The Gold Standard of Thyroid Nodule Examination? Prospective Validation of the ACR TI-RADS in a Secondary Referral Center

Tereza GRIMMICHOVÁ[1,2], Petra PAČESOVÁ[1], Libuše SRBOVÁ[1], Jana VRBÍKOVÁ[1], Terezia HAVRDOVÁ[1], Martin HILL[1]

[1]Institute of Endocrinology, Prague, Czech Republic, [2]Second Department of Internal Medicine, University Hospital Královské Vinohrady and Third Faculty of Medicine, Charles University, Prague, Czech Republic

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Summary

The aim of this prospective study was the validation of the risk stratification of thyroid nodules using ultrasonography with the American College of Radiology Thyroid Imaging, Reporting and Data System (ACR TI-RADS) and partly in comparison to American Thyroid Association (ATA) guidelines in a secondary referral center. Fine needle aspiration biopsy (FNA) (n=605) and histological examinations (n=63) were the reference standards for the statistical analysis. ACR TI-RADS cut-off value: TR4 with sensitivity 85.7 %, specificity 54.1 %, PPV 58.5 %, accuracy 67.7 % (AUC 0.738; p<0.001). ATA cut-off value: "high suspicion" with sensitivity 80 %, specificity 83.3 %, PPV 80 %, accuracy 81.8 % (AUC 0.800; p=0.0025). 18.4 % nodules (3 malignant) could not be assigned to a proper ATA US pattern group (p<0.0001). Both ACR TI-RADS and ATA have allowed fair selection of nodules requiring FNA with superiority of ACR TI-RADS according to classification of all thyroid nodules to the proper group. According to ACR TI-RADS almost one third of the patients were incorrectly classified with 17.9 % missed thyroid carcinomas, exclusively micropapillary carcinomas, even though, the amount of FNA would be reduced to 48 %.

Key words

Thyroid nodule • Thyroid cancer • ACR TI-RADS • ATA • FNA

Corresponding author

T. Grimmichová, Institute of Endocrinology, Národní 8, Prague 1, 11694, Czech Republic. E-mail: tgrimmichova@endo.cz

Introduction

Thyroid nodules are common, with a reported prevalence of up to 68 % in adults on high-resolution ultrasound (Guth *et al.* 2009). Most nodules are benign, but it is crucial to correctly stratify the malignancy risk of nodules to avoid unnecessary invasive procedures and/or surgery but still identify aggressive tumors (Haugen *et al.* 2016).

Fine needle aspiration biopsy (FNA) is the gold standard for the examination of thyroid nodules, but with decreasing sensitivity in multinodular goiter, thyroid nodules >4 ml or follicular tumors (Haugen *et al.* 2016, Nabhan and Ringel 2017, Lasihiotakis *et al.* 2012). For the imaging of thyroid nodules, the gold standard is an ultrasound (US). It is crucial to choose an optimal system for risk stratification of thyroid nodules on ultrasonography for more accurate FNA. Thyroid nodule growth is not a certain predictor of malignancy, therefore various combinations of US features have been studied to differentiate benign and malignant thyroid nodules (Singh *et al.* 2016). In 2002, a combination of four US features was first reported by Kim *et al.* (2002), including microcalcifications, a taller-than-wide shape, irregular borders, and marked hypoechogenicity. Assessment of this combination was considered capable of diagnosing 94 % of thyroid carcinomas, especially PTC (Kim *et al.* 2002, Kratky *et al.* 2014). During the past decade, other US stratification systems have been introduced. In 2009, Horvath *et al.* first published the Thyroid Imaging Reporting and Data System (TIRADS). The grading

Fax +420 241 062 164, e-mail: physres@fgu.cas.cz, www.biomed.cas.cz/physiolres

concept is adapted along the lines of the Breast Imaging Reporting and Data System (BIRADS) that is internationally used in mammography. A score of 1 denotes a normal examination, whereas scores 2,3,4, and 5 correspond to a risk of malignancy of 0 %, <5 %, 5-80 %, and >80 %, respectively. It has been retrospectively and prospectively validated with histological results, with sensitivity, specificity, PPV, and NPV of 88 %, 49 %, 49 % and 88 %, respectively (Horvath *et al.* 2017).

Later, Russ *et al.* presented the French TIRADS system and recently EU-TIRADS, simplifying the original TIRADS (Russ 2017, Russ *et al.* 2017). Finally, the American College of Radiology introduced the point-based classification system ACR TI-RADS. ACR TI-RADS has included recommendations for FNA and follow-up depending on suspicious thyroid nodule features and thyroid nodule size. All TIRADS systems use a lexicon with clear definitions of sonographic features (Grant *et al.* 2015, Tessler *et al.* 2017). The goal of the present study is to validate ACR TI-RADS classification and partly American Thyroid Association (ATA) guidelines in a prospective cytological and surgical series, determining sensitivity, specificity, as well as predictive values allowing confirmation of its role in the management of the thyroid nodules in a low volume thyroid cancer center.

Materials and Methods

The protocol of this prospective study complied with the Declaration of Helsinki and before entering the study, written informed consent was obtained from patients after they received both written and oral information. The study was approved by the ethical committee of Institute of Endocrinology. The study group consisted of 560 patients, 488 women and 72 men in a country with iodine sufficiency (Bilek *et al.* 2020, Bilek *et al.* 2015). The patients were included in the study from March 2017 till December 2018. Basal blood samples for the determination of TSH, fT4, fT3, anti-thyroid peroxidase antibodies (anti-TPO), anti-thyroglobulin (anti-Tg), thyrotropin receptor antibodies (TRAbs) and calcitonin were taken. US, FNA, patient history, and biochemical testing were done at the Institute of Endocrinology and 2nd Department of Internal Medicine, University Hospital Kralovske Vinohrady. FNA was generally performed on thyroid nodule size >1 cm, 45 thyroid nodules were smaller than 1 cm. The thyroid nodules with US suspicious features as hypoechogenicity, irregular or microlobulated margins, taller-than-wide, punctate echogenic foci and solid components were preferentially chosen for FNA. In case of multiple nodules, the most suspicious one was considered. Thyroid nodules were within FNA procedure classified and recorded according to the ACR TI-RADS (n=605) and by ATA risk stratification criteria for thyroid nodule guidance (n=125). Part of the record is a predefined text with description of thyroid nodules localization, size, multiplicity, composition, echogenicity, margin, calcification, shape, and abnormal cervical lymph nodes. A diagram of the location of the thyroid nodules is added to the uniform reports; pointing out the nodule undergoing FNA. In this study, single US features were not evaluated. ACR TI-RADS and ATA thyroid nodule guidance were previously published (Haugen *et al.* 2016, Grant *et al.* 2015, Tessler *et al.* 2017). Briefly, since ACR TI-RADS is a scoring system, points are given for thyroid nodule composition, echogenicity, shape, margin and echogenic foci. It distinguishes 5 groups: TR1-benign, TR2-not suspicious, TR3-mildly suspicious, TR4-moderately suspicious, and TR5-highly suspicious. The ATA thyroid nodule guidance comprises 5 groups with an estimated risk of malignancy as follows: high suspicion (>70-90 %), intermediate suspicion (10-20 %), low suspicion (5-10 %), very low suspicion (<3 %) and benign (<1 %) (Haugen *et al.* 2016, Grant *et al.* 2015, Tessler *et al.* 2017). US was performed on a Phillips Epiq5 (L12-5 linear transducer); elastography was not used in this study.

US-guided FNA of one thyroid nodule was performed in 560 patients and FNAs of two thyroid nodules in the same patient were performed in 47 patients. FNA was performed once for each thyroid nodule by using a 20-gauge needle attached to a 20 ml syringe. Local anesthesia was not applied. Aspirated material was expelled on glass slides and sent for cytopathology examinations. May-Grünwald/Giemsa and hematoxylin and eosin stained specimens were evaluated by expert cytopathologists following the Bethesda System for Reporting Thyroid Cytopathology (TBSRTC) 2017: (I) nondiagnostic or unsatisfactory; (II) benign; (III) atypia of undetermined significance (AUS) or follicular lesion of undetermined significance (FLUS); (IV) follicular neoplasm or suspicious for a follicular neoplasm; (V) suspicious for malignancy; and (VI) malignant (Cibas and Ali 2017). We excluded all thyroid nodules Bethesda I category (n=17; 2.8 %).

To date, histological examination has been done in 63 patients, with 28 findings being malignant (4.6 %) and 35 benign. The thyroidectomy specimens were fixed in formalin and sent to the pathology without information on the US pattern nor TIRADS/ATA category. Standardly, shape, size, color, consistency, presence of capsule, calcification and localization within the gland were recorded for each nodule.

Serum TSH, fT4, fT3, TRAbs, and calcitonin concentrations were measured using the ECLIA method (Roche). Serum anti-Tg and anti-TPO were measured by ELISA (Aeskulisa).

Statistical analysis

All data are given as re-transformed means with 95 % confidence intervals. One-way ANOVA followed by Bonferroni multiple comparisons was used to evaluate differences between groups, and ROC analysis was used to find cut-off values for FNA, ACR TI-RADS and ATA. Afterwards, sensitivity, specificity, positive predictive value (PPV) and area under the curve (AUC) were calculated. The analysis was applied separately on both cytological and histological results. Fisher´s two-tailed exact test was used for evaluation of correlations between dichotomous variables. Due to the non-Gaussian data distribution and the non-constant variance in tested parameters, the original continuous variables for the analysis were transformed by power transformations prior to further processing to attain data symmetry and homoscedasticity (Meloun *et al.* 2000). The transformed data was tested for data symmetry, homoscedasticity and homogeneity using residual analysis as described elsewhere (Meloun *et al.* 2002). Statistical significance was set for p-values <0.05. Statgraphics Centurion 18 software from Statpoint (The Plains, VA, USA) was used for the statistical analysis.

Results

The clinical, biochemical and US parameters of patients are given in Table 1. The group of patients (n=560) was divided into three groups depending on histologically proven results after thyroidectomy: malignant (M) (n=28), benign (B) (n=35) and non-surgery (N) (n=497).

Table 1. Clinical, biochemical and US parameters of patients (shown as re-transformed means with their 95% confidence intervals) after a Bonferroni correction.

Variables	**Malignant surgery** (M)	**Benign surgery** (B)	**Non-surgery** (N)	**Between-group differences** (ANOVA followed by Bonferroni multiple comparisons)
Age [years]	51.9 (46.3, 57.6)	50.4 (45.2, 55.7)	54.4 (53.3, 55.5)	F=1, p=0.353
BMI [kg/m^2]	27.4 (24.5, 30.9)	27.5 (25.0, 30.5)	26.7 (26.2, 27.3)	F=0.2, p=0.834
Thyroid volume [ml]	17.7 (14.2, 22.2)	19.5 (16.0, 23.9)	14.7 (14.2, 15.3)	F=3.8, p=0.024; B>N*
Thyroid nodule volume [ml]	3.56 (2.27, 5.77)	3.95 (2.57, 6.23)	1.69 (1.56, 1.84)	F=9.3, p<0.001; B>N**, M>N*
TSH (0.27-4.2) [mIU/l]	1.91 (1.43, 2.47)	1.71 (1.31, 2.16)	1.41 (1.31, 1.51)	F=2.2, p=0.118
fT4 (12.0-22.0) [pmol/l]	15.7 (14.7, 16.8)	15.6 (14.8, 16.6)	16.5 (16.3, 16.8)	F=1.9, p=0.145
fT3 (3.10-6.80) [pmol/l]	4.74 (4.47, 5.05)	4.84 (4.61, 5.11)	4.81 (4.73, 4.89)	F=0.1, p=0.903
anti-TPO (0.01-40.00) [IU/ml]	97 (21.7, 386)	6.31 (2.27, 16.60)	10.2 (7.99, 12.9)	F=3.5, p=0.032; M>B*, M>N*
anti-Tg (0.01-120.00) [IU/ml]	35.7 (8.21, 144)	0.97 (0.318, 2.83)	1.82 (1.38, 2.39)	F=6.1, p=0.003; M>B**, M>N**
TRAbs (0.30-1.75) [IU/l]	0.36 (0.316, 0.423)	0.394 (0.34, 0.477)	0.383 (0.361, 0.408)	F=0.3, p=0.746
Calcitonin (0.0-6.4) [ng/l]	2.53 (1.61, 4.44)	1.67 (1.06, 2.93)	1.03 (0.931, 1.15)	F=7.6, p<0.001; M>N**

*p<0.05, **p<0.01.

According to ACR TI-RADS TR1 denotes a risk of malignancy 1/80 (1.3 %), TR2 0/53, TR3 3/251 (1.2 %), TR4 11/183 (6 %) and TR5 13/40 (32.5 %) with significant differences between groups ($p<0.001$). According to ATA the risk of malignancy was for sonographic pattern benign 1/13 (7.7 %), very low 0/16, low suspicion 0/32, intermediate suspicion 1/21 (4.8 %), high suspicion 8/20 (40 %) and non-classified 3/23 (13 %) with significant differences between groups ($p=0.0014$). The results of Bethesda system for reporting thyroid cytopathology were in following categories (n=605): II 481 (79.5 %), III 68 (11.2 %), IV 23 (3.8 %), V 16 (2.7 %) and VI 17 (2.8 %). Up to date, histological examination was done in 64 patients, 28 findings were malignant (4.6 %) and 35 benign. The most common type of carcinoma was papillary 78.6 %. Further we had 1 follicular thyroid carcinoma, 1 medullary carcinoma, 2 anaplastic carcinomas, 1 poorly differentiated carcinoma and 1 metastasis.

FNA, ACR TI-RADS and ATA underwent statistical analysis to establish their sensitivity and specificity. Histologically proven results are shown as the reference standard. A cut-off value with the best fit curve was established for FNA, ACR TI-RADS and ATA. The FNA (n=605) cut-off value with the best fit curve was Bethesda V with sensitivity 82 %, specificity 84 %, PPV 79 %, NPV 86.1 %, accuracy 83.1 %, AUC=0.823, Youden's Index=0.659 ($p<0.001$) (Table 2). The ACR TI-RADS (n=605) cut-off value with the best fit curve was TR4 with sensitivity 85.7 %, specificity 54.1 %, PPV 58.5 %, NPV 83.3 %, accuracy 67.7 %, AUC 0.738, Youden's Index=0.39 ($p<0.001$) (Table 3 and Fig. 1). The ATA (n=125) cut-off value with the best fit curve was "high suspicion" group with sensitivity to 80 %, specificity 83.3 %, PPV 80 %, NPV 83.3 %, accuracy 81.8 %, AUC 0.800, Youden Index 0.633 ($p=0.0025$) (Table 4). 18.4 % nodules (3 malignant) could not be assigned to a proper ATA US pattern group. In the group of non-classified nodules were 2 PTC and 1 metastasis.

The interobserver agreement was evaluated in a subset of 38 nodules, and 2 experienced endocrinologists independently examined and rated US images available; absolute difference was 5.95 % and individual SD was 4.20 % as evaluated by ANOVA model consisting of factors observer and subject.

Table 2. FNA Bethesda cytological results with established sensitivity, specificity, PPV and accuracy.

Bethesda	**Sensitivity** (95 % CI)	**Specificity** (95 % CI)	**PPV** (%)	**Accuracy** (%)
II	100.0 (87.7-100.0)	5.4 (0.6-18.2)	44.4	46.2
III	89.3 (71.8-97.7)	27.0 (13.8-44.1)	48.1	53.9
IV	82.1 (63.1-93.9)	64.9 (47.5-79.8)	63.9	72.3
V	82.1 (63.1-93.9)	83.8 (68.0-93.8)	79.3	83.1
VI	50.0 (30.7-69.4)	94.6 (81.8-99.3)	87.5	75.4

PPV – positive predictive value (precision), 95 % CI confidence interval with lower and upper limits.

Table 3. ATA guidance for thyroid nodules with established sensitivity, specificity, PPV and accuracy.

ATA	**Sensitivity** (95 % CI)	**Specificity** (95 % CI)	**PPV** (%)	**Accuracy** (%)
Benign	100.0 (69.2-100.0)	0 (0-26.5)	45.5	45.5
Very low suspicion	90.0 (55.5-99.8)	0 (0-26.5)	42.9	40.9
Low suspicion	90.0 (55.5-99.8)	8.3 (0.2-38.5)	45.5	98.3
Intermediate suspicion	90.0 (55.5-99.8)	50.0 (21.1-78.9)	60.0	68.2
High suspicion	80.0 (44.4-97.5)	83.3 (51.6-97.9)	80.0	81.8

PPV – positive predictive value (precision), 95 % CI confidence interval with lower and upper limits.

Table 4. ACR TI-RADS with established sensitivity, specificity, PPV and accuracy.

ACR TI-RADS	Sensitivity (95 % CI)	Specificity (95 % CI)	PPV (%)	Accuracy (%)
TR1	100.0 (87.7-100.0)	0 (0-9.5)	43.1	43.1
TR2	96.4 (81.7-99.9)	5.4 (0.6-18.2)	43.6	44.6
TR3	96.4 (81.7-99.9)	18.9 (8.0-35.2)	47.4	52.3
TR4	85.7 (67.3-96.0)	54.1 (36.9-70.5)	58.5	67.7
TR5	46.4 (27.5-66.1)	83.8 (68.0-93.8)	68.4	67.7

PPV – positive predictive value (precision), 95 % CI confidence interval with lower and upper limits.

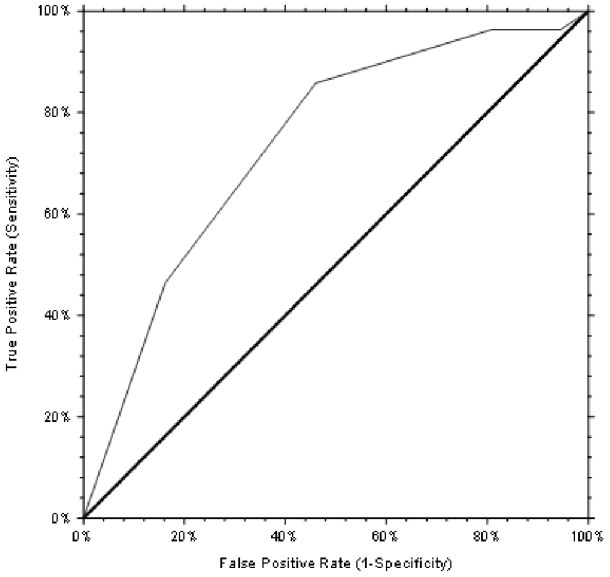

Fig. 1. ROC curve analysis of ACR TI-RADS with the best fit curve for TR4. Sensitivity=85.7 %, Specificity=54.1 %, PPV=58.5 %, NPV 83.3 %, AUC=0.738 (95 % CI 0.596-0.834), Youden Index 0.39; p<0.001 (n=65). PPV – positive predictive value, NPV – negative predictive value.

Discussion

It is suggested that screening is the most important driver of the epidemic of thyroid cancer, especially papillary thyroid microcarcinoma (PTMC) and particularly among females. Among the vast number of thyroid nodules detected, only 5-15 % is proved to be thyroid cancer. For these reasons, it is critical that the physician first determines if a nodule even requires further evaluation by FNA or observation (Vaccarella *et al.* 2016, Ahn *et al.* 2016, Roi *et al.* 2008). At this moment there are many and overlapping US risk stratification systems for guidance in assessing thyroid nodules. In this study we have chosen pattern-based ATA guidance, because in general we have been following ATA guidelines and the point-based ACR TI-RADS scoring system for standardized lexicon with clear and demonstrative explanation (Haugen *et al.* 2016, Grant *et al.* 2015, Tessler *et al.* 2017).

The study assessing differences between ATA, AACE/ACE/AME and ACR TI-RADS demonstrated the highest diagnostic performance for ACR TI-RADS, which was significantly superior to ATA (p=0.008) (Lauria *et al.* 2018). A study by Yoon *et al.* (2016) found that 44 of 1293 nodules (3.4 %) did not meet the criteria for the ATA patterns and were classified as not specified (Yoon *et al.* 2016). The ACR TI-RADS evaluations reduce the percentage of biopsies of benign nodules by more than twice as much as the other systems (52.9 % for ACR TI-RADS, 21.9 % for the ATA guidelines). The ACR TI-RADS criteria that allow for a reduction in the percentage of benign nodules that are biopsied would also be expected to result in a lower percentage of malignant nodules that are biopsied. This is unavoidable because there are some malignancies that have benign sonographic features. Typically, follicular thyroid cancer or uncommon variants of PTC can be solid nodule with various echogenicity, smooth margins and without microcalcifications. In study Middleton *et al.* (2018), biopsy would not have been recommended for 31.8 % of malignant nodules with the use of the ACR TI-RADS, compared with 24.1 % with use of the ATA. The goal of the classification system is to minimize the number of clinically significant cancers that are missed. Follow-up recommendations by ACR TI-RADS are advantageous and should result in later detection of some of the cancers that otherwise would have been overlooked (Middleton *et al.* 2018, Nguyen *et al.* 2018).

The risk of malignancy found in our study for each US ACR TI-RADS category was comparable except TR3 with previously published results by Middleton *et al.* (2018) TR1 (1.3 vs. 0.3 %; p=0.383 Fisher's exact test), TR2 (0 vs.1.5 %; p=1.0), TR 3 (1.2 vs. 4.8 %; p=0.008),

TR4 (6 vs. 9.1 %; p=0.206) and TR5 (32.5 vs. 35 % p=0.864) with a significant differences in malignancy risk between ACR TI-RADS groups (p<0.001).

In our study, FNA had the highest accuracy with sensitivity 82 %, specificity 84 %, PPV 79 %; the proportion of thyroid nodules correctly classified was 83.1 % and incorrectly classified 16.9 % (p<0.001). Both ACR TI-RADS and the ATA guidelines provide effective malignancy risk stratification for thyroid nodules. ATA had higher accuracy in comparison to ACR TI-RADS with sensitivity 80 %, specificity 83.3 %, PPV 80 %; the proportion of thyroid nodules correctly classified was 81.8 % and incorrectly classified 18.2 % (p=0.0025). As mentioned previously, 18.4 % nodules (13 % malignant) could not be assigned to a proper ATA US pattern group. Due to this fact, our study provided similar results as previous studies, with ACR TI-RADS giving improved results over ATA (p<0.0001). ACR TI-RADS had the lowest accuracy with sensitivity 85.7 %, specificity 54.1 %, PPV 58.5 %, the proportion correctly classified thyroid nodules was 67.7 % and incorrectly classified 32.3 %. Our results are comparable with previous published results from tertiary center with a prevalence of thyroid cancer reaching up to 50 % with sensitivity 92 %, specificity 44 % and accuracy 52 % (Middleton *et al.* 2018). If we have closely followed the ATA guidance, non-classified nodules were mixed cystic and solid iso/hyperechoic thyroid nodules with some other suspicious features as microlobulated margins, microcalcification, macrocalcifications, rim calcification and taller-than-wide shape. The number of thyroid nodules that could not be classified was much higher in our study, but supported by other studies (Middleton *et al.* 2018, Lauria *et al.* 2018). ACR TI-RADS offers US stratification system with a possibility to combine more US features, afterwards every nodule can be classified to a proper group. Further, the lexicon with clear explanations and definitions is available. Nevertheless, there are two issues with ACR TI-RADS we feel need to be discussed. If the nodule is of mixed echogenicity, it should be described as predominantly hyperechoic, isoechoic, or hypoechoic, but in some cases is very hard to decide, and description of the thyroid nodule as non-homogenous would be more proper. Alternatively, the physician may choose the most suspicious echogenicity for point-scoring. The second issue regards halo, which is not included in the scheme. A halo may be due to a true fibrous capsule or a pseudocapsule. A uniform halo suggests a benign nodule because most thyroid malignancies are unencapsulated. However, a complete or incomplete halo has been noted in 10-24 % of thyroid carcinoma (Grant *et al.* 2015). These US features have been misleading for our physicians, and we propose that incorporating them into the US stratification scheme could be helpful, as they are very common in clinical US practice. Most likely, resulting in re-grading and more correct classification of our missed PTMCs (17.9 %; 5/28). All missed PTMC in our study, except one, would be in follow-up group, so we can expect later detection. The one missed patient has been under regular follow-up due to autoimmune thyroid disease. We could expect later detection even in this case.

Over-diagnosis can account for 37 % of unnecessary FNA (Horvath *et al.* 2017). If we had strictly followed the ACR TI-RADS and ATA recommendation for FNA depending on thyroid nodule size, up to 48 % FNA according to ACR TI-RADS in comparison to 20.8 % according to ATA would not have been indicated or performed (p<0.0001). In contrast, 5 PTMC (17.9 %; 5/28) according to ACR TI-RADS would have been missed. 1 PTMC (7.7 %) according to ATA would have been missed and 18.4 % nodules (3 malignant) could not be assigned to a proper ATA US pattern group; in total 30.8 % malignancy would be missed by ATA (vs. ACR TI-RADS p=0.429). All 45 thyroid nodules <1 cm in our study should not be biopsied according to both ATA and ACR TI-RADS and none of these nodules was malignant by FNA. According to ATA, clinically manifest carcinoma will be missed in comparison to PTMC according to ACR TI-RADS.

Weaknesses of our study is the low incidence of thyroid carcinoma. However, we are the secondary referral center and we suppose that the incidence of thyroid cancer 4.41 % in our study group corresponds to incidence of thyroid cancer among all malignancies. Further, most of the thyroid nodules were diagnosed on the basis of cytologic findings alone, which could result in some malignancies being missed and, thus, bias in the results. The benefit of this study is its prospective design and unbiased low center volume. US stratification systems are mainly sensitive to most common histotype papillary carcinoma, despite that, other histotypes were detected by ACR TI-RADS and indicated to FNA.

Conclusions

FNA is the gold standard with the best accuracy for the examination of thyroid nodules. Under our

condition of secondary referral center with majority of benign thyroid nodules, both ACR TI-RADS and ATA thyroid nodule ultrasonography stratification systems have allowed fair selection of nodules requiring FNA in consistence with high center volume. ACR TI-RADS is a user friendly with superiority over ATA due to exact thyroid nodule classification. However, almost one third of the patients are incorrectly classified. Despite that, the amount of FNA would be significantly reduced. Individual risk factors and decision of physician must be always taken into account to avoid over-diagnosis and on the other hand to not overlook aggressive thyroid cancer.

Conflict of Interest

There is no conflict of interest.

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Abbreviations

AACE/ACE/AME - American Association of Clinical Endocrinologists, American College of Endocrinology and Associazione Medici Endocrinologi
ACR TI-RADS - American College of Radiology Thyroid Imaging, Reporting and Data System
Anti-Tg - Anti-thyroglobulin antibodies
Anti-TPO - Anti-thyroid peroxidase antibodies
ATA - American Thyroid Association
AUC - Area under the curve
AUS - Atypia of undetermined significance
BIRADS - Breast Imaging Reporting and Data System
FLUS - Follicular lesion of undetermined significance
FNA - Fine needle aspiration biopsy
NPV - Negative predictive value
PPV - Positive predictive value
PTC - Papillary thyroid cancer
PTMC - Papillary thyroid microcarcinoma
TBSRTC - Bethesda System for Reporting Thyroid Cytopathology
TIRADS - Thyroid Imaging Reporting and Data System
TRAbs - Thyrotropin receptor antibodies
US - Ultrasound

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