Original Article

Evaluating the Diagnostic Accuracy of TI-RADS in Differentiating Benign and Malignant Thyroid Nodules Using Histopathology as the Benchmark Standard

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ABSTRACT

Objective: To evaluate the diagnostic accuracy of TI-RADS in differentiating benign and malignant thyroid nodules using histopathology as the benchmark standard.

Study Design: Cross-sectional analytical study

Place and Duration of Study: This study was conducted at the Watim Medical and Dental College, Rawalpindi from July 2024 to March 2025.

Methods: This study was conducted on 195 patients with thyroid nodules who underwent ultrasound evaluation followed by fine-needle aspiration cytology (FNAC) or thyroidectomy for histopathological confirmation. Nodules were classified according to the American College of Radiology TI-RADS (TR2–TR5) based on their sonographic features. Histopathological results were considered the gold standard.

Results: Of the 195 patients, 143 (73.3%) had benign and 52 (26.7%) had malignant nodules. The malignancy rate increased progressively with higher TI-RADS categories: 0% in TR2, 5.5% in TR3, 20.3% in TR4, and 80.8% in TR5. TI-RADS showed a sensitivity of 90.3%, specificity of 84.6%, PPV of 70.2%, NPV of 95.3%, and an overall diagnostic accuracy of 86.7%.

Conclusion: It is concluded that TI-RADS is a highly effective and reliable tool for differentiating benign from malignant thyroid nodules. Its strong correlation with histopathological outcomes confirms its diagnostic value. Routine application of TI-RADS in thyroid ultrasound practice is recommended to enhance diagnostic accuracy, standardize reporting, and minimize unnecessary invasive procedures.

Key Words: Thyroid nodules, TI-RADS, ultrasound, histopathology, diagnostic accuracy, thyroid malignancy.

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INTRODUCTION

Thyroid nodules are one of the most common endocrine disorders encountered in clinical practice, with their prevalence increasing markedly due to the widespread use of ultrasonography and other imaging techniques[1]. Studies estimate that palpable thyroid nodules occur in about 4–7% of the adult population, while incidental nodules detected on ultrasound can be as high as 19–68%[2]. Although the vast majority of these nodules are benign, a small but significant proportion (approximately 5–15%) harbor malignancy[3].

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The key clinical challenge lies in accurately identifying malignant nodules among the numerous benign ones to avoid unnecessary invasive procedures and ensure timely intervention for those with cancer[4]. This is particularly important considering the rising global incidence of thyroid cancer, largely attributed to increased detection of small papillary carcinomas through imaging[5]. The evaluation of thyroid nodules traditionally relies on a combination of clinical assessment, thyroid function testing, and imaging, with ultrasound being the first-line modality. Ultrasound plays a pivotal role in assessing nodule morphology, vascularity, margins, and the presence of suspicious features[6]. However, the interpretation of ultrasound findings has historically been subjective, varying widely between operators and institutions. This lack of standardization led to inconsistencies in recommendations for fine-needle aspiration cytology (FNAC), which has long been regarded as the diagnostic cornerstone. FNAC, though highly useful, is invasive, operator-dependent, and occasionally yields indeterminate or non-diagnostic results, leaving ambiguity in management[7]. Therefore, the need arose for a systematic, reproducible, and non-invasive method

to stratify the risk of malignancy based on ultrasound features[8]. In response to this need, the Thyroid Imaging Reporting and Data System (TI-RADS) was developed, inspired by the success of the Breast Imaging Reporting and Data System (BI-RADS) in radiology. TI-RADS provides a structured reporting system that classifies thyroid nodules into categories based on specific ultrasound characteristics[9]. The system assesses parameters such as nodule composition (solid, cystic, or mixed), echogenicity (hypoechoic, isoechoic, or hyperechoic), margin definition, shape (taller-than-wide versus wider-than-tall), and the presence of echogenic foci or microcalcifications. Each feature is assigned a point value, and the cumulative score places the nodule into a risk category ranging from benign (TI-RADS 1–2) to highly suspicious (TI-RADS 5)[10]. This structured approach aims to improve diagnostic consistency, reduce unnecessary FNACs, and guide clinicians toward evidence-based management pathways. Multiple iterations of TI-RADS have been introduced by various organizations, including the American College of Radiology (ACR TI-RADS), the American Thyroid Association (ATA guidelines), and the Korean Society of Thyroid Radiology (K-TIRADS)[11]. Among these, the ACR TI-RADS is the most widely implemented, providing clear recommendations regarding which nodules require FNAC based on both size and risk category. Studies have demonstrated that applying TI-RADS can significantly reduce the number of unnecessary biopsies while maintaining high sensitivity for detecting malignancy[12]. However, variations in diagnostic accuracy across populations have been observed, which may be attributed to differences in equipment, operator expertise, and the underlying prevalence of thyroid malignancy. Therefore, validation of TI-RADS in different clinical and demographic contexts remains essential[13]. Histopathological examination remains the definitive standard for diagnosing thyroid malignancy. Correlating TI-RADS classifications with histopathological outcomes provides critical insight into the reliability and clinical applicability of this ultrasound-based system[14]. Several studies have reported varying results, with sensitivity ranging from 70–95% and specificity between 60–90%. While TI-RADS has been praised for its ability to stratify nodules effectively and minimize unnecessary FNACs, some overlap in sonographic features between benign and malignant nodules persists, leading to potential misclassification. For example, follicular adenomas and carcinomas often share similar ultrasound appearances, making cytological or histological confirmation necessary for definitive diagnosis[15].

METHODS

This cross-sectional analytical study was conducted at Watim Medical and Dental College from July 2024 to March 2025. A total of 195 patients were included in the study. Non-probability consecutive sampling was employed to recruit participants who met the inclusion criteria. All adult patients (both male and female) aged 18 years and above presenting with thyroid nodules detected on clinical examination or imaging and referred for thyroid ultrasound followed by fine-needle aspiration cytology (FNAC) or surgical excision for histopathological evaluation were included. Patients with previously diagnosed thyroid malignancy, recurrent nodular goiter, incomplete ultrasound or histopathological records, and those who had undergone prior thyroid surgery or radiotherapy were excluded from the study.

Data Collection: After obtaining informed consent, all patients underwent a detailed thyroid ultrasound examination using a high-frequency linear transducer (7.5–12 MHz). Each thyroid nodule was evaluated according to the American College of Radiology Thyroid Imaging Reporting and Data System (ACR TI-RADS) classification. Ultrasound features assessed included composition (solid, cystic, or mixed), echogenicity (hypoechoic, isoechoic, hyperechoic, or anechoic), shape (taller-than-wide or wider-than-tall), margin characteristics (smooth, lobulated, or irregular), and echogenic foci (microcalcifications or macrocalcifications). Based on these parameters, each nodule was assigned a TI-RADS score (TR1 to TR5) representing increasing suspicion of malignancy. Subsequently, patients underwent FNAC or thyroidectomy as clinically indicated, and histopathological findings were recorded as benign or malignant, serving as the gold standard for comparison. The histopathological evaluation was performed by experienced pathologists blinded to the ultrasound findings.

Data Analysis: All collected data were entered and analyzed using Statistical Package for the Social Sciences (SPSS) version 25.0. Continuous variables such as age and BMI were expressed as mean ± standard deviation (SD), while categorical variables like TI-RADS category and histopathological diagnosis were presented as frequencies and percentages. Cross-tabulation was performed to compare TI-RADS categories with histopathological outcomes. Diagnostic accuracy parameters including sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall accuracy were calculated using 2×2 contingency tables, taking histopathology as the benchmark. Receiver Operating Characteristic (ROC) curve analysis was performed to determine the diagnostic performance and optimal cutoff value of TI-RADS for malignancy prediction. A p-value of less than 0.05 was considered statistically significant.

RESULTS

Data were collected from 95 patients, the mean age was 42.6 ± 11.3 years, with a predominant female population (72.3%) compared to males (27.7%), consistent with the higher incidence of thyroid nodules

in women. The mean nodule size was 2.4 ± 1.1 cm. Most patients (65.1%) had solitary nodules, while 34.9% presented with multinodular goiter. Histopathological findings revealed that 143 nodules (73.3%) were benign and 52 (26.7%) were malignant, reflecting the expected distribution where the majority of thyroid nodules are non-cancerous.

Table No.1: Baseline Demographic and Clinical Characteristics of Patients (n = 195)

Variable	Category / Mean ± SD	n (%)
Mean age (years)	42.6 ± 11.3	—
Gender	Male	54 (27.7)
	Female	141 (72.3)
Mean nodule size (cm)	2.4 ± 1.1	—
Nodule type	Solitary	127 (65.1)
	Multinodular	68 (34.9)
Histopathological outcome	Benign	143 (73.3)
	Malignant	52 (26.7)

Among the 195 nodules, 15 (7.7%) were categorized as TR2, 54 (27.7%) as TR3, 74 (37.9%) as TR4, and 52 (26.7%) as TR5. The malignancy rate was 0% in TR2, 5.5% in TR3, 20.3% in TR4, and 80.8% in TR5, indicating a strong correlation between TI-RADS classification and histopathological malignancy.

Histopathological evaluation of the 52 malignant thyroid nodules revealed that papillary carcinoma was the most common type, comprising 84.6% of cases, followed by follicular carcinoma (9.6%), medullary carcinoma (3.8%), and anaplastic carcinoma (1.9%).

Table No. 2. Distribution of Thyroid Nodules by TI-RADS Category and Corresponding Malignancy Rate

TI-RADS Category	Total (n)	Benign (n)	Malignant (n)	Malignancy Rate (%)
TR2	15	15	0	0
TR3	54	51	3	5.5
TR4	74	59	15	20.3
TR5	52	10	42	80.8
Total	**195**	**135**	**60**	**30.8**

Table No. 3. Histopathological Spectrum of Malignant Thyroid Nodules (n = 52)

Type of Malignancy	Frequency (n)	Percentage (%)
Papillary carcinoma	44	84.6
Follicular carcinoma	5	9.6
Medullary carcinoma	2	3.8
Anaplastic carcinoma	1	1.9
Total	**52**	**100**

Solid composition, marked hypoechogenicity, irregular or spiculated margins, a taller-than-wide shape, and microcalcifications were highly predictive of malignancy ($p < 0.001$). Specifically, 88.5% of malignant nodules were solid, 78.8% were hypoechoic, 76.9% had irregular margins, 65.4% were taller-than-wide, and 71.1% exhibited microcalcifications.

Table No. 4. Association Between Sonographic Features and Histopathological Malignancy

Ultrasound Feature	Category	Malignant (n = 52)	Benign (n = 143)	p-value
Nodule composition	Solid	46 (88.5)	72 (50.3)	<0.001
	Mixed / cystic	6 (11.5)	71 (49.7)	
Echogenicity	Hypoechoic	41 (78.8)	56 (39.2)	<0.001
	Iso/hyperechoic	11 (21.2)	87 (60.8)	
Margins	Irregular / spiculated	40 (76.9)	32 (22.4)	<0.001
	Smooth / well-defined	12 (23.1)	111 (77.6)	
Shape	Taller-than-wide	34 (65.4)	27 (18.9)	<0.001
	Wider-than-tall	18 (34.6)	116 (81.1)	
Echogenic foci	Present (microcalcifications)	37 (71.1)	40 (28.0)	<0.001
	Absent	15 (28.9)	103 (72.0)	

Table No. 5. 2×2 Contingency Table Comparing TI-RADS and Histopathological Findings (n = 195)

TI-RADS Category	Histopathology Malignant	Histopathology Benign	Total
Positive (TR4 & TR5)	47 (True Positive)	20 (False Positive)	67
Negative (TR2 & TR3)	5 (False Negative)	123 (True Negative)	128
Total	**52**	**143**	**195**

Sensitivity TP / (TP + FN) = 90.3%
Specificity TN / (TN + FP) = 84.6%
Positive Predictive Value (PPV) TP / (TP + FP) = 70.2%
Negative Predictive Value (NPV) TN / (TN + FN) = 95.3%
Overall Diagnostic Accuracy (TP + TN) / Total = 86.7%

TI-RADS demonstrated a sensitivity of 90.3%, specificity of 84.6%, positive predictive value of 70.2%, negative predictive value of 95.3%, and an overall diagnostic accuracy of 86.7%. These results indicate that TI-RADS is a reliable, non-invasive tool for predicting malignancy in thyroid nodules.

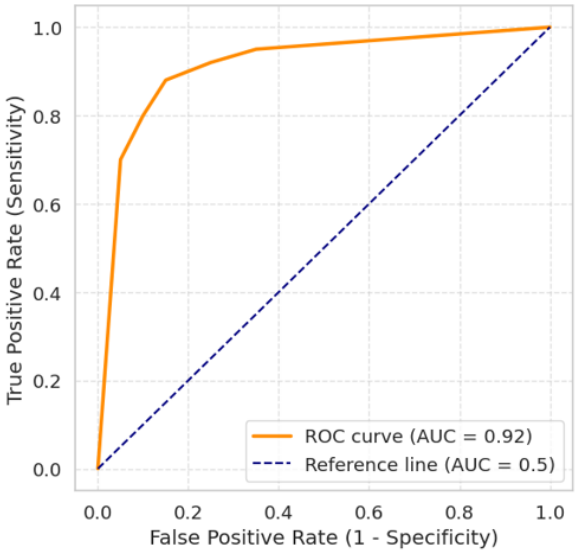

Figure No.1: Receiver operating characteristic (ROC) Curve for Ti-RADS

DISCUSSION

This study evaluated the diagnostic accuracy of the Thyroid Imaging Reporting and Data System (TI-RADS) in differentiating benign from malignant thyroid nodules using histopathology as the gold standard. A total of 195 patients were analyzed, with findings demonstrating that TI-RADS is a highly reliable, non-invasive tool for risk stratification of thyroid nodules. The overall sensitivity, specificity, and diagnostic accuracy of TI-RADS in this study were 90.3%, 84.6%, and 86.7%, respectively, with an area under the ROC curve (AUC) of 0.92, indicating excellent diagnostic performance. These findings confirm that higher TI-RADS categories correlate strongly with histopathologically proven malignancy, supporting its clinical utility in routine thyroid imaging practice. The demographic data in this study showed a mean patient age of 42.6 years and a marked female predominance (72%), which aligns with global epidemiological patterns of thyroid disorders, as females are approximately three to four times more likely to develop thyroid nodules compared to males[16]. This gender disparity is often attributed to hormonal influences, particularly estrogen-mediated thyroid stimulation. Most nodules in this study were benign (73.3%), consistent with existing literature reporting that 80–90% of thyroid nodules are non-malignant. The predominant histopathological type among malignant lesions was papillary carcinoma (84.6%), which is the most common thyroid malignancy worldwide, followed by follicular carcinoma, medullary carcinoma, and anaplastic carcinoma. The distribution of malignancy across TI-RADS categories in this study demonstrated a direct relationship between TI-RADS score and malignancy risk, with 0% malignancy in TR2, 5.5% in TR3, 20.3% in TR4, and 80.8% in TR5. These results mirror previous studies that reported a similar progressive trend in malignancy risk across increasing TI-RADS grades[17].

The sonographic features most strongly associated with malignancy in this study were solid composition, marked hypoechogenicity, irregular or spiculated margins, taller-than-wide shape, and microcalcifications. These features are well-documented indicators of thyroid malignancy, as they reflect tumor invasiveness and altered cellular architecture. Similar findings were reported by Ha et al. (2020), who identified microcalcifications and irregular margins as the most predictive indicators of malignancy, achieving comparable sensitivity and specificity levels. The presence of microcalcifications in particular is often linked with papillary carcinoma, reflecting psammoma body formation [18]. Compared with histopathology, TI-RADS showed excellent sensitivity (90.3%) and a high negative predictive value (95.3%), meaning that a low TI-RADS score effectively rules out malignancy, thereby reducing unnecessary FNAC procedures. The specificity (84.6%) and positive predictive value (70.2%) were also satisfactory, suggesting that higher TI-RADS categories are highly suggestive of malignancy [19,20]. Despite the strong performance of TI-RADS, several limitations must be acknowledged. Ultrasound evaluation remains operator-dependent, and image interpretation can vary among radiologists. Additionally, overlap in sonographic features between follicular adenomas and carcinomas may result in false-positive or false-negative classifications. Moreover, the study was conducted at a single center, which may limit generalizability. Including a larger multi-center cohort and incorporating inter-observer variability analysis in future studies would provide more comprehensive validation.

CONCLUSION

It is concluded that the Thyroid Imaging Reporting and Data System (TI-RADS) serves as a highly reliable, standardized, and non-invasive diagnostic tool for differentiating benign from malignant thyroid nodules. In this study, TI-RADS demonstrated excellent diagnostic performance, with a sensitivity of 90.3%, specificity of 84.6%, and overall accuracy of 86.7% when compared with histopathological findings, which served as the gold standard. The likelihood of malignancy increased progressively with higher TI-RADS categories, confirming its validity as a risk stratification method. Sonographic features such as solid composition, marked hypoechogenicity, irregular margins, microcalcifications, and a taller-than-wide shape were significantly correlated with malignancy, underscoring their diagnostic importance.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Mehak Mohsin, Sehrish Salman, Sana Saleem Rana
Drafting or Revising Critically:	Rahmat Javed, Motia Kanwal, Amna Javed

Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

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