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Original Article

A single-center multidisciplinary study analyzing thyroid nodule risk stratification by comparing the thyroid imaging reporting and data system (TI-RADS) and American thyroid association (ATA) risk of malignancy for thyroid nodules

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ABSTRACT

Objectives: The thyroid imaging reporting and data system (TI-RADS) and 2015 American Thyroid Association (ATA) guidelines are two well-known risk stratification systems for classifying thyroid nodules based on cancer risk. This study aims to evaluate the diagnostic efficacy of these two systems in predicting malignancy in patients undergoing thyroid surgery.

Methods: We studied data on 120 individuals who were scheduled to undergo surgery for benign or malignant nodular diseases of the thyroid gland between October 2017 and October 2019. The TI-RADS category and ultrasound pattern based on ATA guidelines were assigned to dominant thyroid nodule categories by two experienced radiologists blinded to patients' previous thyroid ultrasonography and fine-needle aspiration biopsy results. A pathologist with experience in thyroid diseases blinded to patients' sonographic and clinical data reviewed the thyroidectomy specimens.

Results: A total of 120 patients, 88 women and 32 men, were included in our study. Final histopathological results were as follows: 50% (n=60) papillary thyroid carcinoma, 36.6% (n=44) benign nodular thyroid diseases, 4.1% (n=5) follicular adenoma, 2.5% (n=3) hurtle cell adenoma, 1.7% (n=2) follicular thyroid carcinoma, 1.7% (n=2) medullary thyroid carcinoma, 1.7% (n=2) hurtle cell carcinoma, and 1.7% (n=2) follicular tumor of uncertain malignancy potential. The sensitivity, specificity, positive predictive value, and negative predictive value for TI-RADS were 80%, 56%, 72%, and 67%, respectively, and that for ATA were 80%, 64%, 76%, and 69%, respectively.

Conclusion: The TI-RADS and ATA showed similar rates of sensitivity, specificity, NPV, and PPV. Our observed risk of malignancy was higher than expected for the ACR TI-RADS 3–5 categories and the very low, low, and intermediate suspicion risk strata in the ATA guidelines.

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We found no difference between observed and expected malignancy risk for the ACR TI-RADS 2's and ATA's high suspicion categories.

1. Introduction

Thyroid nodules are frequently encountered in the community, and their rate of detection is increasing as the use of ultrasound (US) has become more widespread [1]. Thyroid US is widely used as an imaging modality for the initial evaluation of thyroid nodules and for the stratification of nodules in association with their risk of malignancy. There are many well-constructed US findings that have distinguished malignant nodules from benign nodules [2–4]. Ultrasonographic features such as echogenicity, shape, margin, dimension, and presence of calcification determine the risk of malignancy in thyroid nodules. Although these characteristics are important factors in determining the risk of malignancy, none are sufficient on their own [5], and a combination of suspicious features has proved to be helpful [6,7]. To classify thyroid nodules according to the risk of cancer, many risk stratification systems based on the combination of US characteristics of thyroid nodules have been developed [6,8,9]. Although these systems focus on the same US characteristics, they each have a different approach and scoring system to determine malignancy risk. The 2015 American Thyroid Association (ATA) management guidelines [10] and the 2017 American College of Radiology thyroid imaging reporting and data system (ACR TI-RADS; 11) are two well-known and frequently used classification systems that have been validated for use in predicting malignancy [12,13]. The ATA guidelines is a qualitative system that separates nodules into five different risk categories, and the ACR TI-RADS also has five different risk categories and determines risk stratification quantitatively. Our main aim in this study is to evaluate the diagnostic efficacy of these two systems in predicting thyroid nodule malignancy in patients undergoing thyroid surgery.

2. Materials and methods

2.1. Patients

Between October 2017 and October 2019, we prospectively analyzed data from 120 patients who underwent an operation because of benign or malignt nodular lesions of the thyroid gland at our hospital's Otolaryngology and Head and Neck Surgery Department. Patients with Graves' disease or toxic nodular goiter were not included in the study. All patients included in the study had a preoperative biopsy. Patients with a biopsy result of Bethesda 3, 4, 5 or 6, and patients with Bethesda 2, but who had cosmetic problems, compression symptoms, or who had suspicious findings on ultrasonography suggesting malignancy were included in the study. This study was approved by the Ethics Committee of Clinical Research of our hospital (Approval number 09.2017.576).

2.2. Thyroid US examination and prospective evaluation

Although thyroid surgery is widely performed in our hospital, we do not use any classification system, such as ATA or ACR TI-RADS, during the ultrasonographic examination of thyroid nodules and for biopsy decisions regarding thyroid nodules. Clinicians direct patients for biopsy according to the size and ultrasound characteristics of the dominant nodule, as determined by radiologists. In this study, all nodular thyroid patients who had previously undergone thyroid ultrasonography and thyroid fine-needle aspiration biopsy (FNAB) and had been indicated for operation were evaluated. Thyroid US was performed again by two experienced radiologists on the morning of the operation day. Radiologists were blinded to patients' previous thyroid US and FNAB results. The two experienced radiologists classified the degree of suspicion of thyroid nodules according to ACR TI-RADS and ATA guidelines together. Postoperative thyroid specimen pathology was examined by a pathologist experienced in the thyroid field who was blinded to patients' US findings. The diagnostic performance of the TI-RADS and ATA classification systems was evaluated by comparing the sonographic benign and malignant nodules with the thyroid specimen pathology.

The diagnostic performance of both risk stratification systems (TI-RADS and ATA) was determined by comparing the ultrasonographic risk of the nodules with the postoperative histopathological findings. TI-RADS 2 (not suspicious) and TI-RADS 3 (mildly suspicious) nodules were grouped as benign nodules; TI-RADS 4 (moderately suspicious) and TI-RADS 5 (highly suspicious) nodules were grouped as malignant nodules. Similarly, ATA very low and low suspicion nodules were grouped as benign nodules; ATA intermediate and high suspicion nodules were grouped as malignant nodules.

2.3. Statistical analysis

Statistical analyses of the results were performed with the Statistical Package for Social Sciences version 17.0 software (IBM). In all analyses, $P < 0.05$ was considered statistically significant. The normal distribution of variables was examined by histogram graphs and the Kolmogorov–Smirnov test. Mean, standard deviation (SD), median, and minimum-maximum values were used while presenting descriptive analyses. Pearson's chi-squared test was used to compare categorical data.

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Table 1. Comparison of observed and expected malignancy risks of TIRADS categories by final histopathological.

TIRADS category	Total	Malignant	Observed malignancy, %	Expected malignancy, %	*p* value
TIRADS 2	8 (6.7%)	0	0	<2	0.49
TIRADS 3	34(28.3%)	14	41	≤5	<0.001
TIRADS 4	38 (31.7%)	18	47	5.1-20	<0.001
TIRADS 5	40 (33.3%)	38	95	>20	<0.001
Total	120	70			

TIRADS: Thyroid imaging reporting and data system.

Table 2. Comparison of observed and expected malignancy risks of ATA categories by final histopathological.

ATA category	Total	Malignant	Observed malignancy, %	Expected malignancy, %	*p* value
High suspicion	48 (40%)	38	79	>70-90	0.49
Intermediate suspicion	26 (21.7%)	18	69	10-20	<0.001
Low suspicion	40 (33.3%)	12	30	5-10	<0.001
Very low suspicion	6 (5%)	2	33	<3	<0.001
Total	120	70			

ATA: 2015 American Thyroid Associatin and Management Guidelines.

Table 3. TIRADS and ATA categories with final histopathological and FNAB results.

Ultrasonographic score	Benign histopathological results (n=50) Bethesda category						Malignant histopathological results (n=70) Bethesda category					
	I	**II**	**III**	**IV**	**V**	**VI**	**I**	**II**	**III**	**IV**	**V**	**VI**
TIRADS 2	0	8	0	0	0	0	0	0	0	0	0	0
TIRADS 3	0	16	4	0	0	0	0	0	0	10	2	2
TIRADS 4	0	10	6	2	2	0	0	2	2	4	2	8
TIRADS 5	0	2	0	0	0	0	0	2	4	0	8	24
ATA VERY LOW RISK	0	4	0	0	0	0	0	0	0	0	0	2
ATA LOW RISK	0	24	4	0	0	0	0	0	0	10	2	0
ATA INTERMEDIATE RISK	0	6	0	2	0	0	0	4	2	4	2	6
ATA HIGH RISK	0	2	6	0	2	0	0	0	4	0	8	26

TIRADS: Thyroid Imaging Reporting and Data System; ATA: 2015 American Thyroid Association and Management Guidelines; FNAB: Fine-Needle Aspiration Biopsy.

3. Results

3.1. Patient demographics and nodules risk groups

A total of 120 patients, 88 women and 32 men, were included in the study. The mean age of the patients was 46.2. Nodules were classified as TI-RADS 2, 3, 4, and 5 in 6.7%, 28.3%, 31.7%, and 33.3% of cases, respectively, as shown in Table 1. Nodules were classified by ATA scores as high risk in 40%, intermediate risk in 21.7%, low risk in 33.3%, and very low risk in 5% of cases, as shown in Table 2.

3.2. Cytological and histopathological results

FNAB results were as follows: 33.3% (n=40) benign (Bethesda 2), 13.3% (n=16) atypia of undetermined significance (AUS) or follicular lesion of undetermined significance (FLUS; Bethesda 3), 13.3% (n=16) suspicious for a follicular neoplasm (Bethesda 4), 11.7% (n=14) suspicious for malignancy (Bethesda 5), and 28.3% (n=34) malignant (Bethesda 6) as shown in Table 3.

The final histopathological results were as follows: 50% (n=60) papillary thyroid carcinoma, 36.6% (n=44) benign nodular thyroid diseases, 4.1% (n=5) follicular adenoma, 2.5% (n=3) hurtle cell adenoma, 1.7% (n=2) follicular thyroid carcinoma, 1.7% (n=2) medullary thyroid carcinoma, 1.7% (n=2) hurtle cell carcinoma, and 1.7% (n=2) follicular tumor of uncertain malignancy potential, as shown in Table 4.

Table 4. Postoperative histopathological diagnosis.

Histopathological diagnosis	n (%)
Papillary thyroid carcinoma	60 (50)
Follicular thyroid carcinoma	6 (5)
Medullary thyroid carcinoma	2 (1.7)
Hurtle cell carcinoma	2 (1.7)
Follicular tumor of uncertain malignancy potential	2 (1.7)
Follicular adenoma	5 (4.1)
Hurtle cell adenoma	2 (1.7)
Benign nodular thyroid diseases	41 (34.1)

3.3. Calculated observed malignancy risk versus expected malignancy risk

The total number of patients who fell into each stratum of the ACR TI-RADS and ATA systems according to calculated observed and expected malignancy risks are shown in Tables 1 and 2. Two patients with follicular tumors of uncertain malignancy potential were classified as benign histopathological results. There was no significant difference

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Table 5. Diagnostic performance based on final histopathological results.

Risk stratification system	Total number of patients	sensitivity	specificity	Positive predictive value	Negative predictive value
ATA	120	80%	64%	76%	69%
TIRADS	120	80%	56%	72%	67%

TIRADS: Thyroid Imaging Reporting and Data System.
ATA: 2015 American Thyroid Association and Management Guidelines.

in observed malignancy risk versus expected malignancy risk in the TI-RADS 1 and 2; however, our calculated observed malignancy risk was significantly higher than the expected malignancy risk in the TI-RADS 3 (41% vs. ≤5%), 4 (47% vs. 5–20%), and 5 (95% vs. >20%). Our calculated observed malignancy risk was significantly higher than the expected malignancy risks for the ATA very low (33% vs. <3%), low (30% vs. 5–10%), and intermediate (69% vs. 10–20%) suspicion categories; however, there was no significant difference in the ATA high suspicion category.

3.4. Diagnostic performance of TI-RADS and ATA

The sensitivity, specificity, positive predictive value, and negative predictive value for TI-RADS were 80%, 56%, 72%, and 67%, respectively, and that for ATA were 80%, 64%, 76%, and 69%, respectively, as shown in Table 5.

4. Discussion

Ultrasonography is an important tool in the evaluation and management of thyroid nodules and is also very helpful for differentiating benign nodules from suspicious or malignant nodules. However, objective evaluations of ultrasonographic features of thyroid nodules are not routinely used in many tertiary health institutions. Thyroid nodule risk stratification systems allow us to make clinicopathological correlations between ultrasonography and histopathology. In this prospective study, we examine the diagnostic performance of two well-known classification systems, TI-RADS and ATA.

We compared the observed versus expected rates of malignancy for each category in the TI-RADS and ATA risk stratification systems [10,11]. Our results showed some inconsistencies. We had a statistically significant higher risk of malignancy than expected for the ACR-TI-RADS 3–5 categories and the very low, low, and intermediate suspicion risk strata in the ATA guidelines. A similar study was performed by Huang et al., who also found significantly higher observed rates of malignancy for the ACR-TI-RADS 3–5 categories and the intermediate ATA risk stratum, but they did not find any statistically significant difference in the very low and low ATA risk strata [14]. In the study by Gao et al., which was done to compare Kwak-TI-RADS with ACR-TI-RADS and ATA systems in 2544 surgically excised nodules, they also found significantly higher observed rates of malignancy for the ACR-TI-RADS 3–5 categories and the intermediate ATA risk stratum [15]. Unlike Huang et al. and Gao et al., we also found significantly higher malignancy rates in the very low and low ATA risk strata. The reason for higher malignancy rates in the very low ATA risk stratum in our study was most likely due to the low number of patients (n=6) in this category. The higher observed malignancy rates in the ACR TI-RADS 3–5 and low and intermediate ATA risk strata in our study are probably due to our hospital being a tertiary referral surgical center. Huang et al. stated that the higher rate of observed malignancy in the TI-RADS 3–5 categories and ATA intermediate suspicion category of their study might be related to the high rate of follicular thyroid cancer (11% of malignant nodules) in their study [14] in contrast to 1% of malignant nodules in the ACR TI-RADS validation study [13] and 5% of malignant nodules in the ATA validation study [12]. They attributed this situation to the higher proportions of follicular cancer in the ATA intermediate risk stratum and TI-RADS 3–4 categories. Follicular cancer constituted 8.5% of all thyroid cancers in our study (6 out of 70 malignant patients), but we did not detect any differences in the distribution of follicular cancer according to the sonographic category. Whatever the reason, these inconsistencies are important to note because the reported risk of malignancy may influence the treatment preferences of patients and providers.

In comparing the diagnostic performance of TI-RADS and ATA according to the final histopathological results, no statistically significant difference was found in terms of sensitivity (80% vs. 80%), specificity (56% vs. 64%), negative predictive value (67% vs. 69%), and positive predictive value (72% vs. 76%). Contrary to our study, many studies found that TI-RADS had higher specificity, and ATA had higher sensitivity [14–16]. However, in the study by Yoon et al. in which 1293 thyroid nodules (diameter >1 cm) were examined, they found that TI-RADS had higher sensitivity, whereas ATA had higher specificity [17]. Recently, Xu's study indicated that the ATA guidelines might yield a higher specificity than TI-RADS for nodules larger than 2 cm [18]. These differences in sensitivity and specificity between studies may be partly due to the study population. Huang et al. also stated that although ATA had higher sensitivity and TI-RADS had higher specificity, they found that overall performance in predicting malignancy was similar for both systems. The performance of both systems in predicting malignancy was similar in our study as well.

There are some limitations to our study. Our hospital is a tertiary referral health institution, and patients with suspected or diagnosed malignancy are referred. Thus, we had a higher rate of malignancy than the general thyroid nodule population of an institution. In addition, there might have been a selection bias resulting in the underestimation of negative predictive values and the overestimation of positive predictive values because all patients underwent thyroidectomy. We also had a relatively small cohort of 120 patients included in the study, with a few patients in specific strata, especially in TI-RADS 2 and the ATA very low stratum, limiting sub-stratification

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analyses. Despite these limitations, ultrasonographic examination of all patients was done in light of the sonographic characteristics of the nodules in the TI-RADS and ATA scoring systems by two radiologists who are experts in thyroid sonography, which limited the misdiagnosis of the nodules. We believe that this well-planned prospective study, based on final histopathological evaluations, adds insight into the utility of these tests and the practice preferences of clinicians.

5. Conclusion

We found that ACR TI-RADS and ATA had similar rates of sensitivity, specificity, NPV, and PPV. Our observed risk of malignancy was higher than expected for the ACR TI-RADS 3–5 categories and the very low, low, and intermediate suspicion risk strata in the ATA guidelines. We found no differences between the observed and expected malignancy risks for the ACR TI-RADS 2 and ATA high suspicion categories.

Compliance with Ethical Standards

The study was approved by the Ethics Comitte for Clinical Researches and confirmation number is 09.2017.576).

Disclosure statement

All the authors declare that they have no conflict of interest

Informed consent

Informed consent was received from all patients.

Declaration of Competing Interest

The authors declare that they have no conflict of interest.

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