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Research Article

Combined Diagnostic Utility of ACR-TIRADS, Fine Needle Aspiration Cytology and Histopathology in the Evaluation of Thyroid Nodules: A Prospective Study

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ABSTRACT
Background: Thyroid nodules are a common clinical problem, with malignancy occurring in approximately 4.5–6.5% of cases. High-resolution ultrasonography, combined with the American College of Radiology–Thyroid Imaging Reporting and Data System (ACR-TIRADS), has emerged as an effective tool for stratifying malignancy risk and guiding the need for fine-needle aspiration cytology (FNAC). Despite its increasing use, limited Indian data exist correlating ACR-TIRADS scores with final histopathology.
Aim: To evaluate the combined diagnostic performance and correlation of ACR-TIRADS, Fine Needle Aspiration Cytology (FNAC), and histopathological examination in patients with thyroid nodules.
Materials and Methods: This prospective observational study included 120 consecutive patients who underwent thyroidectomy after preoperative ultrasonography using ACR-TIRADS at a tertiary care centre in South India. Ultrasound features including composition, echogenicity, margins, shape, and echogenic foci were used to categorize nodules from TR1 to TR5. FNAC was selectively performed, and histopathology served as the gold standard. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and diagnostic accuracy were calculated. Statistical significance was determined using Chi-square test ($p < 0.05$).
Results: Of 120 nodules, 98 (81.7%) were benign and 22 (18.3%) malignant. Malignancy rates increased progressively with higher TIRADS categories. TIRADS demonstrated high sensitivity and NPV but lower specificity, reflecting overlap of suspicious sonographic features between benign and malignant lesions. The correlation between TIRADS score and histopathological outcome was statistically significant ($p = 0.001$).
Conclusion: Although ACR-TIRADS provides effective risk stratification of thyroid nodules, definitive diagnosis cannot be established by ultrasonography alone. FNAC serves as an essential intermediate diagnostic modality, while histopathological examination remains the gold standard. The combined use of TIRADS, FNAC, and histopathology provides the highest diagnostic accuracy and should be adopted for comprehensive evaluation of thyroid nodules.

Keywords: ACR-TIRADS, Thyroid Nodule, Ultrasonography, Histopathology, Risk Stratification, Thyroid Cancer.

INTRODUCTION

Thyroid nodules are a common clinical finding, with their prevalence increasing worldwide over the past decades. Although most thyroid nodules are benign, approximately 4.5–6.5% may be malignant, making accurate differentiation essential to avoid unnecessary thyroidectomies and associated morbidity[1]. Early epidemiological studies reported a palpable nodule prevalence of 3–7%, whereas high-resolution ultrasonography has increased detection rates to 20–76%, emphasizing the role of imaging in modern thyroid evaluation[2,3].

Ultrasonography remains the first-line imaging modality for the assessment of thyroid nodules due to its safety, accessibility, and high diagnostic value. To standardize ultrasound interpretation and improve malignancy risk stratification, several scoring systems have been developed—among them, the American College of Radiology Thyroid Imaging Reporting and Data System (ACR-TIRADS) has gained significant acceptance[4]. TIRADS classifies thyroid nodules into categories based on

ultrasound features such as composition, echogenicity, margins, shape, and calcifications, enabling clinicians to stratify malignancy risk and determine the appropriate need for fine-needle aspiration cytology (FNAC).

FNAC has long served as the gold standard for pre-operative evaluation of thyroid nodules, with sensitivities ranging from 83–99% and specificities between 70–91%[5,6]. However, universal FNAC for all nodules is neither feasible nor cost-effective. TIRADS aims to reduce unnecessary FNAC and surgeries by recommending cytology only for nodules with higher suspicion scores[7].

Despite the increasing adoption of ACR-TIRADS, its diagnostic performance may vary across populations due to differences in iodine status, prevalence of thyroiditis, demographic factors, and operator expertise. Several international studies have validated TIRADS, but Indian data remain limited[8,9]. Given this gap, there is a need for institution-based studies that correlate TIRADS scoring with final histopathology to determine its true diagnostic value in local clinical settings.

While TIRADS effectively stratifies the risk of malignancy, sonographic findings alone are insufficient for establishing a definitive diagnosis. FNAC provides cytological confirmation, whereas histopathological examination remains the definitive standard for diagnosis. Evaluating the correlation among these three diagnostic modalities may improve clinical decision-making and optimize patient management.

Aims and Objectives

Primary Objective

To determine the correlation between ACR-TIRADS score, FNAC (Bethesda category), and final histopathological diagnosis in thyroid nodules.

Secondary Objectives

- To assess the diagnostic performance of TIRADS using FNAC and histopathology as reference standards.
- To determine the agreement between FNAC and final histopathology.
- To evaluate the usefulness of combining ultrasound findings with cytology in surgical decision making.
- To study demographic and clinical characteristics of thyroid nodules.

MATERIALS AND METHODS

Study Design and Setting

This was a prospective observational study conducted in the Department of Otorhinolaryngology, Sree Mookambika Institute of Medical Sciences (SMIMS), Kulasekharam, Tamil Nadu, India. The study period extended from 1 December 2024 to 30 December 2025.

Sample Size Calculation

The sample size was calculated based on the estimated prevalence of malignancy in thyroid nodules in Indian populations (14–20% in previous original studies such as Periakaruppan et al., Srinivas et al., Chandramohan et al.).

Using the formula for diagnostic test sensitivity estimation:

$$n = \frac{Z^2\, P(1-P)}{d^2}$$

Where:

- Z = 1.96 (95% confidence interval)
- P = expected sensitivity of TIRADS = 0.90 (average sensitivity in Indian studies ranges 88–95%)
- d = precision = 0.06

$$n = \frac{(1.96)^2 \times 0.90 \times 0.10}{(0.06)^2} = 96.04 \approx 100$$

Considering a 20% attrition / ineligible rate, the final minimum sample size required = 120.

Thus, 120 consecutive patients meeting eligibility criteria were included.

Study Population

All patients presenting with thyroid nodules to the ENT OPD, ENT ward, and institutional private practice during the study period were screened. Patients undergoing thyroidectomy for diagnostic or therapeutic indications were included.

Inclusion Criteria

- Male and female patients of all age groups.
- Patients with solitary thyroid nodules (STN) or multinodular goiter (MNG).
- Patients with pre-operative ultrasonography performed using ACR-TIRADS scoring.
- Patients undergoing thyroidectomy with complete postoperative histopathology reports. Exclusion Criteria
- Patients with ultrasound grading done with non-ACR TIRADS systems.
- Patients who underwent only FNAC and did not undergo surgery.
- Patients diagnosed with thyroiditis (Hashimoto, De Quervain).
- Patients with toxic multinodular goiter or toxic adenoma.

Rationale: Thyroiditis and toxic goiters alter echotexture and vascularity, affecting TIRADS interpretation.

Ethical Considerations

Ethical clearance was obtained from the Institutional Ethics Committee (IEC) of SMIMS prior to study initiation. Written informed consent was obtained from all participants. Confidentiality was maintained throughout the study.

Data Collection Procedure

1. Clinical Assessment

All participants underwent a standardized clinical evaluation including:

- Duration and progression of neck swelling
- Pain, compressive symptoms (dyspnea, dysphagia)
- Hoarseness of voice
- Thyroid dysfunction symptoms (weight changes, heat/cold intolerance)
- Family history of thyroid disease
- Exposure history (iodine status, radiation)

A detailed ENT examination was performed including inspection, palpation, and direct laryngoscopy to assess vocal cord mobility.

2. Laboratory Investigations

All patients underwent baseline thyroid profile:

- Serum TSH
- Serum Free T3 (FT3)
- Serum Free T4 (FT4)

Basic pre-operative investigations were performed as per institutional surgical protocol.

Ultrasonography and TIRADS Scoring

High-resolution ultrasonography of the thyroid was performed using a 7–13 MHz linear transducer.

Ultrasound was done by a radiology faculty member, and 20% of randomly selected scans were cross-verified for inter-observer reliability by a second radiologist.

Nodule Characteristics Assessed:

- Size
- Composition
- Echogenicity
- Margins
- Shape (tall-than-wide)
- Echogenic foci/microcalcifications
- Cervical lymphadenopathy
- Isthmus involvement

TIRADS Score Was Assigned As Per ACR Criteria:

- TR1: Benign
- TR2: Not suspicious
- TR3: Mildly suspicious
- TR4: Moderately suspicious
- TR5: Highly suspicious

For Diagnostic Comparison:

- TR1–TR2 were grouped as "Benign"
- TR3–TR5 were grouped as "Suspicious/Malignant"

In patients with multiple nodules, the most suspicious nodule was used for analysis.

Fine Needle Aspiration Cytology (FNAC)

Fnac Was Performed Selectively For:

- TR3 and above nodules
- Nodules >1 cm
- Nodules with suspicious sonographic features

FNAC reporting followed the Bethesda System for Reporting Thyroid Cytopathology (TBSRTC).

Surgical Intervention

Thyroidectomy (Hemithyroidectomy Or Total Thyroidectomy) Was Performed Based On:

- FNAC diagnosis
- TIRADS score
- Clinical suspicion of malignancy
- Compressive symptoms
- Cosmetic concerns

Only patients undergoing surgery were included in the study.

Histopathology

Thyroidectomy specimens were processed and reported by qualified pathologists in the Department of Pathology.

Histopathological Diagnosis Was Categorized As:

- Benign (colloid nodule, adenoma, hyperplasia)
- Malignant (papillary, follicular, medullary, anaplastic carcinoma)

Histopathology served as the gold standard for diagnostic accuracy evaluation.

Statistical Analysis

Data were entered into Microsoft Excel and analyzed using SPSS version 26.0.

Parameters Calculated:

- Sensitivity
- Specificity
- Positive Predictive Value (PPV)
- Negative Predictive Value (NPV)
- Diagnostic Accuracy

Formulas Used:

$$Sensitivity = \frac{TP}{TP + FN} \times 100$$

$$Specificity = \frac{TN}{TN + FP} \times 100$$

$$Accuracy = \frac{TP + TN}{TP + TN + FP + FN} \times 100$$

Association between TIRADS and histopathology was tested using Chi-square test.

A p-value < 0.05 was considered statistically significant.

RESULTS

Table 1. Demographic Characteristics of the Study Population (N = 120)

Variable	Category	Frequency (N)	Percentage (%)
Gender	Male	28	23.3
	Female	92	76.7
Age Group (Years)	16–25	10	8.3
	26–35	24	20.0
	36–45	36	30.0
	46–55	28	23.3
	56–65	18	15.0
	66–75	4	3.3
Total		120	100

Table 2. Distribution of ACR-TIRADS Categories (N = 120)

Acr-Tirads Category	Description	Frequency (N)	Percentage (%)
Tr1	Benign	10	8.3
Tr2	Not Suspicious	30	25.0
Tr3	Mildly Suspicious	36	30.0
Tr4	Moderately Suspicious	30	25.0
Tr5	Highly Suspicious	14	11.7
Total		120	100

Table 3. Correlation between ACR-TIRADS Category and Bethesda Cytology (FNAC)

Acr-Tirads	Bethesda Ii	Bethesda Iii	Bethesda Iv	Bethesda V	Bethesda Vi	Total
Tr1	10	0	0	0	0	10
Tr2	28	2	0	0	0	30
Tr3	22	8	4	2	0	36
Tr4	6	6	8	8	2	30
Tr5	0	1	2	5	6	14
Total	66	17	14	15	8	120

Chi-Square Test: $p < 0.001$

Table 4. Correlation between Bethesda Cytology and Final Histopathology

Bethesda Category	Benign Histopathology N (%)	Malignant Histopathology N (%)	Total
Ii	66 (100.0)	0 (0.0)	66
Iii	15 (88.2)	2 (11.8)	17
Iv	10 (71.4)	4 (28.6)	14
V	5 (33.3)	10 (66.7)	15
Vi	2 (25.0)	6 (75.0)	8
Total	98 (81.7)	22 (18.3)	120

Chi-Square Test: $p < 0.001$

Table 5. Diagnostic Performance of Acr-Tirads, Fnac and Combined Assessment Compared With Final Histopathology

Diagnostic Parameter	Acr-Tirads	Fnac (Bethesda V–Vi Positive)	Combined Tirads + Fnac
Sensitivity (%)	90.9	72.7	95.5
Specificity (%)	38.8	92.9	94.9

Positive Predictive Value (%)	25.0	69.6	81.0
Negative Predictive Value (%)	95.0	94.8	98.9
Diagnostic Accuracy (%)	48.3	89.2	95.0

Table 6. Surgical Procedures Performed (N = 120)

Table 6. Surgical Procedures Performed (N = 120)	**Frequency (N)**	**Percentage (%)**
Hemithyroidectomy	22	18.3
Total Thyroidectomy	98	81.7
Completion Thyroidectomy*	2 (Among The 22 Hemithyroidectomy Patients)	1.7
Total Patients	120	100

DISCUSSION

In this prospective observational study of 120 thyroidectomy patients, we evaluated the diagnostic performance of ACR-TIRADS by correlating ultrasound-based risk stratification with final histopathology. Our findings are consistent with patterns reported in Indian and international literature.

Demographic Characteristics

The majority of patients in our study were female (76.7%), with a female-to-male ratio of 3.2:1, and the mean age was 42.6 years. This aligns with the well-documented female predominance in thyroid nodules and thyroid cancer, as reported by Pizzato et al[1]. Indian studies, including Periakaruppan et al[10]. and Chandramohan et al.[9], similarly observed female predominance ranging from 70% to 85% among thyroid nodule patients. The peak age group in our study (36–45 years) is comparable to Srinivas et al.[11], who reported the highest incidence in the 30–50-year age group.

Distribution of Goiter Types

Solitary thyroid nodules (STN) constituted 61.7% of cases in our study. Malignancy was more frequent in STN (24.3%) than in multinodular goiter (MNG) (8.7%). This observation mirrors findings by Horvath et al[7]. and Kwak et al.[5], who reported a higher malignancy risk in STN compared to MNG. Indian studies by Seshadri et al. and Periakaruppan et al[10]. Also reported a higher malignant yield from solitary nodules, confirming that STNs warrant careful evaluation.

Tirads Category Distribution

In our cohort, most benign nodules were classified as TR1–TR3, while suspicious lesions were categorized as TR4–TR5, consistent with ACR-TIRADS pattern descriptions by Russ et al[4]. Malignancy rates increased progressively across categories, from 0% in TR1 to 42.8% in TR5. This trend aligns with previous studies, including Kwak et al[5]. (TR5 malignancy 48%) and Moifo et al[12]. (TR5 malignancy 45%). Indian studies such as Periakaruppan et al[10]. and Chandramohan et al[9]. Also reported escalating malignancy rates with higher TIRADS categories, supporting the reliability of ACR-TIRADS in risk stratification.

Malignancy Rates Compared With Literature

The overall malignancy rate in our study was 18.3%, which is consistent with reported Indian studies showing rates between 14–22%[7,10,13]. This also aligns with ATA guidelines, which estimate malignancy in the general thyroid nodule population to be 5–15%[14], and global averages of 5–7% among nodules evaluated by FNAC or surgery.[15] Thus, the malignancy burden in our cohort is comparable to both regional and international prevalence data.

TIRADS and Histopathology Correlation

Although the incidence of malignancy increased progressively from TR1 to TR5, our study demonstrated that a small proportion of nodules categorized as low-risk (TR1–TR2) were ultimately malignant on final histopathology. This finding indicates that ACR-TIRADS alone cannot completely exclude malignancy. Similar observations have been reported in previous studies where occasional malignant lesions exhibited benign or minimally suspicious ultrasonographic features. Therefore, clinical judgment and cytological assessment remain essential, particularly when clinical suspicion persists despite a low TIRADS category.

Malignancy was observed in 5% of TR1–TR2 nodules, 11.1% of TR3 nodules, 33.3% of TR4 nodules and 42.8% of TR5 nodules. These

findings are comparable with previous studies by Kwak et al.[5], Horvath et al.[7], Moifo et al.[12], and Periakaruppan et al.[10], all of whom demonstrated increasing malignancy rates with increasing TIRADS scores while acknowledging occasional false-negative ultrasound classifications.

Diagnostic Performance

In our study, ACR-TIRADS demonstrated high sensitivity and negative predictive value (NPV), confirming its reliability in ruling out malignancy. The specificity was lower, which is consistent with previous reports and is often attributed to overlapping sonographic features such as hypoechogenicity and microcalcifications seen in both benign and malignant nodules. Russ et al[4]. and Jukic et al[16]. Emphasized that specificity tends to be lower in real-world practice because ultrasound interpretation may overestimate suspicious features. These findings highlight that ACR-TIRADS is highly sensitive but moderately specific, supporting its primary role as a screening and triage tool rather than a definitive diagnostic method.

Comparison with FNAC

Although not all patients underwent FNAC, the correlation between TIRADS categories and FNAC results in our study suggested a parallel diagnostic trend. This concordance has been reported by Periakaruppan et al.[10], Srinivas et al.[11], and Chandramohan et al.[9] Our findings also demonstrate that reliance on ultrasonography alone may result in underestimation of malignancy, particularly in low TIRADS nodules. FNAC substantially improved diagnostic confidence by identifying cytological atypia in several lesions that appeared less suspicious on imaging. The combined assessment achieved markedly higher sensitivity (95.5%), specificity (94.9%), and overall diagnostic accuracy (95.0%) compared with either TIRADS or FNAC alone. These findings support current recommendations that ultrasonography should be used for risk stratification, FNAC for preoperative cytological confirmation, and histopathology as the definitive diagnostic standard. Integration of these modalities provides a more reliable basis for selecting patients for hemithyroidectomy or total thyroidectomy while minimizing both unnecessary surgery and missed malignancies.

Strengths and Clinical Implications

The strengths of this study include its prospective design, which minimizes recall bias, and assessment of inter-observer reliability, enhancing the quality of ultrasound data. This study simultaneously evaluated radiological, cytological, and histopathological findings in the same cohort, enabling comprehensive assessment of the diagnostic pathway for thyroid nodules.

Limitations

The study is limited by its single-center design, which may affect generalizability. Inclusion of only surgically managed nodules may have inflated the malignancy prevalence due to surgical selection bias. Although inter-observer variability was minimized, it cannot be completely excluded. Finally, long-term follow-up for residual or persistent nodules was not

CONCLUSION

Although ACR-TIRADS is an effective risk-stratification tool, our study demonstrates that a small proportion of low TIRADS nodules may still harbor malignancy. Therefore, ultrasonography alone should not determine surgical management. FNAC significantly improves preoperative diagnostic accuracy, while histopathological examination remains the definitive diagnostic standard. The combined use of ACR-TIRADS and FNAC enables more appropriate selection of patients for hemithyroidectomy or total thyroidectomy and reduces the risk of missed malignancies requiring completion thyroidectomy.

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