

# Correlation between Ultrasound-based TIRADS and Bethesda System for Reporting Thyroid-cytopathology: 2-year Experience at a Tertiary Care Center in India

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## Abstract

**Background:** In recent times, high-resolution ultrasound thyroid imaging has paved the way for significant transformation in clinical approach to thyroid nodule. There are several risk stratification systems in thyroid imaging, developed with an aim, not only to reduce the inter-observer variability but also to establish effective communication system. Thyroid image reporting and data system (TIRADS) classification system, which is similar to breast imaging reporting and data system for breast lesion, is the most useful of all. To our knowledge, there is just a handful published research articles available based on Indian population in this regard. In this article, we study the thyroid nodules using high-resolution ultrasound in Indian population and we try to correlate the TIRADS and Bethesda system for reporting thyroid cytopathology. **Materials and Methods:** This prospective study includes 184 patients studied over a period of 2 years (April 2015–April 2017). Patients having thyroid nodule in B-mode ultrasound and are scheduled to get a fine-needle aspiration cytology (FNAC) done. Bethesda classification of these nodules is tabulated in follow-up period simultaneously. By comparing these data, efficacy of TIRADS in differentiating benign from malignant nodules are assessed finally using accuracy, positive predictive value (PPV), cross-tabulation, and Chi-square tests. **Results:** Out of the 117 TIRADS 2 nodules, none turned out to be Bethesda IV or higher, which means none of these nodules turned out to be malignant. The risk of malignancy for TIRADS 2, TIRADS 3, TIRADS 4, and TIRADS 5 was 0, 2.2, 38.5, and 77.8%, respectively. The risk of malignancy percentage in our study is similar to those values obtained in other prominent studies. **Conclusion:** The probability of a particular nodule being malignant can be effectively inferred from the ultrasound-based TIRADS system with a certain level of confidence. Considering our results and other literature reviews, it can be safely assumed that FNAC can be at least deferred in patients having TIRADS 2 nodules, which contribute to majority of newly detected cases. In our experience, there is a remarkable correlation exists between TIRADS ultrasound classification and Bethesda cytology, especially for benign nodules.

**Keywords:** Bethesda, fine-needle aspiration cytology, Indian population, nodules, thyroid image reporting and data system, thyroid

## INTRODUCTION

Nodules in the thyroid are very common and their prevalence rates are largely dependent on the identification method. By just palpation, the prevalence rate ranges from 4 to 7%,<sup>[1,2]</sup> whereas by using the imaging modalities such as the high-resolution ultrasonogram, it ranges from 20 to 76% in the adult population. The nodules discovered with radiographic studies are called “thyroid incidentalomas.”<sup>[2,3]</sup> The correlation between imaging methods and the prevalence reported at surgery and autopsy ranges between 50 and 65%.<sup>[4]</sup>

The main concern for the evaluation of thyroid nodules is the possibility of malignancy. There are wide variations in

the reported proportion of malignancy among the clinically or radiologically detected thyroid nodules. The average prevalence of malignancy rates across the world in thyroid nodules, as evaluated by invasive procedure ranges from 4.0 to 6.5%.<sup>[5,6]</sup>

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Due to the abundant use of ultrasound, the increased access to cytology analysis through fine-needle aspiration cytology (FNAC) guided by ultrasound and with the recent advances in functional imaging modalities such as 18 FDG-PET imaging, the incidental diagnoses of thyroid nodules are increasing every day. It is controversial whether or not such a benefit exists because most of the nodules are generally benign.<sup>[7,8]</sup>

Studies have proposed that, even though incidence of discovery of thyroid nodules during 18 FDG-PET imaging is few (1–2%), the malignant potential may be as high as 27%, these nodules warrant immediate evaluation.<sup>[9]</sup>

### Thyroid nodules

The American Thyroid Association defined thyroid nodules as “discrete lesions within the thyroid gland, radiologically distinct from surrounding thyroid parenchyma.”<sup>[10]</sup>

The literature indicates that the incidence of nodules is around four times higher in women than men.<sup>[2]</sup> The gender disparity is perhaps explained by the hormonal influences of both estrogen and progesterone, as increasing nodule size and new nodule development have been demonstrated to be related to pregnancy and multiparity.<sup>[11]</sup>

The nodules may cause thyroid dysfunction and may rarely cause compressive symptoms due to mass effect. The nodules are critical because of the need to rule out thyroid malignancy.

### Thyroid image reporting and data systems (TIRADS)

TIRADS, proposed by Horvath *et al.*,<sup>[12]</sup> is a classification system based on ultrasound features which was basically introduced to allow for a better selection of thyroid nodules undergoing FNAC, thus avoiding unnecessary procedures. This system also unifies language between radiologists and endocrinologists all over the world.

## MATERIALS AND METHODS

### Ethical committee approval

This study has been approved by the Institutional Research Ethics Committee, Sri Ramachandra University, Porur, Chennai.

### Study design

Prospective study design.

Duration of study: 2 years (April 2015–April 2017).

### Inclusion criteria

Patients who have thyroid nodule in B-mode ultrasound and are scheduled to get an FNAC done are included in this study.

### Exclusion criteria

Normal thyroid scan (TIRADS 1) and proven case of thyroid malignancy (TIRADS 6) were not included in this study.

### Materials

High-resolution B-mode ultrasound done using Toshiba/Canon Aplio™500 with high-frequency probe (12–6.2 MHz).

FNAC reports (follow-up).

### Sample size

A total of 184 patients were included in the final study.

### Sampling method

The study included all the study subjects, who satisfied the inclusion and exclusion criteria, hence no sampling was done.

### Procedure

The patient is made to lie supine. The ultrasound examination starts with B-mode to image the thyroid and the neck. The thyroid nodules, if present, are staged according to TIRADS. The neck is assessed for suspicious lymph nodes. Then FNAC results are followed up for the Bethesda staging.

Additional Software: MicroPure imaging (highly sensitive for microcalcification detection)

### Data collection methods

Data were collected for the study, using a structure case report form. The data were gathered from the history, clinical examination, and the investigation reports of the study participants.

## RESULTS

High-resolution ultrasound along with MicroPure imaging has revolutionized the way thyroid nodules are assessed. The MicroPure imaging is a novel method for detection of microcalcifications. In order to improve the accuracy of reporting and to avoid interpersonal variability, a dedicated team of experienced radiologists and pathologists were involved for this study.

A total of 184 patients were included in this study, out of which 156 were females. These thyroid nodules are predominantly found in and around third–sixth decade of life. The patients in this age group amount to 137 patients, approximately 75% of our study population.

Most of the thyroid nodules mostly come under TIRADS 2 and TIRADS 3 classifications on ultrasound imaging, accounting for around 92% of the nodules picked up on ultrasound. Likewise, most of the nodules (approximately 93%) turn out to be Bethesda I and II on invasive tests. Thirteen out of 184 nodules (7.1%) were detected and proven to be malignant by postoperative studies.

In our study, 184 thyroid nodules which were scheduled to get an FNAC done were initially assessed using ultrasound and TIRADS scoring was given for each case. The cases which were already a proven case of malignancy (TIRADS 6) were not included in this study. Out of the 184 nodules, 117 were categorized under TIRADS 2, 45 were classified under TIRADS 3, 13 were classified under TIRADS 4, and 9 were classified under TIRADS 5. The nodules classified as Bethesda I and II were considered benign, and those nodules classified as Bethesda IV–VI were considered malignant. The results we obtained have been tabulated below in Table 1.

**Table 1: Thyroid imaging reporting and data system [ti-rads] and Bethesda correlation**

	Bethesda 1	Bethesda 2	Bethesda 3	Bethesda 4	Bethesda 5	Bethesda 6	Total
TIRADS 2	10	106	1	-	-	-	117
TIRADS 3	1	42	1	1	-	-	45
TIRADS 4	4	4	-	2	2	1	13
TIRADS 5	1	1	-	2	4	1	9
Total	16	153	2	5	6	2	184

- Out of the 117 TIRADS 2 nodules, none turned out to be under Bethesda IV or higher, which means none of these nodules turned out to be malignant
- Among the 45 nodules labeled as TIRADS 3, 42 nodules were in Bethesda II and 1 nodule each in Bethesda I, III, and IV, respectively.

There were few nodules which appeared suspicious on ultrasound to be classified under TIRADS 4 and TIRADS 5 but turned out to be benign in Bethesda classification. Considering all nodules, the proportion of malignant nodules classified as TIRADS 2, TIRADS 3, TIRADS 4, and TIRADS 5 were 0.0, 7.7, 38.4, and 53.9%, respectively.

Sensitivity, specificity, negative predictive value (NPV), positive predictive value (PPV), and accuracy were also calculated based on histopathological results. TIRADS scores 4 and 5 were considered positive for malignancy, while scores 1–3 were considered negative for malignancy. Cross-tabulation of TIRADS and Bethesda was prepared [Table 2]. Data were analyzed by Chi-square test or Fisher’s exact test for categorical variables of benign and malignant nodules ( $P < 0.001$ ).

We derived at 92.3% sensitivity, 94.15% specificity, 54.54% PPV, and 99.38% NPV for our study. Significant association was noticed between TIRADS and Bethesda system of classification ( $P < 0.001$ ). Area under the curve was 0.932 in ROC curve, which indicated that the results are very good [Figure 1].

On comparing TIRADS result with Bethesda system of classification, the risk of malignancy for TIRADS 2, TIRADS 3, TIRADS 4, and TIRADS 5 was 0, 2.2, 38.5, and 77.8%, respectively.

The risk of malignancy for patients classified TIRADS 4 was estimated at 17.5 times the risk for those rated as 3. The risk of malignancy for patients classified TIRADS 5 was estimated at 35.4 times the risk for those rated as 3.

**FNAC results**

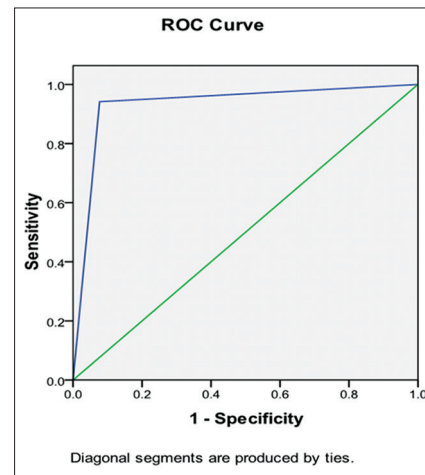
Adenomatoid nodule, colloid nodule, lymphocytic thyroiditis, papillary, and follicular carcinoma of thyroid contributed 40, 34, 10, 7, and 1%, respectively. Eight percent of the nodules were found to be unsatisfactory for evaluation even in repeated FNACs mainly due to cystic nature of the nodules.

**DISCUSSION**

Ultrasound of thyroid should be performed in the initial assessment of the gland and the nodule. Since the prevalence

**Table 2: TIRADS classification \*FNAC results cross tabulation**

TIRADS CLASSIFICATION	FNAC RESULTS		Total
	POSITIVE	NEGATIVE	
POSITIVE			
Count	12	10	22
% of Total	6.5%	5.4%	12.0%
NEGATIVE			
Count	1	161	162
% of Total	0.5%	87.5%	88.0%
Total			
Count	13	171	184
% of Total	7.1%	92.9%	100.0%



**Figure 1:** Accuracy is measured by the area under the ROC curve. 0.90-1.00 = very good (A); 0.80-0.90 = good (B); 0.70-0.80 = fair (C); 0.60-0.70 = poor (D); 0.50-0.60 = fail (F)

of thyroid nodule is very high, patients for whom FNAC should be recommended is still controversial.

FNAC is a useful and inexpensive tool for detecting malignancy of thyroid, but it is a minimally invasive procedure. Performing such test in all thyroid nodules is neither cost effective nor advisable, thus it is important to select the cases according to their malignancy risk.

Several classifications based on sonographic features have been proposed in the recent past, in an attempt to help this selection. However, a general agreement has not been established, given

the difficulty of reproducibility of different classifications proposed or even due to the low correlation between the ultrasound reports and FNAC results.<sup>[13]</sup>

The TIRADS system of classification desires to correlate sonographic features to cytological classification. One of the recent studies revealed the fact that 7.3% of malignant nodules did not have suspicious malignant features on ultrasound.<sup>[14]</sup> Some of the sonographic features gradually increase the risk of malignancy in a nodule. The sonological features included in our study are echogenicity, microcalcifications, taller than wider shape, presence of suspicious lymph node, irregular margins, and peripheral halo. It should be understood that not the presence or the absence of a single particular feature on ultrasound was associated with the nodule's malignancy. It must always be remembered that an amalgam of at least two of the sonological features are more accurate in differentiating a benign nodule and a high-risk nodule for malignancy than just one of these sonological feature alone.<sup>[15,16]</sup>

At the end of our study, we have derived the following results after using several sonological factors to decide the TIRADS scoring of the nodules. Our study has a 0% malignancy risk for TIRADS 1 and TIRADS 2. The risk of malignancy in our study for TIRADS 3, TIRADS 4, and TIRADS 5 were 2.2, 38.5, and 77.8%, respectively.

Among the classifications proposed from all over the world, Horvath *et al.* have offered ten sonological patterns to be analyzed during the ultrasound examination and nodule classification from TIRADS 2–6 (category 4 divided into 4A and 4B).<sup>[13]</sup> They estimated a risk of malignancy of 0% in TIRADS 2, 3.4% in TIRADS 3, 10–80% in TIRADS 4, and 87% in TIRADS 5.

Kwak *et al.* proposed a TIRADS classification by retrospective analysis of thyroid nodules in ultrasound and FNA, using five sonological criteria that can be added during thyroid evaluation.<sup>[17]</sup> This article describes that a malignancy risk of 0% is expected for TIRADS 2, 1.7% for TIRADS 3, a risk of 3.3–72.4% for TIRADS 4, and of 87.5% for TIRADS 5. The main limitation of this study was that each suspicious sonographic feature was given the same importance, even though in reality each ultrasound feature has a different probability for malignancy. For example, a nodule with marked hypoechogenicity/microcalcifications has a higher risk of malignancy than other nodules with irregular margins.

Moifo *et al.* conducted a cross-sectional study carried out at the Centre Hospitalier de Lagny, Marne La Vallée, France.<sup>[18]</sup> Their objective was to determine the reliability of Russ' modified TIRADS classification in predicting thyroid malignancy. In their study, 430 nodules were assessed. Twenty-three nodules out of these 430 nodules (5.3%) were malignant. The malignancy risk of the TIRADS categories were 0% for TIRADS2, 2.2% for TIRADS3, 5.9–57.9% for TIRADS4, and 100% for TIRADS5.

Anuradha *et al.* assessed the practical aspects and accuracy of TIRADS in daily clinical practice observed that PPV for

**Table 3: Study comparison**

	Our study	Horvath <i>et al.</i>	Kwak <i>et al.</i>	Moifo <i>et al.</i>
TIRADS 1	0.0%	0%	0%	0%
TIRADS 2	0.0%	0%	0%	0%
TIRADS 3	2.2%	14.1%	1.7%	2.2%
TIRADS 4	38.5%	45%	3.3%-72.4%	5.9%-57.9%
TIRADS 5	77.8%	89.6%	87.5%	100%

malignancy was 6.6, 32, 36, 64, 59, and 91% for TIRADS 2, 3, 4A, 4B, 4C, and 5 categories.<sup>[19]</sup> According to another similar study from Indian literature by Srinivas *et al.*, it was concluded that the risk of malignancy for TIRADS categories 1, 2, 3, 4A, 4B, 4C, and 5 was 0, 0, 0.64, 4.76, 66.67, 83.33, and 100%, respectively.<sup>[20]</sup>

Our results are within the range suggested by Horvath *et al.*, Kwak *et al.*, Moifo *et al.*, and two other studies based on Indian population [Table 3].

## CONCLUSION

In conclusion, if the nodules are properly classified on ultrasound, the probability of a particular nodule being malignant can be inferred from the ultrasound-based TIRADS system with a certain level of confidence and appropriate measures for management of the nodule can be initiated, thus avoiding unnecessary FNA procedures.

At the end of our study, none of the nodules classified under TIRADS 2 turned out to be malignant; therefore, it can be safely assumed that FNA may be deferred at least in patients having TIRADS 2 nodule, which contribute to majority of newly detected cases and thereby avoiding unnecessary surgeries.

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## Conflicts of interest

There are no conflicts of interest.

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