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ORIGINAL ARTICLE

The relationship between ultrasound-based TIRADS and BETHESDA categories in patients undergoing thyroid biopsy

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Abstract

The TIRADS is a scoring system used for the selection of nodules for FNA and classification of the risk of malignancy based on ultrasound characteristics. The BETHESDA is a standard reporting system used for the classification of FNA results based on six criteria with risks for malignancy. The objective of this study was to evaluate the relationship between TIRADS and BSRTC classifications in patients undergoing thyroid biopsy. A total of 350 consecutive patients were retrospectively evaluated using TIRADS and BETHESDA reporting systems for determining preoperative diagnosis of thyroid nodules. Patients' demographics, size, echogenicity and contour status of the nodules, TIRADS and BETHESDA scores were recorded and analyzed. Data obtained in this study were expressed as mean, standard deviation, frequency and percentage descriptive statistics. The mean age of the patients was 49.03 ± 17.58 years. The mean nodule size was measured as 20.56 ± 10.47 mm. TIRADS TR3 category was found in 165 (47.14%), TR4 in 154 (44%) and TR5 in 31 (8.86%) patients, while BETHESDA II category was found in 288 (82.28%), BETHESDA III category in 1 (0.29%), BETHESDA IV category in 19 (5.43%), BETHESDA V in 37 (10.57%) and BETHESDA VI in 5 (1.43%) patients. There was a general concordance between BETHESDA and TRIADS categories. The most significant concordance was found between BETHESDA IV and TR4 categories (84.21%). Combined use of TRIADS and BETHESDA can be efficiently used to provide the most accurate results for making preoperative diagnosis of thyroid nodules and to determine the risk of malignancy.

Keywords Thyroid nodules · Thyroid cancer · TIRADS · BETHESDA · Ultrasound

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Introduction

Thyroid nodules are defined by the American Thyroid Association as thyroid gland lesions that are radiologically distinct from the surrounding parenchyma [1]. Thyroid nodules are commonly encountered entities and are often identified either incidentally during physical examination or by different imaging modalities [2]. Whereas the prevalence of thyroid nodules varies between 4 and 7 by palpation, this rate raises up to 20–76% using imaging modalities, mainly ultrasound [3]. These nodules are clinically significant because of their potential for malignancy. Thyroid cancer accounts for about 2.1% of all cancers [4]. The global prevalence of malignancy rate in thyroid nodules is between 4.0 and 6.5% as determined by an invasive procedure [5]. Therefore, it is of paramount importance to differentiate benign and malignant nodules in clinical evaluation. The incidental diagnosis of thyroid nodules is increasing in parallel with the common use of ultrasound and advancements in fine needle aspiration

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(FNA) cytology and 18 FDG-PET imaging. FNA cytology remains the gold standard for the investigation and definitive diagnosis of thyroid nodules with 65–99% sensitivity and 72–100 specificity [6].

Studies are ongoing about preoperative diagnosis of thyroid nodules. Thyroid Imaging Reporting and Data Systems (TIRADS) is a radiological classification system proposed by Horvarh et al. and is being successfully used in the selection of nodules for FNA and classification of the risk of malignancy based on ultrasound characteristics [7, 8]. TIRADS reporting is based on ultrasound malignancy characteristics such as hypoechogenicity, solid echostructure of nodules, microcalcifications, irregular margins, taller than wide shape and microlobulated margins [9]. The sensitivity and specificity values for TIRADS for the classification of thyroid nodules were reported as 88% and 49%, respectively [10]. The Bethesda System for Reporting Thyroid Cytopathology (BSRTC) is a standard reporting system used for the classification of FNA results based on six criteria with risks for malignancy [10]. In a recent meta-analysis, the sensitivity of the Bethesda system was found as 97% and specificity as 50.7% [11].

Both TIRADS and BSRTC systems are widely recommended and used in clinical practice worldwide. The use of TIRADS has been proposed to improve the diagnostic accuracy of the Bethesda system [12]. The combined use of invasive and noninvasive examinations may enable surgeons to make more accurate diagnosis for suspected thyroid nodules. The objective of this study was to evaluate the relationship between TIRADS and BSRTC classifications in patients undergoing thyroid biopsy.

Material and methods

Study design and patients

In the present study, a total of 350 consecutive patients aged 18 years or above who were referred to the radiology department of our hospital for imaging of the neck due to several reasons, whose suspicious thyroid nodules were detected by ultrasound and who underwent thyroid biopsy between September 25, 2014, and August 18, 2020, were retrospectively evaluated. Patients with normal thyroid scans (TIRADS-1 and TIRADS-2), those with a history of previous thyroid surgery, parathyroid comorbidity and patients currently diagnosed with thyroid carcinoma (TIRADS-6) were excluded from the study. In addition, thyroid nodules in the BETHESDA I category were not included in the evaluation.

Table 1 TIRADS categorization [7]

Category	Definition	Risk of malignancy
TI-RADS 1	Normal thyroid gland	0
TI-RADS 2	Benign conditions	0
TI-RADS 3	Probably benign nodules	< 5%
TI-RADS 4	Suspicious nodules	5–80%
TI-RADS 5	Probably malignant nodules	> 80%
TI-RADS 6	Biopsy-proven malignancy	100

Table 2 BETHESDA categorization [11]

Category	Description	Risk of malignancy
I	Non-diagnostic/unsatisfactory	0
II	Benign	0–3%
III	Atypia of follicular lesion of unclear significance	5–15%
IV	Follicular neoplasm or suspicious for follicular neoplasm	15–30%
V	Suspicious for malignancy	60–75%
VI	Malignant	97–99%

Data collection

The data used in this study were obtained from the patient files via the hospital information system and archives. Patients' demographics such as age and gender, size, echogenicity and contour status of the nodules, other ultrasound characteristics such as calcification, heterogeneity and internal content, number of biopsies and pathological outcomes were recorded. In addition, TIRADS and BETHESDA categories and concordance between these two systems were also recorded and analyzed.

Data obtained in the study were analyzed using Microsoft® Excel software. Variables were expressed as mean ± standard deviation, frequency and percentage.

Radiological and pathological examinations

All patients underwent ultrasound examination of the thyroid gland and FNA of the nodule at the same session. Ultrasound parameters were read, and the lesion was characterized according to the TIRADS criteria by the same experienced radiologists who were blind to final cytology findings (Table 1). Ultrasound scans were performed using a high-resolution device (GE Logiq E9 Ultrasound USA Domestics, USA) with 3–12 MHz broadband array transducer.

Table 3 Demographic features of the patients

	Minimum	Maximum	Mean ± SD*
Age (years)	18	77	49.03 ± 17.58
Gender			
Female (n/%)	249 / 71.14%		
Male (n/%)	101 / 28.86%		
Nodule size (mm)	5	67	20.56 ± 10.47

SD: Standard deviation

The FNA samples were stained with Papanicolaou and May–Grunwald–Giemsa (MGG), and the smears were interpreted and categorized according to the Bethesda system by an experienced pathologist (Table 2).

Ethics consideration

Before the beginning, the study protocol was approved by the local ethics committee of our hospital with the 23/06/2021 dated and 2/2021.K-51 numbered decision. The necessary permission was received from the hospital management to use the archives of patient files. The study was executed following the ethical principles of the Declaration of Helsinki.

Data expression

Data obtained in this study were analyzed using Statistical Package for Social Sciences (SPSS Inc., Chicago, Illinois, USA) version 22 Software. Continuous variables were expressed as mean ± standard deviation, and categorical variables as frequency and percentage. The concordance between TIRADS and BETHESDA categories was investigated. No further statistics were used.

Results

In this study, a total of 350 patients who met the inclusion criteria were retrospectively evaluated. The mean age of the study population was 49.03 ± 17.58 years, and the female-to-male ratio was 249/101. The mean nodule size of the patients was measured as 20.56 ± 10.47 mm. Demographic characteristics of the patients are given in Table 3.

The mean age was found as 52.62 ± 15.58 in the female and 49.18 ± 17.60 in the male patients. The mean nodule size was calculated as 20.12 ± 10.47 mm in the female and 21.66 ± 10.30 in the male patients.

When TIRADS categories of patients were evaluated based on ultrasound examination, TIRADS TR3 category was found in 165 (47.14%) patients, TR4 in 154 (44%) patients and TR5 in 31 (8.86%) patients. TR1, TR2 and TR6 categories were not included in the study. Figure 1 shows the ultrasound images of TIRADS TR3, TR4 and TR5 thyroid nodules. The majority of the nodules were in TR3 and TR4 categories on ultrasound imaging, accounting for 91.14% of all nodules.

When BETHESDA categories of patients were evaluated based on pathological examination, BETHESDA II category was found in 288 (82.28%) patients, BETHESDA III category in 1 (0.29%) patient, BETHESDA IV category in 19 (5.43%) patients, BETHESDA V in 37 (10.57%) patients and BETHESDA VI in 5 (1.43%) patients. Figure 2 shows the examples of pathological images in different BETHESDA categories.

Among the 288 patients in BETHESDA II category, probably benign nodules (TR3) were found in 159 (55.21%) patients, suspicious nodules (TR4) in 121 (42.01%) patients and probably malignant nodules (TR5) in 8 (2.78%) patients according to the ultrasound findings. One patient in BETHESDA III category had a suspicious thyroid nodule

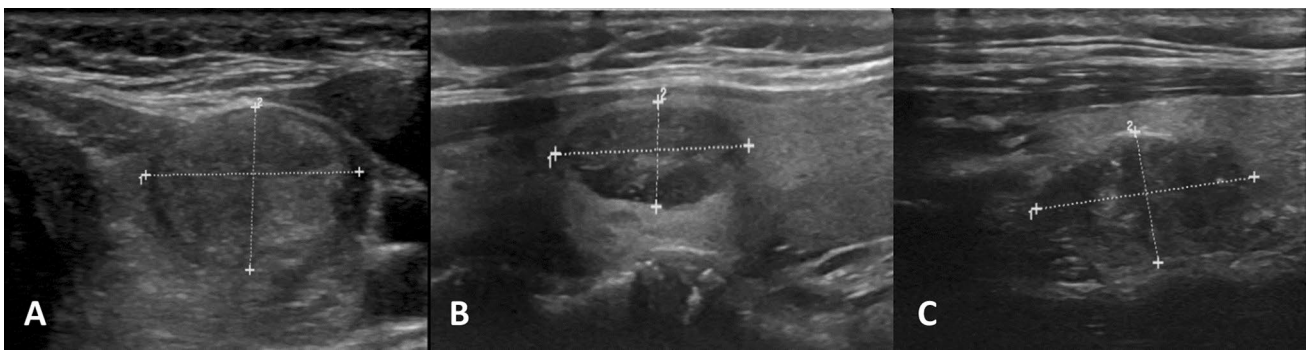

Fig. 1 Ultrasound images of TIRADS TR3, TR4 and TR5 thyroid nodules. **A)** TR3; a nodular lesion in the left lobe with a surrounding thin, complete hypoechoic rim, slightly heterogeneous inner pattern and focal mild hypoechoic and slightly hyperechoic areas. **B)** TR4; a nodular lesion in the right thyroid lobe with slightly lobulated contours, heterogeneous inner pattern, focal hypoechoic and hyperechoic areas. **C)** TR5; a nodular lesion in the left thyroid lobe with irregular contours, faint margins, heterogeneous inner pattern, markedly decreased echogenicity and punctate microcalcifications

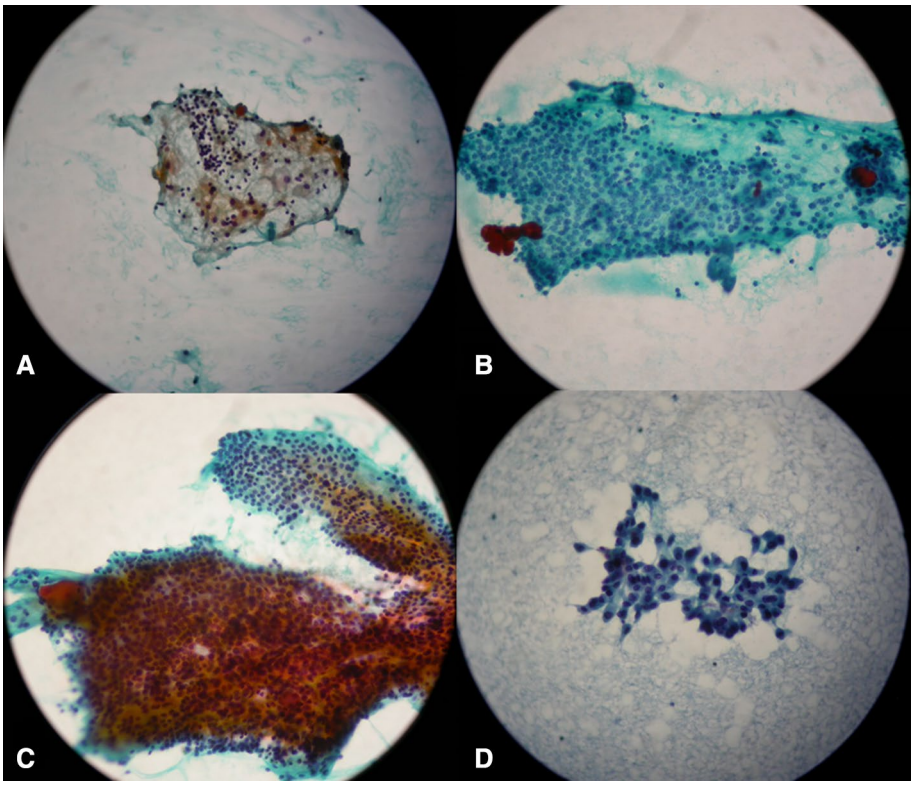

Fig. 2 Pathological images of nodular thyroid lesions based on BETHESDA categories. **A)**; Thyroid nodule showing cystic change, benign thyrocytes and macrophages (BETHESDA II). **B)**; Nuclei with thin chromatin, some of them have prominent nucleolar structure, microfollicle structures (BETHESDA III). **C)**; Hyperplastic thyrocyte groups, some with large nuclei, microfollicular structures. Suspicious for follicular neoplasm (BETHESDA IV). **D)**; Enlargement of nuclei, some of them have thin chromatin, some of the nuclei contain hyperchromasia. Suspicious for papillary thyroid carcinoma (BETHESDA V)

Table 4 TIRADS categories corresponding to BETHESDA categories

BETHESDA	TIRADS					
	TR3		TR4		TR5	
	n	%	n	%	n	%
II ($n=288$)	159	55.21	121	42.01	8	2.78
III ($n=1$)	0	0	1	100	0	0
IV ($n=19$)	3	15.79	16	84.21	0	0
V ($n=37$)	3	8.11	12	32.43	22	59.76
VI ($n=5$)	0	0	40	80	1	20

(TR4). When the 19 patients in BETHESDA IV category were examined, probably benign nodules (TR3) were detected in 3 (15.79%) and suspicious nodules (TR4) in 16 (84.21%) of these patients. Of the 37 patients in BETHESDA V category, probably benign nodules (TR3) were found in 3 (8.11%) patients, suspicious nodules (TR4) in 12 (32.43%) patients and probably malignant nodules (TR5) in 22 (59.76%) patients. Five patients were in BETHESDA VI category, four (80%) of these patients had suspicious nodules (TR4), and one patient (20%) had probably malignant nodules (TR5). The relationship between TIRADS and BETHESDA categories is presented in Table 4. As given in Table 4, there was a general concordance between BETHESDA and TRIADS categories. The most significant concordance was found between BETHESDA IV and TR4 categories (84.21%), followed by BETHESDA V and TR5 (59.76%), BETHESDA II and TR3 (55.21%), and BETHESDA II and TR4 (42.01%).

Discussion

The prevalence of thyroid nodules is as high as 60% in the general population, but only 5% of all nodules ultimately prove to be malignant [13]. However, there has been a significant increase in the cases of thyroid carcinoma in recent years. The incidence of both thyroid nodules and thyroid carcinoma is higher in women than in men. In our study, the rate of female to male was found as 249/101. Studies in the literature have reported similar results. In a study by Yilmaz and Bolukbasi, investigating the combined use of TIRADS and BETHESDA classification systems in the

diagnosis of thyroid cancer, female/male rate was reported as 205/36 [14]. The female/male ratio was reported as 156/28 by Periakaruppan et al. [3] and as 13/56 by Biswas et al. [15]. Although different rates have been stated in the above-mentioned studies, female predominance is evident.

FNA cytology is a useful and cost-effective method to detect thyroid malignancies. However, since the prevalence of thyroid nodules is very high and FNA is a minimally invasive procedure, it is not recommended for all thyroid nodules [16] and patients for whom FNA will be recommended is still debatable [3]. Therefore, it is crucial to select the cases to undergo FNA based on the risk of malignancy. Ultrasonography is widely used for this purpose and provides information about localization, number, size of the nodules and other characteristics that are significant in terms of the risk of malignancy (solidity, calcification, irregular margins, accompanying lymph nodes, etc.) [17].

The introduction of TIRADS classification based on ultrasound patterns has provided an important approach in determining the risk of malignancy in thyroid nodules. This scoring system has been approved by the American College of Radiology, leading to standardization in reporting and an accurate clinicopathological correlation [14]. TIRADS scoring indicates the risk of malignancy in six categories with higher categories showing an increased risk. In our study, we excluded TR1, TR2 and TR6 categories that refer to zero risk, benign conditions and biopsy-proven malignancy, respectively. TR3 was found in 47.14%, TR4 in 44% and TR5 in 8.86% of the patients. In the study by Periakaruppan, TR3 was reported in 26.46%, TR4 in 7.07% and TR5 in 4.89% of the patients [3]. In that study, the majority of the patients were in the T2 category, which was not included in our study. In the study by Yilmaz and Bolukbasi, 8.3% of the patients were in TR3, 43.2% in TR4 and 7.1% in TR5 categories [14]. In another study by Uricoechea et al., TR3 category was found in 27.78%, TR4 in 34.44% and TR5 in 17.78% of the patients [10]. It is seen that there were significant differences among the studies in reported rates of TIRADS categories. These differences might be caused by inclusion of the other TIRAD categories (especially TR1 and TR2) in some of the studies. In addition, overall inclusion and exclusion criteria might cause these differences. On the other hand, the most commonly detected categories are TR3 and TR4 in these studies.

Thyroid USG combined with FNA cytology plays an important role in the preoperative diagnosis and classification of thyroid nodules. It was reported in a study by Adamczewski et al. that classification of a patient in line with the presence of different ultrasound patterns as low, moderate and high risk combined with FNA cytology findings allows optimal clinical decisions regarding treatment strategies [18]. On the other hand, US-guided FNA cytology should be performed in each suspicious cancer case regardless of the nodule size. In a study by Marrazo et al., it was reported that thyroid FNA has a false positive rate of 0.5%, false negative rate of 1%, sensitivity of 94.7%, specificity of 98.4% and accuracy of 99% [19]. However, these rates may vary from one healthcare center to another.

BETHESDA (BSRTC) classification system was introduced in 2007 in order to standardize the terminology used in reporting of thyroid biopsy findings [20]. BSRTC is the standard reporting system for biopsy results that avoids unnecessary surgeries and assists selection of appropriate surgical procedures for patients with thyroid cancer [21]. According to the six criteria of BEDHESTA, the risk of malignancy increases as the categorical number increases. In our study, the most common BETHESDA category was II (82.29%) followed by V (10.57%), IV (5.43%), VI (1.43%) and III (0.29%). Similar to our study, in the study of Periakaruppan et al. BETHESDA II was the most common cytologic category of thyroid nodules, accounting for 82.15% [3]. On the other hand, there are studies reporting much lower rates for BETHESDA II category. For example, the rate of this category was reported as 36.11% by Uricoechea et al. and 9.09% by Yilmaz and Bolukbasi [10, 14]. As mentioned before, we believe that different results among the studies might be attributed to the inclusion and exclusion criteria and subjective nature of evaluations, highly dependent on the individual who performs FNA.

In our study, there was a general concordance between TIRADS and BETHESDA categories. The higher concordance was found among the higher-risk categories (TR4 and BETHESDA IV), which was consistent with the literature [10]. However, the number of patients in these categories was low, making an exact comparison difficult. In addition, studies have used different subtypes and modifications of TIRADS scores, again making a healthy comparison challenging [8, 21].

Study limitations

The main limitation of this study was its retrospective nature and being executed in a single center. A more detailed statistical analysis could be carried out. Finally, TIRADS scores based on ultrasound examination and BETHESDA scores obtained from FNA cytology are highly operator dependent and might be influenced by patients' cooperation. However, the number of our study is higher compared to numerous studies, as a strong aspect of the present study.

Conclusion

There is a general concordance between TIRADS and BETHESDA categories in terms of the risk of malignancy. Combined use of these two scoring systems seems to provide

the most accurate results for the diagnosis of thyroid nodules and for distinguishing benign and malignant nodules in order to make an accurate decision in patients with thyroid carcinoma. However, since these two systems are relatively new, further more comprehensive studies are needed for refinement of these systems to especially increase their specificity values. Yet, these two categorical systems can be efficiently used for preoperative diagnosis of thyroid carcinoma.

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Data availability The data that support the findings of this study are available from the corresponding author upon reasonable request.

Declarations

Conflict of interest The authors declare no conflict of interest to disclose.

Ethics approval Date**:** 23/06/2021 ; No: 2017-KAEK-120/ 2/2021.G-103; Decision No: 2/2021.K-51.

Patient consent Consent from the patients was waived as the study was conducted retrospectively.

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