

# Diagnostic Accuracy of American College of Radiology Thyroid Imaging Reporting Data System: A Single-Center Cross-sectional Study

Pamela Ann Aribon,<sup>1</sup> Emmylou Teope,<sup>2</sup> Anna Lyn Egwolf,<sup>2</sup> Maria Patricia Maningat<sup>1</sup>

<sup>1</sup>Center for Diabetes Thyroid and Endocrine Disorders, St. Luke's Medical Center, Global City, Taguig, Philippines

<sup>2</sup>Department of Radiology, Section of Ultrasonography, St. Luke's Medical Center, Global City, Taguig, Philippines

## Abstract

**Objective.** This study aims to evaluate the diagnostic accuracy of the American College of Radiology Thyroid Imaging Reporting Data System (ACR TI-RADS) in identifying nodules that need to undergo fine-needle aspiration biopsy (FNAB) and identify specific thyroid ultrasound characteristics of nodules associated with thyroid malignancy in Filipinos in a single tertiary center.

**Methodology.** One hundred seventy-six thyroid nodules from 130 patients who underwent FNAB from January 2018 to December 2018 were included. The sonographic features were described and scored using the ACR TI-RADS risk classification system, and the score was correlated to their final cytopathology results.

**Results.** The calculated malignancy rates for TI-RADS 2 to TI-RADS 5 were 0%, 3.13%, 7.14%, and 38.23%, respectively, which were within the TI-RADS risk stratification thresholds. The ACR TI-RADS had a sensitivity of 89.5% and specificity of 54%, LR + of 1.95 and LR - of 0.194, NPV of 97.7%, PPV of 19.1%, and accuracy of 58%.

**Conclusion.** The ACR TI-RADS may provide an effective malignancy risk stratification for thyroid nodules and may help guide the decision for FNAB among Filipino patients. The classification system may decrease the number of unnecessary FNABs for nodules with low-risk scores.

**Key words:** ACR TI-RADS, FNAB, thyroid nodules

## INTRODUCTION

Thyroid nodules are among the most common endocrine pathologies in the general population. The incidence of thyroid nodules is increasing due to the wide use of thyroid ultrasound or other imaging tests that incidentally detect such nodules.<sup>1</sup> With high-resolution ultrasonography, thyroid nodule prevalence ranges from 19-68% in randomly selected individuals.<sup>1,2</sup> In the Philippines, the estimated prevalence of nodular goiter is 8.9% based on PhilTiDes 1 published in 2012.<sup>3</sup> Clinically, thyroid nodules are a significant cause of thyroid dysfunction and, rarely, compressive symptoms and malignancy in 7-15% of cases, depending on the risk factors.<sup>4</sup> Ultrasound is an essential, initial, and the most accurate imaging modality to detect and evaluate thyroid nodules. Specific ultrasound characteristics can identify which thyroid nodules are at higher risk of malignancy. Identifying the risk of malignancy is vital in managing thyroid nodules. It may guide clinicians if FNAB may be required.<sup>1,2</sup>

While fine needle aspiration biopsy is the preferred initial diagnostic method for evaluating thyroid nodules, only approximately 3-7% of thyroid FNAB are malignant.<sup>5</sup> This is why a better classification system is needed to stratify thyroid nodules based on ultrasound characteristics to lessen the number of nodules undergoing unnecessary FNABs. A systematic and reliable method to identify thyroid nodules with a higher risk of malignancy from those that may not need further invasive procedures may be of value.<sup>1,2</sup> There have been several guidelines for the standardization and stratification of nodules based on ultrasound findings.<sup>6-8</sup> The standardized risk stratification system was first introduced by Horvath et al., in 2009, called Thyroid Imaging, Reporting and Data System (TI-RADS), patterned from the BI-RADS system of breast imaging, and is now accepted by several societies.<sup>9</sup> This risk stratification of thyroid nodules based on several ultrasound features has been studied and established; however, it has yet to be universally adopted.<sup>8</sup> In 2017, the American College of Radiology released its paper on Thyroid Imaging

Reporting and Data System (TI-RADS) that stratifies nodules according to a standardized set of terms (lexicon) for reporting sonographic features. These categories are assigned points in 5 ultrasound categories to determine their TI-RADS level.<sup>9-12</sup> The score aids in the decision to perform either biopsy or follow-up, recommending higher size thresholds for biopsy of less suspicious nodules and no biopsy on nodules of any size with benign features.<sup>11</sup> The need for a method to identify nodules that need FNAB is warranted since studies have shown that thyroid cancer has increased in incidence. However, this increase is partly due to screening thyroid sonography in asymptomatic patients causing over-diagnosis of thyroid cancer while mortality remains at a low rate.<sup>11,13</sup> In the study of Hoang et al., ACR TI-RADS guidelines significantly improved the accuracy of recommendations for nodule management, decreasing the number of thyroid nodules recommended for biopsy. Since invasive procedures for thyroid nodules cause a burden on healthcare costs and added anxiety to patients, risk stratification can aid in reducing unnecessary thyroid FNABs.

While FNAB is an accurate and practical method to evaluate thyroid nodules, a stratification system will guide clinicians to discuss and recommend evidence-based management and help patients understand and choose their options, providing better patient-centered management. Limited published studies were done in the Philippines that assess the validity and applicability of TI-RADS. More studies are warranted to test this stratification system to see its strength in identifying a nodule's malignancy risk. This study aims to evaluate the ACR TI-RADS risk stratification system in identifying nodules where FNAB can be safely deferred and its strength in identifying suspicious nodules in a single-center setting.

## OBJECTIVES

### General objective

To assess the diagnostic accuracy of the ACR TI-RADS in identifying nodules that need to undergo FNAB by comparing it to cytopathologic results of patients who underwent FNAB or thyroidectomy at St. Luke's Medical Center Global City, respectively.

### Specific objectives

1. To identify specific thyroid ultrasound characteristics of nodules associated with thyroid malignancy in Filipinos in a single tertiary center.
2. To determine the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy of ACR TI-RADS in detecting malignancy.

## METHODOLOGY

### Study design

This study is a single-center cross-sectional study approved by our institutional review board, and informed consent was waived.

### Study population

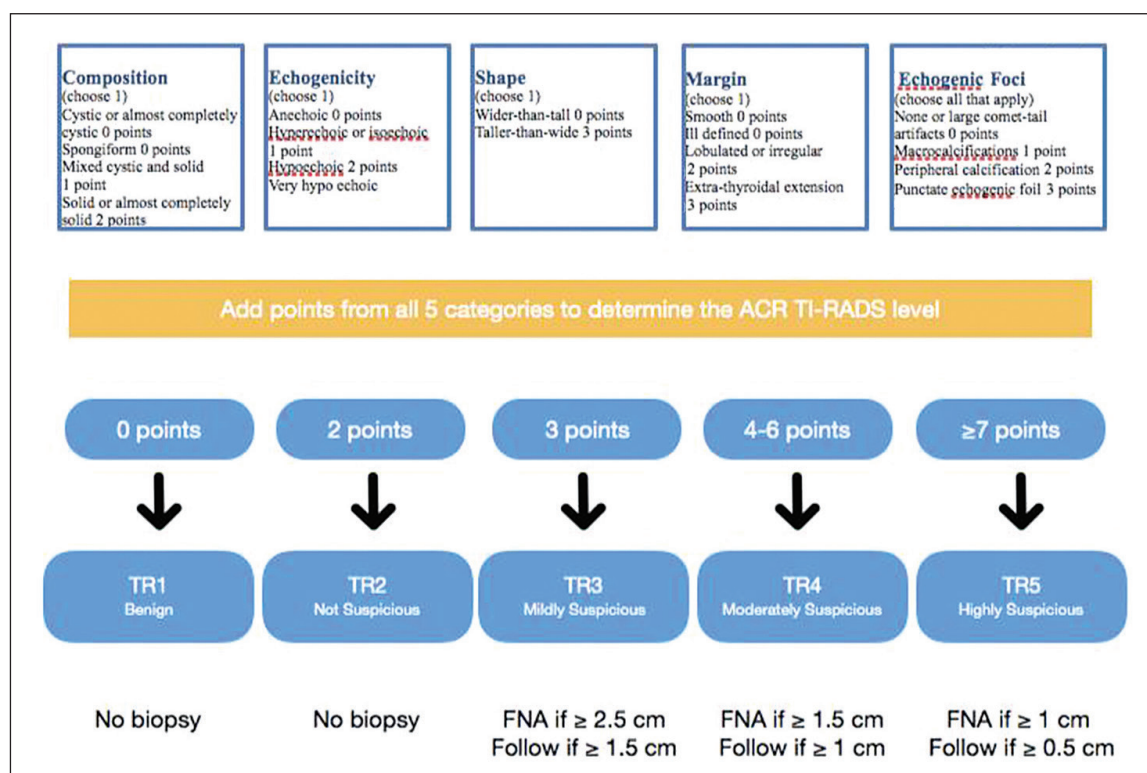
Filipino patients aged 18 years and above who underwent ultrasound-guided FNAB or thyroidectomy at St. Luke's Medical Center Global City from January 2018 to December 2018 were included. Patients whose ultrasounds were performed in other centers were not included due to a lack of consistency in reporting and the unavailability of reviewable images. In addition, those without final cytopathology results or nodules with results of non-diagnostic, indeterminate, suspicious for malignancy (Bethesda category I, III, IV, V) with no repeat fine-needle aspiration biopsy or surgery done to confirm if the nodule is benign or malignant were also excluded. The FNAB results did include the side where the biopsy was done but did not include the specific location of the nodule. However, the best target nodule was selected using the description of the previous ultrasound report. All sub-centimeter nodules were not included in the TI-RADS assessment.

### Sample size

The sample size was computed based on the prevalence of malignant nodules and sensitivity of the TI-RADS 4 based on the study of Horvath et al., which showed a prevalence of 76.13%, sensitivity 99.6% (95% CI: 98.9-100.0) and specificity 74.35% (95% CI: 68.7-80.0).<sup>9</sup> Using G\*Power Application, the computed minimum sample size required was 145 with a margin of error of 5% and actual power of 95% based on the level of significance of 5%.

### Study procedure

The ultrasound scans of the thyroid nodules included in the study were retrieved using the Radiology Information System - Picture Archiving and Communication System (RIS - PACS). Images were reviewed independently by two experienced sonologists blinded from the previous ultrasound report and cytopathology or histopathology result of the thyroid nodules. They stratified the thyroid nodule based on the set criteria of the ACR TI-RADS. Nodules were assigned points for each feature which were then summed up to determine the final TI-RADS score. The total number of points identified the nodule's ACR TI-RADS level and were subsequently categorized (Figure 1). The classification categories were graded according to their characteristic features in ultrasonography based on a TI-RADS point allocation scheme (Table 1). The nodules were classified as benign if the cytopathology result had a Bethesda score of II and malignant if they had a Bethesda score of VI. Nodules with Bethesda scores



FNA= Fine-needle aspiration

**Figure 1.** American College of Radiology Thyroid Imaging Reporting and Data System (ACR TI-RADS) Risk Stratification system and management recommendations.

**Table 1.** Thyroid imaging reporting and data system point allocation scheme

Classification Category	Point(s)
Composition	
Cystic or almost entirely cystic	0
Spongiform	0
Mixed solid and cystic	1
Solid or almost entirely solid	2
Echogenicity	
Anechoic	0
Hyperechoic or isoechoic	1
Hypoechoic	2
Very hypoechoic	3
Shape	
Wider-than-tall	0
Taller-than-wide	3
Margins	
Smooth	0
Ill-defined	0
Lobulated or irregular	2
Extrathyroidal extension	3
Echogenic foci	
None or large comet-tail artifacts	0
Macrocalcifications	1
Peripheral calcifications	2
Punctate echogenic foci	3

of III, IV, and V that underwent repeat biopsy or were surgically removed were also included in the study if their repeat cytopathology or histopathology result returned as Bethesda II or VI or if benign or malignant, respectively.

### Statistical analysis

The data were analyzed using Stata version 12 for Windows. The reference standard for malignancy in this study is cytology and histopathology results. The Shapiro-Wilk Test was used to check if the data is normally distributed. The mean age of patients with malignant and benign nodules was computed and compared using an independent t-test. Categorical variables were evaluated by chi-square test, including the patient sex and ultrasound features. For statistical correlation between pathologic results with ACR TI-RADS level, TR2 or TR3 were considered benign, and nodules with TR4 or TR5 as malignant.<sup>14</sup> To assess the accuracy of ACR TI-RADS in predicting a malignant thyroid nodule, the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and likelihood ratios were computed. Bivariate and multiple logistic regression analyses were performed to identify the sonographic features that are predictive of malignancy. Sonographic features with  $p < 0.25$  in the bivariate analysis were included in the multivariate regression analysis and significant features were selected using the backward-forward method. Crude and adjusted ratio and their corresponding 95% confidence intervals

**Table 2.** Summary of demographic features and ultrasound features

	Benign (N = 157)	Malignant (N = 19)	p
Age, mean (SD)	49.41 (14.00)	48.79 (14.34)	0.859
20-29	12 (7.64%)	-	0.785
30-39	33 (21.02%)	6 (31.58%)	
40-49	33 (21.02%)	4 (21.05%)	
50-59	44 (28.03%)	4 (21.05%)	
60-69	22 (14.01%)	3 (15.79%)	
70 and above	13 (8.28%)	2 (10.53%)	
Sex			0.524
Female	130 (83.87%)	17 (89.47%)	
Male	25 (16.13%)	2 (10.53%)	
Composition			0.884
Cystic or almost entirely cystic / Spongiform	9 (5.73%)	-	
Mixed solid and cystic	20 (12.74%)	2 (10.53%)	
Solid or almost completely solid	128 (81.53%)	17 (89.47%)	
Echogenicity			<0.0001*
Anechoic	4 (2.55%)	-	
Hyperechoic or isoechoic	90 (57.32%)	3 (15.79%)	
Hypoechoic	48 (30.57%)	8 (42.11%)	
Very hypoechoic	15 (9.55%)	8 (42.11%)	
Shape			0.369
Wider than tall	154 (98.09%)	18 (94.74%)	
Taller than wide	3 (1.91%)	1 (5.26%)	
Margin			<0.0001*
Smooth / Ill-defined	147 (93.63%)	11 (57.89%)	
Lobulated or irregular	7 (4.46%)	7 (36.84%)	
Extrathyroidal extension	3 (1.91%)	1 (5.26%)	
Echogenic foci			<0.0001*
None or large comet tail artifacts	115 (73.25%)	5 (26.32%)	
Macrocalcifications	14 (8.92%)	1 (5.26%)	
Peripheral calcifications	7 (4.46%)	1 (5.26%)	
Punctate echogenic foci	21 (13.38%)	12 (63.16%)	
Size			0.924*
Mean (SD)	2.12 (1.14)	2.15 (1.20)	
Median (range)	1.8 (0.5-6.7)	1.8 (0.8-4.2)	

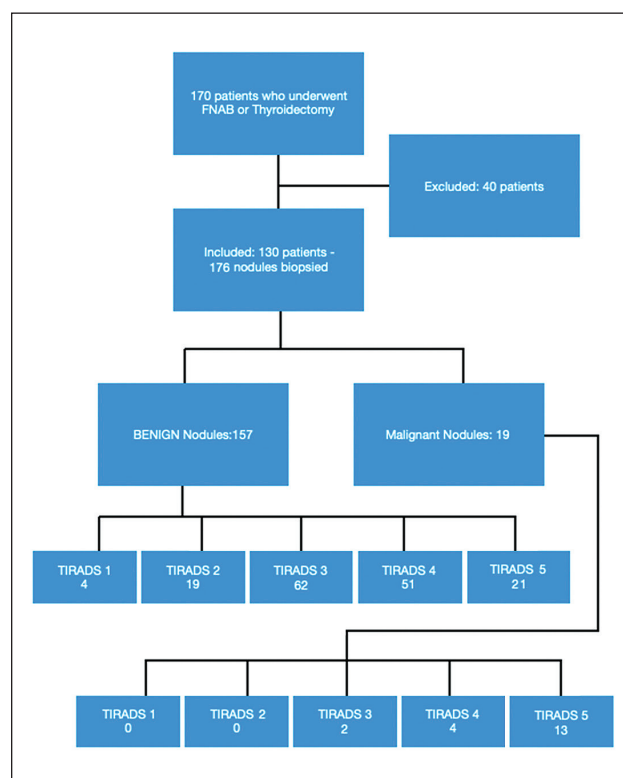
\* Significant at  $p < .01$ 

were determined. A  $p < 0.05$  will mean a significant contribution in predicting malignancy. A negligible amount of missing data was excluded from the analysis.

## RESULTS

### Study population

The total number included in this study was 176 nodules from 130 patients who had undergone a biopsy with cytopathology or histopathology between January to December 2018 at St. Luke's Medical Center-Global City (Figure 2). In this study, all subjects underwent FNAB while only eight proceeded with total thyroidectomy. The histopathology of the eight subjects who underwent thyroidectomy confirmed the FNAB cytopathology results. The mean age was  $50 \pm 14$  (range 20-83). The mean nodule size was  $2.17 \text{ cm} \pm 1.22$  (range 0.6-6.7 cm). There were 19 malignant nodules (11%), with a mean size of 2.15 (SD 1.20). Table 2 summarizes patient demographics and characteristic ultrasound findings. Only records with available digital thyroid ultrasound images and those with definitive cytopathology or histopathology reports were included in this study. The most frequent characteristics of nodules on ultrasound were wider than tall ( $n = 172$ ), smooth or ill-defined margins ( $n = 158$ ), solid composition ( $n = 135$ ), and none or large comet tail artifacts ( $n = 120$ ). The cytopathologic diagnosis was reported using the

**Figure 2.** Flow of Participants.



**Table 3.** Association of clinical features with malignant thyroid nodules on FNA

	Crude OR (95% CI)	P	Adjusted OR (95% CI)	P
Age	1.00 (0.96, 1.03)	0.859	—	—
Sex		0.524	—	—
Female (reference)	1			
Male	0.61 (0.13, 2.82)			
Composition		0.884	—	—
Cystic or almost entirely cystic /Spongiform (reference)	1			
Mixed solid and cystic	0.75 (0.16, 3.51)			
Solid or almost completely solid	—			
Echogenicity		<0.0001		0.073
Anechoic (reference)	1		1	
Hyperechoic or isoechoic	0.06* (0.01, 0.26)		—	
Hypoechoic	0.31* (0.10, 0.98)		—	
Very hypoechoic	—		3.33 (0.89, 12.44)	
Shape		0.369	—	—
Wider than tall (reference)	1			
Taller than wide	2.85 (0.28, 28.88)			
Margins		<0.0001		0.055
Smooth / Ill-defined (reference)	1		1	
Lobulated or irregular	13.36* (3.97, 44.98)		4.20 (0.97, 18.15)	
Extrathyroidal extension	4.45 (0.43, 46.46)		—	
Echogenic foci		<0.0001		0.000
None or large comet-tail artifacts (reference)	1		1	
Macrocalcifications	1.64 (0.18, 15.09)		—	
Peripheral calcifications	3.29 (0.34, 32.08)		—	
Punctate echogenic foci	13.14* (4.19, 41.19)		7.39* (2.41, 22.65)	
Size	1.02 (0.68, 1.54)	0.924	—	—

— Not applicable or not estimable.

\* Significant at  $p < 0.05$ 

Bethesda System of Classification.<sup>7</sup> Diagnosis of benign histopathology included benign follicular nodule goiter (i.e., adenomatous nodule, colloid nodule, etc.) ( $n = 139$ ) and lymphocytic thyroiditis ( $n = 18$ ). Malignant histopathology included Papillary thyroid carcinoma ( $n = 18$ ) and Follicular thyroid carcinoma ( $n = 1$ ). For malignant nodules, the mean age of the patients was comparable to those with benign nodules (mean,  $48.79 \pm 14.34$  (range 20-83) vs.  $49.41 \pm 14$  (range 20-81), respectively;  $P = 0.859$ ). Gender was not statistically significant between malignant and benign lesions ( $P = 0.524$ ). The mean size of both benign and malignant nodules was not statistically different as well (mean  $2.12 \pm 1.14$  (range 0.5-6.7) vs. mean  $2.15 \pm 1.2$  (range 0.8-4.20), respectively ( $P = 0.924$ ). The chi-square test showed a statistically significant relationship between echogenicity, margin, and echogenic foci of the nodules ( $P = <0.0001$ ). Binary logistic regression also showed that only echogenicity, margins, and echogenic foci are associated with malignancy, supporting the chi-square test result. For echogenicity, there are fewer odds of malignancy specifically, 94% and 69% less [crude OR 0.06 (0.01, 0.26) and (crude OR 0.31 (0.10, 0.98), respectively], for patients with hyperechoic and hypoechoic echogenicity, respectively, compared with those with anechoic echogenicity. A higher risk of malignancy is seen for margins as there are 13.36 times higher odds of malignancy (crude OR: 13.36, 95% CI: 3.97-44.98;  $p < 0.0001$ ) for patients with lobulated margins than those with lobulated margins with smooth/ill-defined margins. The odds ratio for malignancy in patients with punctate echogenic foci compared with those without or with large comet-tail artifacts is 13.14 (crude OR: 13.14, 95% CI: 4.19-41.19;  $p = 0.0001$ ). On the other hand, when all factors were considered in a single model

to account for possible confounding factors, echogenicity, margin and echogenic foci were included in the final model. Furthermore, only the echogenic foci were significantly associated with malignancy while controlling for echogenicity and margins. Specifically, there are 7.39 times higher odds of malignancy (adjusted OR (aOR) 7.39, 95% CI 2.41-22.65;  $p < 0.001$ ) for patients with punctate echogenic foci than those with no echogenic foci or with large comet-tail artifacts. Comparing TI-RADS with histopathology, the diagnostic performance of ACR TI-RADS was as follows: sensitivity was 89.5%, specificity of 54%, LR (+) of 1.95 and LR (-) of 0.194, the NPV of 97.7%, the PPV of 19.1% and an accuracy of 58% (Table 4). Table 5 shows that the malignancy rate for TI-RADS 2,3,4 and 5 was 0%, 3.13%, 7.41%, and 39.39%, respectively, which shows a statistically significant malignancy risk across TI-RADS 2 to 5 ( $P < 0.0001$ ).

## DISCUSSION

Ultrasound features have been widely used in predicting the risk of malignancy of thyroid nodules. When taken in isolation, the sensitivity of ultrasound features is predictive of malignancy at 26.7 to 63%, which is not a reliable guide as to when to do FNAB.<sup>11</sup> The ATA guidelines recommend evaluating and managing patients with thyroid nodules based on ultrasound patterns and FNAB results. Individual sonographic characteristics were combined with categorizing ultrasound patterns of thyroid nodules into high suspicion, intermediate suspicion, low suspicion, very low suspicion, and benign pattern. Currently, the ATA recommends biopsy on nodules with ultrasonographic features as follows: (1) thyroid nodules measuring 1 cm and above with intermediate to high sonographic pattern;

**Table 4.** Diagnostic performance of ACR TI-RADS in predicting malignant thyroid nodules (n = 176)

Performance Indicator	Value	95% CI
Prevalence	11%	6.6%-16.3%
Sensitivity	89.5%	66.9%-98.7%
Specificity	54.1%	46%-62.1%
ROC area	0.718	0.637-0.799
LR +	1.95	1.55-2.45
LR -	0.194	0.052-0.727
PPV	19.1%	11.5%-28.8%
NPV	97.7%	91.9%-99.7%
Accuracy	58%	50.30%-65.34%

\* Significant at  $p < 0.01$ **Table 5.** Risk of malignancy by ACR TI-RADS category

ACR TI-RADS	Benign	Malignant	Calculated malignancy rate	p
TR1	4	0	0%	<0.001*
TR2	19	0	0%	
TR3	62	2	3.13%	
TR4	51	4	7.27%	
TR5	21	13	38.24%	

**Table 6.** Comparison of risk of malignancy predicted in ACR TI-RADS

ACR TI-RADS	Risk of malignancy [%]		
	ACR predicted (%)	Middleton et al., <sup>18</sup>	Our study
TR1	<2	0.3	0.0
TR2		1.5	0.0
TR3	5	4.8	3.13
TR4	5.1-20	9.1	7.27
TR5	>20	35.0	38.24

(2) thyroid nodules with low suspicious pattern measuring 1.5 cm and above; and (3) thyroid nodules with very low suspicious ultrasound pattern measuring 2 cm and above.<sup>1</sup>

In 2009, Horvath et al., introduced TI-RADS classification intending to improve the characterization of nodules based on ultrasound features and establish a scoring that would help determine which nodules need to undergo FNAB. Initially, they described ten ultrasound patterns of thyroid nodules with related risk of malignancy.<sup>9</sup> However, due to the complexity of the ultrasound patterns, it only applied to some thyroid nodules, and hence, cumbersome to use in clinical practice. Over the years, several publications and different guidelines were proposed by different institutions to establish recommendations on ultrasound examination of thyroid nodules. In 2014, Kwak et al., investigated a more practical classification of thyroid nodules. They used sonographic characteristics predictive of malignancy such as solid, hypoechoogenicity, marked hyperechoogenicity, microcalcification, micro-lobulation or irregularity of borders and taller-than-wide shape enabling them to classify nodules into five risk levels, TI-RADS 1 to 5.<sup>15</sup> In 2015, the American College of Radiology developed a standard lexicon practical for describing the sonographic characteristics of thyroid nodules that aim to risk stratify and triage nodules for consistent follow-up. They gradually refined and chose terms that demonstrated consistency

regarding performance in describing thyroid nodules as to diagnosing thyroid cancer or classifying a nodule as benign. Allocated points for the different characteristics were based on the likelihood of being associated with malignancy.<sup>16</sup> In 2017, the published ACR TI-RADS enabled easier use among various readers of varying levels of expertise, primarily aiming to decrease the number of unnecessary thyroid nodule biopsies while identifying those that may need further investigation.<sup>11</sup>

A local study in 2017 assessed the accuracy of KWAK-TIRADS in stratifying the risk of malignancy in a single-center setting. The study showed that the solid nodule is the most frequently associated feature predictive of thyroid malignancy and that the higher the TI-RADS score, the higher the risk of malignancy.<sup>17</sup> In our study, sonographic features that showed a significant association with malignancy (Table 3) were echogenicity, margins and echogenic foci. Specifically, there were 94% and 69% fewer odds of having malignancy for patients with hyperechoic and hypoechoic echogenicity with crude OR of 0.06 (0.01, 0.26) and 0.31 (0.10, 0.98), respectively. compared to those with anechoic echogenicity. There are 13.36 times higher odds of malignancy for patients with lobulated margins than those with smooth/ill-defined margins. Lastly, there are 13.14 times more odds of malignancy for patients with punctate echogenic foci than those with no/with large

comet-tail artifacts. When all factors were considered in a single model to account for possible confounding from each factor, echogenicity, margins, and echogenic foci remained in the final model.

The echogenic foci factor was significant in terms of association with malignancy while controlling for echogenicity and margins. Specifically, the odds of malignancy for patients with punctate echogenic foci is 7.39 times that of those with no echogenic foci or large comet-tail artifacts. There have been several studies that have reported that punctate echogenic foci have high specificity for malignant nodules.<sup>18-20</sup> This finding is similar to a local study that was published in 2015, showing that microcalcification was the only significant ultrasound finding that had a significant correlation with malignancy with an odds ratio of 11.3, while a nodule with more than two ultrasound features predictive of malignancy was more likely to be malignant on cytopathology ( $p < 0.001$ ).<sup>21</sup> Another local study showed that microcalcification and irregular margins were significant predictors of thyroid malignancy, similar to international data.<sup>22</sup> We used the ACR TI-RADS classification system in this study, where the predicted malignancy risk for each classification was guided by a multi-center study by Middleton et al. (Table 6). The predicted malignancy for each TI-RADS is as follows: TR1 and TR2 nodules were predicted to have a risk of malignancy lower than 2%, and FNA was not recommended for these nodules. TR3, TR4 and TR5 nodules were predicted to have a malignancy risk of less than 5%, 5.1–20%, and greater than 20%, respectively.<sup>23</sup> In our study, the calculated malignancy rates for TI-RADS 2 to TI-RADS 5 are 0%, 3.13%, 7.14%, and 38.23% which are all within the TI-RADS risk stratification thresholds. However, this was lower than expected by the ATA guideline's recommended malignancy risk for high and moderate suspicion patterns (70–90% and 10–20%, respectively).<sup>1</sup> The calculated malignancy rates of the nodules TR2, TR3, TR4 and TR5 were statistically significant between categories ( $P < 0.0001$ ). With its high sensitivity of 89.5% and a negative predictive value of 97.7%, we can assume that ACR TI-RADS is a reliable way to screen patients with thyroid nodules to recommend whether a biopsy is needed, or close follow-ups may be done, decreasing the number of unnecessary thyroid nodule biopsies. Following the ACR TI-RADS scoring system in this study, FNAB can be avoided in 83 out of 176 nodules or 47.16% of all biopsied nodules.

On the other hand, five malignant nodules (2.84%) of all the nodules biopsied could have been missed. Five nodules not recommended for FNA in the TR5 category were malignant, while three out of the 20 TR4 nodules not recommended for biopsy were malignant. Of the three TR4 malignant nodules, no follow-up was recommended for one of the nodules, while the remaining two were recommended to have a follow-up. These nodules were not recommended for biopsy since the nodule did not reach the size threshold for biopsy. In ACR TI-RADS, the size

threshold to recommend FNAB is for nodules with at least the following sizes: 2.5 cm, 1.5 cm, and 1.0 cm for TI-RADS 3, 4 and 5, respectively.<sup>23</sup> The study of Ito et al., showed that there was no difference in the outcomes between patients with biopsy-proven thyroid carcinoma with nodules of <1 cm who underwent surgery and those who did not undergo surgical intervention, proving that this low-risk papillary carcinoma has an indolent behavior and observation may be prudent for these thyroid nodules.<sup>24</sup> This study does not answer whether the same applies to Filipinos who reported having more aggressive thyroid cancer behavior.

A limitation of this study is that final diagnoses were primarily based on cytopathology results and not surgical histology. However, it has been noted that the probability of a false diagnosis is low at <3% and <1% for TI-RADS 2 and TI-RADS 5, respectively.<sup>17</sup> There may be selection bias as this is an observational retrospective study, rather than a cross-sectional criterion-referenced study where the data is collected in real-time or prospectively from each patient. Finally, only 8 subjects underwent thyroidectomy, so the gold standard of findings taken from surgical pathology reports was not achieved in the greater majority of patients and the ultrasound results were only compared with the FNAB cytopathology reports. In addition, we included nodules biopsied based independently on clinicians' and referring physicians' judgment. During this study, we found that the ACR-TIRADS was not commonly used. Analysis of inter-observer variability was not conducted such that when a discrepancy between the readings was noted, the consultant's reading was followed.

## CONCLUSIONS AND RECOMMENDATIONS

We found that the ACR TI-RADS may be a reliable tool in stratifying thyroid nodules, with its sensitivity of 89.5% and a negative predictive value of 97.7%. ACR TI-RADS can aid in deciding whether an FNAB is warranted or whether close follow-up may be recommended. This could potentially decrease the number of unnecessary thyroid biopsies for nodules with low-risk scores. Specifically, this study showed that hypoechogenicity, irregular margin, and, most significantly, punctate echogenic foci predict the malignant potential of a thyroid nodule. Since several local studies have already shown how strongly echogenic foci are correlated with malignancy, it could be recommended to set a higher score for this feature and probably create a specific scoring system for Filipinos with thyroid nodules. With the increasing familiarity of clinicians with the different classification systems used for thyroid nodules, the need for a single standardized approach to stratifying thyroid nodules is deemed necessary. Using a standardized stratification system will help radiologists and clinicians recommend evidence-based and patient-centered diagnostic and treatment options for our patients. For future studies, we also recommend specifically identifying the location of the nodule (upper, mid, or lower) being biopsied.

## Statement of Authorship

All authors certified fulfillment of ICMJE authorship criteria.

## CRediT Author Statement

**PAA:** Conceptualization, Methodology, Software, Validation, Formal analysis, Investigation, Resources, Data curation, Writing – original draft preparation, Writing – review and editing, Visualization, Project administration; **ET:** Validation, Investigation, Resources; **ALE:** Validation, Investigation, Resources; **MPDM:** Conceptualization, Methodology, Validation, Formal analysis, Investigation, Resources, Writing – original draft preparation, Writing – review and editing, Visualization, Supervision, Project administration.

## Author Disclosure

The authors declared no conflict of interest.

## Funding Source

None.

## References

- Haugen BR, Alexander EK, Bible KC, et al. 2015 American Thyroid Association management guidelines for adult patients with thyroid nodules and differentiated thyroid cancer: The American Thyroid Association Guidelines Task Force on thyroid nodules and differentiated thyroid cancer. *Thyroid*. 2016;26(1):1-133. PMID: 26462967. <https://doi.org/10.1089/thy.2015.0020>
- Gao L, Xi X, Jiang Y, et al. Comparison among TIRADS (ACR TI-RADS and KWAK- TI-RADS) and 2015 ATA Guidelines in the diagnostic efficiency of thyroid nodules. *Endocrine*. 2019;64(1):90-6. PMID: 30659427. <https://doi.org/10.1007/s12020-019-01843-x>.
- Carlos-Raboca J, Jimeno CA, Kho SA, et al. The Philippine Thyroid Diseases Study (PhilTiDeS 1): Prevalence of thyroid disorders among adults in the Philippines. *J ASEAN Fed Endocr Soc*. 2014;27(1):27-33. <https://doi.org/10.15605/jafes.027.01.04>
- Popoveniuc G, Jonklaas J. Thyroid nodules. *Med Clin North Am*. 2012;96(2):329-49. PMID: 22443979. PMID: PMC3575959. <https://doi.org/10.1016/j.mcna.2012.02.002>.
- Cibas ES, Ali SZ; NCI Thyroid FNA State of the Science Conference. The Bethesda system for reporting thyroid cytopathology. *Am J Clin Pathol*. 2009;132(5):658-65. PMID: 19846805. <https://doi.org/10.1309/AJCPPLHWM13JV4LA>.
- Leenhardt L, Erdogan MF, Hegedus L, et al. 2013 European thyroid association guidelines for cervical ultrasound scan and ultrasound-guided techniques in the postoperative management of patients with thyroid cancer. *Eur Thyroid J*. 2013;2(3):147-59. PMID: 24847448. PMID: PMC4017749. <https://doi.org/10.1159/000354537>.
- Shin JH, Baek JH, Chung J, et al.; Korean Society of Thyroid Radiology (KSThR) and Korean Society of Radiology. Ultrasonography diagnosis and imaging-based management of thyroid nodules: Revised Korean Society of Thyroid Radiology consensus statement and recommendations. *Korean J Radiol*. 2016;17(3):370-95. PMID: 27134526. PMID: PMC4842857. <https://doi.org/10.3348/kjr.2016.17.3.370>.
- Gharib H, Papini E, Paschke R, et al. AACE/AME/ETA Task Force on Thyroid Nodules. American Association of Clinical Endocrinologists, Associazione Medici Endocrinologi, and European Thyroid Association Medical guidelines for clinical practice for the diagnosis and management of thyroid nodules: Executive summary of recommendations. *Endocr Pract*. 2010;16(3):468-75. PMID: 20551008. <https://doi.org/10.4158/EP.16.3.468>.
- Horvath E, Silva CF, Majlis S, et al. Prospective validation of the ultrasound-based TIRADS (Thyroid Imaging Reporting And Data System) classification: results in surgically resected thyroid nodules. *Eur Radiol*. 2017; 27(6):2619-28. PMID: 27718080. <https://doi.org/10.1007/s00330-016-4605-y>.
- Hoang JK, Middleton WD, Farjat AE, et al. Reduction in thyroid nodule biopsies and improved accuracy with American College of Radiology thyroid imaging reporting and data system. *Radiology*. 2018;287(1):185-93. PMID: 29498593. <https://doi.org/10.1148/radiol.2018172572>.
- Tessler FN, Middleton WD, Grant EG, et al., ACR Thyroid Imaging, Reporting and Data System (TI-RADS): White Paper of the ACR TI-RADS Committee. *J Am Coll Radiol*. 2017;14(5):587-95. PMID: 28372962. <https://doi.org/10.1016/j.jacr.2017.01.046>.
- Rosario PW, da Silva AL, Nunes MB, Borges MAR. Risk of malignancy in thyroid nodules using the American College of Radiology thyroid imaging reporting and data system in the NIFTP Era. *Horm Metab Res*. 2018;50(10):735-7. PMID: 30312983. <https://doi.org/10.1055/a-0743-7326>.
- Olson E, Wintheiser G, Wolfe KM, Droessler J, Silberstein PT. Epidemiology of thyroid cancer: A review of the National Cancer database, 2000-2013. *Cureus*. 2019;11(2):e4127. PMID: 31049276. PMID: PMC6483114. <https://doi.org/10.7759/cureus.4127>.
- Zheng Y, Xu S, Kang H, Zhan W. A single-center retrospective validation study of the American College of Radiology thyroid imaging reporting and data system. *Ultrasound Q*. 2018;34(2):77-83. PMID: 29596298. <https://doi.org/10.1097/RUQ.0000000000000350>.
- Kwak JY, Han KH, Yoon JH, et al. Thyroid imaging reporting and data system for US features of nodules: A step in establishing better stratification of cancer risk. *Radiology*. 2011;260(3):892-9. PMID: 21771959. <https://doi.org/10.1148/radiol.11110206>.
- Grant E, Tessler F, Hoang J, et al. Thyroid ultrasound reporting lexicon: white paper of the ACR Thyroid Imaging, Reporting and Data System (TIRADS) Committee. *J Am Coll Radiol*. 2015;12(12 Pt A):1272-9. PMID: 26419308. <https://doi.org/10.1016/j.jacr.2015.07.011>.
- Dy JG, Kasala R, Yao C, Ongoco R, Mojica DJ. Thyroid Imaging Reporting and Data System (TIRADS) in stratifying risk of thyroid malignancy at The Medical City. *J ASEAN Fed Endocr Soc*. 2017;32(2):108-16. PMID: 33442093. PMID: PMC7784109. <https://doi.org/10.15605/jafes.032.02.03>.
- Moon WJ, Jung SL, Lee JH, et al.; Thyroid Study Group, Korean Society of Neuro- and Head and Neck Radiology. Benign and malignant thyroid nodules: US differentiation - multicenter retrospective study. *Radiology*. 2008;247(3):762-70. PMID: 18403624. <https://doi.org/10.1148/radiol.2473070944>.
- Papini E, Guglielmi R, Bianchini A, et al. Risk of malignancy in nonpalpable thyroid nodules: Predictive value of ultrasound and color-Doppler features. *J Clin Endocrinol Metab*. 2002;87(5):1941-6. PMID: 11994321. <https://doi.org/10.1210/jcem.87.5.8504>.
- Macedo BM, Izquierdo RF, Golbert L, Meyer ELS. Reliability of Thyroid Rreporting and Data System (TI-RADS), and ultrasonographic classification of the American Thyroid Association (ATA) in differentiating benign from malignant thyroid nodules. *Arch Endocrinol Metab*. 2018;62(2):131-8. PMID: 29641731. PMID: PMC10118978. <https://doi.org/10.20945/2359-3997000000018>.
- Puno-Ramos MPG, Villa ML, Kasala RG, Arzadon J, Alcazaren EAS. Ultrasound features of thyroid nodules predictive of thyroid malignancy as determined by fine needle aspiration biopsy. *Philipp J Intern Med*. 2015;53(2):1-8.
- Cañete EJ, Sison-Peña CM, Jimeno CA. Clinicopathological, biochemical, and sonographic features of thyroid nodule predictive of malignancy among adult Filipino patients in a tertiary hospital in the Philippines. *Endocrinol Metab (Seoul)*. 2014;29(4):489-97. PMID: PMC4285043. <https://doi.org/10.3803/EnM.2014.29.4.489>.
- Middleton WD, Teefey SA, Reading CC, et al., Multi-institutional analysis of thyroid nodule risk stratification using the American College of Radiology Thyroid imaging reporting and data system. *AJR Am J Roentgenol*. 2017;208(6):1331-41. PMID: 28402167. <https://doi.org/10.2214/AJR.16.17613>.
- Ito Y, Miyauchi A, Inoue H, et al. An observational trial for papillary thyroid microcarcinoma in Japanese patients. *World J Surg*. 2010;34(1):28-35. PMID: 20020290. <https://doi.org/10.1007/s00268-009-0303-0>.

Authors are required to accomplish, sign and submit scanned copies of the JAFES Author Form consisting of: (1) Authorship Certification, that authors contributed substantially to the work, that the manuscript has been read and approved by all authors, and that the requirements for authorship have been met by each author; (2) the Author Declaration, that the article represents original material that is not being considered for publication or has not been published or accepted for publication elsewhere, that the article does not infringe or violate any copyrights or intellectual property rights, and that no references have been made to predatory/suspected predatory journals; (3) the Author Contribution Disclosure, which lists the specific contributions of authors; (4) the Author Publishing Agreement which retains author copyright, grants publishing and distribution rights to JAFES, and allows JAFES to apply and enforce an Attribution-Non-Commercial Creative Commons user license; and (5) the Conversion to Visual Abstracts (\*optional for original articles only) to improve dissemination to practitioners and lay readers. Authors are also required to accomplish, sign, and submit the signed ICMJE form for Disclosure of Potential Conflicts of Interest. For original articles, authors are required to submit a scanned copy of the Ethics Review Approval of their research as well as registration in trial registries as appropriate. For manuscripts reporting data from studies involving animals, authors are required to submit a scanned copy of the Institutional Animal Care and Use Committee approval. For Case Reports or Series, and Images in Endocrinology, consent forms, are required for the publication of information about patients; otherwise, appropriate ethical clearance has been obtained from the institutional review board. Articles and any other material published in the JAFES represent the work of the author(s) and should not be construed to reflect the opinions of the Editors or the Publisher.