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Research Article

Correlation of ultrasound and cytological diagnosis of thyroid nodule using TIRADS and Bethesda classifications

TIRADS ve Bethesda sınıflandırmaları kullanılarak tiroid nodülünün ultrason ve sitolojik tanısının korelasyonu

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Abstract

Aim: The objective of this study was to evaluate the compatibility between the two diagnostic methods used in the initial evaluation of individuals with a thyroid nodule, the TIRADS and Bethesda systems.

Material and Methods: Between January 2020 and December 2022, FNA biopsies performed by a single interventional radiologist on 414 patients with thyroid nodules under US guidance were retrospectively reviewed. Demographic information of the patients, size of the nodules, echogenicity, TIRADS and Bethesda scores were recorded and analyzed.

Results: The mean age of the study population was 50.4 ± 14.2 years and the majority were female patients (74.9%). When thyroid nodules were classified according to TRIADS criteria, it was TIRADS TR2 in 29 (7%) patients, TIRADS TR3 in 147 (35.5%) patients, TR4 in 166 (40.1%) patients, and TR5 in 72 (17.4%) patients. The probability of malignant FNAC (Bethesda Class V and Class VI) in TIRADS classes 2, 3, 4, and 5 was 0%, 3.4%, 31.3%, and 66.7%, respectively. The probability of a benign FNAC (Bethesda Class II) in TIRADS category 2 was 100%, while for TIRADS classes 3, 4 and 5 it was 81.6%, 34.9% and 25%, respectively.

Conclusion: Our study shows a good correlation between the Bethesda Classification of thyroid nodule FNAC and thyroid ultrasound reporting using the TIRADS classification. Correct interpretation of the two findings helps the clinician reduce the risk of unnecessary invasive procedures in patients who are unlikely to demonstrate thyroid cancer, while facilitating the identification of patients at high risk of cancer.

Keywords: Fine-needle aspiration cytology, Thyroid nodules, TIRADS, Bethesda, Ultrasonography

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Öz

Amaç: Tiroid nodülü olan bireylerin ilk değerlendirmesinde kullanılan iki tanı yöntemi TIRADS ve Bethesda sistemleri arasındaki uyumu değerlendirmektir.

Gereç ve Yöntemler: Ocak 2020 ve Aralık 2022 yılları arasında tek bir girişimsel radyolog tarafından US kılavuzluğunda yapılan 414 tiroid nodüllü hastaya yapılan İİA biyopsileri retrosepektif olarak incelendi. Hastaların demografik bilgileri, nodüllerin boyutu, ekojenitesi ve kontur durumu, TIRADS ve BETHESDA skorları kaydedildi ve analiz edildi.

Bulgular: Çalışma popülasyonunun ortalama yaşı 50.4 ± 14.2 idi ve çoğunluğu kadın hastalardı (%74.9). Hastaların ortalama nodül boyutu 18.36 ± 12.96 mm olarak ölçüldü. Tiroid nodülleri TIRIADS kriterlerine göre sınıflandırıldığında 29 (%7) hastada TIRADS TR2, 147 (%35.5) hastada TIRADS TR3, 166 (%40.1) hastada TR4 ve 72 (%17.4) hastada TR5 idi. TIRADS 2, 3, 4 ve 5 sınıflarında Bethesda Class V ve Class VI olasılığı sırasıyla %0, %3.4, 31.3 ve %66.7 idi. TIRADS kategori 2'de Bethesda Sınıf II olasılığı %100 iken, TIRADS 3, 4 ve 5 sınıfları için sırasıyla %81.6, %34.9 ve %25 idi.

Sonuçlar: Çalışmamız, tiroid nodülü İİAS'nin Bethesda Sınıflandırması ile TIRADS sınıflandırmasını kullanan tiroid ultrason raporlaması arasında oldukça iyi bir korelasyon olduğunu göstermektedir. İki bulgunun doğru yorumlanması, klinisyenin tiroid kanseri gösterme olasılığı düşük olan hastalarda gereksiz invaziv prosedür riskini azaltmasına yardımcı olurken, yüksek kanser riski taşıyan hastaların belirlenmesini kolaylaştırır.

Anahtar Kelimeler: İnce iğne aspirasyon sitolojisi, Tiroid nodülleri, TIRADS, Bethesda, Ultrasonografi

Introduction

Thyroid nodules are defined as lesions of the thyroid gland that are radiologically different from the surrounding parenchyma [1]. The prevalence of thyroid nodules varies between 4% and 7% by palpation alone, and it increases to 20% and 76% in the adult population using imaging modalities such as high-resolution ultrasonography [2-4]. Nodules detected on radiographic examinations are called "thyroid incidentalomas" [2-5]. The main concern in the evaluation of thyroid nodules is the possibility of malignancy. Therefore, the distinction between benign and malignant nodules is of great importance in clinical evaluation. When invasive procedures are evaluated, the mean prevalence of malignancy rates in thyroid nodules worldwide ranges from 4.0% to 6.5% [6,7]. The incidental diagnosis of thyroid nodules is increasing in parallel with the widespread use of ultrasound, fine needle aspiration cytology (FNAC), and developments in 18 FDG-PET imaging.

Some evidence-based guidelines have been developed for the evaluation of patients presenting with thyroid nodules. The American Thyroid Association (ATA) recommends thyroid US along with cervical lymph node examination in patients with suspected thyroid nodules [8]. Similarly, the National Comprehensive Cancer Network (NCCN) recommends lateral neck compartment ultrasound along with thyroid US in all patients with suspected thyroid nodules. recommends that lymph nodes be evaluated as well. It is a neck mass detected incidentally [9]. The clinical purpose of thyroid USG is to detect nodules with a high risk of thyroid cancer. The presence of findings such as microcalcifications, irregular edges, and significant hypoechogenicity indicates a higher risk of malignancy. Current guidelines divide thyroid nodules into risk categories based on the above-mentioned suspicious features and recommend biopsy.

Thyroid Imaging Reporting and Data Systems (TIRADS) is a classification system based on ultrasound characteristics proposed by Horvath et al. TIRADS Scoring is determined by ultrasound findings in five categories. Ultrasound features assessed for each nodule were composition (solid, cystic, mixed), echogenicity (hyperechoic, isoechoic, hypoechoic), margins (well defined with or without halo sign, microlobulated, ill-defined, irregular), presence of calcification (microcalcification, macrocalcification), and shape of the nodule (round, oval). The higher the cumulative score and the TR (TI-RADS) level increase the probability of malignancy. The findings in each category were detailed in the American College of Radiology (ACR) committee's in 2015 [10]. The primary aim of TIRADS is to improve patient management and cost-effectiveness by avoiding unnecessary fine needle aspiration (FNA) biopsies in patients with thyroid nodules [11]. This system also unifies the language among radiologists and endocrinologists all over the world.

In the classification of thyroid nodules, sensitivity and specificity values for TIRADS have been reported as 88% and 49%, respectively [12]. However, its clinical use is still very limited and its application in clinical practice is questioned. FNA biopsy is the most accurate method for detecting malignancy and is an essential part of current thyroid nodule evaluation. The Bethesda System is a standard reporting system based on six criteria used to classify thyroid FNA biopsy results and includes recommendations for clinical management. A recent

meta-analysis evaluated the validity of the Bethesda reporting system and found 97% sensitivity, 50.7% specificity, and 68.8% diagnostic accuracy; negative and positive predictive values were 96.3% and 55.9%, respectively [13,14]. Although both ultrasonography (US) and FNA biopsy are commonly recommended procedures for examining patients with thyroid nodules, the compatibility between the two methods is still controversial. In conclusion, the aim of this study was to evaluate the compatibility between two diagnostic methods (TIRADS and Bethesda systems) used in the initial evaluation of individuals with thyroid nodules.

The Ankara Bilkent City Hospital Clinical Researches Ethics Committee, (No: E2-23-3988, Date: 25/04/2023) has authorized all techniques used in this work. The authors declare that they adhered to the ethical norms of the 1975 Helsinki Declaration, as revised in 2008.

Material and Methods

The study included 414 consecutive patients who were referred to the interventional radiology department of our hospital from the departments of endocrinology, internal medicine, or general surgery with the diagnosis of nodular or non-nodular "thyroid dysfunction" for neck imaging and who underwent thyroid biopsy after detecting a suspicious thyroid nodule in ultrasonography between January 2020 and December 2022. Patients with normal thyroid imaging (TIRADS 1), Graves-Basedow-associated hyperthyroidism, patients with toxic thyroid nodular disease, and patients with a history of surgically resected thyroid cancer were not included in the study.

Ultrasonography reports and cytology results of all patients were reviewed retrospectively using the hospital data system. Demographic information such as age and gender, ultrasound characteristics such as size and echogenicity of nodules, lesion structure, and pathological results were recorded.

Sonographic evaluation

All procedures were performed using a high-resolution ultrasound device (Acuson Juniper, Siemens Healthineers, Erlangen, Germany) with a 6.7-10 MHz linear transducer probe. TIRADS classification based on sonographic features was performed by an experienced radiologist prior to FNA cytology (Table 1).

Table 1. Thyroid imaging reporting and data system (TIRADS) and the Bethesda System for Reporting Cytopathology	
TIRADS 1: Normal thyroid gland.	I. Nondiagnostic or unsatisfactory.
TIRADS 2: Benign conditions (0% malignancy).	Cyst fluid only.
TIRADS 3: Probably benign nodules (5% malignancy).	Virtually acellular specimen.
TIRADS 4: Suspicious nodules (5–80% malignancy rate). A subdivision into 4a (malignancy between 5 and 10%) and 4b (malignancy between 10 and 80%) was optional.	Other (obscuring blood, clotting artifact, etc.).
TIRADS 5: Probably malignant nodules (malignancy >80%).	II. Benign.
TIRADS 6: Category included biopsy proven malignant nodules	Consistent with a benign follicular nodule (includes adenomatoid nodule, colloid nodule, etc.).
	Consistent with lymphocytic (Hashimoto) thyroiditis in the proper clinical context.
	Consistent with granulomatous (subacute) thyroiditis.
	III. Atypia of undetermined significance/follicular lesion of undetermined significance.
	IV. Follicular neoplasm/"suspicious" for follicular neoplasm. Specify if Hürthle cell type.
	V. Suspicious for malignancy.
	Suspicious for papillary carcinoma.
	Suspicious for medullary carcinoma.
	Suspicious for metastatic carcinoma.
	Suspicious for lymphoma.
	VI. Malignant.
	Papillary thyroid carcinoma.
	Poorly differentiated carcinoma.
	Medullary thyroid carcinoma.
	Undifferentiated (anaplastic) carcinoma.
	Squamous cell carcinoma.
	Carcinoma with mixed features.
	Metastatic.

FNAC procedure

Informed consent for the procedure was obtained from all patients. FNAC was performed by an experienced interventional radiologist under US guidance. FNAC was not performed for completely cystic lesions. An immediate sample adequacy assessment was performed by a cytopathologist, and smears were interpreted and categorized according to the Bethesda system by an experienced pathologist.

All personal data were confidential and managed exclusively by the principal investigator, according to the legal standards on the confidentiality of the medical record and adhering to the rules of the Institutional Review Committee of Human Ethics (reference number: 05.01.2023- 70).

Results

A total of 414 patients who underwent thyroid nodule biopsy were included in the study. The mean age of the study population was 50.4 ± 14.2 years and the majority were female patients (74.9%). The mean nodule size of the patients was measured as 18.36 ± 12.96 mm. Demographic characteristics of the patients are given in Table 2. Malignancy was more common among male patients presenting with a thyroid nodule (P = 0.001). There was significant difference in the mean age of patients with benign (mean age was 51.5 ± 14.1 years) and malignant thyroid nodules (mean age was 44.6 ± 13.1 years) (P = 0.001). There was significant difference in the age of male and female patients with benign nodules (P = 0.014) and patients with malignant thyroid nodules, men (mean age was 50.6 years) were significantly older than women (mean age was 39.4) (P = 0.001). There was no significant difference in the mean size of benign nodules (mean of 18.7 ± 12.1 mm, range 4.6-56.7 mm) and malignant thyroid nodules (mean of 16.4± 17 mm, range 6-67.9 mm) (P = 0.160)

Table 2. Demographic features of the patients

Age (years)	50.4 ± 14.2
Sex	
male	104 (25.1%)
female	310 (74.9%)
Size (mm)	18.36 ± 12.96
Composition	
solid	292 (70.5%)
semi-solid	122 (29.5%)
Echogenicity	
isoechoic	36 (8.7%)
hypoechoic	274 (66.2%)
hyperechoic	104 (25.1%)

When thyroid nodules were classified according to TRIADS criteria, it was TIRADS TR2 in 29 (7%) patients, TIRADS TR3 in 147 (35.5%) patients, TR4 in 166 (40.1%) patients, and TR5 in 72 (17.4%) patients. Cases with an already proven case of malignancy (TIRADS 6) were not included in the study. When the Bethesda categories of the patients were evaluated according to the pathological examination, Bethesda II category in 225 (54.4%) patients, Bethesda III category in 40 (9.7%) patients, Bethesda IV category in 44 (10.6%) patients, Bethesda V in 42 patients (10.1%), and Bethesda VI in 63 patients (15.2%) was found. There were no inadequate or insufficient samples (Bethesda Class I) (Table 3).

Table 3. Thyroid imaging reporting and data system (TIRADS) and Bethesda correlation

	Bethesda II	Bethesda III	Bethesda IV	Bethesda V	Bethesda VI	Total
TIRADS 2	29 (100%)	0	0	0	0	29
	(100%)					
TIRADS 3	120 (81.6%)	17 (11.6%)	5 (3.4%)	0	5 (3.4%)	147
TIRADS 4	58 (34.9%)	23 (13.9%)	33 (19.9%)	36 (21.7%)	16 (9.6%)	166
TIRADS 5	18 (25%)	0	6 (8.3%)	6 (8.3%)	42 (58.3%)	72
Total	225	40	44	42	63	414

The probability of malignant FNAC (Bethesda Class V and Class VI) in TIRADS classes 2, 3, 4, and 5 was 0%, 3.4%, 31.3%, and 66.7%, respectively. The probability of a benign FNAC (Bethesda Class II) in TIRADS category 2 was 100%, while for TIRADS classes 3, 4 and 5 it was 81.6%, 34.9% and 25%, respectively.

Of the 166 cases classified as TIRADS 4, cytology showed that 58 were benign (Bethesda Class II), 33 were follicular neoplasms (Bethesda Class IV), and 23 were indeterminate (Bethesda Class III). Among the 72 cases suspected to be malignant on ultrasound (TIRADS 5), 48 patients had biopsy (FNAC)-proven cancer (66.7% concordance), but 18 cases were cytologically benign (false positive sonographic impression).

Of 225 patients in the Bethesda II category, 120 (53.3%) likely had benign nodules (TR3), 58 (25.7%) suspected nodules

(TR4), and 18 (8%) likely malignant nodules (TR5) was found. When 44 patients in the Bethesda IV category were analyzed, 5 (11.4%) probably had benign nodules (TR3), 33 (75%) had suspicious nodules (TR4), and 6 (13.6%) had possibly malignant nodules (TR5). In Bethesda category V-VI 5 of 105 patients (4.8%) had possibly benign nodules (TR3), 52 patients (49.5%) had suspicious nodules (TR4), and 48 patients (45.7%) had possibly malignant nodules (TR5).

Discussion

A four-step process is used to evaluate a thyroid nodule, which includes clinical examination, thyroid function tests, thyroid ultrasound, and US-guided aspiration cytology, respectively. However, the most important parameter that enables us to reach a pathological diagnosis is cytological diagnosis with FNA biopsy. FNAC is a useful and cost-effective method for detecting thyroid malignancies. However, it is still controversial which patients should be offered FNAC because of the very high prevalence of thyroid nodules and the minimally invasive nature of FNAC [4]. Various classifications based on sonographic features have recently been proposed to aid this selection.

The American College of Radiologists has accepted the suitability of the TIRADS classification system in the ultrasonographic clinicopathological evaluation of thyroid nodules. The TIRADS scoring system consists of six categories. Horvath et al. reported the malignancy risk of the TIRADS scoring system as 0% in TIRADS 2, 14.1% in TIRADS 3, 45% in TIRADS 4, and 89.6% in TIRADS 5 [11]. After 2009, many studies have been conducted to evaluate the reliability of the TIRADS classification system in distinguishing benign thyroid nodules from malignant ones. Reported rates of malignancy for TIRADS 2–5 categories, respectively, were 9.6% (TRIADS 2), 31.1% (TRIADS 3), 76.8% (TRIADS 4) and 100% (TRIADS 5) by Park et al. [15]. In a single-center study evaluating a total of 184 patients, 156 of whom were women, it was reported as 0% (TRIADS 2), 2.2% (TRIADS 3), 38.5% (TRIADS 4) and 77.8 % (TRIADS 5) [16]. In another study including patients with solitary thyroid nodules and clinical maximum size exceeded 1 cm, the thyroid nodules for malignancy was 6.6%, 32%, 36%, 64%, 59%, and 91% for TIRADS 2, 3, 4a, 4b, 4c, and 5 categories, respectively [17]. In these two studies, nodules classified as Bethesda I and II were considered benign, and nodules classified as Bethesda IV-VI were considered malignant. Kwak et al. proposed a TIRADS classification based on retrospective analysis of thyroid nodules on ultrasound and FNA [18]. This article describes that a malignancy risk of 0% is expected for TIRADS 2, 1.7% for TIRADS 3, 3.3-72.4% for TIRADS 4 and 87.5% for TIRADS 5. The main limitation of this study was that each suspicious sonographic feature was given the same importance, even though in reality each ultrasound feature has a different probability for malignancy. For example, a nodule with marked hypoechogenicity/microcalcifications has a higher risk of malignancy than other nodules with irregular margins. In our study, the risk of malignancy for the different TIRADS categories was 0% (TIRADS 2), 3.4% (TIRADS 3), 31.3% (TIRADS 4) and 66.7% (TIRADS 5). There appears to be significant differences between studies in the reported proportions of TIRADS categories. These differences may be due to the inclusion of other TIRADS categories (especially TR1 and TR2) in some studies. Additionally, in our study, follicular neoplasm or susceptible for a follicular neoplasm (Bethesda IV) was not included in the malignant category. Also, general inclusion and exclusion criteria can cause these differences.

Our study shows that there is strong agreement between the TRIADS and Bethesda categories [12,19], both between the lowest risk (TIRADS 2 and Bethesda II) and higher risk groups (TIRADS 5 and Bethesda V), consistent with previously published studies. This indicates that US features suggesting a higher or lower risk of malignancy will be associated with a higher or lower probability of malignancy, respectively, according to the FNA biopsy report (Bethesda).

Our study has several limitations. First, our report is a single institutional study. An inherent weakness of this study is its retrospective nature. Despite having an experienced radiologist, the use of more than one radiologist for the interpretation of ultrasonographic imaging may be helpful because image analysis may differ between radiologists and the extent of interobserver variability in TIRADS classification is unknown. In addition, the fact that the cytopathological evaluation was performed by more than one cytopathologist affects the reliability of the data; however, we have a team of cytopathologists who are experienced in the field and often consult a senior cytopathologist.

Our study shows a good correlation between the Bethesda Classification of thyroid nodule FNAC and thyroid ultrasound reporting using the TIRADS classification. Correct interpretation of the two findings helps the clinician reduce the risk of unnecessary invasive procedures in patients who are unlikely to demonstrate thyroid cancer, while facilitating the identification of patients at high risk of cancer.

Ethics Committee Approval

Ethics committee approval was received for this study from the ethics committee of İstanbul Memorial Şişli Hospital Ethics Committee (References number: 05.01.2023- 70).

Informed Consent

Written informed consent was obtained from all participants who participated in this study.

Author Contributions

Concept, Design, Materials, Data Collection and/or Processing, Literature Search, Writing Manuscript – A.Y.

Declaration of Interests

The authors have no conflicts of interest to declare.

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