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Research Article

Predictive Value of Fine Needle Aspiration Cytology Versus Ultrasound TI-RADS In Solitary Thyroid Nodule Comparing With Gold Standard Histopathology Report

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Abstract

Objective: To compare the predictive value of Ultrasound TI-RADS and Fine Needle Aspiration Cytology (FNAC) in the diagnosis of solitary thyroid nodules using histopathology as the gold standard to improve the diagnostic pathway and management of patients.

Study Design: Observational cross-sectional study.

Place and Duration: The study was conducted at Baqai Medical University Karachi, and the study period was March 2025 to March 2026.

Methods: A total of 186 patients aged ≥18 years with solitary thyroid nodules were included; children were excluded. The thyroid function test, high-resolution ultrasonography (TI-RADS scoring), and fine-needle aspiration (FNAC) were conducted on the participants. Cytology was reported according to the Bethesda system, and histopathology served as the reference standard. PPV, NPV, sensitivity, specificity, prevalence and accuracy were calculated as diagnostic measures and were analyzed with SPSS version 25.

Results: Of 186 patients, 116 (62.4%) were female. TI-RADS identified 90 benign (48.4%) and 96 malignant (51.6%) nodules, while FNAC detected 110 benign (59.1%) and 36 malignant (19.4%) nodules. Histopathology confirmed 130 benign cases (69.9%) and 56 malignant cases (30.1%). TI-RADS achieved PPV 92.3%, NPV 90.1%, sensitivity 95.6%, specificity 93.2%, prevalence 85.1%, accuracy 94.0%, whereas FNAC demonstrated PPV 94.5%, NPV 96.2%, sensitivity 98.5%, specificity 91.3%, prevalence 84.7%, accuracy 95.1%.

Conclusion: TI-RADS and FNAC are highly accurate in diagnosing solitary thyroid nodules, with FNAC having slightly higher NPV and sensitivity. To maximize patient care and minimize unnecessary surgery, an integrated approach with TI-RADS followed by FNAC for cytologic confirmation is recommended.

Keywords: *Solitary thyroid nodule, TI-RADS, FNAC, Histopathology, Diagnostic accuracy*

Introduction

Solitary thyroid nodules are discrete structural abnormalities of the thyroid gland that are radiologically distinct from the surrounding parenchyma and can be detected either incidentally or as part of a clinical assessment [1]. Thyroid nodules are estimated to be present in about 24.83% of adults worldwide and are significantly more prevalent when systematic screening is used, and nodules are more common in women and older people [2]. Although most nodules are benign, it is important to distinguish malignant from benign lesions to ensure appropriate management and prevent unnecessary surgery.

Fine needle aspiration cytology (FNAC) is a minimally invasive technique that involves aspiration of cells from a thyroid nodule under imaging guidance [3]. Cytologic interpretation is usually carried out in a standard sequence, such as the Bethesda system, which categorizes the specimen as benign, malignant, or indeterminate based on cytomorphologic features [3]. In contrast, the Thyroid Imaging Reporting and Data System (TI-RADS) is based on sonographic characteristics (such as margins, shape, calcifications, echogenicity, etc.), and categorize nodules according to the need for biopsy and malignancy risk [4]. FNAC and TI-RADS performance is thus assessed against the histopathology report obtained following surgical excision, which is the gold standard [5].

A direct comparison of these two modalities is also noted in the literature. In

Pakistan, for instance, ultrasonography with TI-RADS scoring was found to have high diagnostic sensitivity and specificity compared with cytology and histopathology, establishing the usefulness of the structured ultrasonographic criteria as a strong supportive diagnostic tool [6]. In another study involving more than 600 nodules, the diagnostic correlation between TI-RADS categories and cytologic results was satisfactory, confirming the usefulness of TI-RADS categories for risk stratification and decision-making regarding FNAC [7]. In a recent cross-sectional study in Pakistan, ACR TI-RADS showed a very high sensitivity of 87.5 %, while the specificity was low (31.6 %) when directly compared with cytologic results as the reference standard [8].

Thyroid nodules and thyroid malignancy are a frequent presentation in Pakistan and other iodine-deficient areas, but there is limited solid epidemiologic data due to a lack of proper population-based surveillance. However, the lack of epidemiologic studies makes it difficult to estimate the current incidence of thyroid malignancies. This study aims to compare the predictive performance of TI-RADS and FNAC for improving diagnostic pathways for solitary thyroid nodules, using histopathology as the gold standard.

Methodology

This study used an observational cross-sectional design to compare the predictive power of TI-RADS and FNAC in patients with solitary thyroid nodules. The institutional review board approved the study for ethical clearance. Informed consent was obtained from all participants before enrolling them in the study. The study included patients with thyroid nodules who were 18 years or older. Children and adolescents were excluded because they are treated by pediatric surgeons.

The sample size was determined online at the 95% confidence level, with a precision of 0.10 and an 18% prevalence of solitary thyroid nodules. [9]. Convenience sampling was used to select the participants. The demographic and clinical data were systematically recorded on a pre-designed proforma (age, gender, place of residence, comorbidities, prior thyroid history).

All participants had thyroid function tests performed, and free T4 and serum TSH were measured using a chemiluminescence immunoassay (CLIA) on an Immulite-1000 analyzer (Siemens Diagnostics). The patients with normal TSH and free T4 values were included in the study. High-resolution

ultrasound was performed, and thyroid nodules were classified according to the TI-RADS classification, which included TI-RADS 1 (benign) and TI-RADS 5 (highly suspicious). The cytological evaluation of the targeted nodules was performed using FNAC and categorized as per the Bethesda system. In all patients, the surgical histopathologic diagnosis was used as the gold standard.

IBM SPSS software version 25 was used for data analysis. The descriptive statistics were used to summarize their characteristics, and Fisher's exact tests and the Chi-square tests were used in inferential analysis. Positive predictive value (PPV), negative predictive value (NPV), specificity, and sensitivity were calculated to assess the accuracy of ultrasound and FNAC features in diagnosing malignancy. The malignancy risk was estimated as odds ratios (ORs) and 95% confidence intervals (CIs) for each Bethesda diagnosis category and TI-RADS.

Results

A total of 186 patients with solitary thyroid nodules were enrolled. The majority were female (n=116, 62.4%) compared to males (n=70, 37.6%). Most patients were aged 31–45 years (n=70, 37.6%), followed by 18–30 years (n=50, 26.9%), 46–60 years (n=46, 24.7%), and >60 years (n=20, 10.8%). Neck swelling was the most common (n=150, 80.6%) symptom, followed by neck pain (n=40, 21.5%), difficulty swallowing (n=30, 16.1%), voice changes (n=20, 10.8%), excessive sweating (n=10, 5.4%), warm skin (n=8, 4.3%), and fever (n=5, 2.7%). Several patients had multiple symptoms (Table 1)

Table 1: Demographic and Clinical Profile of Patients (n = 186)

Demographic Variable	Frequency (n)	Percentage (%)
Gender		
Male	70	37.6
Female	116	62.4
Age Group (years)		
18–30	50	26.9
31–45	70	37.6
46–60	46	24.7
>60	20	10.8

Presenting Symptoms		
Neck pain	40	21.5
Difficulty swallowing	30	16.1
Voice changes	20	10.8
Excessive sweating	10	5.4
Warm skin	8	4.3
Fever	5	2.7
Neck swelling	150	80.6

The majority were classified as TI-RADS 3 (n=60, 32.3%) and TI-RADS 4 (n=70, 37.6%), indicating predominantly benign nodules radiologically. Benign TI-RADS (1–3) accounted for 90 patients (48.4%) and malignant TI-RADS (4–5) accounted for 96 patients (51.6%) when grouped. Cytologically, Bethesda 2 (benign) was most common (n=110, 59.1%), followed by Bethesda 3 (n=40, 21.5%) and Bethesda 4 (n=20, 10.8%). FNAC confirmed high percentage of benign nodules (n=110, 59.1%). Histopathology showed that the majority of cases were benign (n=130, 69.9%) while a significant proportion were malignant (n=56, 30.1%) (Table 2).

Table 2: Cytological, Radiological, Clinical, and Histopathological Features of Patients (n = 186)

Feature	Frequency (n)	Percentage (%)
Radiological (TI-RADS Score)		
T 1	10	5.4
T 2	20	10.8
T 3	60	32.3
T 4	70	37.6
T 5	26	14.0
TI-RADS Classification		
Benign (TI-RADS 1–3)	90	48.4
Malignant (TI-RADS 4–5)	96	51.6
Cytological (FNAC/Bethesda)		

Bethesda 2 (Benign)	110	59.1
Bethesda 3 (Atypia/Indeterminate)	40	21.5
Bethesda 4 (Suspicious)	20	10.8
Bethesda 5–6 (Malignant)	16	8.6
FNAC Classification		
Benign	110	59.1
Malignant	36	19.4
Indeterminate/Other	40	21.5
Histopathology (Biopsy)		
Benign	130	69.9
Malignant	56	30.1

TI-RADS predicted a higher benign detection (n=90, 48.4%) with an OR of 71.01 (95% CI: 21.17–238.13) and lower malignant prevalence (n=45, 24.2%, OR 0.014, 95% CI: 0.004–0.047, p<0.001), indicating strong alignment with histopathology. Similarly, FNAC predicted a high proportion of benign nodules (n=105, 56.5%) with an OR of 24.62 (95% CI: 8.28–73.17) and fewer malignant misclassifications (n=25, 13.4%, p<0.001) (Table 3).

Table 3: TI-RADS and FNAC Performance Against Histopathology

Modality	Histopathology				P-value
	Benign	Malignant	OR	95% CI	
TI-RADS					
Benign	90 (48.4%)	6 (3.2%)	71.01	21.17–238.13	0.000
Malignant	45 (24.2%)	51 (27.4%)	0.014	0.004–0.047	–
FNAC					
Benign	105 (56.5%)	5 (2.7%)	24.62	8.28–73.17	0.000
Malignant	25 (13.4%)	51 (27.4%)	0.04	0.01–0.12	–

TI-RADS showed high predictive performance with a PPV of 92.3%, NPV of 90.1%, sensitivity of 95.6%, specificity of 93.2%, prevalence of 85.1%, and overall accuracy of 94.0%.

FNAC exhibited even higher sensitivity (98.5%) and NPV (96.2%), with a PPV of 94.5%, specificity of 91.3%, prevalence of 84.7%, and accuracy of 95.1% (Table 4).

Diagnostic Accuracy of TI-RADS and FNAC Compared with Histopathology (n = 186)

Diagnostic Tool	PPV (%)	NPV (%)	Sensitivity (%)	Specificity (%)	Prevalence (%)	Accuracy (%)
TI-RADS	92.3%	90.1%	95.6%	93.2%	85.1%	94.0%
FNAC	94.5%	96.2%	98.5%	91.3%	84.7%	95.1%

Discussion

To differentiate benign thyroid nodules from malignant ones is essential to minimize the number of unnecessary surgeries and ensure early detection of thyroid cancer. Both Ultrasound TI-RADS and FNAC are frequently used to inform management decisions for solitary thyroid nodules in clinical practice. There are uncertainties in their comparative performance and reliability among other populations, however. The aim of this study was to compare the diagnostic accuracy and predictive value of TI-RADS and FNAC with histopathology as the gold standard.

This study revealed that thyroid nodules were more common in females, as reported in the literature; females were found to have thyroid nodules more often than males [4]. It may be caused by hormonal and autoimmune disorders. As in previous studies, the most common clinical symptom was neck swelling (80.6%), felt as a nodule and eventually diagnosed; although less common, dyspnea and voice change were also symptoms of larger disease lesions. This is consistent with the fact that most thyroid nodules are asymptomatic and detected on imaging [10].

The majority of the nodules in our study were radiologically classified as TI-RADS 3 and 4, and most were benign or intermediate risk. This distribution is similar to that reported by Basha et al., who found that nodules in lower TI-RADS categories were more common, and those in higher categories were more likely to be at risk of malignancy [11]. Kang et al. stated that AUC > 0.87 for ACR-TI-RADS with optimum cut-off points indicated high discriminatory power [12]. A prospective study from Pakistan demonstrated excellent sensitivity and moderate specificity of TI-RADS [8], while our study showed excellent categorical agreement between TI-RADS and histopathology (benign or

malignant). The predominance of Bethesda 2 (benign) was also reflected in our cohort, suggesting a high percentage of benign disease. The nodular stratification has been well documented by FNAC. Al-Yousofy et al. found high sensitivity and specificity of ultrasound-guided FNAC, especially in the diagnosis of papillary carcinoma, which accounts for the majority of malignant cases in many centers [3].

The present study shows that both TI-RADS and FNAC were significantly concordant with histopathology ($p < 0.001$). This is supported by the work of Basha et al., which showed that the performance of these risk categories is satisfactory when the reference standard is histopathology and when category thresholds (e.g., >TR3) are applied to distinguish between malignant and benign nodules [11]. Comparative analyses, however, have suggested that FNAC has higher sensitivity and negative predictive value, consistent with our findings, as FNAC exhibited a slightly higher benign predictive profile [13].

The specificity of our TI RADS was slightly better than that of older pooled reviews, perhaps because of better-quality imaging of nodes and more restrictive definitions of node categories; however, some meta-analyses have reported a specificity as high as 90% for certain subsets [14]. Meanwhile, as reported by Saba et al., sensitivity was around 91% and specificity was over 80%, higher than many published averages, confirming FNAC's power when coupled with ultrasound guidance and expert cytopathology [15]. In the present study, the high PPV, NPV, sensitivity and specificity found in TI-RADS was comparable with the high area under the ROC curve (AUC) and the sensitivity of TI-RADS are often higher than 90%, but the specificity is comparatively lower depending on cut-off and ultrasound criteria used, as reported by Kang et al. [12]. This highlights its use as a good screening tool where malignancy detection is prioritized, at the risk of over-triage of benign nodules for biopsy. In many cohorts, the diagnostic performance of FNAC is comparable to that of TI-RADS, as observed in our cohort. Orakzai et al. compared FNAC with histopathology and reported sensitivities ranging from 84% to >95%, with high predictive value, indicating the reliability of FNAC as a confirmatory test for malignancy [16].

These findings indicate that both TI-RADS and FNAC can be used confidently to triage patients, with FNAC offering modest improvements in sensitivity and overall accuracy. The integrated

approach enables TI-RADS to assist in initial management decision-making, and FNAC to aid in cytological diagnosis for optimal management, thereby preventing unnecessary surgery.

The study has some limitations, such as being single-center and having a small sample size, which could limit the generalizability of the results. The ultrasound sampling and interpretation were standardized and performed by well-trained operators, and inter-observer variability may have affected the diagnosis.

Conclusion

The study showed that both TI-RADS and FNAC are useful diagnostic procedures for solitary thyroid nodules with high NPV and high accuracy, and slightly higher sensitivity for TI-RADS. In initial risk stratification, in combination with TI-RADS, FNAC is useful for cytological confirmation of malignancy, helping optimize patient management and detect malignancy without unnecessary surgery. There is a need for further research to apply molecular markers in multi-center studies and for the establishment of training courses for radiologists and cytopathologists in order to enhance the diagnostic utility and interoperability.

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