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Original Research Article

Correlation of ACR TI-RADS Ultrasonographic Risk Stratification with Bethesda Cytology and Thyroid Function Status in Patients with Thyroid Nodules

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Abstract

Background: Thyroid nodules are common, and accurate risk stratification is essential to distinguish lesions requiring cytological evaluation from those that can be managed conservatively.

Objective: To evaluate the relationship between ACR TI-RADS ultrasonography, Bethesda cytology, and thyroid function status in patients with thyroid nodules.

Methods: In this study, 200 patients with thyroid nodules were evaluated using thyroid ultrasonography, fine-needle aspiration cytology, and thyroid function tests. Nodules were classified according to ACR TI-RADS and the Bethesda System for Reporting Thyroid Cytopathology.

Results: The mean age was 45.8 ± 12.2 years, and 84.0% were female. TR4 was the most frequent ACR TI-RADS (44.0%), while Bethesda II was the predominant cytology (64.0%). Bethesda V/VI cytology was present in 14.5% of nodules. Increasing ACR TI-RADS showed a significant positive correlation with increasing Bethesda (Spearman's ρ=0.472, $p<0.001$). Suspicious features including solid composition, hypoechogenicity, taller-than-wide shape, irregular margins, and punctate echogenic foci were significantly more frequent in Bethesda V/VI nodules. Using TR4–TR5 as the high-risk threshold yielded 96.6% sensitivity, 48.4% specificity, and 98.4% negative predictive value for Bethesda V/VI cytology. Median TSH increased significantly across higher TI-RADS ($p<0.001$), whereas FT4 did not differ significantly ($p=0.882$).

Conclusion: ACR TI-RADS demonstrated significant concordance with Bethesda cytology and high sensitivity for identifying high-risk cytological lesions. Serum TSH showed an additional positive association with increasing sonographic risk.

Keywords: ACR TI-RADS; Bethesda System; Thyroid Nodule; Ultrasonography; Fine-Needle Aspiration Cytology; Thyroid-Stimulating Hormone.

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Introduction

Thyroid nodules are a common clinical and imaging finding, and their detection has increased substantially with the widespread use of high-resolution ultrasonography. Liao et al., in a 2025 systematic review involving 95,394 asymptomatic adults, reported an ultrasonographic thyroid incidentaloma prevalence of 30.6%, with higher prevalence among women than men (34% vs 23%) and among older than younger adults (42% vs 20%). [1] Although the majority of detected nodules are benign, differentiation of clinically relevant malignancy from the much larger pool of benign lesions remains essential; Durante et al. emphasized that most thyroid nodules are asymptomatic and benign and advocated risk-adapted evaluation to avoid unnecessary diagnostic and therapeutic interventions. [2] Ultrasonography is central to thyroid-nodule risk stratification because morphological characteristics such as composition, echogenicity, shape, margins, and echogenic foci are associated with different probabilities of malignancy. Zheng et al., evaluating 1,033 thyroid nodules, reported malignancy rates of 0%, 1.1%, 13.0%, and 67.1%

for ACR TI-RADS TR2, TR3, TR4, and TR5 nodules, respectively. [3] Rosario et al. similarly reported malignancy risks of 1.7%, 11.2%, and 60.6% for solid TR3, TR4, and TR5 nodules, respectively, demonstrating a marked increase in malignancy risk with higher TI-RADS. [4] In a meta-analysis of 33,748 nodules, Kim et al. found that a threshold of ACR TI-RADS TR4 or higher provided 95% sensitivity and 55% specificity for thyroid cancer detection. [5] Grani et al. further demonstrated that application of ACR TI-RADS could have avoided 53.4% of biopsies, while maintaining a negative predictive value of 97.8%, highlighting its potential to reduce unnecessary FNAC. [6] Nevertheless, Li et al. reported only moderate overall inter-reader agreement for ACR TI-RADS (κ=0.51), with margins showing the lowest agreement (κ=0.34), emphasizing the importance of standardized sonographic interpretation. [7]

Fine-needle aspiration cytology provides complementary cellular-level risk stratification. Cibas and Ali standardized thyroid cytology into six Bethesda categories, with the 2017 system assigning an implied malignancy risk of approximately 0–3% for Bethesda II and 97–99% for Bethesda VI. [8] In an Indian series of 4,532 thyroid FNAs, Mahajan et al. reported Bethesda III, IV, and V frequencies of 2.5%, 3.9%, and 0.5%, respectively, with an overall cytological diagnostic accuracy of 82.4%. [9] Importantly, Modi et al. demonstrated a relationship between imaging and cytology: among 361 nodules with paired assessments, no TR2 or TR3 nodule was Bethesda V/VI, whereas 21.5% of TR5 nodules were Bethesda VI. [10]

Biochemical thyroid status may provide additional risk information. Golbert et al. reported higher TSH concentrations in malignant than benign nodules (2.25 vs 1.50 μU/mL) and an approximately threefold increase in malignancy risk when TSH was ≥2.26 μU/mL. [11] A subsequent meta-analysis involving 5,348 lesions reported pooled sensitivity and specificity of 64% and 72%, respectively, for serum TSH in differentiated thyroid cancer detection, supporting an adjunctive rather than stand-alone diagnostic role. [12] These observations provide the rationale for examining the relationship between ACR TI-RADS ultrasonographic risk stratification, Bethesda cytology, and thyroid function status in patients with thyroid nodules. Against this background, the objective of the present study was to classify thyroid nodules according to the American College of Radiology Thyroid Imaging Reporting and Data System (ACR TI-RADS) and Bethesda System for Reporting Thyroid Cytopathology, to stratify thyroid nodules as benign or malignant based on ultrasonographic features, to assess the concordance between ACR TI-RADS and Bethesda cytological categories, and to evaluate the relationship between ACR TI-RADS classification and thyroid function test findings.

Materials and Methods

This was a single-centre, hospital-based, analytical, cross-sectional study conducted in the Departments of General Medicine and Radiodiagnosis of a tertiary teaching healthcare facility in South India over a period of two years (January 2024–December 2025). The study was approved by the Institutional Human Ethics Committee (IHEC). Each participant was provided with a Participant Information Sheet (PIS) translated into their local language. The information was also explained verbally to ensure clear understanding and voluntary agreement. Written informed consent was obtained prior to enrolling participants in the study. Patients of either sex with one or more clinically or sonographically detected thyroid nodules who underwent thyroid ultrasonography, fine-needle aspiration cytology (FNAC), and thyroid function testing were eligible for inclusion in the study. Thyroid nodules were required to have adequate ultrasonographic information for classification according to the ACR TI-RADS system and corresponding cytological evaluation using the Bethesda System for Reporting Thyroid Cytopathology. Patients with diffuse thyroid disease without a discrete measurable nodule, a history of previous thyroid surgery or previously treated thyroid malignancy, or incomplete ultrasonographic, cytological, or thyroid function test data were excluded.

The sample size was calculated based on Wu et al., that reported a correlation coefficient of r = 0.379 between the ACR TI-RADS and Bethesda cytology. [13] For the present study, a more conservative minimum correlation coefficient of r = 0.20 was considered clinically relevant. Assuming a two-sided significance level of 5% (α = 0.05), 80% statistical power (β = 0.20), and Z values of 1.96 and 0.84, respectively, the sample size was calculated using Fisher's Z-transformation for a correlation coefficient: $n = [(Z_{1-\alpha/2} + Z_{1-\beta})/(0.5 \times \ln((1+r)/(1-r)))]^2 + 3$. For r = 0.20, Fisher's Z value was 0.203, giving a minimum required sample size of 200 patients; enrolled using nonprobability sampling – purposive/convenience sampling technique.

After enrolment, demographic and clinical information, including age, sex, presenting complaints, duration of thyroid swelling, solitary or multinodular presentation, and relevant history of thyroid disease, was recorded using a structured data-collection proforma. Each patient underwent ultrasonographic examination of the thyroid, and the nodule that corresponded to the lesion sampled

for FNAC was considered the index nodule. For patients with multiple nodules, the sonographic characteristics of the nodule selected for cytological evaluation were recorded separately to ensure accurate ultrasound–cytology correlation. On ultrasonography, the location of the nodule, maximum dimensions and maximum diameter were documented, and each nodule was systematically evaluated according to the five ACR TI-RADS sonographic domains: composition, echogenicity, shape, margin, and echogenic foci. Composition was classified as cystic or almost completely cystic or spongiform (0 points), mixed cystic and solid (1 point), or solid or almost completely solid (2 points). Echogenicity was categorized as anechoic (0 points), hyperechoic or isoechoic (1 point), hypoechoic (2 points), or very hypoechoic relative to the strap muscles (3 points). Shape was recorded as wider-than-tall (0 points) or taller-than-wide on the transverse image (3 points). Margins were categorized as smooth or ill-defined (0 points), lobulated or irregular (2 points), or showing extrathyroidal extension (3 points). Echogenic foci were recorded as absent or having large comet-tail artefacts (0 points), macrocalcifications (1 point), peripheral/rim calcifications (2 points), or punctate echogenic foci (3 points); points for applicable echogenic foci were added as specified by the ACR system. The points obtained from all five domains were summed and each nodule was assigned an ACR TI-RADS category as TR1, 0 points (benign); TR2, 2 points (not suspicious); TR3, 3 points (mildly suspicious); TR4, 4–6 points (moderately suspicious); or TR5, ≥7 points (highly suspicious). Nodule size was also assessed in relation to the ACR recommendations for FNAC and follow-up, namely FNAC at ≥2.5 cm for TR3, ≥1.5 cm for TR4, and ≥1.0 cm for TR5 nodules. TR1–TR3 nodules were considered low-risk/likely benign, whereas TR4–TR5 nodules were considered sonographically suspicious for malignancy. FNAC was performed on the index thyroid nodule, and the cytological diagnosis was reported using the Bethesda System for Reporting Thyroid Cytopathology. Cytological findings were classified into six categories: Bethesda I, nondiagnostic; Bethesda II, benign; Bethesda III, atypia of undetermined significance; Bethesda IV, follicular neoplasm; Bethesda V, suspicious for malignancy; and Bethesda VI, malignant. Thyroid function test results obtained during the clinical evaluation were also recorded, principally serum thyroid-stimulating hormone (TSH) and free thyroxine (FT4), with triiodothyronine (T3/FT3) where measured.

Statistical analysis: Statistical analysis was performed using IBM SPSS Statistics for Windows, version 27.0 (IBM Corp., Armonk, NY, USA). Continuous variables were summarized as mean ± standard deviation (SD) or median with interquartile range (IQR), depending on data distribution, while categorical variables were expressed as frequencies and percentages. Differences between categorical variables were assessed using the chi-square test or Fisher's exact test, as appropriate. Continuous variables across ACR TI-RADS categories were compared using one-way analysis of variance (ANOVA) for normally distributed data and the Kruskal–Wallis test for non-normally distributed data. Correlations were assessed using Spearman's rank correlation coefficient. Agreement was evaluated using Cohen's kappa coefficient. Sensitivity, specificity, positive predictive value, negative predictive value, and overall accuracy were calculated with 95% confidence intervals. A two-tailed p value <0.05 was considered statistically significant.

Results

The study included 200 patients with thyroid nodules, with a mean age of 45.8 ± 12.2 years. Females constituted the majority of the study population (84.0%), while males accounted for 16.0%. A solitary thyroid nodule was present in 129 (64.5%) patients, whereas 71 (35.5%) had a multinodular presentation. The mean maximum nodule diameter was 24.7 ± 9.7 mm. The median serum TSH level was 1.83 mIU/L (IQR: 1.24–2.44), with a mean of 2.14 ± 1.74 mIU/L, while the mean FT4 level was 1.19 ± 0.22 ng/dL. Most patients were euthyroid (83.5%), whereas subclinical hypothyroidism and subclinical hyperthyroidism were observed in 6.5% and 5.5% of patients, respectively. According to the ACR TI-RADS classification, TR4 was the most common, accounting for 88 (44.0%) nodules, followed by TR3 in 60 (30.0%) and TR5 in 36 (18.0%) nodules. On cytological assessment using the Bethesda system, Bethesda II (benign) was the predominant category and was observed in 128 (64.0%) nodules. Bethesda VI (malignant) cytology was identified in 18 (9.0%) nodules, while 11 (5.5%) were Bethesda V, suspicious for malignancy. Indeterminate cytology comprised 18 (9.0%) Bethesda III and 15 (7.5%) Bethesda IV nodules, whereas 10 (5.0%) samples were classified as Bethesda I (nondiagnostic). Cross-tabulation of ACR TI-RADS with Bethesda cytology demonstrated a progressive shift toward higher-risk cytological findings with increasing TI-RADS category.

All TR1 nodules were classified as Bethesda II, while 83.3% of TR2 and 80.0% of TR3 nodules were also cytologically benign. In the TR4 group, Bethesda II remained the most frequent category (63.6%), although 4.5% each were classified as Bethesda V and Bethesda VI. In contrast, among TR5 nodules, only 27.8% were Bethesda II, whereas 16.7% were Bethesda V and 38.9% were Bethesda VI. Overall, there was a statistically

significant moderate positive correlation between increasing ACR TI-RADS category and increasing Bethesda cytology (Spearman's ρ = 0.472, p<0.001). All Bethesda V/VI nodules were solid or almost completely solid compared with 71.1% of Bethesda II nodules (p<0.001), while hypoechoic or very hypoechoic echogenicity was observed in 96.6% versus 60.2%, respectively (p<0.001). A taller-than-wide shape was present in 24.1% of Bethesda V/VI nodules compared with only 2.3% of Bethesda II nodules, and lobulated or irregular margins were seen in 69.0% versus 9.4%, respectively (both p<0.001).

Punctate echogenic foci were also significantly more common in Bethesda V/VI nodules (27.6% vs 6.2%, p=0.002), indicating that multiple suspicious ultrasound characteristics were associated with higher-risk cytology. When ACR TI-RADS was dichotomized into TR1–TR3 and TR4–TR5, 28 of 29 nodules with Bethesda V/VI cytology were classified as TR4–TR5, whereas only one was classified as TR1–TR3. This yielded a high sensitivity of 96.6% and negative predictive value of 98.4% for identifying Bethesda V/VI cytology. However, specificity was comparatively low at 48.4%, with a positive predictive value of 29.8% and an overall accuracy of 57.3%. Agreement between the binary ACR TI-RADS classification and definitive Bethesda cytology was statistically significant (Cohen's κ=0.241, 95% CI 0.147–0.335; p<0.001).

Serum TSH levels demonstrated a progressive increase across higher ACR TI-RADS. The median TSH level increased from 1.21 mIU/L in TR1–TR2 nodules to 1.63 mIU/L in TR3, 1.77 mIU/L in TR4, and 2.42 mIU/L in TR5 nodules, with a statistically significant overall difference (p<0.001). In contrast, mean FT4 concentrations were comparable across TI-RADS, ranging from 1.18 to 1.21 ng/dL, with no significant difference (p=0.882). The proportion of euthyroid patients also did not differ significantly between groups (p=0.230). A modest but statistically significant positive correlation was observed between increasing ACR TI-RADS category and serum TSH level (Spearman's ρ=0.321, p<0.001).

Table 1: Baseline demographic, clinical and thyroid function characteristics of the study population

	Value
Age, years, mean ± SD	45.8 ± 12.2
Age, years, range	18–78
Female sex, n (%)	168 (84.0)
Male sex, n (%)	32 (16.0)
Solitary nodule, n (%)	129 (64.5)
Multinodular presentation, n (%)	71 (35.5)
Maximum nodule diameter, mm, mean ± SD	24.7 ± 9.7
TSH, mIU/L, median (IQR)	1.83 (1.24–2.44)
TSH, mIU/L, mean ± SD	2.14 ± 1.74
FT4, ng/dL, mean ± SD	1.19 ± 0.22
Euthyroid, n (%)	167 (83.5)
Subclinical hypothyroidism, n (%)	13 (6.5)
Overt hypothyroidism, n (%)	5 (2.5)
Subclinical hyperthyroidism, n (%)	11 (5.5)
Overt hyperthyroidism, n (%)	4 (2.0)

Table 2: Distribution of ACR TI-RADS and Bethesda cytology

		n (%)
ACR TI-RADS	TR1	4 (2.0)
	TR2	12 (6.0)
	TR3	60 (30.0)
	TR4	88 (44.0)
	TR5	36 (18.0)
Bethesda	I – Nondiagnostic	10 (5.0)
	II – Benign	128 (64.0)
	III – Atypia of undetermined significance	18 (9.0)
	IV – Follicular neoplasm	15 (7.5)
	V – Suspicious for malignancy	11 (5.5)
	VI – Malignant	18 (9.0)

Table 3: Cross-tabulation of ACR TI-RADS with Bethesda cytology

ACR TI-RADS	Bethesda I	Bethesda II	Bethesda III	Bethesda IV	Bethesda V	Bethesda VI
TR1 (n=4)	0 (0.0)	4 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
TR2 (n=12)	1 (8.3)	10 (83.3)	1 (8.3)	0 (0.0)	0 (0.0)	0 (0.0)
TR3 (n=60)	4 (6.7)	48 (80.0)	4 (6.7)	3 (5.0)	1 (1.7)	0 (0.0)
TR4 (n=88)	4 (4.5)	56 (63.6)	11 (12.5)	9 (10.2)	4 (4.5)	4 (4.5)
TR5 (n=36)	1 (2.8)	10 (27.8)	2 (5.6)	3 (8.3)	6 (16.7)	14 (38.9)
Values are n (% within ACR TI-RADS category). Spearman $\rho = 0.472$, $p<0.001$.						

Table 4: Ultrasonographic features according to definitive cytology

Ultrasound	Bethesda II (n=128)	Bethesda V/VI (n=29)	P value
Solid/almost completely solid composition	91 (71.1)	29 (100.0)	<0.001*
Hypoechoic/very hypoechoic echogenicity	77 (60.2)	28 (96.6)	<0.001*
Very hypoechoic echogenicity	11 (8.6)	10 (34.5)	<0.001*
Taller-than-wide shape	3 (2.3)	7 (24.1)	<0.001*
Lobulated/irregular margin	12 (9.4)	20 (69.0)	<0.001*
Punctate echogenic foci	8 (6.2)	8 (27.6)	0.002*

Table 5: Binary ACR TI-RADS risk classification compared with definitive Bethesda cytology

ACR TI-RADS risk group	Bethesda II	Bethesda V/VI	Total
TR1–TR3	62	1	63
TR4–TR5	66	28	94
Total	128	29	157
Performance for identifying Bethesda V/VI cytology			
Sensitivity	96.6% (95% CI 82.8–99.4)		
Specificity	48.4% (95% CI 40.0–57.0)		
Positive predictive value	29.8% (95% CI 21.5–39.7)		
Negative predictive value	98.4% (95% CI 91.5–99.7)		
Overall accuracy	57.3% (95% CI 49.5–64.8)		
Cohen κ	0.241 (95% CI 0.147–0.335); p<0.001		

Table 6: Thyroid function tests according to ACR TI-RADS

	TR1–TR2 (n=16)	TR3 (n=60)	TR4 (n=88)	TR5 (n=36)
TSH, mIU/L, median (IQR)	1.21 (0.98–1.55)	1.63 (1.14–2.21)	1.77 (1.27–2.40)	2.42 (2.04–2.67)
FT4, ng/dL, mean ± SD	1.18 ± 0.18	1.21 ± 0.27	1.18 ± 0.21	1.18 ± 0.19
Euthyroid, n (%)	15 (93.8)	47 (78.3)	72 (81.8)	33 (91.7)
Overall P value	TSH: <0.001* (Kruskal–Wallis); FT4: 0.882 (one-way ANOVA); euthyroid proportion: 0.230 (χ^2 test)			
ACR TI-RADS level also correlated with TSH (Spearman $\rho = 0.321$, $p<0.001$)				

Discussion

The present study evaluated 200 patients with thyroid nodules and demonstrated a marked female predominance (84.0%), with a mean age of 45.8 ± 12.2 years. Boelaert et al., in a prospective cohort of 1,500 patients presenting with palpable thyroid enlargement, similarly reported 1,304 women (86.9%) and a mean age of 47.8 years; 861 patients had solitary nodules and 456 had multinodular goitre. [14] In the present study, 64.5% had a solitary nodule and 35.5% had a multinodular presentation, indicating a comparable clinical spectrum. Most patients were euthyroid (83.5%), while subclinical hypothyroidism and subclinical hyperthyroidism were relatively uncommon. This is clinically relevant because the American Thyroid Association recommends serum TSH measurement during the initial evaluation of a patient with a thyroid nodule, irrespective of whether overt thyroid dysfunction is clinically apparent. [15] ACR TI-RADS classification showed that TR4 was the most common (44.0%), followed by TR3 (30.0%) and TR5 (18.0%). Cytologically, Bethesda II was the largest (64.0%), whereas Bethesda V and VI accounted for 5.5% and 9.0%, respectively. Tessler et al. developed ACR TI-RADS as a structured point-based system incorporating five ultrasound domains – composition, echogenicity, shape, margin, and echogenic foci. [16]

The 2023 Bethesda System similarly provides six cytological groups, namely nondiagnostic, benign, atypia of undetermined significance, follicular neoplasm, suspicious for malignancy, and malignant, with each group associated with an implied risk of malignancy and corresponding clinical management considerations. [17] The

predominance of Bethesda II in the present cohort therefore reflects the expected pattern that the majority of evaluated thyroid nodules are cytologically benign.

A clear stepwise relationship between ultrasonographic and cytological risk was observed. All TR1 nodules and 83.3% of TR2 nodules were Bethesda II, while 80.0% of TR3 nodules were also cytologically benign. In contrast, 55.6% of TR5 nodules were classified as Bethesda V or VI, including 38.9% classified as Bethesda VI. The overall association between the two systems was moderate and statistically significant (Spearman's $\rho=0.472$, $p<0.001$). Wu evaluated ACR TI-RADS in 154 thyroid nodules and reported a correlation coefficient of $r=0.379$ between the converted ACR TI-RADS level and Bethesda cytology, closely supporting the directional relationship observed in the present study. [13] Karatay et al. reported an even stronger positive correlation between ACR TI-RADS and Bethesda ($\rho=0.832$, $p<0.001$) among 73 patients who underwent thyroidectomy. [18] The higher coefficient reported by Karatay et al. may partly reflect the selected surgical population, whereas the present study represented a wider cytological spectrum including benign, indeterminate, suspicious, and malignant.

The individual ultrasonographic characteristics provided further biological and morphological support for this association. Solid or almost completely solid composition was present in 100% of Bethesda V/VI nodules compared with 71.1% of Bethesda II nodules, while hypoechoic or very hypoechoic echogenicity was observed in 96.6% versus 60.2%, respectively. More discriminatory suspicious features also showed marked differences: a taller-than-wide configuration occurred in 24.1% of Bethesda V/VI nodules compared with 2.3% of Bethesda II nodules, lobulated or irregular margins occurred in 69.0% versus 9.4%, and punctate echogenic foci occurred in 27.6% versus 6.2%. Remonti et al., in a meta-analysis of 52 observational studies comprising 12,786 nodules, reported specificity of 96.6% for taller-than-wide shape, 83.1% for irregular margins, and 87.8% for microcalcifications, with corresponding positive likelihood ratios of 8.07, 2.99, and 3.26. [19] Woliński et al. similarly found that taller-than-wide shape was a particularly strong predictor of malignancy (OR 13.7), while irregular margins and microcalcifications showed odds ratios of 7.2 and 7.1, respectively. [20] These observations support the ACR TI-RADS principle that risk assessment is strengthened by integrating several suspicious features rather than relying on any single sonographic sign.

When ACR TI-RADS was dichotomized into TR1–TR3 versus TR4–TR5, 28 of the 29 nodules with Bethesda V/VI cytology were categorized as TR4–TR5. This corresponded to a sensitivity of 96.6% and negative predictive value of 98.4% for identifying Bethesda V/VI cytology, while specificity was 48.4% and positive predictive value was 29.8%. These values should specifically be interpreted as performance against high-risk cytological features rather than as diagnostic performance against histopathologically proven malignancy. Nevertheless, the pattern closely resembles published diagnostic-performance data for ACR TI-RADS. Kang et al., in an updated meta-analysis of 46 studies involving 39,085 patients, reported that using TR4 as the threshold for malignancy yielded a pooled sensitivity of 94.3% and specificity of 52.2%. [21] Thus, the high sensitivity and negative predictive value in the present study suggest that TR1–TR3 classification was strongly associated with absence of Bethesda V/VI cytology, whereas the lower specificity reflects the considerable number of TR4–TR5 nodules that nevertheless had benign cytological findings. The Cohen's κ value of 0.241 indicated only fair binary agreement despite the statistically significant moderate ordinal correlation. This apparent difference is methodologically coherent because Spearman's correlation evaluates whether increasing TI-RADS accompany progressively increasing Bethesda cytology, whereas κ evaluates direct agreement after both systems have been reduced to binary classifications. In the present study, 63.6% of TR4 nodules were still Bethesda II, explaining why overall ordinal correlation could be significant while binary agreement remained modest. This observation also emphasizes the complementary roles of the two systems: ACR TI-RADS provides structural risk stratification and guides selection for FNAC, whereas Bethesda cytology provides cellular-level categorization and more directly informs subsequent clinical management. Wu similarly demonstrated that imaging and cytology were correlated but not interchangeable, reporting an ACR TI-RADS–Bethesda correlation of 0.379. [13]

The secondary analysis demonstrated a significant progressive increase in serum TSH with increasing ACR TI-RADS category. Median TSH increased from 1.21 mIU/L in TR1–TR2 to 1.63 mIU/L in TR3, 1.77 mIU/L in TR4, and 2.42 mIU/L in TR5 ($p<0.001$), with a modest positive correlation between TSH and ACR TI-RADS ($\rho=0.321$, $p<0.001$). This relationship is consistent with previous evidence linking higher serum TSH concentrations with increasing thyroid malignancy risk. In the prospective study by Boelaert et al., compared with patients having TSH <0.4 mU/L, the adjusted odds of malignancy increased to 2.72 (95% CI 1.02–7.27) for TSH 1.0–1.7 mU/L and 3.88 (95% CI 1.48–10.19) for TSH 1.8–5.5 mU/L. [14] The ATA guidelines likewise recognize that higher serum TSH concentrations, including values

within the upper portion of the reference interval, are associated with increased malignancy risk in patients with thyroid nodules. [22] In contrast, FT4 concentrations remained essentially similar across ACR TI-RADS, ranging from 1.18 to 1.21 ng/dL (p=0.882), and the proportion of euthyroid patients did not differ significantly between groups (p=0.230). The presence of a TSH gradient despite relatively stable FT4 concentrations is physiologically plausible because the hypothalamic–pituitary–thyroid relationship permits relatively small variations in circulating thyroid hormone concentrations to produce appreciable reciprocal changes in TSH. Consequently, the observed TSH–TI-RADS relationship is better interpreted as a modest adjunctive biochemical risk association, rather than evidence that thyroid functional status determines sonographic risk. This interpretation is consistent with Boelaert et al., who proposed serum TSH as an adjunct to established clinical and cytological assessment rather than as an independent diagnostic replacement for FNAC. [14] Thus, within the diagnostic framework evaluated in the present study, ACR TI-RADS characterized structural sonographic risk, Bethesda cytology provided cytomorphological risk stratification, and serum TSH contributed additional biochemical information relevant to overall thyroid nodule assessment.

The present study had certain limitations. First, its single-centre design may have limited the generalizability of the findings to populations with different demographic profiles, referral patterns, ultrasound practices, and disease prevalence. Second, the diagnostic comparison was primarily based on ACR TI-RADS and Bethesda cytology, while histopathological confirmation was not available for all nodules; therefore, Bethesda II and Bethesda V/VI were used as cytological reference groups rather than definitive benign and malignant histological outcomes. Third, ultrasound interpretation is inherently operator-dependent, particularly for features such as echogenicity, margins, shape, and echogenic foci, and interobserver variability was not specifically assessed. Fifth, thyroid function tests were evaluated at a single time point, and potential influences such as thyroid medications, autoimmune thyroiditis, iodine status, and other factors affecting serum TSH were not fully accounted for. Finally, the observed association between serum TSH and increasing ACR TI-RADS was cross-sectional and therefore could not establish a causal relationship between thyroid functional status and sonographic malignancy risk.

Conclusion: The present study demonstrated a significant positive relationship between ACR TI-RADS ultrasonography and Bethesda cytology in patients with thyroid nodules, with progressively higher-risk cytology observed as the TI-RADS increased. Suspicious ultrasonographic features, particularly solid composition, marked hypoechogenicity, taller-than-wide shape, irregular or lobulated margins, and punctate echogenic foci, were significantly associated with Bethesda V/VI cytology. ACR TI-RADS showed high sensitivity and a high negative predictive value for identifying nodules with high-risk cytological findings, supporting its usefulness as an effective non-invasive risk-stratification tool and for guiding the selection of nodules for FNAC. Serum TSH levels also increased significantly across higher TI-RADS, suggesting a possible adjunctive role for thyroid function assessment in risk evaluation, whereas FT4 levels and overall euthyroid status showed no significant association. Overall, the findings support the complementary use of ACR TI-RADS, Bethesda cytology, and thyroid function testing for a structured and clinically meaningful assessment of thyroid nodules.

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