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# A SINGLE INSTITUTION EXPERIENCE ON THE CORRELATION OF KWAK THYROID IMAGING REPORTING AND DATA SYSTEM SCORE (KWAK TIRADS) AND MALIGNANCY OF THYROID NODULES SEEN IN A TERTIARY HOSPITAL SETTING

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**Abstract – *Objective:*** *The purpose of this study is to determine the diagnostic accuracy of a surgeon-performed thyroid ultrasound reported using Kwak Thyroid Imaging Reporting and Data System (Kwak TIRADS) in identifying thyroid malignancy.*

***Patients and Methods:*** *This is a retrospective cohort study of patients who underwent preoperative thyroid ultrasound by a surgeon and subsequently underwent thyroidectomy from January 2018 – March 2020 in University of the Philippines - Philippine General Hospital (UP-PGH), Department of Surgery. Correlation between ultrasonographic features and Kwak TIRADS categories with malignancy were analyzed using chi square (univariate analysis) and logistic regression (multivariate analysis).*

***Results:*** *A total of 174 patients with thyroid nodules at least 1 cm in widest diameter were included in the study. There were 85 patients with malignant thyroid disease and 89 patients with benign nodules. Solid composition, hypoechogenicity/marked hypoechogenicity, lobulated/irregular margins, rim/microcalcifications, and shape taller than wide were significantly associated with thyroid malignancy on univariate analysis (all* p*-values < 0.001). However, only solid composition, hypoechogenicity/marked hypoechogenicity, and irregular/lobulated margins were significantly associated with thyroid malignancy on multivariate analysis (*p*-values < 0.001, 0.002 and 0.011, respectively). On the other hand, Kwak TIRADS categories 4a and above are significantly associated with thyroid malignancy (all* p*-values < 0.001), with the risk of malignancy increasing as the Kwak TIRADS category increases. Sensitivity, specificity, PPV and negative NPV are optimal when cutoff for further workup is set at Kwak TIRADS 4a.*

***Conclusions:*** *A surgeon performed thyroid ultrasonography reported using Kwak TIRADS classification can be utilized as a guide in the management of thyroid nodules. The consideration of Kwak TIRADS 4a as a cutoff level for further workup is recommended.*

**KEYWORDS:** *Kwak TIRADS, TIRADS, Thyroid Ultrasonography, Thyroid cancer.*



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## INTRODUCTION

Thyroid nodules are relatively common but have a low clinical significance. These nodules are palpable in about 5% of the general population but can be detected through ultrasound in up to 65 to 70%[1,2]. However, thyroid nodules are usually asymptomatic and are at risk for malignancy in only 5-10% of the time[1-3].

On the other hand, thyroid cancer is the most common endocrine malignancy with a global incidence of 2.1%[4]. Recent data suggest steady increase over the past few decades in the incidence of thyroid malignancy worldwide[5,6]. Conversely, there is a downward trend in mortality rate from thyroid cancer, particularly papillary thyroid cancer[3,5,6]. These may have been brought about by the widespread use of ultrasonography in clinical practice resulting to early diagnosis and treatment of thyroid disease albeit resulting to unnecessary biopsy and surgery[3,7].

Ultrasonography, therefore, has become an indispensable tool in the diagnosis and management of thyroid disease. Its utility in the evaluation and management of thyroid nodules has evolve significantly in the past two decades. The Society of Radiologist in Ultrasound was the first to draft guidelines on the management of thyroid nodules identified in ultrasound in 2005[8]. This lead to the use of stratification grading systems in characterizing risk for malignancy of thyroid nodules in ultrasound by Ito et al[9] and Tae et al[10], both in 2007. Horvath et al[11] published a study in 2009 proposing the use of TIRADS, an evaluation system similar to the Breast Imaging Reporting and Data System (BI-RADS) for a standardized ultrasound characterization and reporting data system of thyroid lesions and stratifying cancer risk for clinical management. However, the ultrasound patterns and equations they presented were difficult to apply clinically due to complexity. Shortly after that, Park et al[12] proposed another classification which employed 12 ultrasound features as basis for predicting the probability of malignancy. Although their approach makes it possible to stratify thyroid nodules into categories, it is cumbersome to assign every thyroid nodule into their equation in clinical practice. Hence, in 2011 Kwak et al[13] proposed a simpler TIRADS classification with a practical and convenient use for the management of thyroid nodules. Thereafter, many other guidelines on the utilization of ultrasound characteristics in determining the risk for malignancy of thyroid nodules have been proposed. Currently, the most widely used is the Kwak TIRADS by Kwak et al[13] in 2011, the ATA guidelines in 2015, and the ACR TIRADS in 2017 [11,13-15]. The authors of these systems have similar intentions, primarily to guide the need for biopsy and probable surgery for malignant nodules, and secondarily to reduce unnecessary invasive procedures for benign lesions. To our knowledge, however, there is no consensus on a single system or guideline to date.

Kwak et al[13] patterned a risk stratification system for thyroid nodules at least 1 cm in greatest diameter based on the BI-RADS system for breast (Table 1). They identified solid composition, hypoechogenicity/marked hypoechogenicity, lobulated/irregular margins, rim/microcalcifications, and shape taller than wide as sonographic features associated with thyroid malignancy [13]. While TIRADS 1 corresponds to a thyroid gland with no distinct nodule, TIRADS 2 to benign nodules (cysts and spongiform nodules) and TIRADS 3 to mixed solid and cystic nodules, TIRADS 4a and higher are differentiated based on the number of suspicious features present (Table 1). Due to the simplicity of this lexicon, it easy to implement, and thus, is used in our institution.

**TABLE 1.** TIRADS classification of Kwak et al[13].

| *Category* | *Description* |
|---|---|
| TIRADS 1 | Negative |
| TIRADS 2 | Benign nodule |
| TIRADS 3 | Probably benign (No suspicious ultrasound features)* |
| TIRADS 4A | One suspicious ultrasound feature* |
| TIRADS 4B | Two suspicious ultrasound features* |
| TIRADS 4C | Three or four suspicious ultrasound features* |
| TIRADS 5 | Highly suggestive of malignancy (Five suspicious ultrasound features)* |

*The following features were considered suspicious: solid component, hypoechogenicity especially marked hypoechogenicity, microlobulated or irregular margins, microcalcifications and taller than wide shape.

Several studies have validated the specificity and sensitivity of Kwak TIRADS in the diagnosis of thyroid nodules. The said stratification system has been found to be comparable[16-18] or even superior[19-21] to other thyroid ultrasound risk stratification systems. To our knowledge, however, there is no local data on the reliability of a surgeon performed thyroid ultrasonography using Kwak TIRADS lexicon.

This study, therefore, aims to validate the diagnostic reliability of surgeon-performed thyroid ultrasonography using Kwak TIRADS in determining malignancy among patients with thyroid nodules in the UP-PGH, Department of Surgery. Specifically, we intend to: (1) determine the diagnostic value of ultrasonographic features of benign and malignant thyroid nodules as identified by Kwak et al[13]; (2) determine the diagnostic performance of Kwak TIRADS lexicon; and finally, (3) determine the optimal Kwak TIRADS category necessitating further investigation.

## PATIENTS AND METHODS

### *Study Design*

This is a retrospective cohort study of patients with thyroid disease, seen and managed between January 2018 and March 2020 in the UP-PGH, Department of Surgery. This study was approved by the University of the Philippines Manila - Research Ethics Board (UPM-REB).

### *Inclusion/Exclusion Criteria*

This study includes consecutive adult patients >18 years of age of the UP-PGH, Department of Surgery between January 2018 to March 2020 who underwent preoperative ultrasound and reported using Kwak TIRADS by a head and neck surgeon. Only lesions with diameter greater than 1 cm in greatest dimension were included. Patients who did not underwent thyroidectomy and patients with no final histopathologic report were excluded from the study.

### *Thyroid Ultrasonographic Technique and Kwak TIRADS Category reporting*

The performance of thyroid ultrasonography in the UP-PGH, Department of Surgery is standardized. The procedures were done using B-mode and Doppler evaluation of the thyroid nodules by head and neck surgeons in-training certified by the Philippine Society of Ultrasound in Surgery, Inc. All the ultrasound scans were performed using a 7.5 – 12 MHz high frequency linear array transducer. Examination was done on realtime, two-dimensional, grayscale and Doppler imaging. The bilateral thyroid lobes, the isthmus and the anterior neck compartments are routinely evaluated with the patient lying supine and neck hyperextended.

Thyroid nodule ultrasonographic features which include size, internal composition, echogenicity, margins, presence and type of calcifications, and the shape, are noted and Kwak TIRADS category determined. A thyroid ultrasonographic result is categorized as TIRADS 1 if there are no distinct nodules identified, TIRADS 2 if spongiform (Figure 1A) or cystic (Figure 1B), and TIRADS 3 if mixed predominantly solid isoechoic nodule (Figure 1C).

Solid composition, hypoechogenicity/marked hypoechogenicity, lobulated/irregular margins,

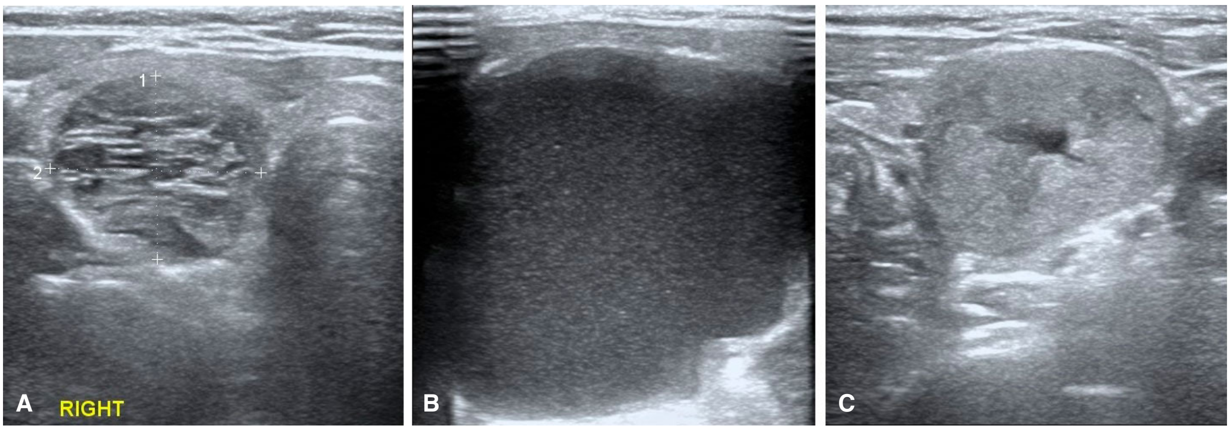


**Fig. 1.** Ultrasound image showing examples of benign thyroid nodules. TIRADS 2 ***(A)*** spongiform, ***(B)*** cystic; TIRADS 3 ***(C)*** mixed predominantly solid isoechoic nodule.

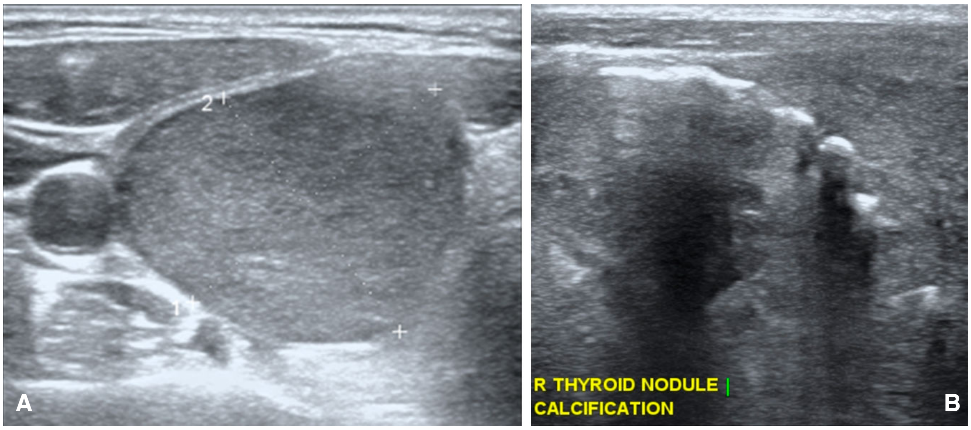


**Fig. 2.** Ultrasound image showing examples of TIRADS 4A. ***(A)*** Solid nodule smooth margin, ***(B)*** mixed nodule with calcifications.

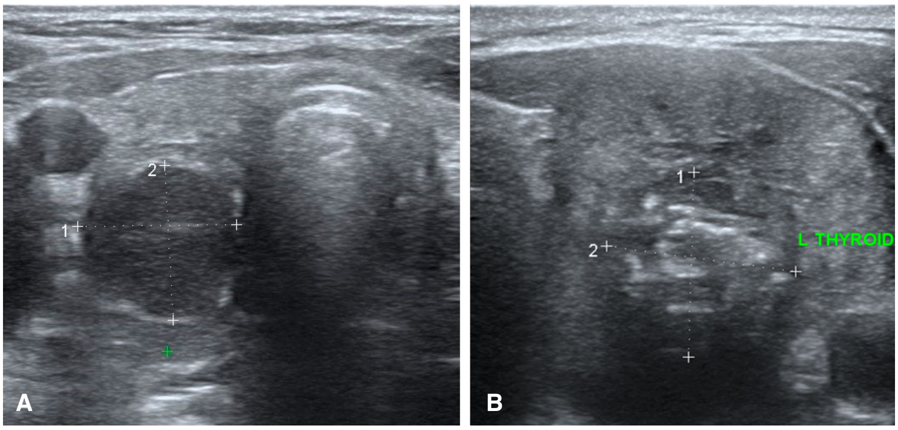


**Fig. 3.** Ultrasound image showing examples of TIRADS 4B. ***(A)*** Solid and hypoechoic nodule, ***(B)*** solid with calcifications nodule.

rim/microcalcifications, and shape taller than wide are considered as suspicious thyroid nodule ultrasonographic features and are scored one (1) each, with the highest possible score of five (5). A thyroid nodule is categorized as TIRADS 4a if it has one (1) suspicious feature (Figure 2), TIRADS 4b if it has two (2) suspicious features (Figure 3), TIRADS 4c if it has 3 - 4 suspicious features (Figure 4) and TIRADS 5 if it has five (5) suspicious features (Figure 5).

Thyroid ultrasound results are recorded in OpenMRS (OpenMRS 2.3.1, OpenMRS Inc., Indianapolis, IN, USA) for future reference. Access to records is limited to authorized persons following the standards of Data Privacy Act of the Philippines.

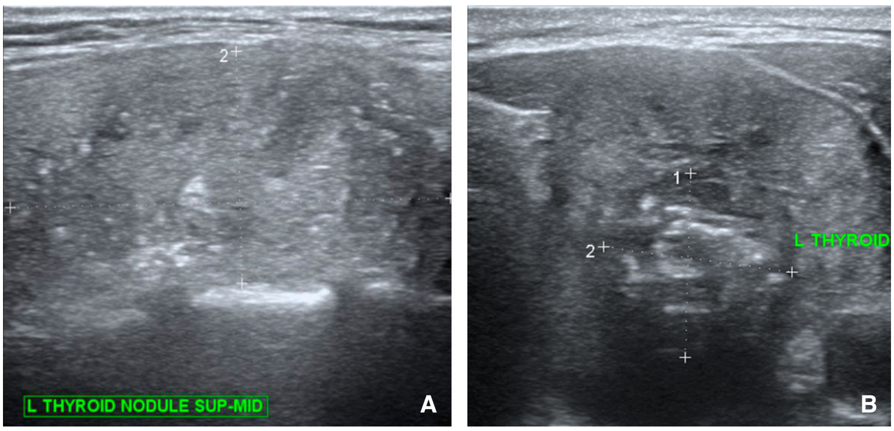


**Fig. 4.** Ultrasound image showing examples of TIRADS 4C. ***(A, B)*** Solid, irregular margin and with microcalcifications nodules.

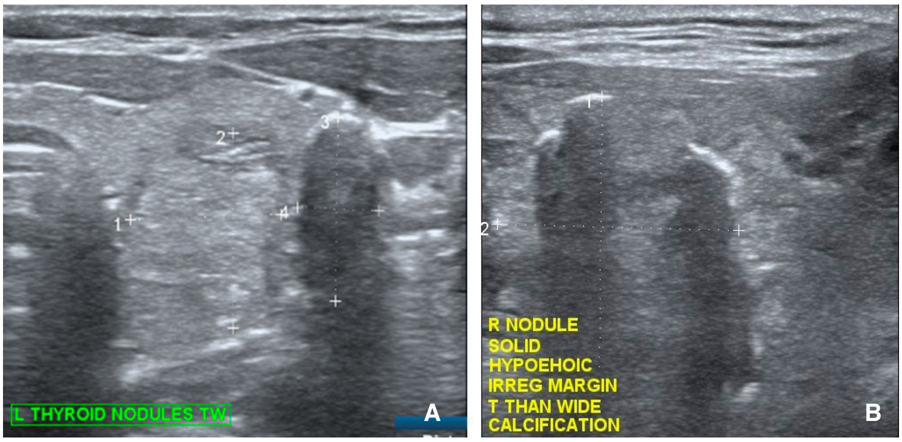


**Fig. 5.** Ultrasound image showing examples of TIRADS 5. ***(A)*** Two solid nodules, hypoechoic and isoechoic, irregular margin, microcalcifications and taller than wide. ***(B)*** solid nodule with hypoechoic, irregular margin, microcalcifications and taller than wide.

### *Data Extraction and Collection*

Data were retrieved from the surgical oncology census and from the medical record system of our institution. These data were entered into an MS Excel file (MS Excel 2019, Microsoft Corporation, Redmond, Washington, IL, USA) and were stored safely within the UP-PGH, Department of Surgery offices. Information was used following the standards of Data Privacy Act of the Philippines.

Demographic profile of patients, the ultrasound results, and histopathology report were collected. Ultrasound results included composition, echogenicity, margins, calcifications, shape and Kwak TIRADS score. In patients with more than one thyroid nodule, the nodule with the greatest number of suspicious ultrasonographic features was considered. All data were then tabulated and recorded in MS Excel file.

### *Statistical Analysis*

The Statistical Product and Service Solutions (SPSS 26.0 for windows; SPSS Inc., Armonk, NY, USA) was used for statistical analysis. Quantitative data are presented as the mean ± standard deviation (SD). Qualitative data are presented as frequencies. Univariate analyses were done using independent *t*-test for quantitative variables and $\chi^2$ test for categorical variables. Logistic regression was used for multivariate analysis. The odds ratio (OR) was determined to quantify the strength of association of suspicious sonographic features and Kwak TIRADS category with thyroid malignancy. In all analysis, a *p*-value < 0.05 was considered statistically significant. The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were calculated to determine diagnostic performance.

## RESULTS

### *Demographic Characteristics*

The distribution of demographic characteristics of the patients are listed in Table 2. A total of 174 patients were included in the study. Eighty-five patients had malignant final histopathology results while 89 patients had benign thyroid disease. The mean age of patients with thyroid malignancy were 43.82 (± 13.17), while those with benign disease were 41.03 (± 10.75). This difference is significant, with a *p*-value of 0.019.

**TABLE 2.** Demographic and clinical profile of thyroidectomy patients.

| | *Histopathologic Findings* | | |
|---|---|---|---|
| | ***Malignant*** | ***Benign*** | ***p-value*** |
| ***No. of Patients (N = 174)*** | 85 | 89 | |
| ***Age (years)*** <br> ***Mean ± Std. Deviation*** | 43.96 (± 13.17) | 41.03 (± 10.75) | 0.019 |
| ***Gender*** | | | |
| Female (n = 151) | 70 (46.4%) | 81 (53.6%) | 0.092 |
| Male (n = 23) | 15 (65.2%) | 8 (34.8%) | |

*The following features were considered suspicious: solid component, hypoechogenicity especially marked hypoechogenicity, microlobulated or irregular margins, microcalcifications and taller than wide shape.

There were more female patients (n = 151) in the study than males (n = 23) (Table 2). Less than half of the female patients (46.4%) had malignant histopathologic results while a greater percentage of male patients (65.2%) had malignant thyroid disease. This difference, however, was not significant, with a $p$-value of 0.092.

### *Suspicious Ultrasonographic Features and Malignancy*

Univariate analysis revealed that solid composition, hypoechogenicity/marked hypoechogenicity, lobulated/irregular margins, rim/microcalcifications, and shape taller than wide are all significantly associated with thyroid malignancy with all $p$-values < 0.001 (Table 3). Solid composition has the highest OR at 24.78 (95% CI: 11.01 - 55.79) followed by irregular/lobulated margins OR = 21.37(95% CI: 4.90 - 93.21), taller than wide shape OR = 20.41 (95% CI: 2.64 - 157.68), micro/rim calcifications OR = 3.34 (95% CI: 4.52 - 40.25), and hypo echogenicity/marked hypoechogenicity.

On multivariate analysis, however, only solid composition, hypoechogenicity/marked hypoechogenicity, and irregular/lobulated margins were found to be significantly associated with thyroid malignancy, with $p$-values < 0.001, 0.002 and 0.011, respectively (Table 3). The OR for these ultrasonographic features on logistic regression were 14.91 (95% CI: 5.84 - 38.06), 4.35 (95% CI: 1.75 - 10.78) and 9.32 (95% CI: 1.68 - 51.89), respectively. It should be noted, however, that the presence of irregular/lobulated margins (n = 30), micro/rim calcifications (n = 37) and shape taller than wide (n = 17) is relatively rare in the study population (N = 174) and have contributed to the acceptance of the non-association of the last two variables, namely micro/rim calcifications and shape taller than wide, with malignancy.

The diagnostic performance of the different suspicious ultrasonographic features in terms of sensitivity, specificity, PPV and NPV are shown in Table 4. Solid composition has the highest sensitivity and negative predictive value at 87.06% and 86.42% respectively. This variable, however, has a specificity and PPV of only 78.65% and 79.57% respectively. On the other hand, taller than wide shape has the highest specificity and PPV at 98.88% and 94.12%. However, this variable has a sensitivity and NPV of only 18.82% and 56.05%, respectively.

**TABLE 3.** Association of suspicious ultrasonographic features and thyroid malignancy.

| Parameter | No. of Malignant Nodules (n = 85) | No. of Benign Nodules (n = 89) | Univariate Analysis | | Multivariate Analysis | |
|---|---|---|---|---|---|---|
| | | | Odds Ratio* | p-Value | Odds Ratio* | p-Value |
| ***Solid Composition*** | | | | | | |
| Yes (n = 72) | 51 | 21 | 24.78 (11.01 - 55.79) | <0.001 | 14.91 (5.84 - 38.06) | <.0.001 |
| No (n = 102) | 34 | 68 | | | | |
| ***Hypo/Very Hypoechogenic*** | | | | | | |
| Yes (n = 72) | 51 | 21 | 4.86 (2.526 - 9.34) | < 0.001 | 4.35 (1.75 - 10.78) | 0.002 |
| No (n = 102) | 34 | 68 | | | | |
| ***Irregular/Lobulated Margins*** | | | | | | |
| Yes (n = 30) | 28 | 2 | 21.37 (4.90 - 93.21) | < 0.001 | 9.32 (1.68 - 51.89) | 0.011 |
| No (n = 114) | 57 | 87 | | | | |
| ***Micro/Rim Calcifications*** | | | | | | |
| Yes (n = 37) | 33 | 4 | 13.49 (4.52 - 40.25) | < 0.001 | 3.34 (0.89 - 12.53) | 0.073 |
| No (n = 137) | 52 | 85 | | | | |
| ***Taller than Wide Shape*** | | | | | | |
| Yes (n = 17) | 16 | 1 | 20.41 (2.64 - 157.68) | < 0.001 | 1.48 (0.15 - 14.91) | 0.737 |
| No (n = 157) | 69 | 88 | | | | |

*Numbers inside the parentheses are confidence intervals (CI).

**TABLE 4.** Diagnostic performance of suspicious ultrasonographic features.

| | Sensitivity (%) | Specificity (%) | PPV (%) | NPV (%) |
|---|---|---|---|---|
| Solid Composition | 87.06% | 78.65% | 79.57% | 86.42% |
| Hypo/Very Hypoechogenic | 60.00% | 76.40% | 70.83% | 66.67% |
| ***Irregular/Lobulation Margins or Extrathyroidal Extension*** | 32.94% | 97.75% | 93.33% | 60.42% |
| Micro/Rim Calcifications | 38.82% | 95.51% | 89.19% | 62.04% |
| Taller than Wide | 18.82% | 98.88% | 94.12% | 56.05% |

### *Kwak TIRADS Categories and Thyroid Malignancy*

There is a significant association of TIRADS 4a and 4b with thyroid malignancy, with $p$-values <0.001 (Table 5). The OR for TIRADS 4a and 4b is 20.70 and 107.33, respectively. The risk for thyroid malignancy increases as the TIRAD category increases, becoming 100% at TIRADS 4c and 5. It should, however, be noted that the three patients with TIRADS 2 lesions (spongiform) and two with TIRADS 3 lesions (mixed solid and cystic) were eventually diagnosed with thyroid malignancy.

The diagnostic performance of Kwak TIRADS was evaluated by computing for sensitivity, specificity, PPV and NPV at different cutoff levels (Table 6). When TIRADS 3 is used as the cut-off level, that is, all nodules' categories 3 and above are considered malignant, the sensitivity and NPV is high at 96.47% and 94.23%, but the specificity and PPV is low at 55.06% and 67.21%. Increasing the cut-off to TIRADS 4a, the sensitivity and NPV decreases to 94.12% and 93.42% but there is a substantial increase in specificity and PPV to 79.78% and 81.63%. Further increasing the cut off to TIRADS 4b, however, results in a low sensitivity of 77.65%. Comparing Table 6 and Table 4, setting the cut off at TIRADS 4a provides the best balance of sensitivity, specificity, PPV and NPV.

## DISCUSSION

Thyroid ultrasonography has become an indispensable tool in the initial assessment of thyroid nodules. Albeit majority of thyroid nodules in the general population were benign, a substantial number of diagnostic aspirations were performed to rule out malignancy[15]. Thyroid ultrasonography is appealing to the patient because it is less invasive, decreasing patient's stress and anxiety. Determining reliable and reproducible ultrasound criteria is integral to permit the selection of nodules warranting aspiration biopsy owing to increased malignancy risk. Our institution and thus, our study, adapted the Kwak TIRADS due to its simplicity and practicality.

In this study, we have evaluated the suspicious ultrasonographic features for thyroid malignancy, to wit, solid composition, hypoechogenicity/marked hypoechogenicity, lobulated/irregular margins, rim/microcalcifications, and shape taller than wide[13]. Univariate analysis of our data demonstrated that all these features are significant predictors of thyroid malignancy (Table 3). However, their diagnostic performance individually, in terms of sensitivity, specificity, PPV and NPV differ, such that using only one ultrasonographic feature with high sensitivity and NPV, e.g., solid composition, would entail accepting low specific-

**TABLE 5.** Association of Kwak TIRADS categories with thyroid malignancy.

| | No. of Malignant Nodules (n = 85) | No. of Benign Nodules (n = 89) | Odds Ratio | p-value | Risk of Malignancy |
|---|---|---|---|---|---|
| T2* (n = 52) | 3 | 49 | 1 | 1 | 5.8% |
| T3** (n = 24) | 2 | 22 | 1.48 (0.23 - 95) | 0.677 | 8.3% |
| T4a (n = 25) | 14 | 11 | 20.79 (5.08 - 84.98) | <0.001 | 56.0% |
| T4b (n = 53) | 46 | 7 | 107.33 (26.18 - 440.11) | <0.001 | 86.8% |
| T4c (n = 13) | 13 | 0 | | | 100.0% |
| T5 (n = 7) | 7 | 0 | | | 100.0% |

*spongiform. **mixed solid and cystic.

**TABLE 6.** Diagnostic Performance Kwak TIRADS at different cutoff levels.

| | Sensitivity (%) | Specificity (%) | PPV (%) | NPV (%) |
|---|---|---|---|---|
| T3* | 96.47% | 55.06% | 67.21% | 94.23% |
| T4a* | 94.12% | 79.78% | 81.63% | 93.42% |
| T4b* | 77.65% | 92.13% | 90.41% | 81.19% |
| T4c* | 9.72% | 100.00% | 100.00% | 57.79% |

ity and PPV. Thus, utilizing this ultrasonographic feature will allow clinicians to detect more of thyroid malignancy from the population (sensitivity = 87.06%), however, the possibility of those with this feature having the actual disease is low (PPV = 79.57%). On the other hand, evaluating nodules in using features with high specificity and NPV, e.g., lobulated/irregular margins, rim/microcalcifications, and shape taller than wide, would also entail accepting low sensitivity and NPV. Thus, while using these features would result to the avoidance of unnecessary further workup, a considerable number of patients having the disease will be missed. Thus, the need to combine these features to come up with acceptable sensitivity, specificity, PPV and NPV.

Multivariate analysis of the correlation of the suspicious ultrasonographic features however, revealed that there is no significant association of micro/rim calcifications and shape taller than wide with thyroid malignancy. It should be noted, however, that these ultrasonographic features are usually found with the other three, namely rim/microcalcifications, shape taller than wide, and irregular/lobulated margins, which by themselves are already significant predictors with OR 14.91 (95% CI 5.84 - 38.06), 4.25 (95% CI: 1.75 - 10.78) and 9.32 (95% CI: 1.68 - 51.89), respectively. Moreover, the former is relatively rare (rim/microcalcifications (n = 37) and shape taller than wide (n = 17)) compared with the study population (N = 174). Thus, the significance of these ultrasonographic features (rim/microcalcifications and shape taller than wide) are undermined when analyzed together with the other three.

The risk of thyroid malignancy was found to increase with Kwak TIRADS categories (Table 5). Our malignancy rates, however, were higher compared to the findings by Kwak et al[13] (Table 7). While Kwak et al[13] found that Kwak TIRADS 2 has a malignancy rate of 0%, our study found that 5.8% of patients with these Kwak TIRADS score have malignant pathology. The difference in malignancy rates increases as the Kwak TIRADS score increases, with our study having the malignancy rates 8.3%, 56%, 86% and 100% with the study by Kwat et al[13] having the malignancy rates of 1.7%, 3.3%, 44.4 – 72.4% and 87.5% for Kwak TIRADS 3, 4a, 4b, and 4c, respectively. This may be reflective of the difference of the behavior of thyroid cancer among Filipinos [22-25].

There is a significant association of Kwak TIRADS categories with thyroid malignancy starting at TIRADS 4a. Expectedly, sensitivity and NPV decreases while specificity and PPV increases with higher TIRADS categories. The sensitivity, specificity, PPV and NPV when TIRADS 4a and above are considered suspicious for malignancy, offers the best scores at 94.12%, 78.78%, 81.63% and 93.42%, respectively (Table 5). This allows 94.12% of thyroid cancers to be detected while minimizing the risk of unnecessary workup.

It should be noted, however, that the risks of malignancy of TIRADS 2 and TIRADS 3 in our study are not negligible (5.8% and 8.3%). These patients have either spongiform lesions, or mixed solid and cystic nodules, which are not considered suspicious ultrasound features for thyroid malignancy. Again, this may be due to the difference in the behavior of thyroid malignancy among Filipinos[22-25] or due to operator dependent limitations. Regardless, there should be careful consideration when forgoing further workup in Filipino patients with TIRADS 2 and TIRADS 3 lesions.

However, it cannot be discounted that the higher malignancy rate in our study could be due to user dependent and equipment factors for which important features were missed resulting to lower Kwak TIRADS scores. Interobserver variability analysis among surgeons and/or sonologists/radiologists cannot be employed due to the retrospective nature of the study and the absence of such controls when the recorded procedures were done. Furthermore, our study included only patients who underwent thyroid ultrasonography

**TABLE 7.** Kwak TIRADS risk of malignancy.

| | Kwak et al[13] | Current study |
|---|---|---|
| TIRADS 2 | 0 | 5.8% |
| TIRADS 3 | 1.7% | 8.3% |
| TIRADS 4a | 3.3% | 56.0% |
| TIRADS 4b | 9.2% | 86.8% |
| TIRADS 4c | 72.4% | 100.0% |
| TIRADS 5 | 87.5% | 100.0% |

and thyroid surgery, thus, may not be representative of all patients with thyroid nodules.

## CONCLUSIONS

A surgeon-performed thyroid ultrasonography utilizing Kwak TIRADS classification as preoperative workup for thyroid nodules is highly predictive of malignancy. This classification can be utilized as a guide in decision making of whether to do further workup in a patient with a thyroid nodule.

Consistent with the findings by Kwak et al[13], setting the cutoff level at Kwak TIRADS 4a for thyroid lesions at least 1 cm in widest diameter to be considered for further workup provides the best diagnostic performance in terms of sensitivity, specificity, PPV and NPV.

### Conflict of interest

The authors declare that they have no conflict of interests and that the article has not been published previously and has not been forwarded to another journal.


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### Data availability:

All relevant data are available from the authors upon request.

### Authorship:

All authors comply with the criteria for authorship.


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## REFERENCES


1. Wong R, Farrell SG, Grossmann M. Thyroid nodules: diagnosis and management. Med J Aust 2018; 209: 92-98.
2. Durante C, Grani G, Lamartina L, Filetti S, Mandel SJ, Cooper DS. The Diagnosis and Management of Thyroid Nodules: A Review. JAMA 2018; 319: 914.
3. Gharib H, Papini E, Garber JR, Duick DS, Harrell RM, Hegedus L, Paschke R, Valcavi R, Vitti P. American Association of Clinical Endocrinologists, American College of Endocrinology, and Associazione Medici Endocrinologi Medical Guidelines for Clinical Practice for the Diagnosis and Management of Thyroid Nodules - 2016 Update Appendix. Endocr Pract 2016; 22: 1-60.
4. Ferlay J, Soerjomataram I, Dikshit R, Eser S, Mathers C, Rebelo M, Parkin DM, Forman D, Bray F. Cancer incidence and mortality worldwide: Sources, methods and major patterns in GLOBOCAN 2012: Globocan 2012. Int J Cancer 2015; 136: E359-E386.
5. La Vecchia C, Malvezzi M, Bosetti C, Garavello W, Bertuccio P, Levi F, Negri E. Thyroid cancer mortality and incidence: A global overview: Thyroid Cancer Mortality and Incidence. Int J Cancer 2015; 136: 2187-2195.
6. Miranda-Filho A, Lortet-Tieulent J, Bray F, Cao B, Franceschi S, Vaccarella S, Dal Maso L. Thyroid cancer incidence trends by histology in 25 countries: a population-based study. Lancet Diabetes Endocrinol 2021; 9: 225-234.
7. Grant EG, Tessler FN, Hoang JK, Langer JE, Beland MD, Berland LL, Cronan JJ, Desser TS, Frates MC, Hamper UM, Middleton WD, Reading CC, Scoutt LM, Stavros AT, Teefey SA. Thyroid Ultrasound Reporting Lexicon: White Paper of the ACR Thyroid Imaging, Reporting and Data System (TIRADS) Committee. J Am Coll Radiol. 2015; 12: 1272-1279.
8. Frates MC, Benson CB, Charboneau JW, Cibas ES, Clark OH, Coleman BG, Cronan JJ, Doubilet PM, Evans DB, Groellner JR, Hay ID, Hertzberg BS, Intenzo CM, Jeffrey RB, Langer JE, Larsen PR, Mandel SJ, Middleton WD, Reading CC, Sherman SI, Tessler FN. Management of Thyroid Nodules Detected at US: Society of Radiologists in Ultrasound Consensus Conference Statement. Radiology 2005; 237: 794-800.
9. Ito Y, Amino N, Yokozawa T, Ota H, Ohshita M, Murata N, Morita S, Kobayashi K, Miyauchi A. Ultrasonographic Evaluation of Thyroid Nodules in 900 Patients: Comparison Among Ultrasonographic, Cytological, and Histological Findings. Thyroid 2007; 17: 1269-1276.
10. Tae HJ, Lim DJ, Baek KH, Park WC, Lee YS, Choi JE, Lee JM, Kang MI, Cha BY, Son HY, Lee KW, Kang SK. Diagnostic Value of Ultrasonography to Distinguish Between Benign and Malignant Lesions in the Management of Thyroid Nodules. Thyroid 2007; 17: 461-466.
11. Horvath E, Majlis S, Rossi R, Franco C, Niedmann JP, Castro A, Dominguez M. An Ultrasonogram Reporting System for Thyroid Nodules Stratifying Cancer Risk for Clinical Management. J Clin Endocrinol Metab 2009; 94: 1748-1751.
12. Park JY, Lee HJ, Jang HW, Kim HK, Yi JH, Lee W, Kim SH. A Proposal for a Thyroid Imaging Reporting and Data System for Ultrasound Features of Thyroid Carcinoma. Thyroid 2009; 19: 1257-1264.
13. Kwak JY, Han KH, Yoon JH, Moon HJ, Son EJ, Park SH, Jung HK, Choi JS, Kim BM, Kim EK. Thyroid Imaging Reporting and Data System for US Features of Nodules: A Step in Establishing Better Stratification of Cancer Risk. Radiology 2011; 260: 892-899.
14. Ha EJ, Baek JH, Na DG. Risk Stratification of Thyroid Nodules on Ultrasonography: Current Status and Perspectives. Thyroid 2017; 27: 1463-1468.
15. Mahajan A, Vaidya T, Vaish R, Sable N. The journey of ultrasound-based thyroid nodule risk stratification scoring systems: Do all roads lead to Thyroid Imaging, Reporting and Data System (TIRADS)? J Head Neck Physicians Surg 2017; 5: 57.
16. Migda B, Migda M, Migda MS, Slapa RZ. Use of the Kwak Thyroid Image Reporting and Data System (K-TIRADS) in differential diagnosis of thyroid nodules: systematic review and meta-analysis. Eur Radiol 2018; 28: 2380-2388.

17. Migda B, Migda M, Migda MS. A systematic review and meta-analysis of the Kwak TIRADS for the diagnostic assessment of indeterminate thyroid nodules. Clin Radiol. 2019; 74: 123-130.
18. Qi Q, Zhou A, Guo S, Huang X, Chen S, Li Y, Xu P. Explore the Diagnostic Efficiency of Chinese Thyroid Imaging Reporting and Data Systems by Comparing With the Other Four Systems (ACR TI-RADS, Kwak-TIRADS, KSThR-TIRADS, and EU-TIRADS): A Single-Center Study. Front Endocrinol 2021; 12: 763897.
19. Gao L, Xi X, Jiang Y, Yang X, Wang Y, Zhu S, Lai X, Zhang X, Zhao R, Zhang B. Comparison among TI-RADS (ACR TI-RADS and KWAK- TI-RADS) and 2015 ATA Guidelines in the diagnostic efficiency of thyroid nodules. Endocrine 2019; 64: 90-96.
20. Schenke S, Klett R, Seifert P, Kreissl MC, Görges R, Zimny M. Diagnostic Performance of Different Thyroid Imaging Reporting and Data Systems (Kwak-TIRADS, EU-TIRADS and ACR TI-RADS) for Risk Stratification of Small Thyroid Nodules (≤10 mm). J Clin Med 2020; 9: 236.
21. Seifert P, Schenke S, Zimny M, Stahl A, Grunert M, Klemenz B, Freesmeyer M, Kreissl MC, Herrmann K, Görges R. Diagnostic Performance of Kwak, EU, ACR, and Korean TIRADS as Well as ATA Guidelines for the Ultrasound Risk Stratification of Non-Autonomously Functioning Thyroid Nodules in a Region with Long History of Iodine Deficiency: A German Multicenter Trial. Cancers 2021; 13: 4467.
22. Lo TEN, Uy AT, Maningat PDD. Well-Differentiated Thyroid Cancer: The Philippine General Hospital Experience. Endocrinol Metab 2016; 31: 72.
23. Nguyen MT, Hu J, Hastings KG, Daza EJ, Cullen MR, Orloff LA, Palaniappan LP. Thyroid cancer mortality is higher in Filipinos in the United States: An analysis using national mortality records from 2003 through 2012. Cancer 2017; 123: 4860-4867.
24. Rashid FA, Munkhdelger J, Fukuoka J, Bychkov A. Prevalence of BRAFV600E mutation in Asian series of papillary thyroid carcinoma—a contemporary systematic review. Gland Surg 2020; 9: 1878-1900.
25. Shah BR, Griffiths R, Hall SF. Thyroid cancer incidence among Asian immigrants to Ontario, Canada: A population-based cohort study: Thyroid Cancer Incidence in Asians. Cancer 2017; 123: 3320-3325.