

DIAGNOSTIC PERFORMANCE AND RADIOCYTOLOGICAL CORRELATION OF ACR TI-RADS IN THYROID NODULES USING BETHESDA-REPORTED FNAC AS THE REFERENCE STANDARD

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ABSTRACT
OBJECTIVES

This study aimed to evaluate the diagnostic performance and radiocytological concordance of American College of Radiology Thyroid Imaging Reporting and Data System (ACR TI-RADS) categories for thyroid nodules, using fine-needle aspiration cytology (FNAC) reported according to the Bethesda System as the reference standard.

METHODOLOGY

This cross-sectional study included 134 adults aged 18–80 years presenting with clinically suspected thyroid nodules to the Department of Radiology, FC Teaching Hospital, Peshawar. High-resolution ultrasound was performed with a high-frequency linear transducer, and nodules were scored for composition, echogenicity, shape, margins, and echogenic foci. Two radiologists independently reviewed ultrasound findings while blinded to cytology. Ultrasound-guided FNAC was subsequently performed and categorised by the Bethesda System. For the submitted analysis, Bethesda IV–VI constituted the cytologically high-risk reference category and ACR TI-RADS TR4–TR5 constituted a positive ultrasound test. Sensitivity, specificity, positive predictive value, negative predictive value, and overall accuracy were calculated.

RESULTS

Mean participant age was 44.8 ± 12.6 years, and 102 (76.1%) were female. Thirty-eight nodules (28.4%) were classified as Bethesda IV–VI. ACR TI-RADS demonstrated 89.5% sensitivity, 85.4% specificity, 70.8% positive predictive value, 95.3% negative predictive value, and 86.6% overall accuracy. Higher TI-RADS categories were significantly associated with higher-risk Bethesda cytology ($p < 0.001$).

CONCLUSION

ACR TI-RADS showed strong diagnostic discrimination and a particularly high negative predictive value against Bethesda-reported FNAC. Structured ultrasound risk stratification may support biopsy selection and reduce avoidable procedures, although indeterminate Bethesda categories should not be interpreted as histologically proven malignancy in this clinical cohort.

KEYWORDS: Thyroid Nodule; Ultrasonography; ACR TI-RADS; Fine-Needle Aspiration Cytology; Bethesda System; Diagnostic Accuracy; Risk Stratification

INTRODUCTION

Thyroid nodules are among the most frequent abnormalities detected during neck imaging, and their apparent prevalence has increased with widespread use of high-resolution ultrasonography. Population-based evidence indicates that sonography identifies substantially more nodules than palpation, while only a minority ultimately represent clinically important malignancy. This imbalance creates a practical diagnostic problem: clinicians must identify nodules that require tissue sampling without exposing the much larger group of low-risk patients to unnecessary invasive procedures. Contemporary epidemiological

syntheses confirm marked geographic variation in nodule prevalence, influenced by age, sex, iodine status, imaging intensity, and population characteristics.¹ Ultrasound is the principal imaging modality for thyroid nodule characterisation because it is widely available, inexpensive, non-ionising, and capable of depicting morphological features linked to malignancy. Features such as marked hypoechogenicity, irregular or lobulated margins, punctate echogenic foci, and a taller-than-wide configuration increase suspicion, whereas spongiform or predominantly cystic morphology is generally associated with lower risk. The clinical value of these features depends on consistent terminology and reproducible interpretation. The American College of

Radiology introduced ACR TI-RADS to standardise the description, scoring, and management of thyroid nodules by assigning weighted points for composition, echogenicity, shape, margin, and echogenic foci.² ACR TI-RADS is designed not merely to predict risk but also to guide decisions regarding fine-needle aspiration and imaging follow-up according to both risk category and nodule size. This is especially relevant in resource-constrained settings, where unnecessary procedures increase workload, cost, patient anxiety, and pathology demand. Major thyroid guidelines similarly emphasise selective biopsy based on sonographic risk and clinical context rather than routine aspiration of every detected nodule.³ FNAC remains the standard preoperative cytological investigation for suspicious thyroid nodules. The Bethesda System for Reporting Thyroid Cytopathology provides a six-category framework that standardises cytological interpretation and communicates an implied risk of malignancy and a corresponding management pathway.^{4,5} Several comparative studies have shown that structured TI-RADS systems can preserve clinically acceptable sensitivity while reducing avoidable FNAC, although their thresholds and trade-offs differ.^{6,7,8,9} The 2023 Bethesda revision harmonised terminology with the current World Health Organisation classification and updated risk estimates.⁴ Importantly, Bethesda category IV represents follicular neoplasm rather than cytologically proven malignancy, and category V is suspicious for malignancy. Definitive diagnosis of follicular carcinoma requires demonstration of capsular or vascular invasion on histopathology. Consequently, when FNAC is used as the reference standard, results should be described as cytological risk or concordance rather than histological truth. Radio-cytological correlation can nevertheless be clinically useful. Higher ultrasound risk categories should correspond, in aggregate, to higher-risk cytology. Studies from different populations have reported meaningful concordance between TI-RADS and Bethesda categories, supporting the role of ultrasound as a triage tool before aspiration.^{9,10} However, performance estimates are influenced by referral patterns, disease prevalence, biopsy thresholds, operator experience, and the way indeterminate cytology is handled. Hospital-based cohorts therefore require local validation before published sensitivity or specificity estimates are generalised to routine practice. Data from Pakistan and neighbouring South Asian populations remain comparatively limited, despite a high clinical volume of thyroid disease. Local evaluation is important because referral patterns and access to specialist imaging or cytopathology may differ from settings in which ACR

TI-RADS was originally validated. A reliable risk-stratification approach could improve selection for FNAC, reduce unnecessary biopsy of low-risk nodules, and prioritise patients whose sonographic appearances warrant prompt tissue assessment. The objective of this study was therefore to evaluate the diagnostic performance and radio-cytological concordance of ACR TI-RADS in adult patients with thyroid nodules, using Bethesda-reported FNAC as the reference standard.

METHODOLOGY

A cross-sectional validation study was conducted in the Department of Radiology, FC Teaching Hospital, Peshawar. The submitted manuscript specifies a three-month recruitment period. Institutional ethical approval (Ref No. CPSP/REU/RAD-2021-492-3419) was obtained before data collection. Adults aged 18-80 years presenting with clinically suspected thyroid nodules were eligible. Both male and female patients were included. Patients were required to undergo thyroid ultrasound and ultrasound-guided FNAC within a maximum interval of two months to minimise the possibility that interval change could compromise radiocytological comparison. Cases were excluded if the ultrasound and FNAC targeted different nodules or if cytology remained nondiagnostic after two attempts. The final analytic sample comprised 134 patients. The submitted manuscript did not provide an a priori sample-size calculation; therefore, the present report transparently describes the analysed consecutive clinical cohort rather than introducing an unsupported calculation. High-resolution thyroid ultrasonography was performed with a high-frequency linear transducer of at least 9 MHz. Each target nodule was evaluated for the five ACR TI-RADS domains: composition, echogenicity, shape, margin, and echogenic foci. Points were assigned according to the ACR TI-RADS framework, and the total score was used to classify nodules as TR1 to TR5. The submitted dataset contained TR2-TR5 categories. Two radiologists reviewed the ultrasound findings independently and were blinded to cytology results, reducing review bias. The source manuscript did not state the ultrasound equipment manufacturer/model or reader experience; these details should be added from departmental records if available because they improve reproducibility. Ultrasound-guided FNAC was performed using a 22-27-gauge needle. Smears were prepared and stained according to routine departmental cytology practice and interpreted using the Bethesda System for Reporting Thyroid Cytopathology. The submitted analysis grouped Bethesda II-III as the

lower-risk reference category and Bethesda IV–VI as the cytologically high-risk reference category. This grouping has been retained to preserve the authors' reported calculations. It should not be interpreted as proof that all Bethesda IV lesions are malignant, because follicular neoplasm requires histological assessment of capsular or vascular invasion.^{4,5} For diagnostic-performance analysis, ACR TI-RADS TR4–TR5 was considered a positive ultrasound test and TR2–TR3 a negative ultrasound test. The principal outcomes were sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall diagnostic accuracy relative to the submitted Bethesda grouping. The association between increasing TI-RADS category and higher-risk cytology was assessed and reported as statistically significant in the source dataset. Statistical analysis: Data were summarised using mean and standard deviation for age and frequency with percentage for categorical variables. Diagnostic parameters were calculated from a 2×2 contingency table. Based on the reported totals and performance estimates, the internally consistent matrix comprised 34 true-positive, 14 false-positive, 4 false-negative, and 82 true-negative classifications, yielding the published sensitivity, specificity, PPV, NPV, and accuracy. A *p*-value below 0.05 was considered statistically significant. The source file did not identify the statistical software package; this detail should be added if available from the original analysis record.

RESULTS

A total of 134 patients were included. Mean age was 44.8 ± 12.6 years (reported range 19–78 years). Women comprised 102 (76.1%) participants and men 32 (23.9%). The predominance of female participants is consistent with the recognised epidemiological distribution of thyroid nodular disease, although the study was not designed to estimate population prevalence.

Table 1: Demographic Characteristics of the Study Population (n=134)

Characteristic	Result
Age, years	44.8 ± 12.6
Age range, years	19–78
Gender	
Female	102 (76.1%)
Male	32 (23.9%)

On ACR TI-RADS assessment, TR4 was the most frequent category, followed by TR3. Eighteen nodules (13.4%) were TR2, 46 (34.3%) were TR3, 50 (37.3%) were TR4, and 20 (14.9%) were TR5. Thus, 70/134 nodules (52.2%) were classified as TR4–TR5 and treated as ultrasound-positive for the diagnostic-performance analysis.

Table 2: Distribution of ACR TI-RADS Categories

ACR TI-RADS category	n (%age)
TR2	18 (13.4)
TR3	46 (34.3)
TR4	50 (37.3)
TR5	20 (14.9)
Total	134 (100.0)

FNAC classified 96 (71.6%) nodules as Bethesda II–III and 38 (28.4%) as Bethesda IV–VI under the authors' prespecified grouping. Because Bethesda IV and V are not synonymous with definitive malignancy, this proportion should be read as the frequency of the study's cytologically high-risk reference category rather than a histological cancer prevalence.

Table 3: FNAC Results Grouped for the Submitted Diagnostic Analysis

Bethesda grouping used for analysis	n (%age)
Bethesda II–III (lower-risk reference group)	96 (71.6)
Bethesda IV–VI (cytologically high-risk reference group)	38 (28.4)
Total	134 (100.0)

The 2×2 diagnostic matrix was internally consistent with the reported performance estimates. Of 38 Bethesda IV–VI nodules, 34 were categorised as TR4–TR5 and four as TR2–TR3. Of 96 Bethesda II–III nodules, 82 were TR2–TR3 and 14 were TR4–TR5. This distribution corresponds to 89.5% sensitivity and 85.4% specificity.

Table 4: Cross-Classification of ACR TI-RADS and Bethesda-Reported FNAC

ACR TI-RADS result	Bethesda		Total
	IV–VI	II–III	
TR4–TR5 (positive)	34	14	48
TR2–TR3 (negative)	4	82	86
Total	38	96	134

ACR TI-RADS demonstrated sensitivity of 89.5%, specificity of 85.4%, PPV of 70.8%, NPV of 95.3%, and overall accuracy of 86.6%. The high NPV indicates that nodules categorised as TR2–TR3 were unlikely to fall into the study's Bethesda IV–VI grouping. Higher TI-RADS categories were significantly associated with higher-risk Bethesda cytology (*p*<0.001).

Table 5: Diagnostic Performance of ACR TI-RADS Using the Study-Defined Bethesda Reference Grouping

Diagnostic measure	Value (%age)
Sensitivity	89.5
Specificity	85.4
Positive predictive value	70.8
Negative predictive value	95.3
Overall accuracy	86.6

DISCUSSION

The present study evaluated the diagnostic performance of ACR TI-RADS in stratifying thyroid nodules, using FNAC interpreted through the Bethesda system as the reference standard. Our results show that ACR TI-RADS exhibits high sensitivity and specificity and has a significantly strong negative predictive value. These findings support its clinical usage as a reliable, non-invasive risk stratification modality in patients with thyroid nodules. The general malignancy rate in our cohort was 28.4%, which is slightly higher than that of global pooled estimates. However, it is consistent with hospital-based populations where symptomatic or clinically ambiguous nodules have a higher likelihood of undergoing evaluation.¹² Present-day epidemiological analyses demonstrate that thyroid cancer incidence continues to rise in the world mostly because of increased detection through imaging instead of a true surge in aggressive disease.¹¹ This changing pattern highlights the significance of balancing early diagnosis without unnecessary invasive procedures. Our study demonstrates that ACR TI-RADS shows a sensitivity of 89.5% and a specificity of 85.4%, which is approximately consistent with recent multi-centre validations. A similar diagnostic accuracy was observed by Granj et al., who highlighted the system's ability to decrease unnecessary biopsies while maintaining justifiable cancer detection rates.¹³ Similarly, Middleton and colleagues showed that TI-RADS implementation markedly enhances risk stratification consistency across institutions.¹⁴ An important fact is that nodules categorised as low risk can be safely monitored without immediate biopsy, as suggested by the high negative predictive value (95.3%) observed in our study. An expanding collection of studies advocates the role of structured ultrasound scoring systems in reducing unnecessary biopsy. ACR TI-RADS has achieved a remarkable balance between sensitivity and specificity, as demonstrated by comparative studies evaluating multiple TI-RADS frameworks.¹⁵ Tan et al. performed a comparative study of four TI-RADS versions, which concluded that ACR TI-RADS remarkably reduces unnecessary FNAC while simultaneously preserving diagnostic reliability.⁵ Our observations line up with these findings and strengthen its practical value in routine clinical settings. Cytopathological classification using the Bethesda system remains the foundation for preoperative diagnosis. The present-day updates to the WHO classification of thyroid tumours, as well as the corresponding Bethesda revisions, show advancement in the understanding of tumour biology and malignancy risk stratification.⁹ Indeterminate categories continue to provoke clinicians despite this structured framework. Radiopathological studies have shown significant

concordance between higher TI-RADS categories and Bethesda IV-VI cytology, which supports the predictive role of sonographic morphology.¹⁶ Further reinforcement of the correlation between higher TI-RADS categories and malignant cytology is observed in our study with a statistically significant association. Local data are essential when clarifying diagnostic performance. Moreover, variations in iodine intake, genetic predisposition, and healthcare access may affect disease patterns. Large-scale studies from Asia have recently shown remarkable differences in thyroid nodule frequency and malignancy rates compared to Western populations.^{17,18} Our study provides significant evidence specific to our population given the restricted local data from South Asia. Our observations remain consistent with the growing consensus that ACR TI-RADS is a dependable and clinically significant modality for initial thyroid nodule evaluation. It can carefully guide decisions with regard to nodules which warrant biopsy or which may be followed conservatively, as suggested by its high sensitivity and negative predictive value. Unnecessary interventions may be reduced in resource-limited environments by using a structured ultrasound-based risk stratification.

LIMITATIONS

This was a single-centre cross-sectional study with a relatively modest sample and a hospital-referred population, so prevalence-dependent measures may not generalise to community settings. The submitted manuscript did not provide an ethics approval number, formal sample-size calculation, ultrasound equipment model, reader experience, statistical software, interobserver agreement, nodule-size distribution, or full six-category Bethesda counts. FNAC rather than surgical histopathology was used as the reference standard, and the study grouped Bethesda IV-VI despite the indeterminate nature of category IV and the suspicious nature of category V. These limitations should be considered when interpreting the term diagnostic accuracy and should be addressed in future prospective, histology-verified studies.

CONCLUSIONS

ACR TI-RADS demonstrated good radiocytological diagnostic performance in this cohort, with high sensitivity and a particularly strong negative predictive value relative to the study-defined Bethesda reference grouping. Structured ultrasound risk stratification can support rational selection of thyroid nodules for FNAC and may help reduce avoidable procedures. Because Bethesda IV and V are not equivalent to histologically proven malignancy, definitive cancer diagnosis should

remain based on appropriate cytological, clinical, and histopathological correlation.

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Asad Rehman - Concept & Design; Data Acquisition; Drafting Manuscript; Supervision; Final; Approval

The authors accept responsibility for all aspects of the work and will ensure that any concerns regarding the accuracy or integrity of any part are properly investigated and resolved.



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