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Non-Invasive Risk Stratification Of Thyroid Nodules With Its Histopathological Correlation: A Cross Sectional Study At A Tertiary Care Centre In Pondicherry

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Abstract

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Introduction

The thyroid nodules are very common and almost occur in about 50% adult population with less than 7% being malignant [(1).] The superficial location of the thyroid gland makes the gland easy to scan and high resolution grey scale and color doppler techniques can demonstrate the normal thyroid anatomy and delineate the pathology of the gland with increased clarity [(2).] Ultrasonography of the thyroid gland provides detailed information of the gland and helps in stratification of the nodules and help in making decision regarding FNACs [(3,4).]The thyroid gland is examined using high frequency transducer.The ultrasound of the thyroid gland should be done as a diagnostic ultrasound in patients with suspected thyroid nodule to characterize the lesion [(5).]

The ultrasound of the thyroid gland nodule were categorised under a reporting system named "Thyroid Imaging, Reporting and Data system(TIRADS)" based on five ultrasound features with improvement in guidelines which are helpful in managing the patient [(6).]Further the reporting system was simplified with various studies published by Kwak et al. and Park et al [(7,8)]. Finally, an algorithm was followed in which the thyroid nodules were assigned points on the basis of the echogenicity, shape, composition, size, echogenic foci and margins of the nodule simplified by Tessler et al. and approved by ACR committee widely followed for day to day use thus simplifying, providing a uniform reporting and managing a ndule and reducing the number of FNACs of the nodule[(9)]

Materials And Methods

Affiliation: The study was carried out at the department of Radio-diagnosis, Sri Lakshmi Narayana Institute of medical sciences from January 2020 to July 2021 with aim to evaluate the ultrasound characteristics of thyroid nodules

Source of data –All adult patients referred for USG thyroid to department of Radiodiagnosis, Sri Lakshmi Narayana Institute of Medical Sciences were included in study .

Sample size: 50

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

Study period: 18 months

Study design: Time bound Cross sectional study

Inclusion Criteria

1. Patient who were referred to radiology department for ultrasound thyroid and found to have nodules.
2. Patients with an ability to understand and sign informed consent

Exclusion Criteria

1. Patients not giving consent for the study.
2. Patients who were a known case of thyroid malignancy or for whom nodules were categorized in previous studies.
3. Bleeding disorders as FNAC was contraindicated in such patients.
4. Lactating mothers

Methods

We enrolled the patients referred for ultrasound thyroid and revealed nodule on USG. All the patients with thyroid nodules were examined with hyper extended neck in supine position using Sonix SPQ + Colour doppler and SIEMENS high frequency probe (7MHz). The transverse and longitudinal measurements are taken. Grey mode USG and colour doppler techniques are used to evaluate thyroid nodules.The thyroid nodules were delineated into five categories of TIRADS and were compared with FNAC and histopathology results. The neck was assessed for suspicious lymph nodes.

Statistical Methods:

Categorical variables like age, gender, echogenicity, composition, margins, calcification, shape of lesion, FNAC's and TIRADS categories were presented as percentages. The initial analysis was done using mean and standard deviation for quantitative variables. Association of tumor characteristics with diagnosis (HPE) was assessed using Chi square test and a p value of less than 0.05 was considered as statistically significant. Diagnostic validity of TIRADS categories for diagnosing malignancy was assessed using sensitivity, specificity, positive and negative predictive values against FNAC's and HPE findings. HPE diagnosis was considered as gold standard.(Bethesda system).

Observation And Results:

A total number of 50 participants were included in analysis. The mean age of study population was 40.4 years (range 15 – 60 years).Of the total 50 patients, females (96%) have high predilection in developing thyroid nodule.

The nodules were studied on the basis of five ultrasound features and further differentiated into benign and malignant with the FNAC and histopathological finding.

Echogenecity: In our study out of 50 cases; 37 nodules were hyperechoic, in which 75% benign and 25% malignant. 6 nodules were anechoic which was 100% benign. 5 nodules were hypo echoic in which 20% were benign and 80% malignant and 2 lesion which appeared very hypoechoic was 100% malignant.

Composition:

Of the 50 nodules which were evaluated, 10 nodules appeared cystic/ spongiform nature 80% nodules of this category were benign and 20% malignant. The 33 nodules with mixed composition were 75.8% benign and 24.2% wmalignant and 7 nodules with solid composition turned out to be 28.6% and 71.4% benign and malignant nature respectively.

Margins:

Majority of the nodules (45) were well defined with 77.8% benign nature and remaining 22.2% were malignant. Four nodules were showing irregular margin and one nodule which had extrathyroidal extension both were 100% malignant.

Echogenic Foci(Calcification):

Of the 50 nodules, 33 nodules (66%) were not having calcification or comet tail artefact which were 84.9% benign and 15.1% nodules were proven malignant. The 4 nodules (8%) which had macrocalcification were 100% benign. The 2 nodules (4%) with peripheral/rim calcification were also 100% benign. The 11 nodules (22%) proved 90.9% malignant and 9.1% benign.

Dimensions:

Predominantly, 47 nodules (94%) which were wider than taller was 74.5% benign and 25.5% malignant. The remaining 3 nodules (6%) which were taller than wider were 100% malignant.

All the nodules were evaluated with five salient ultrasound features and was scored with TIRADS scoring. There were 14 nodules (28%) under the category TIRADS 1, 20 nodules (40%) under

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TIRADS 2, 4 nodules (8%) under TIRADS 3 and nodules (12%) in each category TIRADS 4 and 5.

Distribution of sample based on Sensitivity and specificity for ultrasound features

	Total (n=50)	**Malignant (HPE) (n=15)**	**Sensitivity**	**Specificity**	**PPV**	**NPV**
Echogenicity						
Anechoic	6	0	0	82.3	0	66
Hyper echoic	37	9	60	20	24.3	53.9
Hypo echoic	5	4	26.7	97.1	80	75.6
Very hypo	2	2	13.3	100	100	73
Composition						
Cystic/spongiform	10	2	13.3	77.1	20	67.5
Mixed	33	8	53.3	28.6	24.2	58.8
Solid	7	5	33.3	94.3	71.4	76.7
Margins						
Smooth / ill defined	45	10	66.7	0	22.2	0
Lobulated/ irregular	4	4	26.7	100	100	76.1
Extra-thyroidal extension	1	1	6.7	100	100	71.4
Calcification						
None/ large comet-tail	33	5	33.3	20	15.2	41.2
Macro-calcification	4	0	0	88.6	0	67.4
Peripheral/rim calcification	2	0	0	94.3	0	68.8
Punctate echogenic foci	11	10	66.7	97.1	90.9	87.2
Shape (Dimension)						
Wider than taller	47	12	80	0	25.5	0

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Taller than wider	3	3	20	100	100	74.5

The ultrasound features were analyzed separately in our study and found that nodules that are very hypoechoic, irregular margins/extrathyroidal extension, punctate echogenic foci and taller than wider lesions have significant positive predictive value. To further asses the reliability of the scoring system the nodules were followed with cytology and surgical histopathology.FNAC results were as follows.The nodules under TIRADS 1 category were 100% benign. 80% nodules of TIRADS 2 category were benign, 10% malignant and 10% were inconclusive.The TIRADS 3, nodules were 75% benign and 25% inconclusive. However, malignant results were nil. In TIRADS 4, 50% were benign,33.3% was malignant and 16.7% were inconclusive. TIRADS 5 category showed 66.6% malignant nodules, 16.7% nodules were benign and 16.7% were inconclusive.

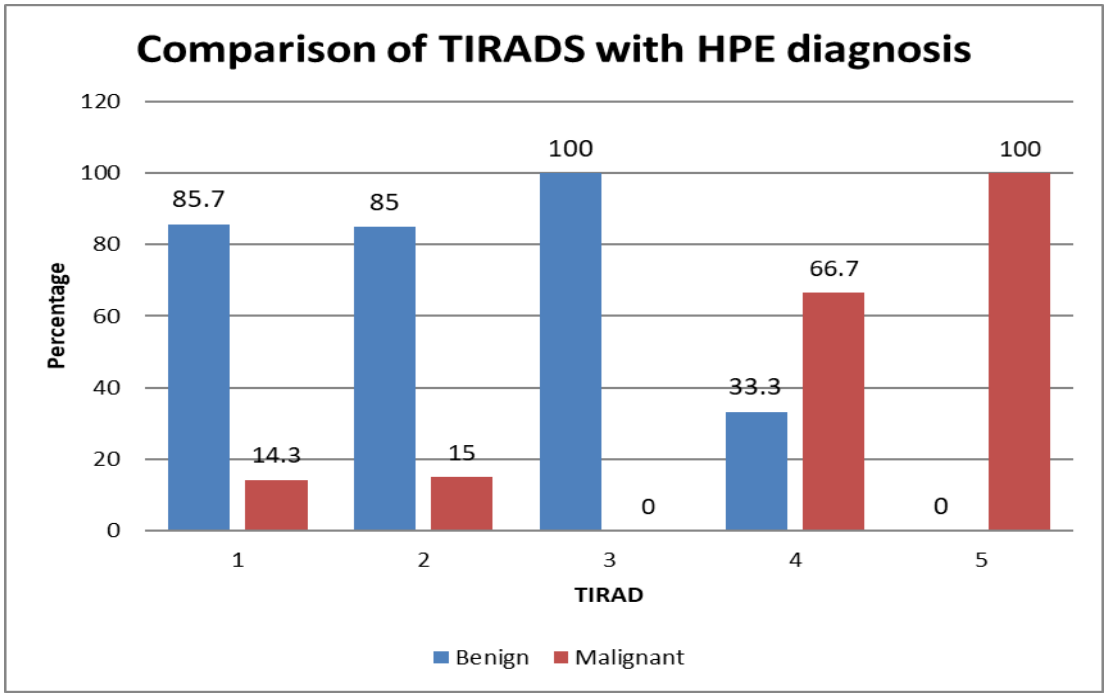
Histopathology:

Out of the 50 nodules, 35 nodules (70%) were benign and 15 nodules (30%) were malignant. The 15 malignant nodules were further characterized based on the types into papillary carcinoma, medullary carcinoma and follicular carcinoma.

Distribution of sample based on benign and different malignant nodules

HPE	Frequency (n=50)	Percentage(%)
Benign	35	70
Papillary carcinoma	11	22
Medullary carcinoma	2	4
Follicular carcinoma	2	4

Bar diagram showing comparison of TIRADS and HPE



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TIRADS category were compared to the histopathological findings for assessing the diagnostic reliability of ultrasound. There is strong correlation between TIRADS category and histopathological findings with significant P value <0.001.The histopathology of nodules in TIRADS 1 were 85.7% benign and 14.3% malignant, TIRADS 2 were 85% benign and 15% malignant, TIRADS 3 were 100% benign, TIRADS 4 were 33.3% benign and 66.7% malignant and TIRADS 5 nodules were 100% malignant.

Distribution of sample based on FNAC and HPE comparison

FNAC	HPE Benign		HPE Malignant		P value
	Number	Percent	Number	Percent	
Inconclusive	3	60	2	40	<0.001
Benign	31	83.8	6	16.2	
Malignant	1	12.5	7	87.5	

The FNAC results were compared with final histopathological findings. Out of the inconclusive nodules (n = 5), 60% were benign and 40% were malignant. In the 37 nodules which were benign in FNAC, 83.8% (n =31) were benign and 16.2% (n =6) were malignant. One nodule which was malignant in the initial cytology was benign when sent for histopathology. 87.5% nodules(n=7) was malignant in both FNAC and histopathology.

Discussion

Ultrasound is a non-invasive method, safe and easily reproducible method in characterization of thyroid nodules based on the five sonological features used to assign a TIRADS score.The current study has been planned to assess the diagnostic utility of TIRADS in differentiating benign and malignant thyroid nodules in a tertiary care teaching hospital. The study has included 50 participants who had nodules more than 1 cm, was graded for a risk of malignancy with TIRADS and were compared with cytology and surgical histopathology.The features which mostly helped in predicting malignancy were punctate echogenic foci, taller than wider lesion and very hypoechoic. The hypo echogenicity were compared echogenicity of strap muscles..Hoang et al. published the ultrasound features which helps in differentiating benign and malignant thyroid nodules(1).

In our study, totally 14 nodules were categorized under TIRADS 1, 12 nodules (85.7%) were benign and 2 nodules (14.3%) with a positive predictive value for malignancy being 14.3%, and 65.7% specificity. Srinivas et al. published that nodules which were completely cystic in nature and hyperechoic were almost always benign (24). The presence of macrocalcification in 4 nodules was 0% malignant which was also substantial to the study published by Srinivas et al. (24).

The 20 nodules which belonged to TIRADS 2 category, 17 nodules (85%) were benign and 3 nodules (15%) were malignant with positive predictive value of and specificity of in our study

In current study, the nodules which were categorized under TIRADS 3 were benign with positive predictive value for malignancy was 0% and 88.6% specific.The nodules which belonged to TIRADS 4 and 5 were 12 nodules with suspicious features.

There were 6 nodules with TIRADS 4 in which 2 were benign (33.3%) and 4 nodules were malignant (66.7%) with positive predictive value 66.7% and specificity value of 94.3%.

The 6 nodules (100%) which belonged to TIRADS 5 category were all malignant in final histopathological correlation in our study.The findings in our study were similar to a prospective study done by Srinivas et al. where the nodules which were categorized under TIRADS 5 showed 100% malignancy risk(24).A study was published by Chng et al. which evaluated 167 nodules from 150 patients and found that malignant nodules were hypoechoic, solid, irregular margins, taller than wider morphology and microcalcification with a good positive predictive value similar to our study (31). However, the features in favour of malignancy were substantial.The cystic/

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spongiform nodule were 12 nodules were 77% specificity and 20% positive predictive value which was similar to a study done by Bonavita et al. in which benign patterns were described based on the spongiform feature as type 1 and colloid nodules were predominantly benign (20).The presence of complete halo around lesion with well-defined/ smooth margins were benign in our study with 0% positive predictive value for malignancy with similar results to studies done by researchers(19,24). The nodules which were well defined/smooth margin were almost benign in a study published by Popli et al and found that the loss of this feature / irregular margin had 88.7% specificity and sensitivity 77.2% for malignancy (32).The nodules with macrocalcification in our study was 4 and all were benign, which was substantial to a retrospective study in which the thyroid nodules were evaluated using five ultrasound features focusing on macrocalcification were 91% benign (33)To compile in our study the features of a benign nodule were echogenicity of nodule more than of the thyroid parenchyma which, absence of calcification and nodule with well-defined margins.The 2 nodules which were very hypoechoic in our study were malignant which were studies to multiple studies. However, the hypoechoic nodule with no suspicious features were found to have intermediate risk whereas the nodules with additional features of suspicion were found to have high risk for malignancy (34).The nodules in our study with irregular margins or extrathyroidal extension were 4 and 1 respectively. Both the features were suspicious with positive predictive value of 100% and found to be malignant on histopathological correlation. Grani et al. described that the interval period could be extended for follow up of patients with nodules which were benign (35).In our study, the nodules with more than one suspicious feature which were categorized under TIRADS 4 and TIRADS 5 were 66.7% and 100% helpful in stratifying malignant risk of a nodule.Finally, when the nodules are assigned to a TIRADS category the results were followed by cytology and surgical histopathology and found to be promising. The TIRADS scoring system would be an important tool in precluding the unnecessary FNAC and stratify the nodules risk for malignant which would be useful in future to radiologist for everyday use. This scoring system will be an invaluable tool in diagnosis of malignant nodules in a non-invasive approach.

Limitations

1. Firstly, the major limitation of our study was sample size (50 patients with nodules). The smaller study population may have biased analysis.
2. All patients underwent FNAC which may have led to selection bias of the patients excluding patients who did not require an invasive procedure.
3. The study was done over a limited period, the follow up of patients could not be carried out which led to many patients who were excluded from the study.
4. The gold standard method was histopathology which includes FNAC and surgical excision. Hence, the number of patients who were involved in the study were limited

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.The positive predictive value of TIRADS in stratifying a risk for malignancy in a nodule for category 1,2,3,4 and 5 were 14.3%, 15%, 0%, 66.7% and 100% respectively.Many studies have shown the USG characteristics of thyroid nodules using TI-RADS system.But our study was based on the hypothesis that USG based risk stratification of nodules is accurate and hence unnecessary invasive procedure like FNAC/biopsy can be avoided in cases of a benign nodule and thus pave a way for better patient care.Further studies with larger sample size and follow up are required to prove this hypothesis which can reduce the patients cost, avoid unnecessary invasion and to prevent complications.

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