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Agreement between Sonographic Features and Fine Needle Aspiration Cytology in the Diagnosis of Thyroid Nodules in a Tertiary Hospital

Danette Pabalan and Ricardo Victorio Quimbo

Department of Pathology and Laboratory Medicine, National Kidney and Transplant Institute, Quezon City, Philippines

ABSTRACT

Objective. Management of thyroid nodules relies on the Thyroid Imaging Recording and Data System (TIRADS) for sonographic findings and the Bethesda System for Reporting Thyroid Cytopathology (TBSRTC). The proponents aimed to determine the concordance between sonographic TIRADS findings and cytological diagnosis by TBSRTC in the evaluation of malignancy of patients with thyroid nodules.

Methodology. Sonographic and cytology results collected from 2018 to 2022 were obtained to determine whether there is an agreement between TIRADS and TBSRTC findings.

Results. Two hundred sixty-two (262) samples were obtained. Overall accuracy of predicting TIRADS category was highest for echogenic foci. Thyroid nodule distribution was highest for TIRADS 3 and 4 sonographically and TBSRTC II cytologically. There is low agreement between TBSRTC and TIRADS in the categorization of nodules as benign, implying that nodules may show sonographic features suspicious of malignancy despite being categorized as TBSRTC I or II by cytology. However, nodules categorized as TBSRTC III to VI show sonographic features suspicious for malignancy at the very least.

Conclusion. The correctness of TIRADS prediction is highest for echogenic foci although not significantly higher than other parameters. The overall predicting power of TIRADS for the absence of malignancy is high for TIRADS 1 and 2, whereas TIRADS 5 predicts a 31.11% risk of malignancy making it a strong indication for FNAC. However, prediction of malignancy in TIRADS 3 and 4 nodules must be in association with other factors since a significant percentage may turn out to be TBSRTC II.

Key words: thyroid nodules, thyroid ultrasound, TIRADS, fine-needle aspiration cytology, TBSRTC

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Corresponding author: Danette V. Pabalan, MD
E-mail: danettepabalanmd@gmail.com
ORCiD: https://orcid.org/0000-0003-1932-792X

INTRODUCTION

Thyroid nodules are focal well-defined lesions of altered echogenicity having estimated global prevalences of 4-8% and 19-67% by palpation and ultrasonography, respectively.[1,2] In the local setting, clinicians follow the 2015 criteria established by the American Thyroid Association (ATA) in managing thyroid nodules which recommends ultrasound-guided fine-needle aspiration as the mainstay for diagnosis.[3] The guideline stratifies thyroid nodules based on the thyroid imaging recording and data system (TIRADS) for sonographic findings and the Bethesda System for Reporting Thyroid Cytopathology (TBSRTC) for cytologic diagnosis which respectively categorize thyroid nodules into five and six categories.[1]

Although widely available, data on concordance of thyroid nodule ultrasound (US) and fine-needle aspiration cytology (FNAC) findings remains unsettled and scarcely available in the Philippines hence this study aims to provide local data on this matter by assessing these findings among patients with thyroid nodules in-a tertiary hospital setting.

METHODOLOGY

Research design

This study is a retrospective cross sectional analytical review of results of patients who underwent thyroid ultrasound and subsequent fine-needle aspiration cytology regardless of thyroid function test results in a five-year period from 2018 to 2022.

Sampling strategy

This study employed purposive sampling which is a non-probability approach that relied on the primary investigator's discretion in selecting patients who underwent thyroid ultrasound and subsequent fine-needle aspiration cytology regardless of thyroid function test results. Based on the institution's data from 2018 to 2022 which showed a total population size of 423, a sample size of 202 was calculated considering the following assumptions: a hypothesized frequency of 50%, a margin of error of 5% with a 95% confidence interval, and a design effect of 1. Two hundred sixty-two individuals (262) qualified for the study. Their demographic data and thyroid ultrasound and fine-needle aspiration cytology results were retrieved from hospital's radiology and laboratory information systems and recorded using Microsoft Excel Sheet Software ver. 16.66.1.

Analysis

Descriptive statistics were be used to assess the age, US findings and final diagnosis of the patients. Categorical variables were analyzed using frequency and percentage, while continuous variables were assessed using the mean and standard deviation.

The polychoric correlation coefficient was employed to assess the strength of the relationship between the ordinal variables under investigation (sonographic TIRADS findings and the cytological diagnosis determined by TBSRTC scoring). Subsequently, the dataset was divided into two subsets: training and testing data.

To establish a model for the training subset, Univariate Regression Analysis was conducted. The cutoff score will be derived from the area under the receiver operating characteristic of the training dataset. Following this, Sensitivity and Specificity, accompanied by 95% confidence intervals, along with positive (PPV) and negative (NPV) predictive values, were computed for each major ultrasound feature strongly indicative of malignancy, using cytology as the reference test.

All statistical tests were two-tailed tests. Null hypotheses were rejected at 0.05α-level of significance. RStudio version 4.2.0 software was used for data analysis.

RESULTS

Table 1 presents population characteristics of patients who underwent thyroid ultrasound and subsequent fine-needle aspiration cytology. The data is organized by age groups and gender, with a total of 262 patients. Noteworthy trends include a concentration of cases in the age groups of 45-54 and 55-64, which collectively represent a significant portion of the total cases.

Table 1. Population characteristics of patients who underwent thyroid US and subsequent FNAC

Age group (years)	Female (N = 217)	Male (N = 45)	Total (N = 262)
	Frequency (%)		
15-24	5 (1.9%)	1 (0.4%)	6 (2.3%)
25-34	18 (6.9%)	2 (0.8%)	20 (7.6%)
35-44	30 (11.5%)	1 (0.4%)	31 (11.8%)
45-54	51 (19.5%)	13 (5.0%)	64 (24.4%)
55-64	80 (30.5%)	18 (6.9%)	98 (37.4%)
Greater than or equal to 65	33 (12.6%)	10 (3.8%)	43 (16.4%)

Across all age groups, the number of female patients is notably higher than male patients. Specifically, in the age group of 55-64, there are 80 female patients (30.5%) compared to 18 male patients (6.9%).

Table 2 summarizes the findings from thyroid ultrasound, categorized by parameters such as TIRADS category, composition, echogenicity, echogenic foci, margin, and shape. Solid composition is prevalent in the majority of cases (73.7%), while complex (20.2%) and cystic (4.2%) compositions are also observed. Regarding echogenicity, a significant number of nodules are hypoechoic (60.3%), followed by isoechoic (20.6%) and hyperechoic (18.3%) types. Macro/microcalcifications are the most common echogenic foci findings accounting 45% of the population, while other foci such as peripheral calcifications (10%) and punctate echogenic foci (7%) are less frequent. Nodules with smooth margins are predominant (73.3%), and the majority exhibit a wider-than-tall shape (93.5%).

Table 3 presents the statistical characteristics of various radiologic parameters in predicting the TIRADS category of a patient. Each parameter (composition, echogenicity, echogenic foci, margin, and shape) has associated sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall accuracy. In terms of sensitivity, echogenic foci perform the best at 57.1%, indicating its ability to correctly identify patients with the TIRADS category. Specificity, measuring the ability to correctly identify patients without the TIRADS category, is highest for echogenic foci at 89.3%. PPV, representing the probability of a positive TIRADS prediction being accurate, is consistently matched with sensitivity for each parameter. NPV, indicating the probability of a negative TIRADS prediction being accurate, is also consistently high, ranging from 86.7% to 89.3%.

Table 4 provides a comprehensive overview of the ultrasound and cytology results, categorized by diagnostic classifications defined by both TIRADS and TBSRTC. The table presents the number and percentage of cases falling into specific intersections of TBSRTC and TIRADS categories.

The distribution across TIRADS classifications is as follows:

- 8 TBSRTC I nodules – TIRADS 1 to 4;
- 186 TBSRTC II nodules – TIRADS 1 to 5;
- 10 TBSRTC III nodules – TIRADS 1 and TIRADS 3;
- 14 TBSRTC IV nodules – TIRADS 1 and TIRADS 4 to 5;
- 17 TBSRTC V nodules – TIRADS 3 to 5; and
- 14 TBSRTC VI nodules – TIRADS 3 to 5.

Table 2. Thyroid ultrasound findings

Parameter	TIRADS category					Total
	1	2	3	4	5	
	Frequency (%)					
Composition						
Solid	-	-	47 (17.9%)	109 (41.6%)	37 (14.1%)	193 (73.7%)
Complex	1 (0.4%)	3 (1.1%)	20 (7.6%)	21 (8.0%)	8 (3.1%)	53 (20.2%)
Cystic	7 (2.7%)	1 (0.4%)	3 (1.1%)	-	-	11 (4.2%)
Spongiform	-	-	2 (0.8%)	2 (0.8%)	1 (0.4%)	5 (1.9%)
Echogenicity						
Hypoechoic	-	-	18 (6.9%)	96 (36.6%)	44 (16.8%)	158 (60.3%)
Isoechoic	4 (1.5%)	3 (1.1%)	27 (10.3%)	19 (7.3%)	1 (0.4%)	54 (20.6%)
Hyperechoic	2 (0.8%)	1 (0.4%)	27 (10.3%)	17 (6.5%)	1 (0.4%)	48 (18.3%)
Cystic	2 (0.8%)	-	-	-	-	2 (0.8%)
Echogenic foci						
Macro/Microcalcification	1 (0.4%)	-	16 (6%)	86 (33%)	14 (5%)	117 (45.0%)
Peripheral calcifications	-	-	1 (0.4%)	10 (4%)	15 (6%)	26 (10%)
Punctate echogenic foci	-	-	1 (0.4%)	3 (1%)	15 (6%)	19 (7%)
None/Comet Tail	7 (2.7%)	4 (1.5%)	54 (21.0%)	36 (14.0%)	4 (1.5%)	105 (40.0%)
Margin						
Smooth	8 (3.1%)	4 (1.5%)	63 (24.0%)	93 (35.5%)	24 (9.2%)	192 (73.3%)
Ill defined	-	-	7 (2.7%)	21 (8.0%)	7 (2.7%)	35 (13.4%)
Irregular	-	-	1 (0.4%)	18 (7.0%)	11 (4.2%)	30 (11.0%)
Extension	-	-	1 (0.4%)	0 (0.0%)	4 (1.5%)	5 (1.9%)
Shape						
Wider than tall	8 (3.1%)	4 (1.5%)	72 (27.5%)	126 (48.1%)	35 (13.4%)	245 (93.5%)
Taller than wide	-	-	-	6 (2.3%)	11 (4.2%)	17 (6.5%)

Table 3. Statistical characteristics of radiologic parameters in predicting TIRADS category of a patient

Parameter	Sensitivity	Specificity	PPV	NPV	Accuracy
Composition	46.7%	86.7%	46.7%	86.7%	78.7%
Echogenicity	52.4%	88.1%	52.4%	88.1%	81.0%
Margin	46.7%	86.7%	46.7%	86.7%	78.7%
Shape	48.6%	87.1%	48.6%	87.1%	79.4%
Echogenic foci	57.1%	89.3%	57.1%	89.3%	82.9%

The overall distribution across TIRADS categories indicates a substantial proportion of cases classified as TIRADS 3 (27.5%) and TIRADS 4 (49.6%).

The distribution across TBSRTC categories is as follows:
- TBSRTC I – 18 cyst fluid only (100%);
- TBSRTC II – 186 follicular nodular disease (71%);
- TBSRTC III – atypia of undetermined significance;
- TBSRTC IV – 3 follicular neoplasm (Hürthle cell type) (21.43%), 11 follicular neoplasms (78.57%);
- TBSRTC V – 15 suspicious for papillary carcinoma (88.24%), 1 suspicious for metastatic carcinoma (5.88%), 1 suspicious for lymphoma (5.88%);
- TBSRTC VI – 9 papillary thyroid carcinoma (64.29%), 1 high-grade follicular cell-derived non-anaplastic thyroid carcinoma (7.14%), 1 medullary thyroid carcinoma (7.14%), 1 undifferentiated (anaplastic) carcinoma (7.14%), 2 metastatic carcinoma (14.29%).

The overall distribution across TBSRTC categories indicates a substantial proportion of cases classified as TBSRTC II.

Table 5 provides an overview of the correlation between TIRADS classification and risk of malignancy which evidently shows a 4 to 5-fold and 15 to 16-fold estimated risk of malignancy for TIRADS 4 and 5 compared to category 3 with respective p-values of 0.05 and 0.0004, respectively. All TIRADS 1 and 2 and majority of TIRADS 3 cases turned out to be benign.

DISCUSSION

The institution utilizes the GE Logiq P9 ultrasound machine and employs TIRADS for classifying thyroid nodules based on composition, echogenicity, echogenic foci, margins, and shape, with each descriptor giving a point. Adding all points of all descriptors provides the TIRADS score which divides thyroid nodules into 5 categories namely TIRADS 1(benign), 2 (not suspicious for malignancy), 3 (mildly suspicious for malignancy), 4 (moderately suspicious for malignancy), and 5 (highly suspicious for malignancy) with respective malignancy risk of 0%, 1.7%, 3.3-72.4%, and 87.5% for categories 2-5.[4] Suspicious sonographic features include solid or mixed composition, hypoechogenicity, taller than wider in shape, irregular margins, and evidence of extrathyroid extension and risk of malignancy being 7-15%.[5-7]

The Bethesda System for Reporting Thyroid Cytopathology is utilized in classifying thyroid nodules into 6 categories namely I ("non-diagnostic" – cyst fluid only,

Table 4. Ultrasound findings (TIRADS) and FNAC correlation

Diagnostic Categories		TIRADS					Total
		1	2	3	4	5	
TBSRTC	I	3 (1.1%)	1 (0.4%)	10 (3.8%)	4 (1.5%)	-	18 (6.9%)
	II	3 (1.1%)	3 (1.1%)	59 (22.5%)	96 (36.6%)	25 (9.5%)	186 (71.0%)
	III	1 (0.4%)	-	1 (0.4%)	7 (2.7%)	1 (0.4%)	10 (3.8%)
	IV	1 (0.4%)	-	-	8 (3.1%)	5 (1.9%)	14 (5.3%)
	V	-	-	1 (0.4%)	10 (3.8%)	6 (2.3%)	17 (6.5%)
	VI	-	-	1 (0.4%)	5 (1.9%)	8 (3.1%)	14 (5.3%)
	Total	**8 (3.1%)**	**4 (1.5%)**	**72 (27.5%)**	**130 (49.6%)**	**45 (17.2%)**	**259 (98.9%)**
Polychoric coefficient					**0.4962 – Moderate**		

Table 5. Proportion of malignancy per TIRADS classification

TIRADS Classification	Benign, n (%)	Malignant, n (%)	Total, n	Risk of Malignancy	OR (95% CI)	*P*-value
1	8 (100%)	0 (0%)	8	**0.00%**	**1.66 (0.07-37.52)**	**0.75**
2	4 (100%)	0 (0%)	4	**0.00%**	**3.13 (0.13-75.53)**	**0.48**
3	70 (97.22%)	2 (2.78%)	72	**2.78%**	**Reference**	
4	115 (88.46%)	15 (11.54%)	130	**11.54%**	**4.57 (1.01-20.56)**	**0.05**
5	31 (68.89%)	14 (31.11%)	45	**31.11%**	**15.81 (3.39-73.79)**	**0.0004**
Total	228 (88.03%)	31 (11.97%)	259			

virtually acellular, other); II ("benign" – follicular nodular disease, chronic lymphocytic (Hashimoto) thyroiditis, granulomatous (subacute) thyroiditis, other); III ("atypia of undetermined" – nuclear type, other); IV ("follicular neoplasm" – oncocytic (Hürthle cell) type); V ("suspicious for malignancy" – papillary thyroid carcinoma, medullary thyroid carcinoma, metastatic carcinoma, lymphoma, other); and VI ("malignant" – papillary thyroid carcinoma, high-grade follicular cell-derived non-anaplastic thyroid carcinoma, medullary thyroid carcinoma, anaplastic carcinoma, squamous cell carcinoma, carcinoma with mixed features, metastatic malignancy, non-Hodgkin lymphoma, other), with respective risk of malignancy of 13%, 4%, 22%, 30%, 74%, and 97% based on follow-up of surgically resected nodules.[8]

The age groups 45-54 and 55-64 represent a significant portion of the total cases with the number of female patients being notably higher in this study which corroborated with previous literature.[9] Among all the ultrasound parameters, overall sensitivity, specificity, PPV, and NPV of predicting TIRADS category is highest for echogenic foci and lowest for composition in contrast to a previous study where values were highest for echogenic foci and lowest for composition.[10]

The 14 out of 18 (22.22%) TBSRTC I nodules exhibit TIRADS 3 to 5 categorization, suggesting that non-diagnostic nodules may also show sonographic features suspicious for malignancy. There is 3.23% agreement between TBSRTC and TIRADS in the categorization of TBSRTC II nodules as benign given that only 6 out of 186 TBSRTC category II nodules are under TIRADS 1 and 2 and the remaining 180 (96.77%) are under TIRADS 3 to 5, implying that despite being benign, majority of TBSRTC II nodules will show sonographic features suspicious for malignancy with considerable overlap between TIRADS 3 and 4. Among TBSRTC category III (9 out of 10 – 90%) and IV (13 out of 14 – 92.86%) nodules, the majority show TIRADS 3 to 5 categorizations, suggesting that nodules with atypia of undetermined significance and follicular nodules will primarily exhibit sonographic features suspicious for malignancy. All 17 (100%) TBSRTC category V and 14 (100%) TBSRTC category VI nodules are under TIRADS 3 to 5, implying that malignant nodules will probably show suspicious sonographic features at the very least.

The investigators found that results for nodules categorized as TBSRTC II, V, and VI are comparable to previous studies.[9-11] Findings for nodules categorized as TBSRTC I and III were not previously elucidated.

CONCLUSION

The correctness of TIRADS prediction is highest for echogenic foci although not significantly higher than other parameters. The overall predicting power of the TIRADS system for the absence and presence of malignancy is high in both ends of the spectrum and TIRADS 1 and 2 are reassuring whereas TIRADS 5 is a strong indication for FNAC. However, the decision to proceed with FNAC in TIRADS 3 and 4 nodules must only be indicated in association with other factors since a significant percentage may turn out to be TBSRTC II.

STATEMENT OF AUTHORSHIP

The authors certified fulfillment of ICMJE authorship criteria.

AUTHOR DISCLOSURE

The authors declare no conflict of interest.

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