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Prediction of Thyroid Malignancy Using the American College of Radiology Thyroid Imaging Reporting and Data System (ACR-TIRADS): A Local Multicenter Study

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Objective: To evaluate the diagnostic performance of the American College of Radiology Thyroid Imaging Reporting and Data System (ACR-TIRADS) for predicting histopathologically confirmed malignancy in thyroid nodules in three Cordillera Consortium hospitals.

Methods: This retrospective multicenter cross-sectional study included patients who underwent thyroidectomy and had complete preoperative ultrasound and histopathology records from January 2019 to December 2021. ACR-TIRADS categories were reviewed and assigned based on recorded sonographic features. Diagnostic performance was evaluated using sensitivity, specificity, likelihood ratios, predictive values, accuracy, and receiver operating characteristic (ROC) analysis. The empirical area under the ROC curve (AUC) and achieved precision were characterized post hoc using the standard Hanley–McNeil and conservative Blume frameworks.

Results: Of 117 patients, 38 (32.5%) had malignant and 79 (67.5%) had benign histopathologic findings. Malignant nodules were more frequently solid or almost completely solid, hypoechoic, lobulated or irregular, and associated with punctate echogenic foci. ACR-TIRADS classification differed significantly between malignant and benign nodules ($P<0.001$). At a cutoff of ACR-TIRADS categories 4–5, sensitivity was 73.68% (95% CI, 56.90–86.60), specificity was 67.09% (95% CI, 55.60–77.25), and accuracy was 69.23% (95% CI, 60.03–77.43). The empirical AUC was 0.7532. Under the Hanley–McNeil framework, the 95% CI was 0.664–0.843, whereas the conservative Blume framework yielded a 95% CI of 0.616–0.890.

Conclusion: ACR-TIRADS demonstrated fair discriminatory ability and moderate diagnostic performance in this selected thyroidectomy cohort. Its principal value may be in risk stratification rather than as a stand-alone confirmatory test. The post hoc precision estimates indicate that the observed diagnostic performance should be interpreted in light of the retrospective design, selected study population, and differences between standard and conservative precision frameworks.

Key words: ACR-TIRADS, thyroid nodules, thyroid malignancy, ultrasonography, diagnostic accuracy

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Thyroid cancer is the ninth most common cancer worldwide and the most common endocrine malignancy in the Philippines. Thyroid nodules are common, but only a minority are malignant, making accurate risk stratification important for identifying patients who may benefit from further evaluation while limiting unnecessary invasive procedures.[1,2] High-resolution ultrasonography is central to thyroid nodule assessment, while fine-needle aspiration biopsy (FNAB) provides cytologic evaluation when indicated.[3]

Ultrasound-based risk-stratification systems have been developed to standardize the assessment of sonographic features associated with malignancy. Studies comparing ACR-TIRADS with other systems have reported favorable diagnostic performance, and contemporary evidence continues to support its use in thyroid nodule risk stratification.[4,5] ACR-TIRADS has also been evaluated in Philippine patients, where higher categories were associated with thyroid malignancy.[6] International studies have likewise shown that structured ultrasound risk stratification can reduce unnecessary biopsy while maintaining diagnostic performance.[5,7,8,9]

However, diagnostic performance may vary according to case mix, disease prevalence, referral patterns, and clinical practice. Evidence from multicenter Philippine cohorts is limited, particularly among patients managed in the Cordillera region. A local multicenter evaluation is therefore important to determine whether the performance of ACR-TIRADS observed elsewhere is applicable to patients seen across different hospitals in this setting.

This study evaluated the association between ACR-TIRADS sonographic characteristics and histopathologically confirmed thyroid malignancy and determined the diagnostic performance of ACR-TIRADS

in a multicenter cohort of patients who underwent thyroidectomy in three Cordillera Consortium hospitals.

Methods

Study Design and Setting

This retrospective multicenter cross-sectional study was conducted in three Cordillera Consortium hospitals: Benguet General Hospital, Notre Dame de Chartres Hospital, and Pines City Doctors' Hospital. The study period covered January 2019 to December 2021.

Participants and Selection

The study population consisted of patients with thyroid nodules who underwent thyroidectomy at any of the three participating hospitals. Eligible patients had a complete preoperative ultrasound examination containing the sonographic features required for ACR-TIRADS categorization and a histopathologic result. Patients with incomplete ultrasound or histopathologic records and those with prior interventional procedures that could affect the ultrasound assessment were excluded. Since the study was based on surgical cases with available records, the final cohort represents a selected thyroidectomy population rather than all patients with thyroid nodules.

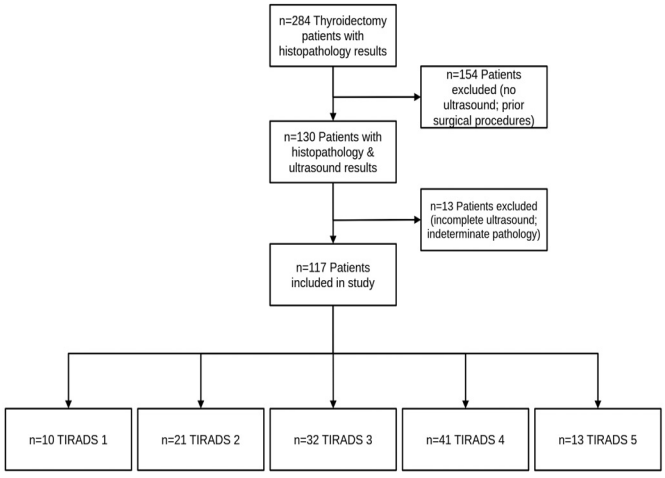


Figure 1. Flow of patient selection and distribution of analyzed thyroid nodules by ACR-TIRADS category and histopathologic findings. Cordillera Consortium, 2025.

Since this was a retrospective study based on a complete enumeration of eligible records, no prospective sample-size target was imposed. Of the 284 patients who underwent thyroidectomy with histopathologic examination, 130 had both preoperative ultrasound and histopathology records and no previous surgical or interventional procedure. Thirteen patients were subsequently excluded because of incomplete ultrasound findings or indeterminate histopathologic results, leaving 117 patients for analysis. Since the final cohort size and the distribution of malignant and benign outcomes were determined by the available retrospective records and could not be controlled prospectively, the sample-size projections were not used to impose a recruitment target. Instead, the achieved precision of the diagnostic accuracy estimates was characterized using 95% confidence intervals and post hoc power, as appropriate.

Reference Standard

Histopathologic diagnosis from the participating hospitals served as the reference standard. Nodules were classified as malignant or benign based on the final histopathologic report.

Ultrasound Assessment

Data were abstracted using a standardized data collection tool. Variables included age, sex, fine-needle aspiration biopsy results when available, ultrasound findings, ACR-TIRADS category, and histopathologic diagnosis. ACR-TIRADS categorization was based on composition, echogenicity, shape, margins, and echogenic foci. The recorded sonographic findings were reviewed by a sonologist for validation of the categorization. The study records did not specify whether this review was performed using stored ultrasound images, printed images, or written ultrasound reports; this limitation is considered in the interpretation of the findings.

The diagnostic accuracy of the ACR-TIRADS classification system was evaluated using Area Under the Receiver Operating Characteristic Curve (AUC-ROC) analysis. Diagnostic performance metrics were calculated by defining an ACR-TIRADS score of 4 or 5

as a positive test for malignancy, while scores of 1, 2, or 3 were treated as negative.

Statistical Analysis

Categorical variables were summarized using frequencies and percentages, while normally distributed continuous variables were summarized using means and standard deviations. The Shapiro–Wilk test was used to assess normality. Differences in continuous variables between malignant and benign groups were assessed using the independent-samples t-test. Differences in categorical variables were assessed using the chi-square test or Fisher's exact test, as appropriate. The distributions of composition, echogenicity, shape, margins, echogenic foci, and ACR-TIRADS classification were compared between malignant and benign histopathologic findings.

Given the retrospective nature of the data, post hoc frameworks were used to characterize the stability of the empirical AUC, including its margin of error (MoE) and confidence boundaries. Inference was conducted at a two-sided α=0.05. The AUC was computed using the nonparametric Mann–Whitney U-statistic. Post hoc power was evaluated as the probability of detecting the observed effect size at the specified α, using the corresponding AUC-to-effect-size relationship.

Two statistical frameworks were applied to evaluate the achieved MoE and 95% confidence intervals (CI):

1. Standard Non-Parametric Framework (Hanley–McNeil): Direct variance estimation was computed from the raw rank-order data matrices to determine the standard error (SE) of the AUC.[10]
2. Distribution-Free Conservative Framework (Blume): Alternatively, to safeguard against potential structural distortions or severe data skewness common in categorical TIRADS indexing, Blume's model-free upper-bound variance method was applied to ensure interval validity regardless of the underlying data distribution.[11]

Sensitivity, specificity, positive and negative likelihood ratios, and overall accuracy were calculated with 95% confidence intervals. Since predictive values depend on prevalence and the study cohort was selected from thyroidectomy patients, PPV and NPV were interpreted cautiously. Prevalence-adjusted PPV and NPV were calculated using the observed sensitivity and specificity and the 10.1% prevalence reported in a previous thyroid-nodule cohort as an illustrative reference. Missing values were neither replaced nor estimated. Statistical analyses were performed using Stata (Version 12.0, StataCorp LLC, College Station, TX).

Results

A total of 117 patients were included in the analysis. The overall mean age was 45.13 ± 13.17 years, and 85 (72.65%) were younger than 55 years. Thirty-eight patients (32.48%) had malignant histopathologic findings and 79 (67.52%) had benign findings. The mean age was lower among patients with malignant nodules than among those with benign nodules (39.82 ± 14.20 vs 47.68 ± 11.92 years; *P*=.002). However, age group (<55 vs ≥55 years) was not significantly associated with malignancy (*P*=.133). Most patients were female in both groups, and sex was not significantly associated with malignancy (*P*=0.528) (Table 1).

Table 1. Demographic profile of the patients, by histopathologic findings. Cordillera Consortium, 2025.

Variable	Total (n=117)	Malignant (n=38)	Benign (n=79)	*P* value
Age, years, mean ± SD	45.13 ± 13.17	39.82 ± 14.20	47.68 ± 11.92	0.002
<55 years	85 (72.65)	31 (81.58)	54 (68.35)	0.133
≥55 years	32 (27.35)	7 (18.42)	25 (31.65)	
Male	18 (15.38)	7 (18.42)	11 (13.92)	0.528
Female	99 (84.62)	31 (81.58)	68 (86.08)	

Sonographic Characteristics

Nodule composition differed significantly between malignant and benign groups (*P*=0.004). Solid or almost completely solid nodules accounted for 81.58% of malignant nodules compared with 51.90% of benign nodules, whereas mixed cystic and solid nodules were more common among benign nodules (37.97% vs 10.53%). Echogenicity was also significantly associated

with malignancy (*P*=0.003); hypoechoic nodules were more frequent in the malignant group (55.26% vs 25.32%), while hyper- or isoechoic nodules were more common in the benign group (63.29% vs 34.21%). (Table 2)

Nodule shape was not significantly different between groups (*P*=0.100). Most nodules were wider than tall. Taller-than-wide nodules occurred in 7.89% of malignant cases and 1.27% of benign cases. Margin characteristics were significantly different (*P*<.001), with lobulated or irregular margins more frequent among malignant nodules than benign nodules (23.68% vs 2.53%). Both nodules with extrathyroidal extension were malignant, although the small number of observations limits interpretation.

Echogenic foci were significantly associated with histopathology (p=.001). Punctate echogenic foci were present in 26.32% of malignant nodules compared with 3.80% of benign nodules. In contrast, no echogenic foci or large comet-tail artifacts were more common among benign nodules (78.48% vs 50.00%).

Risk of Malignancy by ACR-TIRADS Category

The observed risk of malignancy increased across ACR-TIRADS categories overall, from 10.0% in category 1 and 9.5% in category 2 to 21.9% in category 3, 43.9% in category 4, and 76.9% in category 5 (Table 3). Category 5 had the highest proportion of malignant nodules, whereas category 2 had the lowest observed proportion among the five categories.

Diagnostic Performance

The corresponding 2×2 contingency table is shown in Table 4. At a cutoff of ACR-TIRADS categories 4–5 as a positive result and categories 1–3 as a negative result, sensitivity was 73.68% (95% CI, 56.90–86.60) and specificity was 67.09% (95% CI, 55.60–77.25), with an overall accuracy of 69.23% (95% CI, 60.03–77.43). The positive likelihood ratio was 2.24 (95% CI, 1.55–3.23), and the negative likelihood ratio was 0.39 (95% CI, 0.23–0.68). The observed prevalence of malignancy

Table 2. Sonographic profile of thyroid nodules, by histopathologic findings. Cordillera Consortium, 2025.

Variable	Total (n=117)	Malignant (n=38)	Benign (n=79)	*P* value
Composition				**0.004**
Cystic/almost completely cystic	9 (7.69)	2 (5.26)	7 (8.86)	
Spongiform	2 (1.71)	1 (2.63)	1 (1.27)	
Mixed cystic and solid	34 (29.06)	4 (10.53)	30 (37.97)	
Solid/almost completely solid	72 (61.54)	31 (81.58)	41 (51.90)	
Echogenicity				**0.003**
Anechoic	12 (10.26)	3 (7.89)	9 (11.39)	
Hyper- or isoechoic	63 (53.85)	13 (34.21)	50 (63.29)	
Hypoechoic	41 (35.04)	21 (55.26)	20 (25.32)	
Very hypoechoic	1 (0.85)	1 (2.63)	0	
Shape				**0.100**
Wider than tall	113 (96.58)	35 (92.11)	78 (98.73)	
Taller than wide	4 (3.42)	3 (7.89)	1 (1.27)	
Margin				**<0.001**
Smooth	98 (83.76)	25 (65.79)	73 (92.41)	
Ill-defined	6 (5.13)	2 (5.26)	4 (5.06)	
Lobulated/irregular	11 (9.40)	9 (23.68)	2 (2.53)	
Extrathyroidal extension	2 (1.71)	2 (5.26)	0	
Echogenic foci				**0.001**
None or large comet-tail artifacts	81 (69.23)	19 (50.00)	62 (78.48)	
Macrocalcifications	18 (15.38)	7 (18.42)	11 (13.92)	
Peripheral (rim) calcifications	5 (4.27)	2 (5.26)	3 (3.80)	
Punctate echogenic foci	13 (11.11)	10 (26.32)	3 (3.80)	

P values are based on the categorical test (chi-square or Fisher's exact test, as appropriate).

Table 3. Observed risk of malignancy by ACR-TIRADS category. Cordillera Consortium, 2025.

ACR-TIRADS category	Total nodules	Malignant, n (%)	Benign, n (%)	Observed risk of malignancy
1	10	1 (10.0)	9 (90.0)	10.0%
2	21	2 (9.5)	19 (90.5)	9.5%
3	32	7 (21.9)	25 (78.1)	21.9%
4	41	18 (43.9)	23 (56.1)	43.9%
5	13	10 (76.9)	3 (23.1)	76.9%
Total	117	38 (32.5)	79 (67.5)	32.5%

Table 4. Two-by-two contingency table of ACR-TIRADS classification using categories 4–5 as positive and 1–3 as negative, by histopathologic findings. Cordillera Consortium, 2025.

ACR-TIRADS classification	Benign	Malignant	Total
Negative (TIRADS 1, 2, 3)	53 (67.09%)	10 (26.32%)	63 (53.85%)
Positive (TIRADS 4, 5)	26 (32.91%)	28 (73.68%)	54 (46.15%)
Total	79 (100.00%)	38 (100.00%)	117 (100.00%)

in this selected cohort was 32.48%. Using the 10.1% prevalence reported in a previous thyroid-nodule cohort as an illustrative reference prevalence, the observed sensitivity and specificity corresponded to a prevalence-adjusted PPV of approximately 20.5% and NPV of approximately 95.8%. These estimates illustrate the dependence of predictive values on disease prevalence and should not be interpreted as estimates of the actual prevalence in the Cordillera population.

ROC Analysis

Based on the enrolled cohort, the empirical ROC-AUC was 0.753 (SE=0.0456, 95% CI 0.66371–0.84262), indicating fair overall diagnostic performance (Figure 2).

Under the standard Hanley–McNeil framework, the AUC's standard error was 0.046, corresponding to a 95% confidence interval of 0.664–0.843 (MoE = ±8.9%) and a post hoc power of 99.7%. Under the more conservative Blume framework, the worst-case 95% confidence interval was 0.616–0.890 (MoE = ±13.8%) with post hoc power of 84.7%.

The lower boundaries of the 95% CIs of both frameworks (0.664 and 0.616, respectively) lie beyond the random-chance threshold of 0.50, supporting ACR-TIRADS ≥4 as a statistically significant discriminator between malignant and benign thyroid nodules.

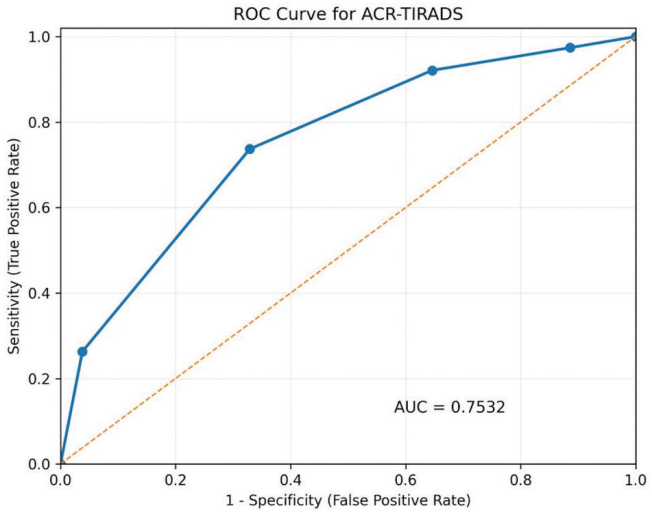


Figure 2. Receiver operating characteristic (ROC) curve for ACR-TIRADS in distinguishing malignant from benign thyroid nodules. AUC, 0.7532. Cordillera Consortium, 2025.

Discussion

In this multicenter cohort of 117 thyroidectomy patients, ACR-TIRADS classification was significantly associated with histopathologic malignancy, and the observed risk of malignancy increased across higher ACR-TIRADS categories. The cohort was predominantly female, consistent with the demographic pattern reported in previous thyroid nodule studies.[6,12] Patients with

malignant nodules had a lower mean age than those with benign nodules, although age group and sex were not significantly associated with malignancy. Since the study population was restricted to patients who underwent thyroidectomy, these demographic findings should not be interpreted as estimates of the distribution of all patients with thyroid nodules.

Several sonographic features differed significantly between malignant and benign nodules. Solid or almost completely solid composition was more frequent among malignant nodules, as were hypoechogenicity, lobulated or irregular margins, and punctate echogenic foci. These findings are biologically and clinically consistent with the role of structured ultrasound assessment in thyroid malignancy risk stratification.[4,6,8] In contrast, nodule shape did not reach statistical significance in this cohort. The lack of significance may partly reflect the small number of taller-than-wide nodules. Similarly, only one very hypoechoic nodule and two nodules with extrathyroidal extension were observed; these sparse findings limit the precision of estimates and should not be interpreted as evidence that these features lack diagnostic importance.

The distribution of malignancy across ACR-TIRADS categories showed a clear upward pattern: 10.0% in category 1, 9.5% in category 2, 21.9% in category 3, 43.9% in category 4, and 76.9% in category 5. The higher observed risks in categories 4 and 5 support the ability of ACR-TIRADS to stratify nodules according to malignancy risk. However, the malignancy proportions in this study were higher than those reported in large unselected or broader clinical cohorts.[13] This difference should not be interpreted as evidence that patients in the Cordillera region inherently have a higher population prevalence of thyroid cancer. The present study included only patients who underwent thyroidectomy and had retrievable preoperative ultrasound and histopathology records, a selection process that likely enriched the sample for clinically suspicious nodules. This selection is an important source of selection bias and limits generalizability.

Using ACR-TIRADS categories 4–5 as a positive test and categories 1–3 as a negative test, sensitivity was 73.68% and specificity was 67.09%, with an overall accuracy of 69.23%. The positive likelihood ratio of 2.24 indicates a modest increase in the likelihood of malignancy after a positive result, whereas the negative likelihood ratio of 0.39 indicates a meaningful reduction in likelihood after a negative result. The AUC of 0.7532 indicates fair discriminatory ability. The achieved AUC precision was characterized post hoc: the Hanley–McNeil framework yielded a 95% CI of 0.664–0.843 (MoE ±8.9%) with 99.7% post hoc power, while the conservative Blume framework yielded a 95% CI of 0.616–0.890 (MoE ±13.8%) with 84.7% post hoc power. These findings support the use of ACR-TIRADS as a risk-stratification tool, but they do not support describing it as a definitive or confirmatory diagnostic test.

Predictive values require particular caution in this study because they depend strongly on disease prevalence. The observed cohort prevalence was 32.48%, which reflects the selected thyroidectomy population rather than the general population of patients with thyroid nodules. Using the 10.1% prevalence reported in a previous thyroid-nodule cohort as an illustrative reference prevalence,[14] the sensitivity and specificity observed in this study correspond to an estimated PPV of approximately 20.5% and NPV of approximately 95.8%. These values are prevalence-dependent and should not be interpreted as estimates of the actual prevalence or predictive values in the Cordillera population. A locally representative prevalence estimate would be needed for more precise population-level predictive values.

The study also has important methodological limitations. Of 284 patients who underwent thyroidectomy with histopathology, only 117 were ultimately analyzed, representing a substantial loss of potentially eligible cases. Many records lacked preoperative ultrasound information, while others had incomplete ultrasound data or indeterminate histopathologic findings. This retrospective record-based selection can introduce selection bias. In addition, the study relied on the sonographic information available in the medical records. Although ACR-TIRADS categorization was reviewed by a sonologist, the available study documentation does not specify whether the review was performed from stored ultrasound images, image prints, or written reports. This limits assessment of interobserver agreement and should be addressed in future prospective studies using standardized image review.

Finally, the findings should be interpreted within the context of a three-hospital Cordillera Consortium cohort and should not be generalized to all Filipino patients with thyroid nodules. Future multicenter prospective studies that include consecutive patients at the time of ultrasound assessment, use standardized independent image interpretation, and establish a representative local prevalence of thyroid malignancy would provide stronger evidence regarding the generalizability and clinical utility of ACR-TIRADS.

Conclusion

In this selected multicenter thyroidectomy cohort, higher ACR-TIRADS categories were associated with greater observed risk of histopathologically confirmed malignancy. Current findings support ACR-TIRADS as a risk-stratification tool but not as a stand-alone confirmatory test. Since the study included only thyroidectomy patients with retrievable records, further prospective studies involving consecutive patients and standardized ultrasound image review are needed to establish population-level diagnostic performance in the Philippines.

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