

DIAGNOSTIC ACCURACY OF TIRADS CLASSIFICATION IN DIFFERENTIATING BENIGN AND MALIGNANT THYROID NODULES KEEPING FINE NEEDLE ASPIRATION CYTOLOGY (FNAC) AS GOLD STANDARD

SAQIB HA^{*1}, SAEED U¹, ZAHRA M², NOREEN A², FIRDOUS A³, ISLAM ZU³

¹Department of Radiology, CPEIC Multan, Pakistan

²Department of Peads Radiology, CH & ICH Multan, Pakistan

³Department of Radiology, MMDC Multan, Pakistan

*Corresponding author email address: drkash226@gmail.com

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Abstract: *Thyroid nodules represent a joint clinical presentation of various benign and malignant thyroid diseases. Diagnostic ultrasound, particularly utilizing the Thyroid Imaging Reporting and Data System (TI-RADS), has emerged as a pivotal tool for stratifying the risk of malignancy in thyroid nodules and guiding decisions regarding fine-needle aspiration biopsy (FNAC). However, comprehensive validation studies are warranted to assess the diagnostic accuracy of ultrasound-based TI-RADS classification compared to FNAC as the gold standard. This cross-sectional validation study, conducted at the Department of Radiology, CPE Institute of Cardiology Multan from August 2, 2021, to February 1, 2022, enrolled 243 patients presenting with thyroid nodules, including multiple and solitary nodules. Baseline demographic variables, including age, gender, and nodule duration, were recorded for each participant. Ultrasonography was performed in all patients, and TI-RADS scores were calculated. Subsequently, fine-needle aspiration biopsies, guided by ultrasound, were obtained in the radiology department and sent to the histopathology department for confirmation of malignancy. The mean age of the cohort was 42.05 ± 12.27 years, with a mean nodule duration of 6.87 ± 3.56 months. The mean TI-RADS score was 3.46 ± 2.00. Of the participants, 176 (72.43%) were male and 67 (27.57%) were female. Malignancy was detected in 84 (34.57%) patients based on TI-RADS score, whereas FNAC confirmed malignancy in 50 (20.58%) patients. Evaluating diagnostic accuracy with FNAC as the gold standard, the TI-RADS score demonstrated a sensitivity of 84.0%, specificity of 78.2%, positive predictive value (PPV) of 50.0%, and negative predictive value (NPV) of 95.0%. Our findings indicate that the TI-RADS scoring system is reliable in predicting malignancy in patients with thyroid nodules. With a sensitivity of 84.0% and specificity of 78.2%, TI-RADS represents a valuable adjunctive tool in the diagnostic algorithm for thyroid nodules, offering considerable potential for improved clinical decision-making and patient management strategies.*

Keywords: TI-RADS Classification, Fine Needle Aspiration Cytology (FNAC), Malignant Thyroid Nodules

Introduction

Thyroid nodules pose a significant health concern globally, particularly in regions like Pakistan, where iodine deficiency prevails, increasing the risk of thyroid diseases among its population (Mohammadi et al., 2018). Despite advancements in diagnostic techniques, fine-needle aspiration cytology (FNAC) remains the gold standard for diagnosing malignant thyroid nodules. However, ultrasound-based thyroid imaging, employing the Thyroid Imaging Reporting and Data System (TI-RADS), has emerged as a promising adjunct for risk stratification and decision-making regarding FNAC (Al Dawish et al., 2020; Noortman et al., 2023).

This study aims to evaluate the diagnostic accuracy of TI-RADS classification in detecting malignant thyroid nodules, utilizing FNAC as the reference standard. While various classification systems exist for thyroid nodules, TI-RADS, adapted from the Breast Imaging Reporting and Data System (BI-RADS), offers a standardized approach, integrating ultrasound findings to distinguish between benign and malignant lesions.

Recent studies by Huang et al. and Kunapinun et al. have provided valuable insights into the performance of TI-RADS in malignancy differentiation, albeit with differing

results (Huang et al., 2020; Kunapinun et al., 2023). By Huang et al. reported sensitivity and specificity of 78.4% and 73.2%, respectively, while Kunapinun et al. found sensitivity of 100% and specificity of 61.1%. These variations underscore the need for further investigation to ascertain the accurate diagnostic accuracy of TI-RADS (Huang et al., 2020; Kunapinun et al., 2023).

Our study, conducted in a population at heightened risk of thyroid diseases due to iodine deficiency, aims to fill this gap by prospectively evaluating the diagnostic accuracy of TI-RADS. By correlating ultrasound findings with FNAC results, we seek to determine the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of TI-RADS in our population.

The findings of this study hold significant implications for clinical practice, particularly in resource-constrained settings like Pakistan. If TI-RADS demonstrates high diagnostic accuracy, it could be a cost-effective and accessible alternative to FNAC, thereby facilitating timely diagnosis and management of malignant thyroid nodules. Moreover, by establishing a standardized risk stratification system, this research enhances the diagnostic algorithm for thyroid nodules, ultimately improving patient outcomes.

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Methodology

This cross-sectional validation study was conducted at the Department of Radiology, CPE Institute of Cardiology Multan, from August 2, 2021, to February 1, 2022. The sample size of 243 patients was determined based on the expected sensitivity and specificity of TI-RADS and the estimated frequency of malignant lesions. Non-probability consecutive sampling was employed to include patients meeting the predefined inclusion criteria.

Patients referred to the radiology department with thyroid nodules, aged 20 to 70 years, with a duration of thyroid nodules ranging from 1 month to 2 years, and having multiple or solitary thyroid nodules were considered eligible for inclusion. Patients who were unwilling to participate in the study were excluded.

Following approval from the Research Ethics Unit (REU) of CPSP and the Ethics Review Committee (ERC) of CPE Institute of Cardiology Multan, written consent was obtained from all participating patients. Baseline variables, including age, gender, and duration of nodules, were recorded. Ultrasonography was performed, and a consultant radiologist calculated TI-RADS scores with at least three years of post-fellowship experience. Fine needle aspiration biopsy was conducted under ultrasound guidance in the radiology department, and samples were sent to the histopathology department for diagnosis of malignancy. Data were collected using a pre-designed proforma.

Data analysis was performed using SPSS v23.0 software. Mean and standard deviation were calculated for quantitative variables, while qualitative variables such as gender and presence/absence of malignant lesions were analyzed using TI-RADS and FNAC. The sensitivity, specificity, positive predictive value, and negative predictive value of TI-RADS were calculated using 2x2 contingency tables, with FNAC as the gold standard. Stratification was used to control for effect modifiers such as age, gender, and duration of nodules. Post-stratification analysis was conducted to assess the impact of these modifiers on the diagnostic accuracy of TI-RADS.

Results

The mean age of patients included in this study was 42.05±12.27 years. The minimum age was 20, and the maximum age was 70 years. The mean duration of nodules was 6.87±3.56 months. The minimum duration was 02 months, and the maximum was 24 months. The mean TIRADS score was 3.46±2.00. The minimum TIRADS score was 01, and the maximum was 08 (Table 1). There were more female patients as compared to males. There were 176 (72.43%) males and 67 (27.57%) females (Figure 1).

Table 1: Demographics of study population

Variables	Mean	S.D	Minimum	Maximum
Age (Years)	42.05	12.27	20	70
Duration of Nodules (Months)	6.87	3.56	02	24
TI-RADS	3.46	2.00	01	08

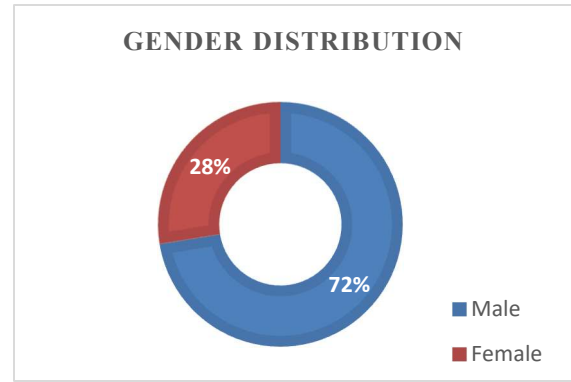


Figure 1: Gender distribution of the study population

Malignancy in TIRADS score was found in 84 (34.57%), and it was not found in 159 (65.43%) patients (Figure 2). Malignancy of FNAC was found in 50 (20.58%), and it was not found in 193 (79.42%) patients (Figure 14). Regarding diagnostic accuracy, taking FNAC as the gold standard, the TIRADS score was 84.0% sensitive, 78.2% specific, 50.0% PPV, and 95.0% NPV (Table 2).

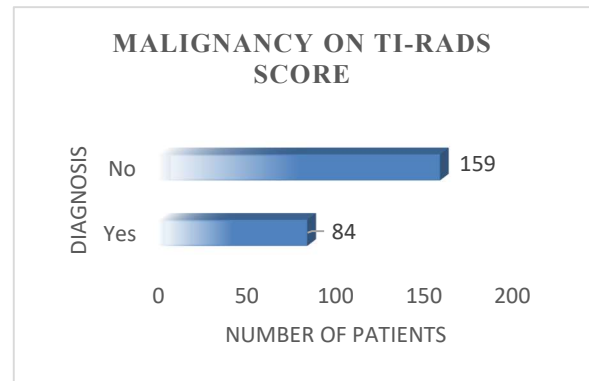


Figure 2: Malignancy Findings Based on TI-RADS Score

Stratification of age was performed. In patients aged 20-39, the TIRADS score was 92.3% sensitive, 75.8% specific, 50.0% PPV, and 97.4% NPV. In patients aged 40-70 years, the TIRADS score was 75.0% sensitive, 80.9% specific, 50.0% PPV, and 92.7% NPV. Stratification of gender was performed. In females, the TIRADS score was 81.1% sensitive, 78.4% specific, having 50.0% PPV and 94.0% NPV. In males, the TIRADS score was 92.3% sensitive, 77.8% specific, having 50.0% PPV and 97.7% NPV. Stratification of the duration of nodules was performed. In patients having nodules for 02-06 months, the TIRADS score was 90.5% sensitive, 77.5% specific, 45.2% PPV, and 97.5% NPV. In patients having a duration of nodules of 07-24 months, the TIRADS score was 79.3% sensitive, 79.1% specific, 54.8% PPV and 92.3% NPV (Table 3).

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Table 2. Diagnostic Accuracy of malignancy on TI-RADS taking malignancy of FNAC as gold standard

Malignancy on TIRADS	Malignancy on FNAC	
	Yes	No
Yes	42	42
No	08	151

Sensitivity: 84.0% , Specificity: 78.2%, PPV: 50.0% , NPV: 95.0%

Table 3. Age stratification is used to determine the association of age groups, genders, and duration of nodules with diagnostic accuracy of malignancy on TI-RADS, taking malignancy of FNAC as the gold standard

Variables	Constructs	Malignancy on TIRADS	Malignancy on FNAC		
			Yes	No	
Age	Age Group = 20-39 Years	Yes	24	24	Sensitivity: 92.3% Specificity: 75.8% PPV: 50.0% NPV: 97.4%
		No	02	75	
	Age Group = 40-70 Years	Yes	18	18	Sensitivity: 75.0% Specificity: 80.9% PPV: 50.0% NPV: 92.7%
		No	06	76	
Gender	Female	Yes	30	30	Sensitivity: 81.1% Specificity: 78.4% PPV: 50.0% NPV: 94.0%
		No	07	109	
	Male	Yes	12	12	Sensitivity: 92.3% Specificity: 77.8% PPV: 50.0% NPV: 97.7%
		No	01	42	
Duration of nodules	02-06 Months	Yes	19	23	Sensitivity: 90.5% Specificity: 77.5% PPV: 45.2% NPV: 97.5%
		No	02	79	
	07-24 Months	Yes	23	19	Sensitivity: 79.3% Specificity: 79.1% PPV: 54.8% NPV: 92.3%
		No	06	72	

Discussion

Thyroid nodules are a common occurrence (Niedziela, 2014). They are found in 4% to 8% of adults by palpation, 10% to 41% by ultrasound, and 50% by autopsy (Singh Ospina et al., 2016). The prevalence of thyroid nodules increases with age. However, only 5% to 10% of all thyroid nodules are malignant. Therefore, it's essential to use imaging techniques to rule out thyroid cancer. While various imaging modalities are used for thyroid diagnosis, ultrasound is the most commonly used technique for evaluating thyroid nodules due to its cost-effectiveness, safety, and non-invasiveness (Ishtiaq et al., 2022). Based on ultrasound findings, many studies have been conducted to predict whether a thyroid nodule is benign or malignant. Several ultrasound features like calcifications, hypoechogenicity, irregular margins, absence of a halo, predominantly solid composition, and introduced

vascularity have been associated with an increased risk of thyroid cancer (Borowczyk et al., 2021; Rago and Vitti, 2022). However, the sensitivity, specificity, and positive and negative predictive values for these criteria are highly variable, and no ultrasound feature has a high sensitivity and a high positive predictive value for thyroid cancer (Smith-Bindman et al., 2013). The combination of factors somewhat improves the positive predictive value of ultrasound.

A TIRADS scoring system has been developed to determine the malignancy of thyroid nodules in patients. A study was conducted to evaluate the diagnostic accuracy of this system using FNA reporting as the gold standard. The study found that TIRADS has a sensitivity of 84%, specificity of 78.2%, positive predictive value of 50%, and negative predictive value of 95% (Dong et al., 2023). Another study conducted in India showed that TIRADS had a sensitivity of 72%, specificity of 68.8%, positive predictive value of 63.9%,

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negative predictive value of 76.2%, and accuracy of 70.2% (Bhushan Shah et al., 2020). The ACR TI-RADS had a sensitivity of 85.7% and a specificity of 51.1%. Another study showed that TIRADS had a sensitivity of 80%, specificity of 87.5%, positive predictive value of 61.5%, and negative predictive value of 94.6% (Bhushan Shah et al., 2020; Ma et al., 2024). A Turkish study showed a sensitivity of 87%, specificity of 71.7%, NPV of 97.4%, PPV of 31.1%, and diagnostic accuracy of 73.6% (Çolakoğlu and Deniz, 2019). Another study showed that TIRADS had a sensitivity of 78.4%, specificity of 73.2%, PPV of 52.3%, and NPV of 90.1% (Ahmadi et al., 2019). Finally, a study showed that TIRADS had a sensitivity of 100%, specificity of 61.1%, PPV of 100%, and NPV of 63.0% (Nighat et al., 2021). By adopting the indication for FNAB as test positivity, the EU-TIRADS was able to identify nodules with low malignancy risk whose FNAB could be safely avoided.

In conclusion, EU-TIRADS provides effective malignancy risk stratification that can guide the selection of thyroid nodules for biopsy. Applying the guideline criteria for FNAB in clinical practice will significantly reduce the number of unnecessary FNABs. A recent meta-analysis investigating the efficiency of the five most common US stratification systems showed that NPV was high in almost every study.

Limitations of our study include its single-center design, which may restrict the generalizability of findings, and the relatively small sample size, potentially limiting statistical power. Non-probability consecutive sampling may introduce selection bias while using FNAC as the gold standard for malignancy determination may have limitations. Interobserver variability among radiologists and incomplete data could affect the accuracy of our analyses, and the lack of long-term follow-up limits our understanding of nodule behavior over time. Additionally, including published studies in the discussion may introduce publication bias. These limitations underscore the need for more extensive, multi-center studies with rigorous methodology to validate our findings and enhance the understanding of the diagnostic accuracy of TIRADS in thyroid nodule assessment.

Conclusion

The TI-RADS scoring system is reliable in predicting the presence of malignancy in patients with thyroid nodules. In this study, TI-RADS's sensitivity was 84%, and specificity was 78.2%.

Declarations

Data Availability statement

All data generated or analyzed during the study are included in the manuscript.

Ethics approval and consent to participate

Approved by the department Concerned.

Consent for publication

Approved

Funding

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Conflict of interest

The authors declared absence of conflict of interest.

Author Contribution

HAMMAD AHMAD SAQIB (Assistant Professor)

Study Design, Review of Literature

Conception of Study, Development of Research Methodology Design, Study Design., Review of manuscript, final approval of manuscript

UMAMA SAEED (Assistant Professor)

Coordination of collaborative efforts.

Conception of Study, Final approval of manuscript

MAHWISH ZAHRA (Assistant Professor)

Manuscript revisions, critical input.

Coordination of collaborative efforts.

AFSHAN NOREEN (Assistant Professor)

Data acquisition, analysis.

Manuscript drafting.

ATQA FIRDOUS (Associate Professor)

Data entry and Data analysis, drafting article

Data acquisition, analysis.

ZIA UL ISLAM (Associate Professor)

Coordination of collaborative efforts

Study Design, Review of Literature.

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