



Evaluation of Thyroid Nodule: Thyroid Imaging Reporting and Data System (TIRADS) and Clinicopathological Correlation

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Abstract Ultrasound is one of the accepted modality for the initial assessment of thyroid nodules. Thyroid image reporting and data system (TIRADS) classification system is the most useful of the risk stratification systems of thyroid imaging in predicting malignancy. The purpose of this study is to assess the clinical usefulness of TIRADS in the evaluation of thyroid nodule and compare it with final histopathological results. This was a prospective observational study conducted in a tertiary care hospital over a period of one year. Preoperative ultrasound was performed in 85 patients admitted for thyroid surgery. Thyroid nodules were classified according to TIRADS into five groups. The TIRADS category was compared with the final histopathological diagnosis following surgery. Sensitivity, specificity, positive as well as negative predictive value and risk of malignancy for each TIRADS category was assessed. The risk of malignancy for TIRADS 2, TIRADS 3, TIRADS 4, and TIRADS 5 was 4.2%, 13.3%, 57.9% and 100%, respectively. The usefulness of TIRADS classification in prediction of malignancy was 77.8% sensitive, 89.6% specific, had a positive predictive value of 66.6% and negative predictive value of 93.8%. The probability of a particular nodule being malignant can be inferred from ultrasound based TIRADS system. Hence ACR TIRADS classification is a valuable tool for diagnosis of thyroid nodule and should be adopted in our routine clinical practice.

Keywords Thyroid nodule · Thyroid imaging reporting and data system (TIRADS) · Histopathological correlation · Ultrasonography

Introduction

Thyroid lesions are commonly seen in our routine clinical practice. The prevalence of thyroid nodules is about 8.5% and more common among women [1]. Different diagnostic modalities are available to evaluate thyroid nodules. The main concern in evaluation of thyroid nodule is the possibility of malignancy. There are wide variations in the reported proportion of malignancy among clinically and radiologically detected thyroid nodules. Clinical examination cannot reliably distinguish between benign and malignant nodules.

Ultrasound is the widely accepted imaging modality for the initial assessment of thyroid nodules. However, ultrasound has low specificity due to the considerable overlap between the sonographic features of benign nodules and thyroid cancer. Hence, the surgical excision of the nodule and its histopathological examination is the way to differentiate between the more common benign and much less common malignant nodules.

The American College of Radiology Thyroid Imaging Reporting and Data Systems (ACR TIRADS) is a risk stratification system for classifying thyroid lesions. It is a five-point classification to determine the risk of cancer in thyroid nodules based on ultrasound characteristics. Nevertheless, ultrasound has lot of limitations including the difference in resolution of the equipment, observer variations and overlapping of findings. TIRADS classification tries to minimize these shortcomings.

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The purpose of this study is to assess the clinical usefulness of TIRADS in the evaluation of thyroid nodule and compare it with final histopathological results in our setup.

Materials and Methods

This is a prospective observational study conducted in a tertiary care hospital over a period of one year. All patients of either sex with thyroid swelling with ultrasound TIRADS classification undergoing thyroid surgery were included in the study. Patients with TIRADS 1 category and those not willing to participate in the study were excluded. Ethical clearance was obtained from the Institutional human ethical committee.

All patients underwent high resolution B- mode ultrasound done using Toshiba Aplio™500 with 5–14 MHz linear transducer. An additional software—MicroPure imaging, which is highly sensitive for microcalcification detection was used.

The thyroid nodules if present were staged according to Thyroid Imaging Reporting and Data System (TIRADS) classification. All the nodules were assessed for the following features: size, composition, echogenicity, margins, taller than wider shape, microcalcification, macrocalcification, intranodular vascularity and abnormal cervical lymphadenopathy. A score was assigned for feature (s) noted in each category of ACR TIRADS and scored accordingly as: (1) normal thyroid gland, (2) benign lesions, (3) probably benign lesions, (4) suspicious lesions, (5) probably malignant lesions. The patients were then subjected to surgery. The choice of surgery was determined based on clinical, ultrasound and FNAC reports. The surgically resected specimens were fixed in 10% buffered formalin for 24 h and histological evaluation was performed by pathologist. The results of the ultrasound TIRADS category was interpreted and compared with the final histopathological results.

Results

A total of 85 patients were included in this study. Patients aged 31–60 years made up the greatest number of cases, accounting for 76.4% of the cases totally. This study included 15 males and 70 females. The female: male ratio was 4.6: 1. Female predominance was seen among most of the age groups. However, in the age group of 61–70 years the number of male patients outnumbered the females. The distribution of age group and gender among study subjects is shown in Table 1.

The distribution of thyroid nodules based on TIRADS category is given in Table 2. Out of the 85 nodules, 48 were

classified into TIRADS 2, 15 were classified into TIRADS 3, 19 came under TIRADS 4 and 3 were categorized into TIRADS 5.

Out of 85 nodules, 67 were benign and 18 were malignant. 78.8% of the nodules were benign and 21.2% of the nodules turned out to be malignant. Of the benign lesions, 27/67 (40.3%) of them were adenomatoid nodules, 12/67 (17.9%) of them were colloid goitre, 5/67 (7.4%) of them were follicular adenoma, 19/67 (28.4%) of them were nodular goitre and 4/67 (6.0%) cases were lymphocytic thyroiditis. Among 85 nodules, 18 (21.2%) were malignant. 15/18 (83.3%) of them were papillary carcinoma and 3/18 (16.7%) of them were follicular carcinoma. The distribution of thyroid nodules with respective to TIRADS category and histopathological diagnosis is given in Table 3.

Out of the 48 nodules in TIRADS 2 category, 46/48 (95.8%) were benign and 2/48 (4.2%) were diagnosed to be malignant by histopathology. In TIRADS 3 category, 13/15 (86.7%) nodules were benign and 2/15 (13.3%) were malignant. Among 19 nodules of TIRADS 4 category, 11/19 (57.9%) were malignant and 8/19 (42.1%) were benign. In TIRADS 5 category, all 3/3 (100%) nodules had malignant character on histopathology. The distribution of TIRADS category among histopathologically confirmed benign and malignant nodules is shown in Fig. 1.

Thus the risk of malignancy in TIRADS 5 was 100% and in TIRADS 4 was 57.9%. TIRADS 3 category had a risk of 13.3% and TIRADS 2 had 4.2% risk of malignancy as shown in Fig. 2. Among 18 patients with thyroid malignancy, 13 were females and 5 were males. Occurrence of malignancy was highest in extremes of age groups. Below 30 years, 5 out of 14 patients had malignancy (35.7%). Above 60 years, 3 out of 6 patients had malignancy (50%).

Sensitivity, Specificity, Positive Predictive value and Negative predictive value were calculated based on TIRADS results. TIRADS category 4 and 5 were considered positive for malignancy while TIRADS 2 and TIRADS 3 were considered negative for malignancy. Data was analyzed by Chi- Square test, Fischer exact test and Likelihood ratio for categorical variables of benign and malignant nodules. It was found that the *p* value of TIRADS 2, TIRADS 4 and TIRADS 5 was significant ($p = 0.00$). However, the *p* value in TIRADS 3 category was insignificant ($p = 0.31$).

Hence, TIRADS 4 and 5 were found to be statistically significant in prediction of malignancy and TIRADS 2 had significant prediction for benign lesions. Using this, we calculated a 77.8% sensitivity, 89.6% specificity, 66.6% positive predictive value and 93.8% negative predictive value. According to this study TIRADS classification has a strong negative predictive value, good specificity and fairly

Table 1 Distribution of age group and gender among the study subjects

Age group	Gender		Total
	Male	Female	
≤30 years	1	13	14
31–40 years	3	26	29
41–50 years	2	19	21
51–60 years	4	11	15
61–70 years	4	0	4
> 70 years	1	1	2
Total	15	70	85

Table 2 Distribution of thyroid nodules based on TIRADS category

TIRADS category	Frequency	Percentage
TIRADS 2	48	56.5
TIRADS 3	15	17.6
TIRADS 4	19	22.4
TIRADS 5	3	3.5
Total	85	100

Table 3 The distribution of thyroid nodules with respective to TIRADS category and histopathological diagnosis

Tirads Category	Histopathological Diagnosis							Total
	Adenomatoid nodule	Colloid goitre	Follicular adenoma	Nodular goitre	Lymphocytic thyroiditis	Follicular CA	Papillary CA	
TIRADS 2	20	9	1	12	4	0	2	48
TIRADS 3	4	2	1	6	0	0	2	15
TIRADS 4	3	1	3	1	0	2	9	19
TIRADS 5	0	0	0	0	0	1	2	3
Total	27	12	5	19	4	3	15	85

good sensitivity. The positive predictive value of TIRADS classification as per this study was low.

Discussion

Thyroid swelling is a common disorder and almost 12% of adult Indians have been shown to have a palpable nodule in a population based study by Menon et al. in the year 2009 [2]. However, the incidence of malignancy in these thyroid lesions is low [3]. Identification of these high risk nodules is crucial and should not be missed. Ultrasound is the initial investigation of choice for assessment of thyroid nodules.

Several attempts have been made to create a standardized system to classify thyroid nodules according to their risk of malignancy. Many international societies have published different ultrasound classification systems for diagnosing thyroid malignancy. In 2017, the American College of Radiology published a paper on Thyroid Imaging Reporting and Data System (ACR TIRADS) that enabled one to precisely predict clinical and pathological correlation and did not recommend FNAC of nodules with benign ultrasound characteristics regardless to size.

Recently in 2018, Pantano et al. compared the performances of American Thyroid Association (ATA), American Association of Clinical Endocrinologists (AACE),

Fig. 1 Distribution of TIRADS category among histopathologically confirmed benign and malignant nodules

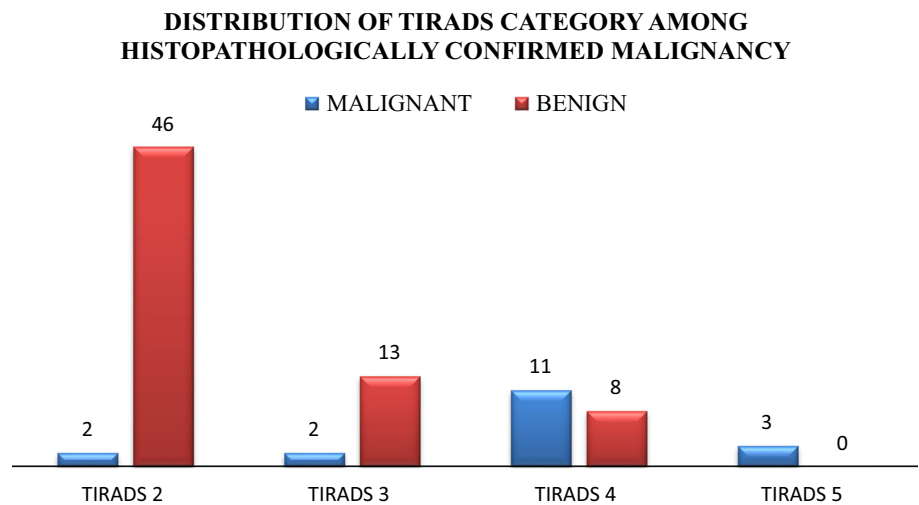
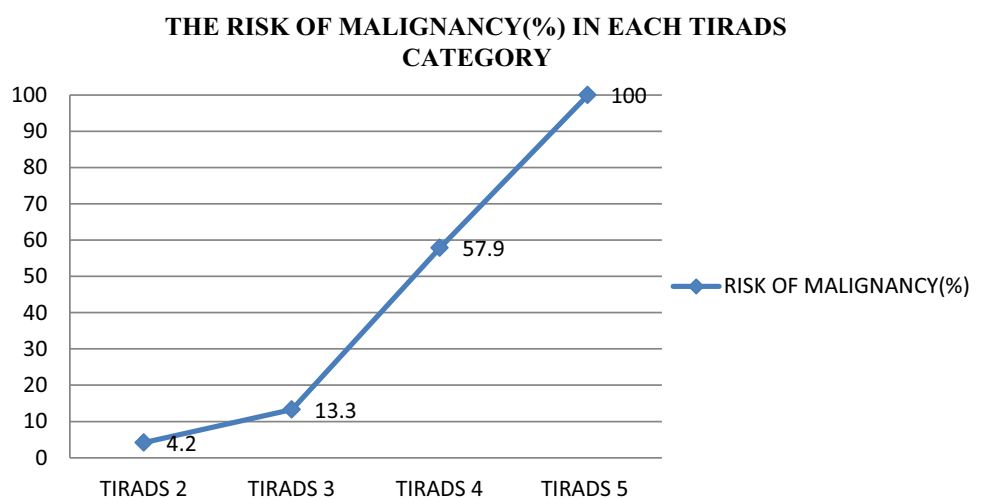


Fig. 2 The risk of malignancy (%) in each TIRADS category



American College of Endocrinology (ACE), Associazione Medici Endocrinologi (AME) and American College of Radiology Thyroid Imaging Reporting and Data System (ACR TIRADS) classifications for the identification of thyroid nodules with high risk cytology [4]. They concluded that using ATA and AACE/ACE/AME was less accurate when compared to TIRADS system in classification of thyroid nodules. This study further stated that ACR TIRADS classification system had the highest area under ROC (Receiver Operating Characteristics) curve for the identification of cytologically high risk nodules.

In many countries, surgeons, radiologists and endocrinologists have adopted the TIRADS classification for evaluation of thyroid lesions and use it regularly. The benefit of TIRADS classification is its simplicity and it was designed to make it simple to assess the risk of malignancy in clinical practice and to reduce the number of FNAC procedures in subjects presenting with a low risk of malignancy. However, the drawback of TIRADS score is its limited value to confirm malignancy and to guide

subsequent management of patients in those patients with indeterminate cytological results.

Many previous studies have compared the diagnostic performance of ultrasound TIRADS with those nodules that were diagnosed based on cytological findings. This could result in some malignant nodules being missed and lead to potential bias in the results. Thus, a strong clinico-pathological correlation will guide us in defining the risk of malignancy and direct our proper management of thyroid lesions. The strength of this present study lies in the fact that only those nodules that were resected were included and the final histology was used as the reference standard, since histology provides the greatest certainty on the eventual diagnosis.

In this study, out of 85 patients 15 patients were males and 70 were females. Thyroid nodules were found to occur 4.6 times higher in female population than male in our study. The youngest patient was 21 years and the eldest patient was 74 years. Most of the patients were in the age group 31–40 years. A similar study by Bakhos et al. and

Virk et al. showed thyroid nodules are most commonly found in the age group 20–40 years [5, 6].

On correlating TIRADS classification with the histopathological results it was observed that the risk of malignancy in histopathologically proven nodules was 4.2% in TIRADS 2, 13.3% in TIRADS 3, 57.9% in TIRADS 4 and 100% in TIRADS 5. Though TIRADS 2 category was considered as benign, patients underwent surgery in these cases for management of multinodular goitre and also for cosmetic purposes in case of huge goitre.

Horvath et al. concluded that less than 5% of patients in TIRADS 2 category had risk of malignancy [7]. However in the study done by Mofio et al. and Sanchez et al., the risk of malignancy in TIRADS category 2 was 0% which was lower when compared to this study [8, 9]. The risk of malignancy in TIRADS 3 in this study was 13.3%, similar to the study by Horvath et al. who reported 5–10% risk of malignancy in these nodules [7]. However, this is slightly higher when compared to studies done by Mofio et al. and Sanchez et al. [8, 9]. Both these studies showed the risk of malignancy in TIRADS 3 to be 2.2% [8, 9]. The risk of malignancy in TIRADS 4 category in this study is similar to the study by Mofio et al. [8]. Both these studies showed a risk of 57.9%. The study by Sanchez et al. showed malignancy risk in TIRADS 4 to be 48%, slightly lower than that observed in these studies [9]. The TIRADS 5 category had a similar risk of malignancy in all the studies.

All these studies point out that TIRADS 5 category is strongly suggestive of malignancy whereas TIRADS 2 category has the least risk of malignancy. However, these patients with TIRADS 2 category should not be neglected and need regular follow up for the progress of thyroid nodules.

From this study, TIRADS classification was 77.8% sensitive, 89.6% specific, had a positive predictive value of 66.6% and negative predictive value of 93.8% for the prediction of malignancy. When comparing these results to the outcome of a study done by Singaporewalla et al., this study had a comparable sensitivity in predicting malignancy (77.8% vs. 70.6%) and comparable specificity and negative predictive value (89.6% vs. 90.4% and 93.8% versus 93.8% respectively) [10]. On the other hand, on comparing results with the data reported by Horvath et al., this study had a lower sensitivity (77.8% compared to 88%) but higher specificity (89.6% compared to 49%). This study also had a comparable negative predictive value of TIRADS score predicting malignancy as well (93.8% compared to 94%) [7].

The study done in Indian subcontinent by Anuradha et al. assessed the practical aspects and accuracy of TIRADS in daily clinical practice and observed that predictive value for malignancy in TIRADS 2 was 6.6%, TIRADS 3

was 32%, TIRADS 4 was 64% and TIRADS 5 was 91% [11]. Similar Indian study done by Srinivasan et al. concluded the risk of malignancy for TIRADS 2 was 0%, TIRADS 3 was 6.4%, TIRADS 4 was 66.6% and TIRADS 5 was 100% [12].

Though the risk of malignancy in TIRADS 2 and 3 is considered to be low, the rate of incidence of malignancy in young female patients is considerably high. There should always be an index of suspicion for malignancy in these patients and follow up is essential through serial ultrasound or cytopathological diagnosis especially in young females.

This study did not define pathological correlation of TIRADS 4 subgroups 4a, 4b and 4c to the histopathological results which is a limitation of this study.

Conclusion

Ultrasound of thyroid plays a major role in the evaluation of thyroid swellings. If the nodules are classified according to ultrasound based TIRADS classification, the probability of a particular nodule being malignant can be inferred with confidence. Hence ACR TIRADS classification is a reliable indicator for prediction of malignancy and is a highly specific and accurate system for categorizing benign and malignant nodules. TIRADS classification should be a recommended standard for evaluation of thyroid nodules.

Though TIRADS 2 and 3 category is generally considered benign, they should be viewed with caution as false negative results do occur and these patients should be followed up if clinical suspicion of malignancy is present. TIRADS 5 has a strong prediction of malignancy as seen in this study.

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