

Correlation of the Thyroid Nodules' Sonographic Features With Fine Needle Aspiration (FNA) Cytology Results

Hossein Ghanaati

Tehran University of Medical Sciences

Alireza Arefzadeh (✉ arefzadeh@iautmu.ac.ir)

Assistant professor of Endocrinology, Department of Endocrinology Amiralmomenin & Bouali Hospitals
Tehran Medical Sciences Islamic Azad University, Tehran, Iran <https://orcid.org/0000-0001-8484-3088>

Hamidreza Hosseinpour

Shiraz University of Medical Sciences

Mahsa Alborzi Avanaki

Islamic Azad University of Tehran: Islamic Azad University Central Tehran Branch

Alireza Abrishami

Shahid Beheshti University of Medical Sciences School of Medicine

Research

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Abstract

Background: Thyroid nodules are a common finding in clinical practice. Although ultrasonography is an accepted method for evaluating and following these nodules, Fine Needle Aspiration (FNA) is the procedure of choice for assessing the risk of malignancy. This study aims to determine the correlation between sonographic features of thyroid nodules based on Thyroid Imaging Reporting and Data System (TIRADS) classification and the cytology results obtained by FNA of thyroid nodules.

Methods: In this prospective cohort study, 147 patients with thyroid nodules underwent FNA under the guide of ultrasonography based on TIRADS classification, and their sonographic features were recorded. The pathologic findings were also obtained according to the Bethesda system. Finally, the association between sonographic features and cytology results were analyzed.

Results: 147 patients with a mean \pm SD age of 49.8 ± 13.7 years were assessed. 16 (10.9%) nodules were malignant, and 131 nodules (89.1%) were benign. The association of TIRADS categories with the risk of malignancy is as follows: TIRADS 1 (0%), TIRADS 2 (16.9%), TIRADS 3 (10.5%), TIRADS 4 (16.7%), and TIRADS 5 (0%). The location of thyroid nodules and their bloody lamellae were significantly correlated with the risk of malignancy (P value < 0.05). However, the association between the risk of and gender, calcification, hardness, halo sign and nodules' echogenicity were not statistically significant.

Conclusions: Although there are trusted classifications for categorizing the thyroid nodules, there is still uncertainty in utilizing them as an accepted method of choice for managing the thyroid nodules, as various sonographic features are shared between benign and malignant ones.

Background

In clinical practice, thyroid nodule is a frequent finding, which is revealed during a precise physical exam or a variety of imaging procedures [1]. According to epidemiological documents, in iodine sufficient regions of the world, near 5% of the females and 1% of the males are detected with palpable thyroid nodules [2]. However, they can be discovered in 10–41% of adults by ultrasonography (US), which is increasing with recently growing use of this imaging procedure [3] and it is stated that most of these nodules are benign [4]. Although there is an increasing incidence of thyroid nodules due to improved health care access of population [5], there is still an urge to increase the rate of diagnosis at the lowest cost and least possible time.

Ultrasonography (US) is one of the most common first-line modality of evaluating palpable thyroid nodules or detecting them incidentally [6]. However, most of these nodules should undergo Fine Needle Aspiration (FNA), which is the keystone of assessing nodular thyroid disease, to increase the accuracy of predicting their potential cancer risk [7, 8]. FNA under the guide of US has made biopsy the most important tool for making decision about conservative management or surgery of thyroid nodules [9]. There has also been a substantial controversy over assessing clinically asymptomatic nodules by FNA biopsy or close observation [10].

Thyroid Imaging Reporting and Data System (TIRADS) classification, which was first established in 2009, is a model for evaluating the thyroid nodules based on specific patterns of US that enhances the selection of nodules for further evaluation by FNA biopsy [11]. Although there are some sonographic features which are suggestive of malignancy of the thyroid nodules, there is extreme variability in reported sensitivity and specificity of these findings in correlation with final cytology results from study to study [3].

The aim of our study was to compare the cytology reports of thyroid nodules' FNA biopsy with their specific sonographic features in predicting the risk of thyroid malignancy. In other words, we tried to determine US characteristics which have the most correlation with malignant tumors to reduce the number of unnecessary FNA procedures in patients with thyroid nodules and their suitable selection.

Methods

In this prospective cohort study, a total of 147 consecutive patients with thyroid nodules, who referred for FNA biopsy due to any reason, underwent cytological study and US after obtaining informed consent at an institution from December 2018 to September 2019. Our inclusion criteria were based on any patient who referred for further evaluation of his/her suspicious thyroid nodules due to any reason. Those who had a history of benign cytology result and previous thyroid malignancy were excluded from the study.

Neck US was performed for each patient by our experienced radiologist using a high-resolution US apparatus (Medison Accuvix V10, Korea) with 7 MHz linear transducer. Every thyroid nodule was assessed based on ACR TI-RADS criteria such as composition, echogenicity, shape, margin, and echogenic foci [12]. The TIRADS model categorizes the nodules into 5 groups ranging from 1 (benign) to 5 (highly suspicious), as summarized in Table 1. It is noteworthy that all 147 patients underwent FNA, regardless of the nodules' TIRADS grade, to determine the accuracy of ACR-TIRADS classification system.

Table 1
ACR TI-RADS categories and criteria for FNA and follow up sonography

ACR TI-RADS	Definition	Indicated management
1	Benign	No FNA
2	Not suspicious	No FNA
3	Mildly suspicious	FNA if ≥ 2.5 cm
		Follow if ≥ 1.5 cm
4	Moderately suspicious	FNA if ≥ 1.5 cm
		Follow if ≥ 1 cm
5	Highly suspicious	FNA if ≥ 1 cm
		Follow if ≥ 0.5 cm

Every suspicious nodule according to TIRADS scoring and those which were requested by patients' clinician underwent FNA biopsy under the guide of US, which was performed for them in supine position with a mid-extended neck position under standard sterilized condition by our qualified interventional radiologist. Lidocaine was used as the local anesthesia. Target nodules were aspirated with a 21-gauge needle attached to a 20 cc syringe, using aspiration technique; the obtained samples were fixed with alcohol on glass slides. Our pathologist reported the cytology based on Bethesda system.

Finally, the cytology results and TIRAD scoring of these nodules were recorded and analyzed using SPSS software. The statistical tests used included Chi-square and Fisher and Kappa for comparison of categorical variables. The P-value less than 0.05 was considered statistically significant. In addition, the sensitivity, specificity, positive predictive value, and negative predictive value of TIRADS were determined.

It is noteworthy that all 147 patients underwent FNA regardless of the nodules' TIRADS grade to determine the accuracy of ACR-TIRADS classification system.

Results

Totally, 147 nodules of 147 patients were assessed. The patients' mean age was $49.8 \text{ years} \pm 13.7$ (standard deviation) and 126 patients were female (85.7%). The age ranges of patients were from 20 to 80 years.

In histopathologic assessment, absolutely 16 nodules were malignant (10.9%), in which 15 were Papillary Thyroid Carcinoma (PTC) (83.3%), and 3 were Hurthle cell neoplasm. Hence, benign lesions were seen in 131 nodules (89.1%), in which the most common lesion was follicular nodules (86, 66.7%). Table 2 summarizes different histological findings of these nodules.

Thyroid nodules were also analyzed from other aspects. Mean suction time for each nodule was 13.7 ± 4.8 (standard deviation) (range: 4–35). Mean lamellae provided for patients was 3.7 ± 1 (1–8). Mean anteroposterior diameter was $14.2 \pm 7.3 \text{ mm}$ (1–40) and mean transverse diameter was $15 \pm 8.5 \text{ (1–50)}$ and also mean score of vacuum force was 9.5 ± 1.7 (2–10); none of them had a significant correlation with malignancy of the thyroid nodules.

According to our results, TIRADS categories had different associations with the risk of malignancy which is as follows: TIRADS 1 (0%), TIRADS 2 (16.9%), TIRADS 3 (10.5%), TIRADS 4 (16.7%), and TIRADS 5 (0%). The most common location of the nodules was in the right lobe (77, 52.4%) and 67 of them were benign. Cystic transformation was seen in 69 nodules (46.9%) and calcification was seen in 88 nodules (59.9%). Other characteristic US findings of 147 nodules are mentioned in Table 3.

Table 2
Distribution of Different Histopathological Findings among the Nodules

Malignancy	Finding	Number (%)
<i>n = 147</i>		
Benign lesions	Benign Follicular Nodule	86 (58.5)
	Hashimoto disease	9 (6.1)
	Non-Diagnostic	2 (1.3)
	Cystic fluid only	21 (14.3)
	Atypia of Undetermined Significance	11 (7.5)
	Hurtle cell benign adenoma	2 (1.3)
Malignant lesions	PTC	15 (10.2)
	Hurthle Cell Neoplasm	1 (0.7)

Table-3. Demographic and sonographic features of the thyroid nodules

Variable	Thyroid nodule		P-value
	Benign <i>n</i> = 129	Malignant <i>n</i> = 18	
	No (%)	No (%)	
Gender			
Male	20 (95.2)	1 (4.8)	0.47
Female	109 (86.5)	17 (13.5)	
TIRADS			
1	14 (100)	0 (0)	0.45
2	49 (83.1)	10 (16.9)	
3	51 (89.5)	6 (10.5)	
4	10 (83.3)	2 (16.7)	
5	3 (100)	0 (0)	
Cystic formation			
Yes	61 (88.4)	8 (11.6)	0.82
No	68 (87.2)	10 (12.8)	
Location			
Right	67 (87)	10 (13)	0.013*
Left	60 (92.3)	5 (7.7)	
Isthmus	2 (66.7)	1 (33.3)	
Left upper	0 (0)	1 (100)	
Left lower	0 (0)	1 (100)	
Calcification			
Yes	77 (87.5)	11 (12.5)	0.9
No	52 (88.1)	7 (11.9)	
Bloody lamellae			
Tiny	36 (97.3)	1 (2.7)	0.047*
somewhat	71 (83.5)	14 (16.5)	
Intermediate	15 (93.8)	1 (6.3)	
High	5 (71.4)	2 (28.6)	

Variable	Thyroid nodule		P-value
	Benign <i>n</i> = 129	Malignant <i>n</i> = 18	
	No (%)	No (%)	
Angle			
Equal to 75°	126 (88.1)	17 (11.9)	0.41
Other than 75°	3 (75)	1 (25)	
Hardness			
No	107 (89.9)	12 (10.1)	0.19
Mild	15 (78.9)	4 (21.1)	
Moderate	5 (83.3)	1 (16.7)	
Completely	2 (66.7)	1 (33.3)	
Halo sign			
Yes	67 (89.3)	8 (10.7)	0.95
No	52 (89.7)	6 (10.3)	
Echogenicity			
Hyperecho	27 (87.1)	4 (12.9)	0.058
Hypoecho	32 (80)	8 (20)	
Isoecho	37 (97.4)	1 (2.6)	
Heterogenous	23 (95.8)	1 (4.2)	
* Indicator of significant correlation			

Discussion

Fine Needle Aspiration Biopsy (FNAB) is accepted as a precise, safe, and cost-effective tool for diagnosis of the thyroid nodules, especially for preoperative decision making [13], and Sonography guided FNAB has also improved its diagnostic accuracy remarkably recently [14]. Most of the time, the purposeful or incidental finding of a thyroid nodule is first diagnosed by Ultrasonography (US) [15]. Therefore, physicians usually decide if the nodule needs further evaluation based on these nodules' sonographic features. However, most of these sonographic characteristics are shared between benign and malignant lesions [16]. In this study, we tried to compare these sonographic features based on the ACR TIRADS model with final cytology reports of the thyroid nodules and evaluate how these features could make a physician suspicious of malignancy and additional procedures.

Despite an increased rate of thyroid nodule diagnosis following a growing variety of modalities, most of the nodules are benign [17]. As in our study, 89.1% of the nodules were benign lesions, including benign follicular nodule, cystic fluid only, Colloid nodules, etc. However, different factors affect this prevalence, such as iodine deficiency, post-radiation therapy, and even patients' level of health service accessibility in different societies [17, 18].

According to our experience, like some other studies [19, 20], the size of the nodules is not a good indicator of the risk of malignancy of thyroid nodules. However, some researches claim that there is a strong association between these two factors as the larger size of the nodules correlates with a higher malignancy rate with a threshold of 2.0 cm [21, 22]. Generally, the nodules' size is not an important predictive indicator of thyroid malignancy unless accompanied by other malignant features [19].

In this study, surprisingly, we found no significant correlation between the TIRADS model and the risk of malignancy (p value = 0.45); this is in contrast with what Singaporewalla et al. [23] claimed in their research. They showed that there was an accuracy of 83% in predicting the risk of malignancy based on using TIRADS. However, the maximum correlation that we found was in TIRADS 2, with 16.9% of malignancy association. There are other studies by Horvath et al. [11], Park et al. [24], and Kwak et al. [25] that reported the leading association of TIRADS with the risk of malignancy 89.6%, 100%, and 87.5%, respectively. This may be due to our limited sample size, but notably, the TIRADS model is somehow operator dependent, as some studies suggest using this model by two radiologists at the same institution.

As mentioned above, all 147 patients underwent FNA under the guide of sonography to determine the accuracy of ACR-TIRADS classification and the correlation of histologic findings in accordance with sonographic features. In our experience, interestingly, TIRADS 2 had the most correlation with the risk of malignancy, which increases the uncertainty of using this scoring system as an indicator of thyroid nodules' FNA necessity. We believe that this discrepancy may cause the misdiagnosis of patients who present with thyroid nodules with TIRADS 2 and will not be further assessed according to ACR-TIRADS.

Our study showed that there was a statistically significant (p = 0.013) correlation between malignancy and the location of thyroid nodules, and most of our cytologically malignant nodules were located in the right lobe. Although 67 out of all 77 nodules of the right lobe were benign, 10(13%) were malignant compared to 5 (7.7%) out of 65 nodules of the left thyroid lobe. Most studies claim that there is no relationship between the location of the thyroid nodules and malignancy and despite the absence of association, the isthmus and mid-lobar nodules were the most sites of the thyroid, which correlates with the risk of malignancy [26, 27].

In accordance with a retrospective observational cohort study conducted by Frates et al. [28], one of the sonographic characteristics which correlate with malignancy would be the existence of microcalcification. This finding is also in contrast with our study in which there was no association between the nature of calcification and the risk of malignancy (p value = 0.9). In another study by Rago et al. [29], only a combination of the presence of microcalcification plus the absence of halo sign had a

significant relationship with the possibility of malignancy, which is associated with high specificity (93.0%) but low sensitivity (36.0%). Our research did not differentiate the subtypes of calcifications (such as micro, macro, coarse, and peripheral) and this may affect the results as some studies showed that although malignant thyroid nodules might correlate with microcalcifications, benign lesions are even associated with macro-calcification [30, 31].

Several studies have tried to determine if Fine Needle Capillary (FNC) sampling is superior to Fine Needle Aspiration due to a higher amount of cellular material, but they did not obtain statistically significant data [32, 33]. Although FNA sampling provides a more specific field and more diagnostic parameters than the FNC technique [33], our experience revealed that the samples accompanied by blood were significantly associated with more risk of malignancy (p value = 0.047).

In this study, we evaluated a relatively new variable to determine if the angle of the needle entry to thyroid nodules during FNA sampling affects the risk of malignancy. According to the results, there was no significant (p value = 0.47) correlation between the group of patients in whom the needle was induced in the angle of 75° and the other group who underwent this procedure with any other angle of needle entry.

Based on our experience in this research, hypoechoogenicity is somehow associated with malignancy with a p -value of 0.058, which was statistically insignificant. However, Nabahati et al. revealed that there was a considerable positive correlation between malignancy and hypoechoogenicity [odds ratio (OR) 3.577, 95% confidence interval (CI) 2.045–6.256] as their 29 nodules out of all 221 hypoechoic nodules were malignant (p value < 0.001). In our study, 26% of the thyroid nodules were hypoechoic, and 20% were malignant. Overall, echogenicity is one of the criteria of ACR TI-RADS, and as in our study, the more hypoechoogenic the thyroid nodule, the higher the risk of malignancy.

Conclusions

Thyroid nodules are a common finding of clinical practice worldwide. The clinical approach to this clinical finding is based on the first sonographic features and the FNA biopsy results. Although there are accepted models such as TIRADS to distinguish malignant lesions with high sensitivity and specificity, our study demonstrates that even these relatively trusted scoring systems may not be trustworthy enough and most of these sonographic features are mutual between malignant and benign lesions.

Abbreviations

FNA

Fine Needle Aspiration; TIRADS:Thyroid Imaging Reporting and Data System; ACR-TIRADS:American College of Radiology-Thyroid Imaging Reporting and Data System; US:ultrasonography; PTC:Papillary Thyroid Carcinoma; FNAB:Fine Needle Aspiration Biopsy; FNC:Fine Needle Capillary.

Declarations

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Authors' contributions

HG, AAr designed the study and obtained ethical approval, MA collected the clinical data and HH carried out the data gathering. AAr and HH drafted the manuscript while HG and AAb edited and prepared the final version of the article. All author proofread and approved the final version of the manuscript.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

The study protocol was approved by the medical Ethics Committee of Tehran University of Medical Sciences (Ethics ID: IR.TUMS.VCR.REC.1398.686)

Consent for publication

Consent was obtained from the patient parent/guardian regarding the publication of this case report.

Competing interests

The authors declare that they have no competing interests.

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