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Assessment of Vascularity Patterns and Sonographic Criteria in Distinguishing Benign from Malignant Thyroid Nodules

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Abstract

Introduction: Thyroid nodules are a prevalent concern, prompting extensive research into diagnostic criteria for malignancy. While sonographic criteria in TIRADS have been widely studied, the role of nodule vascularity pattern, a less explored factor, remains uncertain. This study aims to investigate various vascularity patterns in different types of thyroid nodules, evaluating their potential utility in determining nodule malignancy.

Methods: A prospective study was conducted at Imam Reza (AS) Birjand Hospital from November 2022 to November 2023, involving 92 patients with thyroid nodules presenting for fine-needle aspiration (FNA). Skilled radiologists performed ultrasound exams, documenting nodule characteristics according to Tirads criteria and predefined vascularity patterns. Pathology reports were included for correlation. Data analysis was performed using SPSS-22, with an epidemiologist conducting statistical analyses.

Results: Qualitative analysis of 92 thyroid nodules revealed four vascularity index categories: no vascularity (31.6%), peripheral vascularity (49.4%), central vascularity (13.9%), and central/peripheral vascularity (5.1%). The observed distribution was statistically significant ($p < 0.001$). Simultaneous consideration of central or central/peripheral vascularity as indicators of malignancy and peripheral vascularity or absence of vascularity as indicators of benign nodules yielded a diagnostic sensitivity and specificity of 76.9%. When applying this criterion, the specificity increased to 81%. Moreover, the positive predictive value was 40%, and the negative predictive value was 95.5%.

Conclusion: Combining vascularity patterns with established sonographic criteria in thyroid assessments significantly aids in distinguishing between benign and malignant nodules. However, caution should be exercised, as malignant nodules may exhibit any of the four vascularity patterns investigated in this study.

Key Words: TIRADS, thyroid nodule, vascularity, pathology.

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INTRODUCTION

The thyroid gland, an endocrine organ resembling a delicate butterfly in shape, spans from the fifth cervical vertebra to the first thoracic vertebra (1). It receives a bountiful dual blood supply from the superior and inferior thyroid arteries, enhancing its vital function (2). Remarkably, the thyroid takes precedence as the initial endocrine gland to manifest during the fetal period. Throughout fetal development, the thyroid's weight maintains a constant ratio in relation to the fetal weight, exhibiting minimal disparity between male and female fetuses (3). Thyroid disorders manifest in two distinct categories: diffuse and focal Diseases. In contemporary times, the presence of thyroid nodules has become prevalent within significant segments of the population. Screening ultrasounds reveal that between 33% and 68% of asymptomatic individuals, ostensibly in good health, harbor thyroid nodules (4).

Presently, the burgeoning utilization of diagnostic ultrasound and aspiration techniques, alongside the traditional practice of palpating nodules, has led to an upsurge in the identification of both differentiated and undifferentiated thyroid malignancies. Notwithstanding the potential contribution of these diagnostic tools to the increased detection, the escalating incidence of thyroid cancers cannot be disregarded (5). Although more than 90% of nodules identified through ultrasound typically exhibit a benign pathology upon final examination, due to the lack of spontaneous regression, it remains challenging to definitively discern which nodules require treatment (6). In recent times, the advent of ultrasound devices featuring higher frequencies, coupled with significant advancements in nodule characterization, has fostered widespread adoption of the

Thyroid Imaging Reporting and Data System (TIRADS) for classifying nodules as benign or malignant. This classification scheme serves as a valuable adjunct for early diagnosis and differentiation of nodules necessitating further investigation, offering a heightened discriminatory capacity beyond histopathology (8, 7).

Thyroid nodules represent a frequent pathological condition, with approximately 4-7% of the adult population demonstrating palpable nodules. Of paramount importance in the evaluation of thyroid nodules lies the accurate diagnosis of malignancy, prompting comprehensive initiatives in pursuit of this objective. Presently, the Thyroid Imaging and Reporting Data System (TIRADS) classification system has emerged as an instrumental tool for meticulous scrutiny of thyroid nodules, exhibiting commendable efficacy in discerning their benign or malignant nature, as documented by extant investigations (10, 9). Various societies have witnessed marginal disparities in the classification schema of TIRADS, featuring five distinct types, all of which have demonstrated favorable sensitivity and specificity in diverse comparative studies. However, the ACR-TIRADS classification stands as the superior choice, excelling in both sensitivity and specificity for thyroid nodule diagnosis (11). Radiologists employ specific TIRADS scoring to stratify nodules based on parameters encompassing echogenicity, nodule shape, nodule composition, nodule margins, and the presence or absence of calcifications (12).

Contemporary scholarship proposes that the amalgamation of TIRADS criteria in conjunction with histopathological examination has considerably facilitated the distinction between benign and malignant nodules. Nonetheless, the integration of qualitative and quantitative color Doppler assessments represents a novel avenue for enhancing the precision of diagnostic endeavors. These additional modalities hold promise in delineating patients necessitating pathological examination and refining the determination of TIRADS classification (13). Thus, this study endeavors to investigate whether the concurrent evaluation of color Doppler findings, in conjunction with established TIRADS criteria, can augment the accurate identification of benign nodules, delineating the need for further histopathological analysis.

Material and Methods

The study's statistical population comprised all patients referred to Imam Reza Hospital (AS) in Birjand city with thyroid nodules, who exhibited nodules in the ultrasound examination and met the sonographic criteria for aspiration. Nodules with insufficient or inappropriate samples reported from laboratory analysis were excluded from the study. Additionally, dissatisfaction with participation in the study served as an exclusion criterion.

Sample Size

Based on T Rago et al.'s (14) study, which utilized criteria of hypoechogenicity in benign nodules (13.30) and malignant nodules (6.74), sample size determination employed the formula for comparing proportions in two independent groups with a 95% confidence level and 80% power. Accordingly, a total of 23 individuals were calculated for each group. Considering the prevalence of benign and malignant nodules, 92 patients were included in the study.

$Z(1-\beta) = 0.84$, $Z(1-\alpha/2) = 1.96$

$$\frac{\left\{\left(z_{1-\frac{\alpha}{2}}\sqrt{2p\bar{q}} + z_{1-\beta}\sqrt{p_1q_1 + p_0q}\right)\right\}^2}{(p_1 - p_0)^2}$$

Procedure

In this study, patients referred for thyroid nodule needle aspiration underwent evaluation by an experienced radiologist. Utilizing the TIRADS criteria, all thyroid nodules subjected to needle aspiration were categorized into six groups: benign, probably benign, suspected malignant, malignant, and previously proven malignant. Sonographic criteria, encompassing echogenicity, shape, margin, and other factors, were employed to define these six categories. Moreover, the radiologist assessed the vascularity of the thyroid nodules in addition to the TIRADS sonographic criteria. Notably, nodule vascularity assessments were conducted prior to biopsy to prevent biopsy-related inflammation from interfering with the vascularity evaluation. After acquiring the necessary information for TIRADS classification and examining the vascularity patterns of the nodules, such as lack of vascularity, peripheral or central vascularity, or simultaneous peripheral and central vascularity, the desired samples were sent to the pathology laboratory. The detailed pathological examination of the samples facilitated the classification of thyroid nodules into four categories: benign, indeterminate, malignant, and insufficient samples. The obtained information was subsequently recorded in the corresponding patient checklist.

Data Analysis

The collected data were entered into SPSS-22 software throughout the study's implementation and subjected to statistical analysis. Descriptive statistics, including relative and absolute frequencies for qualitative data, were reported. The comparison of variables relied on the chi-square test or Fisher's exact test. Furthermore, the sensitivity and specificity of the examined variables in diagnosing benign and malignant thyroid nodules will be reported. The significance level was set at 0.05.

Ethical Considerations

The researcher adhered to ethical requirements, including the preservation of patient confidentiality, in accordance with the Declaration of Helsinki. The study commenced after receiving approval from the ethics committee. No additional costs were imposed on the patients, and all research stages involved informed consent from the participants.

Results

A total of 92 patients were included in this study, with the youngest patient being 33 years old and the oldest patient being 64 years old. The average age of the study population was 50.03 ± 7.58 years. Out of the total population, 53 (42.4%) were female and 39 (57.6%) were male. To provide a comprehensive analysis, the patients were further categorized into four age groups: 14 patients under 40 years old, 35 patients between 40 and 50 years old, 33 patients between 50 and 60 years old, and 10 patients over 60 years old. The majority of patients with thyroid nodules were women in the age group of 40 to 60 years.

Regarding the nature of thyroid nodules, 47 (51.1%) were solid nodules, 36 (39.1%) were mixed solid cystic nodules, and 9 (9.8%) were cystic nodules. Analysis of nodular echogenicity revealed that the highest proportion (40.2%) exhibited hypoechoic characteristics, followed by 31 people (33.7%) with hyper-isoechoic characteristics, 17 people (18.5%) with no echo, and 7 people (7.6%) with markedly hypoechoic characteristics. In terms of nodule shape, 70 individuals (76.1%) had wider nodules, while 22 individuals (23.9%) had taller nodules. When examining the nodule margins, the majority (66.3%) exhibited regular margins, while 6 (6.5%) had irregular margins, and 24 (26.1%) had lobulated margins. The frequency distribution of nodule classifications was 48 people (52.2%), 21 people (22.8%), 23 people (25%), and 23 people (52.8%).

In this study, nodules were categorized into four vascularity patterns, with peripheral vascularity being the most common (Table 1).

Tab.1. Frequency of Vascularity Patterns.

Frequency	Percent	The cumulative frequency	Vascularity pattern
26	28.3	28.3	No vascularity
41	44.6	72.8	Peripheral vascularity
17	18.5	91.3	Central vascularity
8	8.7	100	Central and peripheral vascularity

In the assessment of thyroid nodule types based on pathological examinations, 85.9% were classified as benign and 14.1% as malignant. Additionally, the association between thyroid nodules and benign or malignant types was examined. Most benign tumors were associated with thyroid nodules grade 3, while malignant tumors were more frequently associated with thyroid nodules grade 5. This correlation between thyroid nodules and benign or malignant types was statistically significant (p = 0.001) (Table 2).

Tab.2. Investigation of the Relationship between TIRADS and Pathology Types.

			Tirads			Total
			3	4	5	
pathology	benign	Count	47	17	15	79
		% within pathology	59.50%	21.50%	19.00%	100.00%
	malig	Count	1	4	8	13

	malignant	% within pathology	7.70%	30.80%	61.50%	100.00%
Total		Count	48	21	23	92
		% within pathology	52.20%	22.80%	25.00%	100.00%

When exploring the relationship between the nature of thyroid nodules and pathology types specifically within the benign nodules group, 36 cases exhibited a solid consistency, while 34 cases displayed a mixed solid cystic nature. Furthermore, 9 cases of benign nodules were entirely cystic. Among the 13 nodules with malignant pathology, 11 cases demonstrated solid consistency, while 2 cases presented a cystic solid nature (Table 3).

Tab.3. Correlation between Pathology and Nodule Nature.

			composition			Total
			cystic	mixed solid cystic	solid	
pathology	benign	Count	9	34	36	79
		% within pathology	11.40%	43.00%	45.60%	100.00%
	malignant	Count	0	2	11	13
		% within pathology	0.00%	15.40%	84.60%	100.00%
Total		Count	9	36	47	92
		% within pathology	9.80%	39.10%	51.10%	100.00%

In the analysis of echogenicity patterns, 30 out of 79 benign nodules exhibited hyper or isoechoic characteristics. Additionally, 26 cases demonstrated hypoechoic characteristics, while 6 cases displayed severe hypoechoic characteristics. Among the malignant thyroid nodules, 11 cases were hypoechoic, 1 case was severely hypoechoic, and 1 case was hyper or isoechoic (Table 4).

Tab.4. Relationship between Echogenicity and Nodule Type.

			echogenicity				Total
			anecho	hyper/iso	hypo	extremely hypo	
pathology	benign	Count	17	30	26	6	79
		% within pathology	21.50%	38.00%	32.90%	7.60%	100.00%
	malignant	Count	0	1	11	1	13
		% within pathology	0.00%	7.70%	84.60%	7.70%	100.00%
Total		Count	17	31	37	7	92
		% within pathology	18.50%	33.70%	40.20%	7.60%	100.00%

Among the studied benign nodules, 65 cases were wider than tall, while 14 cases were taller than wide. In malignant nodules, 8 cases were taller than wide, and 5 cases were wider than tall.

The analysis of nodule margins revealed that 70.9% of benign nodules had clear margins, 24.1% had lobulated margins, and 3.8% had unclear margins. Among the malignant nodules, 38.5% exhibited clear margins, 23.1% had unclear margins, and the remaining 38.5% displayed lobulated borders. The investigation of echogenic focus (calcification) and nodule pathology demonstrated that among benign nodules, 48.1% had no calcification, 35.4% exhibited macrocalcification, 6.3% displayed point calcification, and 10.1% demonstrated rime calcification. Among malignant nodules, 53.8% had no microcalcification, 38.5% exhibited point calcification, and 7.7% displayed rimlike calcification.

In the logistic regression model, which included variables such as age, sex, vascularity pattern, and TIRADS, it was observed that individuals with high TIRADS had 25.3 times higher odds of central vascularity and a 22.3 times higher probability of malignancy (Table 5).

Tab.5. Logistic Regression Model.

B	S.E.	Wald	df	Sig.	Exp (B)	95% C.I.for EXP(B)		
						Lower	Upper	
1.18	0.466	6.417	1	0.011	3.253	1.306	8.103	Tirads
1.17	0.429	7.434	1	0.006	3.22	1.389	7.465	Vascularity pattern
0.0	0.0	0.7	1	0.3	1.04	0.94	1.1	Age

45	52	56		85	6	5	57	
0.972	0.837	1.349	1	0.245	2.642	0.513	13.618	sex
-13.333	3.911	11.623	1	0.001	0			constant

The diagnostic value of TIRADS 3, 4, and 5 was assessed in this study. Among nodules with TIRADS 4 and 5, 12 demonstrated malignant pathology, while 32 cases had benign pathology. In TIRADS 3, one nodule exhibited malignant pathology, while 47 cases presented benign pathology. The sensitivity and specificity of TIRADS in nodule examination were determined to be 92.3% and 59.45%, respectively. Additionally, the positive predictive value of TIRADS in nodule examination was 27.2%, and the negative predictive value was 97.9%.

In the evaluation of the diagnostic value of the vascularity pattern of nodules, the majority of malignant nodules (10 out of 13 cases) displayed both central and peripheral vascularity. Among the total of 79 nodules with benign pathology, 64 cases exhibited no vascularity or peripheral vascularity, while 15 cases demonstrated central and peripheral-central vascularity patterns simultaneously. The examination of the vascularity pattern of nodules in the diagnosis of benign and malignant types exhibited a sensitivity of 76.9% and a specificity of 81%. The positive predictive value for vascularity patterns was 40%, and the negative predictive value was 95.5% in this study.

Discussion

The investigation of TIRADS indices in determining the benignity or malignancy of thyroid nodules has been extensively studied and analyzed in terms of diagnostic accuracy and the frequency of different ultrasound characteristics. The current classification system, TIRADS, is widely trusted by internal medicine practitioners and endocrinologists. However, several studies have proposed the consideration of additional nodule characteristics, such as vascularity, to enhance the accuracy of diagnosing benign and malignant thyroid nodules, highlighting potential limitations in the existing diagnostic criteria (15).

In this particular study, a qualitative classification of 92 thyroid nodules was conducted, categorizing them into four groups: nodules without vascularity, nodules with peripheral vascularity, nodules with central vascularity, and nodules with both central and peripheral vascularity. Among the benign nodules, 31.6% exhibited No vascularity, 49.4% displayed peripheral vascularity, 13.9% demonstrated central vascularity, and 5.1% exhibited both central and peripheral vascularity simultaneously. In the malignant nodules, 46.2% showed peripheral vascularity, 30.8% exhibited both central and peripheral vascularity, and 15.4% displayed peripheral vascularity without central vascularity. Additionally, 7.7% of malignant nodules demonstrated No vascularity. The study findings also indicated that considering the presence of Central and both central and peripheral vascularity as a malignancy indicator, as well as the absence of vascularity or presence of peripheral vascularity as a benignity indicator, resulted in a nodule diagnostic sensitivity of 76.9% and a specificity of 81% for distinguishing malignancy from benignity. Furthermore, the positive predictive value was 40%, and the negative predictive value was 95.5%. These results suggest that although the positive value of these indicators in distinguishing benign from malignant nodules may be relatively modest, the negative predictive value can be relied upon to a significant extent when these indicators are negative.

In a study conducted by Raghavan et al. in 2014, a total of 229 thyroid nodules were evaluated in 130 patients to explore the relationship between certain ultrasound variables, such as single nodule presence, hypoechoic nodule, and irregular margin, and the presence of malignancy. The results confirmed the significance of these ultrasound variables in predicting malignancy. Additionally, the study found that internal vascularity was significantly more common in malignant nodules (16). Furthermore, it was observed in their study that all nodules categorized as TIRADS 3 were benign, while 13.4% of TIRADS 4 cases were malignant. Moreover, 91% of TIRADS 5 cases were malignant. In Our study, 97.91% of nodules categorized as TIRADS 3 were found to be benign, while 19.047% of nodules categorized as TIRADS 4 were malignant. These findings are consistent with the study conducted by Raghavan et al., except for the cases categorized as TIRADS 5, where 34.78% of nodules were malignant based on pathological examination. Although This Difference Exists In These Two Studies in nodules categorized as TIRADS 5, But our study findings sre closer to which indicated in review studies available in online radiopedia references (17).

Borlea et al. conducted a study involving 131 nodules and explored the use of additional sonographic criteria, such as vascularity and elastography pattern, alongside TIRADS criteria. The authors concluded that evaluating nodule vascularity pattern, in conjunction with the established TIRADS criteria, could aid in distinguishing between benign and malignant nodules, a finding that aligns with the findings of the present study (18).

Horvath et al. conducted a research in China, involving 502 nodules from 210 patients, where the histopathology of the nodules was compared with TIRADS findings to assess the accuracy of TIRADS criteria in identifying benign and malignant nodules. The study reported a sensitivity of 99.6% and specificity of 74.3% for TIRADS criteria, while the present study yielded a sensitivity of 92.3% and specificity of 59.45%. These findings demonstrate overall agreement with Horvath et al.'s research (19).

In a study by Matthew Debnam et al. focusing on vascular flow in Doppler ultrasound examinations of 200 colloid nodules and 166 nodules with papillary cancer, the patterns of vascularity between colloid and malignant papillary nodules were examined by a neuroradiologist under blind conditions. The study concluded that there was no clear distinction in the vascularity pattern between colloid and malignant papillary nodules, which contrasts with the findings of the present study (20).

According to a meta-analysis study conducted by Khadra et al., which encompassed 89 relevant articles on the prevalence of hypervascularity in malignant nodules, the following outcomes were obtained: out of the 4154 nodules examined, 1419 cases were identified as malignant, constituting approximately 34% of the cases. Among these malignant nodules, 33% exhibited no internal vascularity, while 17% displayed peripheral vascularity and 50% manifest internal vascularity. The study concluded that there was no definitive distinction between peripheral and internal vascularity patterns in benign and malignant nodules, suggesting that the assessment of internal vascularity within thyroid nodules may not necessarily predict benign or malignant status. These findings are incongruent with the outcomes of the present study (21).

In Rago's study, which involved 104 thyroid nodules, it was concluded that the simultaneous assessment of a significant internal vascularity pattern, along with the presence of microcalcifications and the absence of a hypoechoic halo, is highly specific for identifying malignant nodules. The researchers categorized nodule vascularity patterns into three categories: no vascularity, peripheral vascularity, and internal vascularity. Among the 30 malignant nodules, internal vascularity was observed in 20 cases, whereas among the non-malignant nodules, 38 cases exhibited internal vascularity. This suggests that vascularity, when considered in conjunction with other TIRADS criteria, contributes predictively, although its standalone significance is not significant. This finding aligns with the results of the current study (14).

In conclusion, based on the findings of the present study, the sonographic criteria utilized in TIRADS demonstrate a significant ability to differentiate between benign and malignant nodules. Benign nodules frequently fell within TIRADS 3, whereas malignant nodules were predominantly classified as TIRADS 5. Moreover, the qualitative analysis of the vascularity index, categorized into four groups, proved helpful in distinguishing between benign and malignant nodules. Malignant nodules often exhibited internal or combined internal and peripheral vascularity patterns, while peripheral vascularity or lack of vascularity was more frequently observed in benign nodules.

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