Validity Of TIRADS In Diagnosing Malignant Thyroid Nodules With Histopathological Correlation

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Abstract

Introduction: Thyroid nodules are a very common clinical presentation with the estimated prevalence of 3-7% by palpation and 19-67% by high resolution ultrasonography (USG).

Aim:The aim of this study is to determine the risk of malignancy, accuracy in each Thyroid Imaging Reporting and Data System (TIRADS) categories and determine the specific ultrasonographic features associated with malignancy by using histopathologic diagnosis as the reference standard.

Material and Methods: This is a single-centre prospective observational study carried out on 60 patients with a suspected thyroid nodule referred from department of Otorhinolaryngology, Surgery and Internal Medicine to the department of radiology and imaging over a period of 6 months . All patients are subjected to ultrasound and the lesions were characterized according to TIRADS categories. Patients in TIRADS 3,4 and 5 categories underwent Fine needle aspiration cytology (FNAC) as per the guidelines. Correlation of TIRADS category with histopathologic diagnosis were assessed. The sensitivity, specificity, positive predictive value, negative predictive value and accuracy of the screening test along with their 95% CI were calculated. The threshold for statistical performance was set at 0.05. Each ultrasonographic features were also compared with its histopathologic results.

Results: The sensitivity, specificity, positive predictive value, negative predictive value and accuracy of TIRADS 4 and 5 categories in relation to histopathologic diagnosis were 92.00%, 25%, 50%, 80%, and 55% respectively.
Among individual USG parameters, microcalcification was most sensitive (76%) and specific (81%) feature with an adjusted OR 14.44 (95% Cl 2.387 to 87.426, *p*=0.00173) followed by irregular margin and taller-than-wider shape with a specificity of 88% and 88% respectively.

Conclusion:Due to the high incidence of thyroid nodule among general population ultrasound screening using TIRADS scoring is a sensitive reliable predictor of thyroid malignancy. Risk of malignancy increases significantly with higher TIRADS score. Microcalcification is the most frequent ultrasound feature that is predictive of thyroid malignancy.

Keywords:TIRADS,ultrasound,histopathology,sensitivity,specificity,PPV,NPV,accuracy

INTRODUCTION

Thyroid nodules are very common among general population, especially in women. It is defined as an focal discrete area of unusual growth of thyroid cells with altered echogenicity within thyroid gland that is radiologically and pathologically distinct from surrounding normal thyroid parenchyma[0,**Error! Reference source not found.**]. Its estimated incidence is around 3-7 % on clinical examination and can go as high as 67% with the use of high resolution ultrasound which as a sensitivity of 95% for detection of nodule as small as 1-3 mm[**Error! Reference source not found.**,**Error! Reference source not found.**]. Majority of thyroid nodules are benign, but malignancy can be detected in approximately 5–15% of cases, mainly affecting patients younger than 20 or older than 60 years[**Error! Reference source not found.**]. High resolution ultrasound (USG) is the first line imaging modality in assessment of thyroid nodule followed by ultrasound-guided fine-needle aspiration cytology (FNAC), and surgical decision is mostly relied upon on the FNAC result.
Recently, various studies have been performed using ultrasound to determine features which are predictive of malignancy in a thyroid nodule like taller than wider shape, microcalcifications, hypoechogenicity, and irregular margin.
The purpose of this study is to determine the diagnostic value of ultrasound and its features in the evaluation of thyroid nodule in comparison with the final histopathologic diagnosis.

Materials And Methods

This study was a single centre prospective cross-sectional observational study of 60 patients with suspected a thyroid nodule. The study conducted in the Department of Radiology and Imaging Sciences over a period of six months between March 2021 and August 2021 in a tertiary care hospital. Ethical clearance was obtained (IEC No: KIMS/PG/2021/32) from the Institutional Ethics Committee prior to commencement of the study. After obtaining the informed consent the study was carried out.

METHODOLOGY

High Frequency Ultrasound of thyroid gland

All 60 patients were subjected to an ultrasound examination of thyroid gland using a high frequency 7–15 MHz linear transducer in transverse and longitudinal planes, with the patient in the supine position with the neck extended. Each thyroid nodule was evaluated and the report was prepared according to the TIRADS categories and TIRADS Score. Then USG guided FNAC was done from the suspicious nodules if indicated.

Ultrasound guided -Fine needle aspiration cytology

After the explanation of the Ultrasound guided-FNAC procedure, the signed informed consent is obtained from the patients. It was done using a 22-gauge needle by an experienced radiologist. The sample is prepared and fixed by alcohol. The cytological analysis was classified according to Bethesda category[6] as shown in [Table/Fig 1].

DIAGNOSTIC CATEGORY	DESCRIPTION
I	Non-diagnostic/unsatisfactory
II	Benign
III	Atypia or follicular lesion of undetermined significance (AUS or FLUS)
IV	Follicular neoplasm or suspicious for follicular neoplasm
V	Suspicious for malignancy
VI	Malignant

Table 1: Bethesda classification for thyroid cytopathology

HISTOPATHOLOGY

Of the total 60 subjects with thyroid nodules, 29 of them underwent surgery most of them were Bethesda 4 and 5 categories. The surgical specimens were embedded in paraffin blocks, sectioned and were stained by haematoxylin and eosin stain and examined under light microscope. Histopathology slides was evaluated by a single pathologist. Out of 29 biopsy proved subjects, 8 were of "Bethesda 2" cytology and thus having a benign etiology were also operated due to increasing size, compressive symptoms or due to cosmetic concern.

STATISTICAL ANALYSIS

Data were collected in standardized form. All the data collected was compiled in MS Excel and IBM SPSS software package version 23.0. A 2x2 table was constructed to determine accuracy measures (sensitivity, specificity, predictive values, likelihood ratios) of TIRADS compared to histopathology. The Chi-square test were performed to see whether correlation existed between the major ultrasound features and malignancy. Odds ratio (risk estimates) were calculated and presented using 95% confidence interval (CI).The threshold for statistical significance was set at 0.05.

RESULTS

In this study a total of 60 patients were included. There were 52 (86.66%) female and 8 (13.33%) male patients, with the male to female ratio of 13 : 2 Mean age of subjects is 42.18 ± 12.64 years. The predominantly involved was right lobe ot thyroid.

The individual characteristics of thyroid nodule according to TIRADS classification is shown the [Table/Fig 2].

TIRADS	
COMPOSITION	
Cystic	8 (13.33%)
Spongiform	10 (16.66%)
Mixed Cystic/Solid	10 (16.66%)
Solid	32 (53.33%)
ECHOGENICITY	
Anechoic	16 (26.66%)
Hyper Or Isoechoic	14 (23.33%)
Hypoechoic	26 (43.33%)
Very Hypoechoic	4 (6.66%)
SHAPE	
Wider Than Tall	49 (81.66%)
Taller Than Wide	11 (18.33%)
MARGIN	
Smooth	44 (73.33%)
Ill Defined	4 (6.66%)
Lobulated Or Irregular	10 (16.66%)
Extra Thyroidal Extension	2 (3.33%)
ECHOGENIC FOCI	
None Or Large Comet Tail Artifact	32 (53.33%)
Macrocalcification	8 (13.33%)
Peripheral Calcification	4 (6.66%)
Punctate Echogenic Foci	16 (26.66%)

Table 2: Baseline characteristics of thyroid according to TIRADS

The most frequent characteristics of thyroid nodules on ultrasound were solid composition (53%), hypoechoic (43%) or anechoic (27%), well-circumscribed (73%), and wider than tall (82%) nodule. Microcalcification were present in 27% of nodules, while macrocalcification were seen in 13% cases.

TIRADS CATEGORIES	
TIRADS 3	36 (60%)
TIRADS 4	15 (25%)
TIRADS 5	9 (15%)

Table 3: Distribution of patients in various TIRADS categories

Distribution of patients in TIRADS 3, 4, and 5 categories were 60%, 25%, and 15% respectively as shown in the [Table/Fig 3]. Patients in TIRADS categories 3, 4, 5 underwent USG-guided FNAC as per the guidelines.

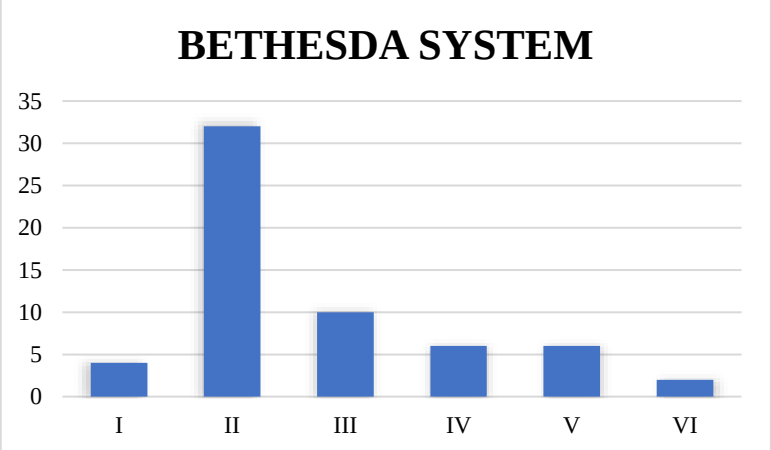

Figure 1: Distribution of patients in Bethesda classification

[Table/Fig 4] shows distribution of nodules according to Bethesda classification. About 53% of nodules were classified as benign by Bethesda classification after FNAC. Of total 60 patients, 29 underwent surgery with 16 patients having benign pathology and 13 having thyroid malignancy on HPE.

	HISTOPATHOLOGY			
TIRADS CATEGORY	**MALIGNANT**	**BENINGN**	**TOTAL**	**RISK OF MALIGNANCY**
TIRADS 3	1	4	**5**	**20%**
TIRADS 4	5	10	**15**	**33.33%**
TIRADS 5	7	2	**9**	**77.70%**
	13	**16**	**29**	

Table 4: Comparison of TIRADS with risk of malignancy

TIRADS categories and risk of malignancy in patients who underwent thyroidectomy are shown in the [Table/Fig 5]. The risk of developing malignancy of TIRADS categories 3, 4 and 5 in our study were 20% (1 out of 5), 33.33% (5 out of 15) and 77.70% (7 out of 9) respectively.

	HISTOPATHOLOGY		
TIRADS	**MALIGNANT**	**BENINGN**	**TOTAL**
TIRADS 4 AND 5	12	12	24
TIRADS 3	1	4	**5**
	13	**16**	**29**
SENSITIVITY	92.30% (89.25-94.82)	**POSITIVE LIKELYHOOD RATIO**	1.238 (0.11-1.26)
SPECIFICTY	25% (9.70-25.76)	**NEGATIVE LIKELYHOOD RATIO**	0.192 (0.01-1.95)
Positive predictive value (PPV)	50% (48.50-51.53)		
Negative predictive value (NPV)	80% (0.97-82.45)		
ACCURACY	55%		

Table 5: Predictive validity of TIRADS versus Histopathology (Gold Standard)

Preoperative TIRADS score with final histopathologic diagnosis is shown in the [Table/Fig 6]. Combining TIRADS 4 and 5 category as probably a malignant USG findings, and TIRADS 3 category as probably benign USG findings and the approximate sensitivity, specificity, PPV, and NPV of USG in predicting malignancy were 92%, 25%, 50%, and 80% respectively. The overall accuracy was about 55%. Hence, we can clearly see that USG can be used as a good initial screening modality but with poor specificity.

On subgroup analysis using HPE as the reference standard, the individual characteristics of thyroid nodule like echogenicity, shape, nodule margin and presence of microcalcification were studied. Major ultrasound features associated with malignancy according to TIRADS are shown in [Table/Fig 7].

ULTRASOUND FEATURES	**HISTOPATHOLOGY**			
	MALIGNANT	**BENINGN**	**TOTAL**	***p* Value**
TALLER THAN WIDE				
PRESENT	5	2	**7**	**0.1042**
ABSENT	8	14	**22**	
HYPOECHOIC				
PRESENT	9	4	**13**	**0.0172**
ABSENT	4	12	**16**	
MICROCALCIFICATION				
PRESENT	10	3	**13**	**0.0017**
ABSENT	3	13	**16**	
IRREGULAR MARGIN				
PRESENT	3	2	**5**	**0.4533**
ABSENT	10	14	**24**	

Table 6: Association of major ultrasonographic feature with histopathology

Sensitivity, specificity, PPV, NPV, OR, and likelihood ratio of major ultrasound features that are predictive of malignancy were calculated and along with performance in respect to histopathology using different statistical analysis are shown in the [Table/Fig 8].

FEATURES	SENSITIVTY	SPECIFICITY	PPV	NPV	Odd Ratio (0R)	LIKELIHOOD RATIO
TALLER THAN WIDE	38%	88%	71	64	4.37 (0.67-27.41)	3.07
HYPOECHOGENICITY	69%	75%	69	66	6.75(1.64-34.91)	2.76
MICROCALCIFICATION	76%	81%	77	81	14.4(2.38-87.42)	4.00
IRREGULAR MARGIN	23%	88%	60	58	2.10(0.30-15.28)	1.84

Table 7: Diagnostic attributes of different ultrasonographic features. PPV-Positive Predictive Value.NPV-Negative predictive value.

Major ultrasound features that is predictive of malignancy is microcalcification that is highly sensitive (76%) and specific (81%) followed by hypoechogenecity which is highly specific (75%) but not very sensitive (69%) . Taller than wider nodule had a high specificity of 88% with a lesser sensitivity of 38% and irregular margin had a sensitivity 23 % and specificity of 88% respectively. Hence, microcalcification and echogenicity helps to differentiate benign from malignant nodule.

DISCUSSION

High resolution Ultrasonography of the thyroid gland increases the detection of thyroid nodule even in an asymptomatic population. Most of the patients in this study was euthyroid with a female preponderance of 87%.These were in accordance with previous studies done by Joanna Grace Dy et al. [7] and Debanu De et al. [8] with a prevalence of 86% among female population. According to the previous report by Naveen et al. [9] right lobe was commonly involved which was also found in this study.

In this present study majority number of patients were in the 21–40 years age group (55%), followed by 51–60 years age group (33%). The results were in accordance to reports published earlier by Joanna Grace Dy et al [7] and Debanu De et al. [8] in which they noted that majority of the cases were between 21 and 40 years age group .

We adapted the TIRADS classification proposed by Kwak et al.[10]. Their study showed the malignancy risk expected for TIRADS 3 category to be 1.7% ,TIRADS 4 category to be 3.3-72.4%,TIRADS 5 category to be 87.5% respectively. This study shows the malignancy risk for TIRADS 3 category to be 20%, 33.33% for TIRADS 4 category and 77.70% for TIRADS 5 category respectively.

In this study the accuracy of TIRADS versus histopathology was 55 % which was in accordance with study done by Joanna Grace Dy et al. [7] (53%) and was slightly lower as compared to others studies done by Debanu De et al. [8] (61%), Ha et al. [11] (69.5%) and Russ et al. [12] (62%) respectively. The reason for low accuracy is possibly due to high false positive rate. The overall sensitivity of TIRADS categories 4 and 5 for malignancy in this study was 92.00% which was lower than that reported by Joanna Grace Dy et al. [7] (98%), Ha et al.[11] (95.5%) and Yoon et al.[13] (97.4%) and higher than the study done by Debanu De et al. [8] (80%).PPV of our study was 50% which was in comparison to PPVs of Debanu De et al. [8] (51%), Horvath et al.[14] (49%) and Ha et al. [15] (44.5%) and higher than the study done by Joanna Grace Dy et al. [7] (35%).The specificity of this study was only 25% which was lower in comparison to other studies (29%-75%).

On reviewing through literatures, there are some suspicious ultrasonographic features that are predictive of malignancy namely, microcalcification, echogenicity, taller than wide nodules and irregular margin with different statistical accuracies.

In the present study microcalcification for prediction of malignancy had Sensitivity, specificity, PPV and NPV of 76%,81%,71% and 64% respectively. The results from the present study revealed that microcalcification is the best suspicious ultrasonographic feature that should be relied upon on the prediction of malignancy in a thyroid nodule. Debanu De et al. [8],Papini et al.[15],Yunus et al. [16],and Salmaslıoğlu et al.[17], found that microcalcification was one of the best specific feature of thyroid malignancy. The features which was second most appreciated was hypoechogenicity which had a sensitivity and specificity of 69% and 75% respectively which was in line with the previous study reports.

The Taller than wide and ill-defined margins had a good specificity at 88% and 88% respectively but lacked sensitivity. Low sensitivity in case of taller than wide category could have occurred by chance. Controversy regarding the ill-defined margin is due to entangled definitions and observer variability.

In spite of having relatively a low accuracy ,this study showed that TIRADS still can be used has a good screening tool for the prediction of malignancy in a patient presenting with a thyroid nodule. Specific ultrasound features such as microcalcification, hypoechogenicity, taller than wide nodule and irregular margins may help in the prediction of malignancy in a thyroid nodule which helps in further management whether to observe or proceed with further appropriate investigation such as FNAC.

LIMITATIONS(S)

Few limitations to this study were identified. First, wide confidence interval was relatively due small sample size. Secondly, it did not represent equally the different TIRADS categories since the majority of the population had at least 1 suspicious ultrasound feature suggestive of malignancy. Third, since it is a single institution study it may not be reflective of the entire population. In order to validate this study findings, we recommend a prospective multicentre study in evaluating the use of TIRADS.

CONCLUSION(S)

TIRADS scoring plays an incremental role in differentiating benign from an malignant thyroid nodule due to its high sensitivity. Risk of malignancy increases significantly with higher TIRADS score. Among individual sonographic features, microcalcification and hypoechogenecity are highly suspicious for malignancy. Hence USG can very well predict malignancy in a patient who is presenting with a palpable thyroid nodule.

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Conflicts of interest

None.

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