

Risk Stratification of Thyroid Nodules Comparative Study Between Ti-Rads, Cytology and Histopathology

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Introduction

A thyroid nodule is defined as a lesion that is distinct and may be differentiated from the surrounding thyroid parenchyma by clinical examination, Ultrasound or other sensitive imaging modalities.¹ The prevalence varies from 4 to 7% by just palpation^{2,3} When patients were assessed by ultrasound, the prevalence of a thyroid nodule was as high as 80% among the iodine-deficient parts of India.⁴ This is much higher than diagnosed on clinical examination. The nodules discovered with imaging studies are called "thyroid incidentalomas."^{5,6} The correlation between imaging methods and the prevalence reported at surgery and autopsy ranges between 50 and 65%.⁷

The importance of the evaluation of thyroid nodules is the possibility of malignancy. The incidence of thyroid cancer is low (1-1.8 per 100,000).⁸ There are vast differences in the reported percentage of malignancy among the clinically or thyroid nodules detected by radiologically.

The average prevalence of malignancy rates across the world in thyroid nodules, from 4.0 to 6.5% on evaluation by an invasive procedure.^{9,10} There are well-established ultrasound findings

that differentiate benign and malignant thyroid nodules.^{11,12,13} There are several classification systems which categorise thyroid nodules according to the risk of cancer.^{14,15,16}

The ultrasonographic characteristics of a thyroid nodule associated with a higher incidence of malignancy include hypo echogenicity, increased intra-nodular vascularity, irregular margins, micro calcifications, absent halo, and a taller than-wide shape measured in the transverse dimension.¹⁷

Several benign and malignant ultrasound gray scale and Doppler features have emerged in the last decade that may be used in various ways to assign probabilities, along with another method based on the Breast Imaging Reporting and Data System (BIRADS), Thyroid Imaging Reporting and Data Systems (TIRADS) of thyroid nodules have been proposed for risk stratification.¹⁸

Fine-needle aspiration (FNA) is considered a cost-effective method and accurate for evaluating thyroid nodules, for the differential diagnosis of these thyroid nodules, with high diagnostic sensitivity and specificity.^{19,20,21}

The purpose of the current research is to evaluate the reliability of TIRADS in determining the malignancy in the thyroid nodules that invasive cytology and surgery can be avoided in the low-risk group.

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Materials and Methods

Type of Study: Prospective observational study.

Study Setting: Department of General Surgery, Tertiary Care Centre.

Study Period: November 2017 to September 2019.

Study Sample: 77 cases admitted in General Surgery Ward with nodular thyroid enlargement and underwent thyroidectomy.

Methodology

Demographic data and risk factors for thyroid malignancy, along with the history of the patient were recorded in the proforma. All selected cases subjected to Ultrasonography, and ACR-TIRADS score obtained. FNAC was done and reported according to the Bethesda system of Cytopathology reporting.

Patients posted for thyroidectomy, and Histopathological report of the specimen collected. In the end, TIRADS score compared with the FNAC, and HPE reports in assessing or predicting the malignancy in a thyroid nodule.

Results

Table 1: Age distribution in the study population.

| Age in years | No of Cases | Percentage |
|--------------|-------------|------------|
| 13-20 | 1 | 2 |
| 21-30 | 10 | 13 |
| 31-40 | 23 | 28 |
| 41-50 | 24 | 31 |
| 51-60 | 12 | 16 |
| 61-70 | 5 | 7 |
| >70 | 2 | 3 |
| Total | 77 | 100 |

Table 2: Sex distribution in the study population.

| Sex | No of Cases | Percentage |
|--------|-------------|------------|
| Male | 10 | 13 |
| Female | 67 | 87 |
| Total | 77 | 100 |

Table 3: Composition of the Thyroid Nodules.

| Composition | Score | No of Cases | Percentage |
|----------------------|-------|-------------|------------|
| Cystic/spongiform | 0 | 0 | 0 |
| Mixed cystic & solid | 1 | 58 | 75 |
| Completely solid | 2 | 19 | 25 |

Table 4: Echogenicity of the Thyroid Nodules.

| Echogenicity | Score | No of Cases | Percentage |
|--------------------|-------|-------------|------------|
| Anechoic | 0 | 8 | 10 |
| Hyper or isoechoic | 1 | 47 | 61 |
| Hypoechoic | 2 | 22 | 29 |
| Very hypoechoic | 3 | 0 | 0 |

Table 5: Shape of the Thyroid Nodules.

| Shape | Score | No of Cases | Percentage |
|------------------|-------|-------------|------------|
| Wider than tall | 0 | 67 | 87 |
| Taller than wide | 3 | 10 | 13 |

Table 6: Margin of the Thyroid Nodules.

| Margin | Score | No of Cases | Percentage |
|---------------------------|-------|-------------|------------|
| Smooth /ill-defined | 0 | 71 | 92 |
| Lobular /irregular | 2 | 6 | 8 |
| Extra thyroidal extension | 3 | 0 | 0 |

Table 7: Echogenic foci in the Thyroid Nodules.

| Echogenic foci | Score | No of Cases | Percentage |
|------------------------------|-------|-------------|------------|
| None or comet tail artefact | 0 | 44 | 57 |
| Macrocalcifications | 1 | 8 | 10 |
| Peripheral rim calcification | 2 | 1 | 2 |
| Punctate echogenic foci | 3 | 24 | 31 |

Table 8: TIRADS score for the Thyroid Nodules.

| TIRADS | Grade | No of Cases | Percentage |
|-----------------------|-------|-------------|------------|
| Benign | TR1 | 0 | 0 |
| Not suspicious | TR2 | 32 | 42 |
| Mild suspicious | TR3 | 16 | 21 |
| Moderately suspicious | TR4 | 12 | 15 |
| Highly suspicious | TR5 | 17 | 22 |

Table 9: FNAC of the Thyroid Nodules.

| FNAC | Bethesda Class | No of Cases | Percentage |
|-----------------------------------|----------------|-------------|------------|
| Non diagnostic | I | 0 | 0 |
| Benign | II | 52 | 68 |
| AUS/FLUS | III | 1 | 2 |
| Suspicious of follicular neoplasm | IV | 5 | 6 |
| Suspicious for malignancy | V | 7 | 9 |
| Malignant | VI | 12 | 15 |

Table 10: Histopathology Report of Thyroidectomy specimen.

| Histopathology Report | No of Cases | Percentage |
|------------------------|-------------|------------|
| Nodular Goitre | 44 | 57 |
| Hashimotos Thyroiditis | 9 | 12 |
| Papillary Carcinoma | 18 | 23 |
| Follicular Adenoma | 4 | 5 |
| Follicular Carcinoma | 2 | 3 |

Table 11: Comparison of TIRADS, FNAC and Histopathology Reports.

| TIRADS Grade | | FNAC | | | HPE | |
|--------------|---------|---------|-----------|-------------------|---------|-----------|
| | | Benign | Malignant | Follicular lesion | Benign | Malignant |
| TR1 | 0 | - | - | - | - | - |
| | 32 | 32 | - | - | 32 | - |
| TR2 | (41.5%) | (100%) | | | (100%) | |
| | 16 | 15 | 1 | - | 15 | 1 |
| TR3 | (21%) | (93.7%) | (6.3%) | | (93.7%) | (6.3%) |
| | 12 | 5 | 2 | 5 | 9 | 3 |
| TR4 | (15.5%) | (41.7%) | (16.6%) | (41.7%) | (75%) | (25%) |
| | 17 | 1 | 16 | - | 1 | 16 |
| TR5 | (22%) | (5.8%) | (94.2%) | | (5.8%) | (94.2%) |

Table 12: Comparison of TI-RADS with FNAC.

| | FNAC Malignant (Positive) | FNAC Benign (Negative) | Total |
|---------------------|---------------------------|------------------------|-------|
| TR4, TR5 (Positive) | 23 | 6 | 29 |
| TR2, TR3 (Negative) | 1 | 47 | 48 |
| Total | 24 | 53 | 77 |

Table 13: Comparison of TIRADS with histopathology.

| | HPE Benign | HPE Malignant | Total |
|---------------------|------------|---------------|-------|
| TR2, TR3 (Negative) | 47 | 1 | 48 |
| TR4, TR5 (Positive) | 10 | 19 | 29 |
| Total | 57 | 20 | 77 |

Discussion

Initial analysis of thyroid nodules based on the following.

- Proper history, along with a clinical examination of the patient,
- Lab tests -thyroid function tests,
- Thyroid USG, and
- USG-guided FNAC based on TI-RADS features.²²

It is similar to the triple assessment of the breast lumps. Unlike breast lumps, TI-RADS US features are still not routinely used in several medical institutes.²³

The accessibility of TI-RADS and validation of this USG classification system by the ACR permit a precise both clinical and pathological correlation.

As noted from the previous studies, a robust clinical and pathological correlation will guide in defining the risk of malignancy and proper direct management of thyroid lesions.²⁴⁻²⁷ However, a general agreement not yet mentioned gives the difficulty in reproducing different classification systems or even the low correlation between the USG reports and FNAC.²⁸

Of all the systems, the classification proposed by ACR-TIRADS is simple and similar to BIRADS system, which is in use for many years and is familiar to many radiologists. Therefore, we assessed thyroid nodules based on ACR-TIRADS.²⁹⁻³⁸

Age and Sex Distribution

In this study, the peak incidence noted in the age group of 41-50 years. The youngest patient was 18yrs, and the eldest was 72 yrs. In this study, 67 were female, and 10 were males. A female to male's ratio in the study was 6.7:1.

Abdelkader et al.³⁹ studied 100 patients; 22 males and 78 females with mean age 43.7 ±11.5; range: 22-60 years.

In Periakaruppan, et al.,⁴⁰ A total of 184 patients included in the study, out of which females are 156. These nodules mostly found among 30-60 years of life. The patients in this age group are 137 patients, about 75% of our study population.

In Chandramohan, et al.⁴¹ Out of 272 nodules, 154 benign nodules (119 were females, 35 were males) and among 118 malignant nodules (75 were females, 43 were males). Malignancy was more common among male patients presenting with a thyroid nodule (P=0.01).

When comparing our results with the results of a study done by Singaporewalla et al.⁴² the US of thyroid nodules in our study had a comparable sensitivity in predicting malignancy (82.45% versus 71.5%) and specificity (95% versus 84%). We also had a better NPV of TI-RADS score predicting malignancy (65.5% versus 91.5%) and PPV 97.92%.

In our study, there were no cases with TR1. Among the 32 cases in TR2 FNAC and histopathology was proved to be benign in all the 100% cases. 16 cases were in TR3 among them FNAC and histopathology showed benign aetiology in 15 and malignant features in 1 case subsequently. In 12 cases with TR4 5 were benign, two were malignant, and 5 showed follicular lesions on FNAC, and on histopathology 9 turned out to be benign lesions, and three were of malignancy. Among the 17 cases in TR5 16 were malignant and one was benign on FNAC and histopathology.

Among 77 cases, of a total 48 cases which labeled as benign (mostly TR2, TR3), 47 cases are also proven to be benign, and only one case turned out as malignant on FNAC. Of a total of 29 cases which labelled as malignant (TR 4, TR 5) on TR-RADS, 23 are proven to be malignant on FNAC, and only six turned out as benign on FNAC.

According to these findings, TI-RADS have a sensitivity of about 95.83%, Specificity of approximately 88.67%, the positive predictive value of approximately 79.31%, the negative predictive value of approximately 97.92% compared with FNAC (cytology).

Among 77 cases, of a total 48 cases which labeled as benign (mostly TR2, TR3), 47 cases are also proven to be benign, and only one case turned out as malignant on HPE. Of a total of 29 cases which labeled as malignant (TR4, TR5) on TR-RADS, 19 are proven to be malignant, and 19 turned out as benign on HPE.

According to these findings, TI-RADS have a sensitivity of about 82.45%, Specificity of about 95%, positive predictive value (PPV) of approximately 97.92%, negative predictive value (NPV) of approximately 65.52% compared with HPE.

In Singaporewalla et al.⁴² study, they had 20 patients classified as TI-RADS 5 (malignant on the US), FNAC biopsy showed only 12 confirmed as malignant, and the remaining were benign. That gives them a 60% accuracy of US in predicting malignancy. Similarly, in this study, they found that among the 14 cases categorized as TIRADS 5, 10/14 cases had an FNAC biopsy established as cancer (71.4% accuracy).

Ultrasound impression of thyroid nodules had lower sensitivity in predicting malignancy (70.6% compared to 88%) but higher specificity (90.4% compared to 49%). They also had a higher positive and negative predictive value of TIRADS score predicting malignancy as well (60% compared to 49%, and 93.8% compared to 88%, respectively). Accuracy was 83% overall. In this study, the risk of malignancy for the different TIRADS categories was 0% (TIRADS2), 9.5% (TIRADS 3), 33.3% (TIRADS 4) and 60% (TIRADS 5).

Abdelkader et al.³⁹ study in 55 patients with thyroid nodules of probably benign (TI-RADS3) nature and FNA cytology established the same in 45/55 patients showing 82% concordance rate between US and FNAC.

Among the 31 cases that categorized as TI-RADS4 (indeterminate), 8/31 cases were benign on FNAC (Bethesda II), 1/31 cases had an FNAC biopsy established as cancer. Remaining 22/31 patients were under Bethesda III, IV, and V, giving a 70.9% concordance rate between the US and FNAC.

Among the 14 cases that categorized as TI-RADS 5 (malignant on the US), 2/14 patients were benign on FNAC biopsy (false-positive of the US), 5/14 cases were suspicious on FNAC (Bethesda IV), and 7/14 cases had an FNAC biopsy established as cancer giving a 50% concordance between the US and FNAC. From the previous results, the overall concordance rate between US TI-RADS and Bethesda is 67.6%.

The final concordance rate of US TI-RADS with the final histopathological results for predicting malignancy was 75.4% with a sensitivity 76.9% and specificity 91.3%, PPV 71.4%, and NPV 76.4%. The concordance rate of FNAC with the final HPE findings for identifying malignancy was 95% with a sensitivity and specificity of 81.8% and 98% respectively, PPV 90%, and NPV 96%.

In Chandramohan, et al.⁴⁴ study in 168 cases, The PPV for malignancy of TIRADS 2, 3, 4a, 4b, 4c, and 5 categories was 6.6%, 32%, 36%, 64%, 59%, and 91%, respectively. In conclusion, the PPV for malignancy was high for TIRADS category five and 4c nodules. Reassigning TIRADS category 4a nodules as TIRADS3 will improve the PPV and specificity of TIRADS. In Kwak et al.⁴⁵ describes 0%, 1.7%, 3.3%, 9.2%, 44.4–72.4%, and 87.5% risk of malignancy for TIRADS 2, 3, 4a, 4b, 4c, and 5 categories, respectively. However, in a subsequent retrospective validation study, the authors found a 7.3% and 8.3, 96.6% risk of malignancy in TIRADS 3 and TIRADS 4,5 categories of thyroid nodules.

According to Periakaruppan, et al.⁴⁰, study out of the 184 nodules, 117 categorised under TIRADS 2, none turned out to be under Bethesda IV or higher, which means none of the nodules turned out to be malignant. Thirteen classified under TIRADS4, and 9 as TIRADS 5 category. Among the 45 nodules labelled as TIRADS 3, 42 nodules are Bethesda II and one nodule each in Bethesda I, III, and IV, on FNAC respectively.

Few nodules which appeared suspicious on USG are classified as TIRADS 4 and TIRADS5 but turned out to be benign in FNAC according to Bethesda classification. Considering all nodules, the proportion of nodules being malignant classified as TIRADS2 were 0.0, TIRADS3 were 7.7, TIRADS 4 was 38.4, and TIRADS5 was 53.9%. In this study, sensitivity is 92.3%, specificity is 94.15%, and PPV is 54.54%, and NPV is 99.38%. A significant association is noted between TIRADS and Bethesda system of classification ($P < 0.001$). In a study by Stephanie A. Fish⁴³, a total of 832 nodules evaluated with ultrasound before FNA cytology. Seventy-nine nodules measured lower than 1cm and removed from the study. Another 251 nodules excluded due to indeterminate cytology results. The final study included 502 nodules in 477 patients.

Thirty-six (7.2%) nodules determined to be malignant. In general, strictly following the recommendations from the risk-stratification systems decreased the number of FNAs to between 17.1% and 53.4%. The most effective method was ACR TIRADS, which would have reduced the biopsy number by greater than half (53.4%) with 2.2% false-negative rate. The false-negative rate was due to nodules with a final diagnosis of malignancy, but no biopsy recommendation based on the risk-stratification system. Many more biopsies recommended as most of the systems had similar discriminatory capacities to identify malignancy. K-TIRADS was the poor performer, as it reduced the number of biopsies by only 17.1%. Eleven nodules diagnosed as malignant would have misclassified as not requiring FNA by at least one of the TIRADS systems. All five systems missed three cancers; which were either isoechoic or hyperechoic and had no other suspicious features. The best performance is by ACR TIRADS by classifying more than half of FNA cytology as unnecessary with only 2.2% false-negative rate.

Conclusion

In conclusion, from the study, it was made out that the PPV for malignancy was high for TIRADS

category 5 and 4 nodules. TIRADS is a straight forward and practical method of assessing thyroid nodules and can be used in practice as the overall agreement between observers for assigning TIRADS category was substantial.

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Conflict of Interest: Nil

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