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Evaluation of Sonographic Features with TIRADS of Malignant Cytology, Suspicious for Malignancy, and Follicular Neoplasm Thyroid Nodules According to the Bethesda Reporting System

Bethesda Raporlama Sistemine Göre Malign Sitoloji, Malignite Açısından Kuşkulu ve Foliküler Neoplazi Olan Tiroid Nodüllerinin Sonografik Özelliklerinin TIRADS ile Değerlendirilmesi

Hülya ÇETİN TUNÇEZ[1], Ahmet BOZER[1], Merve SANAĞ[1], Asuman ARGON[2]

[1]İzmir City Hospital, Clinic of Radiology, İzmir, Türkiye
[2]İzmir City Hospital, Clinic of Pathology, İzmir, Türkiye

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ABSTRACT

Objective: Thyroid nodules are common and prevalence is 19-68% in the population. The gold standard diagnosis is fine needle aspiration cytology (FNAC). In this study, we examined the sonographic features of thyroid nodules with IV, V, VI [malignant cytology, malignancy suspected cytology (MC-MSC), and follicular neoplasia (FN)] according to the Bethesda Thyroid Cytopathology Reporting System (BTCRS). We aimed to evaluate its correlation with the American College of Radiologists' (ACR) Thyroid Imaging Reporting and Data System (TIRADS) classification.

Methods: Ultrasound (US) features of 198 nodules detected as IV, V, and VI according to BTCRS in FNAC results were retrospectively examined. They were classified according to the ACR-TIRADS categorization from 1 to 5.

Results: Of the 198 nodules, 153 were in MS-MSC and 45 were in FN. Female/male ratio; 155/43 and the mean age was 48.8±13.1. The mean size of the nodules was 18.7±9.3 mm. The mean size was 21.2±9.2 mm in the FN group and 18±9.3 mm in the MS-MSC group. Nodule size was found to be statistically significant in the FN group (p=0.013). The TIRADS score was found to be higher in the MS-MSC group (p=0.041). Ninety-three percent of the FN group and 92% of the MS-MSC group were based on a single nodule.

Conclusion: TIRADS helps determine the malignant potential of thyroid nodules and prevent unnecessary biopsies. The presence of a single nodule may be a significant finding in malignancy. US features of follicular thyroid carcinoma may differ from typical TIRADS criteria, and size is a significant finding in distinguishing it from papillary thyroid carcinoma.

Keywords: Thyroid nodule, TIRADS, Bethesda, fine needle aspiration cytology

ÖZ

Amaç: Tiroid nodülleri oldukça yaygın olup prevalansı toplumda %19-68'dir. Tanıda altın standart ince iğne aspirasyon sitolojisidir (İİAS). Çalışmamızda Bethesda Tiroid Sitopatolojisini Raporlama Sistemine (BTSRS) göre IV, V, VI (malign sitoloji, malignite kuşkulu sitoloji (MS-MKS) ve foliküler neoplazi (FN) olan tiroid nodüllerinin sonografik özelliklerini inceledik. Amerikan Radyologlar Koleji'nin (ACR) Tiroid Görüntüleme Raporlama ve Veri Sistemi (TIRADS) sınıflandırması ile korelasyonunu değerlendirmeyi amaçladık.

Yöntem: 2019 ile 2023 tarihleri arasında İİAS sonuçları BTSRS'ye göre IV, V, VI saptanan 198 nodülün ultrason (US) özellikleri retrospektif olarak incelendi. ACR-TIRADS kategorizasyonuna göre 1 ila 5 arasında sınıflandırıldı. İİAS sonucu tanısal olmayan sitoloji, benign sitoloji ve önemi belirsiz atipi saptanan nodüller çalışma dışı bırakıldı.

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Corresponding Author/ Sorumlu Yazar:
Hülya ÇETİN TUNÇEZ MD,
İzmir City Hospital, Clinic of Radiology, İzmir, Türkiye
Phone: +90 507 790 48 16
drhulyacetintuncez@gmail.com
ORCID: 0000-0002-0830-0070

Bulgular: Yüz doksan sekiz nodülden 153'ü MS-MKS, 45'i FN grubundaydı. Kadın/erkek oranı; 155/43 ve yaş ortalaması 48,8±13,1'di. Nodüllerin ortalama boyutu 18,7 mm idi (minimum: 6 mm, maksimum: 66 mm). FN grubunda boyut ortalaması 21,2±9,2 mm, MS-MKS grubunda 18±9,3 mm saptandı. FN grubunda nodül boyutu istatistiksel olarak anlamlı bulundu (p=0,013). Nodüllerin 16'sı (%8) TR 2, 33'ü (%16) TR 3, 113'ü (%57) TR 4, 36'sı (%19) TR 5 grupta idi. MS-MKS grubunda TIRADS skoru daha yüksek bulundu (p=0,041). FN grubunun %93'ü, MS-MKS grubunun %92'si tek nodül zeminindeydi. Diğer verilerde her iki grubun karşılaştırmasında istatistiksel anlamlı farklılık saptanmadı.

Sonuç: TIRADS raporlama sistemi tiroid nodüllerinin malignite potansiyelinin belirlenmesi ve gereksiz biyopsilerin önüne geçilmesinde yardımcı olmaktadır. Tek nodül varlığı malignite açısından anlamlı bir bulgu olabilir. Ayrıca foliküler tiroid karsinomunun US özelliklerinin tipik TIRADS kriterlerinden farklı olabileceği ve papiller tiroid karsinomundan ayrımda boyutun anlamlı bir bulgu olduğu akılda tutulmalıdır.

Anahtar Kelimeler: Tiroid nodülü, TIRADS, Bethesda, ince iğne aspirasyon sitolojisi

INTRODUCTION

Thyroid nodules have become increasingly common, often being an asymptomatic clinical finding, with the advancement of imaging techniques. Epidemiological studies have reported the prevalence of thyroid nodules diagnosed by high-resolution ultrasound (US) in the general population to be between 19% and 68%.[1] Because cancer constitutes 7-15% of all nodules, distinguishing benign nodules from malignant ones is crucial.[2] US is widely used in thyroid examinations because of its non-invasive nature, ease of application, rapid results, and ability to assess the risk of malignancy. However, because of the overlapping sonographic features of benign and malignant nodules, US alone cannot accurately diagnose benign or malignant nodules. US-guided fine-needle aspiration cytology (FNAC) has high sensitivity and specificity for distinguishing benign nodules from malignant ones. Based on the FNAC results, the Bethesda Thyroid Cytopathology Reporting System (BTCRS) has been developed, classifying the risk of malignancy into six categories.[3] These categories include non-diagnostic cytology, benign cytology, atypia of undetermined significance, follicular neoplasm (FN), suspicious cytology for malignancy, and malignant cytology (MC).

Various professional associations have published guidelines to assist in clinical decision-making based on the US features of thyroid nodules.[4] In 2009, Horvath et al.[5] initially proposed the Thyroid Imaging Reporting and Data System (TI-RADS) classification. Subsequently, various modified TI-RADS classification systems based on clinical practice have been suggested. In 2017, the Thyroid Imaging Reporting and Data System Committee of the American College of Radiology (ACR) published a new risk classification system comprising five categories, including internal structure, echogenicity, echogenic foci, margin, and shape characteristics.[6] All categories are scored according to their features, and the sum of the scores from each category determines the TIRADS score. They are classified as TR1 benign, TR2 non-suspicious, TR3 mildly suspicious, TR4 moderately suspicious, and TR5 highly suspicious.

The aim of this study was to evaluate the sonographic features and correlation with TIRADS of thyroid nodules with MC, cytology suspicious for malignancy (MSC), and FN according to the Bethesda Classification.

METHODS

The records of patients who were referred to the radiology clinic with a biopsy request and underwent US-guided fine needle aspiration cytology (FNAC) between January 2019 and August 2023 were retrospectively evaluated. Our research was approved by the University of Health Sciences Türkiye, İzmir Bozyaka Training and Research Hospital Ethics Committee (decision no: 2023/105, date: 19.07.2023). A total of 198 nodules diagnosed with FN MSC and MC based on FNAC results according to the BTCRS were included in the study for patients aged 18 and older. Nodules with non-diagnostic cytology, benign cytology, and atypia of undetermined significance, patients with unavailable US results in the system, children, pregnant women, and lactating women were excluded from the study.

Before the procedure, thyroid US and US-guided FNAC were performed by two radiology experts with 7 years of experience in the same clinic. A Samsung RS85 trademark (Samsung, Schwalbach am Taunus, Germany) US device and a 2.0-14.0 MHz frequency LA2-14A linear probe were used for all procedures. The internal structure, echogenicity, presence of echogenic foci, and margin and shape characteristics of the nodule were evaluated. US reports were retrospectively reviewed from the Hospital Information Management System and categorized according to the ACR-TIRADS classification. For ACR-TIRADS, 0-2 points were assigned for the internal structure of the nodule (cystic, predominantly cystic, and spongiform 0 points; cystic and solid mixed 1 point; solid or predominantly solid 2 points); 0-3 points for echogenicity (anechoic 0 points; isoechoic or hyperechoic 1 point; hypoechoic 2 points; markedly hypoechoic 3 points); 0-3 points for shape (parallel to the skin 0 points; perpendicular to the skin 3 points); 0-3 points for margin characteristics (smooth and well-defined 0 points; lobulated and irregular 2 points; extrathyroidal extension 3 points); and all present in the echogenic focus category were scored (none or comet-tail artifact 0 points; macrocalcification 1 point; peripheral rim calcification 2 points; punctate echogenic

focus 3 points). The total score was recorded according to the ACR-TIRADS classification, where 0 points were TR1, 2 points were TR2, 3 points were TR3, 4-6 points were TR4, and ≥7 points were TR5 (Figure 1, 2).

During FNAC material acquisition, aspiration was performed using a 21-gauge needle and a 5 mL syringe. One of the two thin smear samples spread from the samples taken from the patient was air-dried and stained with May Grunwald Giemsa, whereas the other was fixed with alcohol and stained with Papanicolaou (PAP). A PAP-stained slide was prepared from the samples in red solution using liquid-based cytology (BD Diagnostics, SurePath test), and a cell block was created. Sections obtained from cell blocks were stained with hematoxylin and eosin. All preparations were evaluated according to BTCRS by a cytopathologist with 20 years of experience.

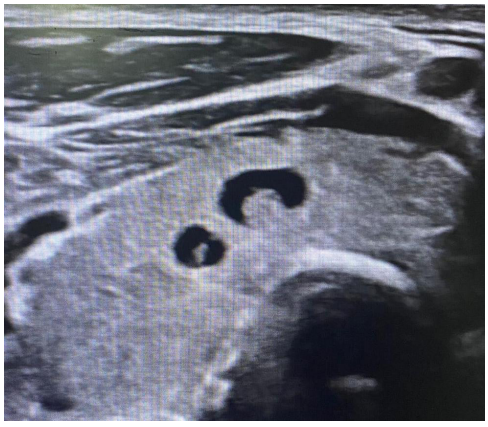

Figure 1. Fifty-five y, female. TIRADS score is 2 (TR2) (mixed cystic and solid composition 1 point, isoechoic echogenicity 1 point, wider than tall shape 0 point, smooth margin 0 point, none echogenic foci 0 point) FNAC result: Benign cytology according to Bethesda classification

FNAC: Fine needle aspiration cytology

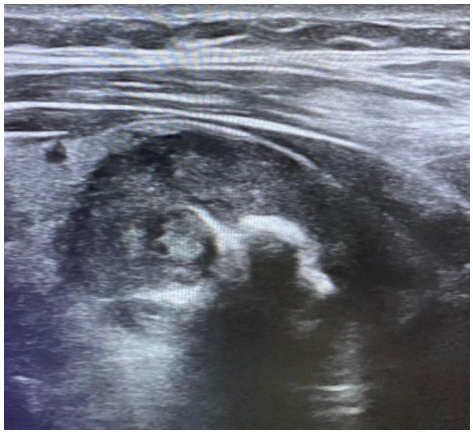

Figure 2. Forty-eight y, female. TIRADS score is 7 (TR5) (solid composition 2 point, hypoechoic echogenicity 2 point, wider than tall shape 0 point, lobulated and irregular margin 2 point, macrocalcification 1 point) FNAC result: malignant cytology according to Bethesda classification

FNAC: Fine needle aspiration cytology

Statistical Analysis

Analyses were performed using IBM Statistical Package for the Social Sciences statistics for Windows, version 25.0 (IBM Corp. Released 2017, Armonk, NY) package program. The normal distribution suitability of age, size, and TI-RADS score variables was evaluated using the Kolmogorov-Smirnov test ($n \geq 50$) or Shapiro-Wilk test ($n < 50$). Independent two-sample t-test (for those conforming to normal distribution) and Mann-Whitney U test (for those not conforming to normal distribution) were used for comparisons between the two groups (FN and MC-MSC) for these variables. Comparison of categorical variables between the two groups was performed using the chi-square test or Fisher's exact test. The presence of linear relationships between numerical and ordinal variables was examined using Spearman's rho correlation analysis. All hypothesis tests were performed at a significance level of 0.05.

RESULTS

Of the patients with 198 included nodules in the study, 155 were female and 43 were male. The mean age was 48.8±13.1 (minimum: 20, maximum: 80). Of the patients, 45 had FN according to the BTCRS pathology results, whereas 153 nodules had suspicious and malignant cytologies. Fifty-three percent of the nodules were located in the right lobe, 38% in the left lobe, and 9% in the isthmus. There was no statistical difference between the groups in terms of gender and localization ($p=0.614$, $p=0.173$, respectively). Thyroiditis background was present in the gland parenchyma of 24 patients (12%). The mean size of the nodules was 18.7±9.3 mm (minimum: 6 mm, maximum: 66 mm). The mean size in the FN group was 21.2±9.2 mm (minimum: 7, maximum: 55), whereas in the MC-MSC group, it was 18±9.3 mm (minimum: 6, maximum: 66) (Table 1). In the comparison of the two groups, the size criterion in the FN group was found to be statistically significant ($p=0.013$). Ninety-three percent of the FN group and 92% of the MC-MSC group had a single nodule. The distribution of the FN and MC-MSC groups according to the TIRADS category is shown in Table 2. In the comparison of the two groups, the TIRADS score was higher in the MC-MSC group and was found to be statistically significant ($p=0.041$). The characteristics of the nodules according to the TIRADS criteria are shown in Table 3. In the comparison of the two groups, the margin feature was found to be statistically significant. Apart from this result, no statistically significant difference was found in the comparison of the two groups in other results.

DISCUSSION

With the widespread use of imaging methods, especially US, the incidence of thyroid nodules and cancer is increasing in the community. Our study highlights the importance of using TIRADS to differentiate malignant from benign nodules. Although TIRADS scores were higher in the MC-MSC group, nodule sizes were larger in the FN group. Both nodules and thyroid cancers are observed 3-4 times more in women than in men.[7] In our study, this ratio was found to be 3.6 (155/43).

The ACR-TIRADS system helps to determine the malignancy risk of detected nodules in daily practice and guides us in deciding on FNAC. In the study by Horvath et al.[5], the malignancy rates reported according to the TIRADS category were found to be 0% in TR2, 14.1% in TR3, 45% in TR4, and 89.6% in TR5. In the study by Park et al.[8], these rates were reported as 9.6%, 31.1%, 76.8%, and 100% for TR2, TR3, TR4, and TR5, respectively. Kwak et al.[9] reported these rates as 0.1%, 1.7%, 3.3%, 9.2%, 44.4-72.4%, and 87.5% for TR2, TR3, TR4a, TR4b, TR4c, and TR5, respectively. In our study, these rates were found to be 8% in TR2, 16% in TR3, 57% in TR4, and 19% in TR5. When compared with

Table 1. Distribution of age, size and TIRADS score of the groups

	FN (mean±SD)	MC-MSC (mean±SD)	p value
Age (years)	49.78±11.80	48.54±13.55	**0.581**
Size (mm)	21.20±9.30	18.00±9.31	**0.013**
TIRADS score	4.1±1.5	4.9±1.9	**0.041**

FN: Follicular neoplasm, MC-MSC: Malign cytology, cytology suspicious for malignancy, TIRADS: Thyroid Imaging Reporting and Data System, SD: Standard deviation

Table 2. Distribution of FN and MC-MSC groups according to TIRADS category

TIRADS	FN (n)	MC-MSC (n)	Total (n)
TR 1	0 (0%)	0 (0%)	0 (0%)
TR 2	5 (11%)	11 (7%)	16 (8%)
TR 3	7 (16%)	26 (17%)	33 (16%)
TR 4	28 (62%)	85 (56%)	113 (57%)
TR 5	5 (11%)	31 (20%)	36 (19%)
Total	45 (100%)	153 (100%)	198 (100%)

FN: Follicular neoplasm, MC-MSC: Malign cytology, cytology suspicious for malignancy, TIRADS: Thyroid Imaging Reporting and Data System, n: Number of patients

Table 3. Distribution of TIRADS criteria of nodules according to groups

TIRADS criteria		FN	MC-MSC	p value
Composition				
	Cystic and solid mixed	5 (11%)	13 (8.5%)	0.564
	Solid	40 (89%)	140 (91.5%)	
Echogenicity				
	Hyper-isoechoic	16 (35.6%)	57 (37.3%)	0.835
	Hypoechoic	29 (64.4%)	96 (62.7%)	
Shape				
	Parallel to the skin	44 (97.8%)	151 (98.7%)	0.541
	Perpendicular to the skin	1 (2.2%)	2 (1.3%)	
Contour				
	Smooth and well-defined	41 (91.1%)	113 (73.9%)	**0.046**
	Lobulated or irregular	2 (4.4%)	26 (17%)	
	Extrathyroidal extension	2 (4.4%)	14 (9.2%)	
Echogenic focus				
	None or comet-tail	37 (82.2%)	108 (70.6%)	0.404
	Macrocalcification	4 (8.9%)	14 (9.2%)	
	Peripheral rim calcification	0 (0%)	3 (2%)	
	Punctate microcalcification	4 (8.9%)	28 (18.3%)	
Internal structure				
	Homogeneous	29 (64.4%)	94 (61.4%)	0.715
	Heterogeneous	16 (35.6%)	59 (38.6%)	

FN: Follicular neoplasm, MC-MSC: Malign cytology, cytology suspicious for malignancy, TIRADS: Thyroid Imaging Reporting and Data System

the literature, the malignancy risk of nodules defined as TR4 was slightly higher, whereas the malignancy risk of TR5 nodules was slightly lower. This may be because TR4 nodules cover nodules in the range of 4-6 points, making it a more heterogeneous group, and the relatively high number of nodules with 6 points.

In our study, it was noteworthy that malignant nodules developed in a single-nodule background in 92-93% of cases. Similarly, in a study by Keskin et al.[10], it was found that lesions with a single nodule on US were 3.6 times more likely to be malignant.

US features such as hypoechoic/markedly hypoechoic echogenicity, irregular or spiculated margins, and micro or macrocalcifications increase the risk of malignancy in thyroid nodules.[2,11] While these criteria are helpful in diagnosing papillary thyroid carcinoma (PTC), they are less helpful in diagnosing follicular thyroid carcinoma (FTC).[12] Compared with PTC, FTC is generally larger in size, isoechoic with a hypoechoic halo, and often lacks suspicious US features that suggest PTC.[13,14] Hoang et al.[13] found statistically significant differences between PTC and FTC in the following features: orientation to the long axis of the skin (74.0% vs. 26.1%), hypoechoic appearance (72.4% vs. 34.8%), irregular margin (92.9% vs. 60.9%), fine calcifications (33.9% vs. 0%), absence of hypoechoic halo (74.0% vs. 13.0%), and absence of cystic changes (98.4% vs. 82.6%). The combination of these features indicates distinct differences in US images between PTC and FTC. Additionally, a comprehensive evaluation using the SEER database revealed that, on average, PTC nodules have a smaller diameter compared with FTC, and nodules larger than 4 cm are less common in PTC (8% compared to 27% in FTC).[15] In our study, nodules with FN were found to be statistically significantly larger than nodules with MC-MSC (p=0.013). Additionally, in the comparison of the two groups in our study, the TIRADS score was found to be statistically significantly higher in the MC-MSC group, which is consistent with the literature and confirms that the TIRADS criteria are more meaningful in the diagnosis of PTC. In the literature, the evaluation of TIRADS categorization by two radiology experts in our study is an important advantage.

Study Limitations

Our limitations include the small number of patients and the retrospective nature of the study, scoring records that do not include a TIRADS score in the US report. Moreover, the evaluation of patients with cytology suspicious for malignancy along with the results of MC in our study may have led to misleading results.

CONCLUSION

In conclusion, the ACR-TIRADS reporting system should be used as a common language by radiologists and clinicians to determine the malignancy potential of thyroid nodules and avoid unnecessary biopsies. However, it should be kept in mind that the US features of FTC may be different from typical TIRADS criteria, and size is a significant finding in distinguishing FTC from PTC.

Ethics

Ethics Committee Approval: Our research was approved by the University of Health Sciences Türkiye, İzmir Bozyaka Training and Research Hospital Ethics Committee (decision no: 2023/105, date: 19.07.2023).

Informed Consent: Retrospective study.

Authorship Contributions

Surgical and Medical Practices: H.Ç.T., M.S., Concept: H.Ç.T., Design: H.Ç.T., A.B., Data Collection or Processing: H.Ç.T., A.B., M.S., A.A., Analysis or Interpretation: H.Ç.T., A.B., M.S., A.A., Literature Search: H.Ç.T., A.B., A.A., Writing: H.Ç.T.

Conflict of Interest: No conflict of interest was declared by the authors.

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