (2.1)	1 (1.6)
no	95 (97.9)	165 (99.4)
Papillary carcinoma		
yes	12 (12.4)	2 (1.2)
no	85 (87.6)	164 (98.8)
Micropapillary carcinoma		
yes	11 (11.3)	7 (4.2)
no	86 (88.7)	159 (95.8)
Malignant tumors of other organs		
yes	4 (4.1)	3 (1.8)
no	93 (95.9)	163 (98.2)
Arterial hypertension		
yes	42 (43.3)	61 (36.7)
no	55 (56.7)	105 (63.3)
Diabetes mellitus		
yes	4 (4.1)	14 (8.4)
no	93 (95.9)	152 (91.6)
ABO		
A	26 (36.6)	59 (41.3)
B	11 (15.5)	26 (18.2)
AB	2 (2.8)	8 (5.6)
0	32 (45.1)	50 (35.0)
Rh		
positive	61 (87.1)	117 (81.8)
negative	9 (12.9)	26 (18.2)
Benign thyroid diseases (family)		
yes	24 (25.0)	30 (18.2)
no	72 (75.0)	135 (81.8)
Malignant thyroid diseases (family)		
yes	2 (2.1)	7 (4.3)
no	92 (97.9)	157 (95.7)
Other malignant diseases (family)		
yes	9 (9.6)	14 (8.6)
no	85 (90.4)	148 (91.4)

All variables with a p value < 0.05 were included in the multivariate logistic regression model (Table 5). Independent predictive factors were elevated preoperative thyroglobulin concentration, ≥ 500 ng/mL, and a presence of more than one nodule. Scintigraphy findings were excluded from analysis because of a small number of patients with them. The whole model with all predictors was statistically significant ($p < 0.001$). There was no significant multi-collinearity among the predictors.

According to multivariate regression analysis, statistically significant predictors for follicular thyroid cancer were: type of nodule (dominant and non-dominant/solitary) (OR = 2.71, 95% CI 1.36–5.38), which means that patients with more than one nodule have almost three times a bigger chance to have follicular cancer in relation to patients with a solitary nodule; preoperative serum thyroglobulin concentration ≥ 500 ng/mL with OR = 4.18, 95% CI 1.14–15.33. Patients with Tg ≥ 500 ng/mL had over four times a bigger chance for follicular cancer.

Based on our results we formed a nomogram, a two-dimensional diagram designed to enable calculation of preoperative probability of malignancy (Figure 1). It may help to improve clinical management of patients with follicular lesions.

Discussion

The incidence of malignancy in patients with thyroid follicular tumors lies between 12% and 30% [4–7]. In our study it was 63.1%. The research of Paramo and Mesko [8] (71 patients with follicular neoplasm) showed that the incidence of malignancy was 13% in men and 13% in women. In the study of Petric et al. [9], the malignancy rate was 43% in males and 23% in female patients with follicular and Hurthle cell neoplasms with a diameter of 2 cm or less.

The frozen section findings and FNAB are not a reliable method for distinguishing between benign a malignant follicular nodules. The discrimination between follicular adenoma and carcinoma can only be made postoperatively. Possible predictive factors of follicular carcinoma can help a surgeon to indicate operative treatment and to perform an adequate operation for each patient with a follicular thyroid neoplasm.

Average age of our patients was similar in both groups (adenoma group 48 years, carcinoma group 50 years). Our findings extend previous reports that age and gender are not predictive factors of malignancy [4, 5, 7, 8, 10, 11], but the findings of Petric et al. [9] were the opposite, where male patients had a higher risk of carcinoma. Similar result regarding sex reported Reparia et al. [12], but they also reported that age of the patient was not a predictor of malignancy. Unlike this, according to the research of Paramo and Mesko [8] age ≤ 45 years was a predictive parameter of malignancy in follicular neoplasm of the thyroid.

In the present study, univariate analysis showed that a tumor diameter < 30 mm was significantly more frequent in patients with follicular carcinoma.

Table 4

Univariate regression analysis

Independent variable	*p*	OR	95% CI	
Gender (male/female)	0.772	0.91	0.49	1.70
Age	0.195	0.99	0.97	1.01
Age (50 years)	0.109	0.66	0.40	1.10
Smoking (smokers/nonsmokers)	0.840	0.94	0.53	1.68
Disease duration (> 60/≤ 60 months)	0.399	0.80	0.48	1.34
Tumor diameter (< 30 mm/≥ 30 mm)	**0.022**	1.81	1.09	3.00
Type of nodule (dominant and non-dominant/solitary)	**0.022**	1.81	1.09	3.00
Microcalcifications (yes/no)	0.265	1.49	0.74	3.02
Echostructure (iso, hyper, heteroechoic/hypoechoic)	0.360	0.73	0.38	1.42
Nodule vascularization (irregular/regular)	0.222	1.80	0.70	4.62
Scintigraphy (afunctional and hypofunctional/functional and hyperfunctional)	**0.005**	5.47	1.68	17.81
Thyroid functional status	0.501	0.77	0.37	1.63
Serum Tg	0.157	1.00	1.00	1.00
Serum Tg (≥ 78 ng/mL/< 78 ng/mL)	0.672	1.16	0.59	2.28
Serum Tg (≥ 500 ng/mL/< 500 ng/mL)	**0.045**	3.65	1.03	12.91
Anti-TPOAb (positive/negative)	0.805	1.11	0.47	2.63
Coexisting Hashimoto thyroiditis. (yes, no)	0.190	0.62	0.30	1.27
Coexisting goiter (yes, no)	0.109	0.65	0.38	1.10
Coexisting Graves' disease (yes, no)	0.999	-	-	-
Arterial hypertension (yes, no)	0.294	0.76	0.46	1.27
Diabetes mellitus (yes, no)	0.191	2.14	0.68	6.70

OR – odds ratio; CI – confidence interval; Tg – thyreoglobulin; Anti TPOAb – antithyreoperoxidase antibodies.
Note: statistically significant values are bolded.

Table 5

Multivariate regression analysis

Independent variable	*p*	OR	95% CI	
Tumor diameter (< 30 mm / ≥ 30 mm)	0.063	1.92	0.96	3.83
Type of nodule (dominant and non-dominant/solitary)	0.004	2.71	1.36	5.38
Thyroglobulin (≥ 500 ng/mL/< 500 ng/mL)	0.031	4.18	1.14	15.33

OR – odds ratio; CI – confidence interval.

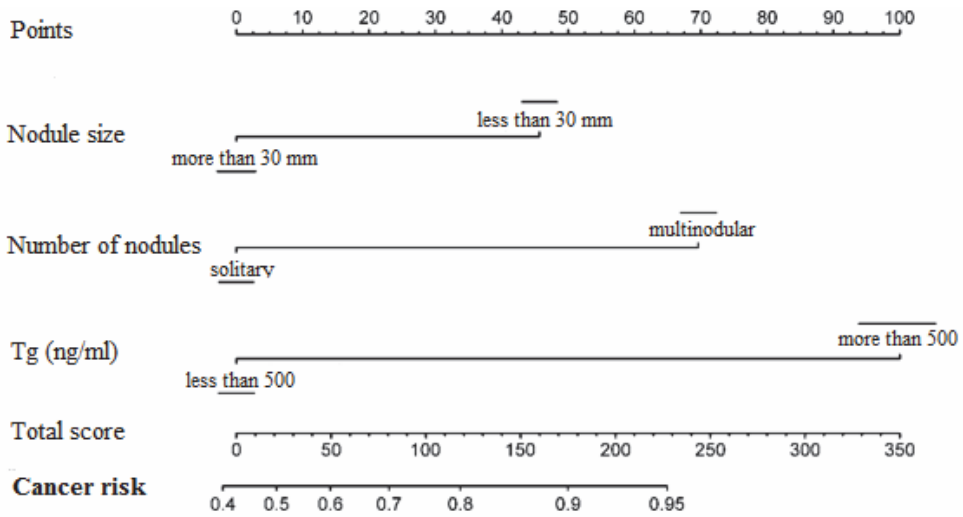

Fig. 1 – Nomogram-preoperative probability of malignancy for follicular thyroid tumors.

The diameter of follicular tumors as a predictive factor for carcinoma has been mentioned in literature many times [1, 9, 12, 13]. In the study of 616 patients with follicular adenoma, follicular carcinoma and follicular variant of papillary cancer, nodules ≥ 4 cm were associated with increased odds of a benign lesion which is in correlation to our research. In the same study, a family history of thyroid cancer was associated with increased odds of malignancy which was not proven in our study [10]. Paramo and Mesko [8] reported that a tumor > 4 cm is a predictive parameter of malignancy in follicular neoplasms. Gulcelik et al. [2] in their study of 98 patients with follicular neoplasm did not find a statistical significance, although the mean nodule size was slightly larger in malignant nodules. Risk of malignancy was higher in nodules measuring 2 cm or larger according to the results of Reparia et al. [12]. In the study of Petric et al. [9] the tumor diameter did not correlate with the malignancy rate. Tumor volume was found to be an independent predictor for follicular thyroid cancer (FTC) in all patients with a cytological diagnosis of follicular lesion [14].

Adenomas are usually solitary, less than 3 cm, but a significant numbers of exceptions exist [15]. In our study, univariate analysis showed that the presence of more than one thyroid nodule was significantly more frequent in patients with follicular carcinoma and it was an independent predictive factor in the multivariate logistic regression model. Gulcelik et al. [2] published similar results, in their study the presence of a solitary nodule was not predictive for malignancy. Unlike this, Najafian et al. [16] came out with data that multinodularity on physical examination was associated with an increased odds of a benign lesion.

Deviation of our results regarding incidence of malignancy, tumor size and type of nodule may be caused by a minority of follicular carcinomas in regard to the number of follicular variant of papillary carcinomas in the carcinoma group.

Serum thyroglobulin is primarily used in the postoperative cancer monitoring for differentiated thyroid carcinomas, but it could indicate differentiated cancer with controversial usefulness. In our study, the mean preoperative thyroglobulin level in the adenoma group was 226.6 ng/mL and 320.3 ng/mL in the carcinoma group. Thyroglobulin level over 500 ng/mL were significantly more frequent in patients with follicular carcinoma. Patients with thyroglobulin level over 500 ng/mL have over four times a bigger chance to have cancer. Petric at al. [9] showed that patients with a preoperative thyroglobulin values over 80 ng/mL had a malignancy rate of 35%, while in those with a lower level it was 19%. Several investigators published that there is a higher level of preoperative thyroglobulin in patients with well differentiated thyroid carcinomas compared to patients with benign goiters [17–19]. Kim et al. [14] showed that it was found to be an independent predictor for follicular cancer in all patients with a cytological diagnosis of a follicular lesion. On the other hand, Suh et al. [20] claimed that an elevated thyroglobulin level had no predictive value in follicular tumors, even in a high threshold value of 500 ng/mL.

The presence of hypoechoic solid features is generally considered to be the most reliable suspicious finding, but the value of ultrasonography is still controversial [21, 22]. Our results didn't confirm that echostructure (hypoechoic nodule) and the presence of microcalcifications had a higher frequency of malignancy, although it was reported by many authors [2, 4, 5, 21, 22]. Calò et al. [10] published, in accordance with our research, that the presence of microcalcifications was not significantly associated with malignancy. The results of Zdon et al. [11] also showed that the disease duration was not a significant predictor of malignancy.

Interestingly, coexisting primary hyperparathyroidism was not found in any of the 263 patients. Out of the 4,033 patients who underwent thyroidectomy at our institution from 2009–2014, in 114 (2.8%) a parathyroidectomy was simultaneously performed. Out of these 114 patients, 42 (37 %) had normocalcaemic primary hyperparathyroidism [23].

One of the main limitations of our study was the low rate of patients with follicular carcinoma, but it is considered a rare tumor. To overcome this limitation it would be necessary to analyze a higher number of such patients which would be possible through a multicentric study or in a longer period of time. On the other hand, the relatively short period where all operations were performed in one tertiary referral centre at a highly specialized endocrine surgery unit with thyroid expert pathologists and the uniformity of data can be considered a strength of the study.

Conclusion

According to our results, an elevated preoperative thyroglobulin concentration level, greater than or equal to 500 ng/mL, and the presence of more than one thyroid nodule are independent predictors of malignancy for follicular thyroid carcinomas. The nomogram presented in this study could help to improve the clinical management of patients with follicular thyroid lesions.

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