Radio Pathological Correlation of Thyroid Nodules Using Tirads Based Ultrasound Classification and Bethesda Classification for FNAC: a Prospective Study

Richa TIWARI1, Ruchi GUPTA2, Amit Kumar VERMA3, Sanjeev KUMAR4, Yogita KATIYAR5

Abstract

Background: Thyroid gland is afflicted by various pathologies amongst which nodules are the cause of maximum concern because of their malignant potential. With the introduction of high resolution ultrasound and use of Thyroid imaging reporting and data system (TIRADS) classification as a widely used universal grading system, there has been reduced inter-observer variability and increased inter-departmental communication. In this study, we studied the TIRADS ultrasound grading as a screening tool and compared it with the BETHESDA grading on FNAC. Material and methods: 200 patients with thyroid nodules were subjected to ultrasound and USG guided FNAC. Each was assigned a TIRADS and Bethesda grade. Findings were compared to assess the sensitivity, specificity, PPV (positive predictive value) and NPV (negative predictive value) of ultrasound in differentiating benign from malignant nodules. Result: Out of 200 nodules examined, 116 nodules belonged to TIRADS 2 while 44, 13 and 27 belonged to TIRADS 3, 4 and 5 respectively. On FNAC, 162 patients belonged Bethesda 2 & 12, 7, 15 and 4 to Bethesda 3, 4, 5 and 6 respectively. The sensitivity, specificity, PPV and NPV of ultrasound were found to be 92.3, 90.8, 60 and 98.75 % respectively. Conclusion: TIRADS is an effective risk stratification system which should be routinely used in our clinical practice as it can predict the possibility of a particular nodule for being malignant to a great extent. Especially keeping in mind its high negative predictive value, FNAC can be deferred in TIRADS 2 patients which form a majority of cases reporting to pathology department for thyroid FNAC. Keywords: TIRADS (thyroid image reporting and data system), thyroid nodules, fine-needle aspiration cytology, Bethesda.

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INTRODUCTION

Thyroid gland is afflicted by various pathologies ranging from diffuse enlargement (goiter) to nodular lesions and thyroiditis.

Nodules are the cause of maximum concern among all thyroid pathologies because of their malignant potential. There is a wide range of malignant potential among the clinically or radiologically detected thyroid nodules. The average prevalence of malignancy rates across the world in thyroid nodules, as shown by invasive procedure ranges from 4.0 to 6.5%.

The American Thyroid Association defines thyroid nodules as “discrete lesions within the thyroid gland, radiologically distinct from surrounding thyroid parenchyma.” These nodules may be first identified clinically or incidentally on thyroid imaging ( incidentalomas).

Earlier in the absence of any standardized system of USG reporting, there was difficult communication between radiologists and endocrinologists. Then, the introduction of the Thyroid Imaging Reporting and Data System (TIRADS) by the American College of Radiologists was an attempt to study and compare sonographic findings of thyroid nodules to cytological findings. This system was originally proposed by Horvath et al. as a risk stratification system and subsequently modified by Jin Kwak et al. into a more practical and reproducible format.

TIRADS classification originally proposed by Horvath et al. and subsequently modified by Kwak et al. is as follows: TIRADS 1—normal thyroid gland; TIRADS 2—benign lesions (including simple cyst, spongiform nodule, isolated macro calcification and typical sub acute thyroiditis); TIRADS 3—probably benign lesions (no suspicious ultrasound [US] features or nodules that are iso or hyperechogenic); TIRADS 4—suspicious lesions, TIRADS 5—probably malignant lesions (all five suspicious US features); and TIRADS 6—biopsy-proven malignancy.

Ultrasound imaging characteristics which were considered suspicious were (I) solid nodule (II) microcalcifications, (III) irregular or microlobulated margins, (IV) marked hypoechogenicity and (V) taller-than-wide shape. TIRADS 4a had a 5–10% risk of malignancy, while 4b and 4c had a 10–80% risk of malignancy. TIRADS 5 category lesions have 80% risk of malignancy.

The fine-needle aspiration method for studying the thyroid was first developed in Sweden in the Ruduunhelmet hospital of Stockholm in the 1950s. Bethesda classification system established a standar-
Radio Pathological Correlation of Thyroid Nodules Using Tirads Based Ultrasound Classification and Bethesda Classification

Table 1. TIRADS and Bethesda distribution of nodules

<table>
<thead>
<tr>
<th>TIRADS</th>
<th>BETHESDA 2</th>
<th>BETHESDA 3</th>
<th>BETHESDA 4</th>
<th>BETHESDA 5</th>
<th>BETHESDA 6</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>TIRADS 2</td>
<td>114</td>
<td>2</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>116</td>
</tr>
<tr>
<td>TIRADS 3</td>
<td>38</td>
<td>4</td>
<td>1</td>
<td>1</td>
<td>-</td>
<td>44</td>
</tr>
<tr>
<td>TIRADS 4</td>
<td>5</td>
<td>3</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>13</td>
</tr>
<tr>
<td>TIRADS 5</td>
<td>5</td>
<td>3</td>
<td>4</td>
<td>12</td>
<td>3</td>
<td>27</td>
</tr>
<tr>
<td>TOTAL</td>
<td>162</td>
<td>12</td>
<td>7</td>
<td>15</td>
<td>4</td>
<td>200</td>
</tr>
</tbody>
</table>

been tabulated in Table 1.

For all the calculations, TIRADS 4/5 and BETHESDA 4/5/6 considered positive for malignancy and the rest as negative.

Thus 80% of nodules (160) belonged to benign and probably benign categories on ultrasound, i.e. TIRADS 2 and TIRADS 3 while 20% belonged to suspicious (TIRADS 4) and malignant (TIRADS 5) categories. Similarly approx 81% nodules belonged to benign (Bethesda 2) grade on FNAC while only 13 were malignant (Bethesda 4, 5 and 6).

Out of 116 nodules belonging to TIRADS 2, none turned out to be Bethesda 4/5/6, thus risk of malignancy in TIRADS 2 was 0%. Out of the two indeterminate FNAC (Bethesda III) amongst these, one patient insisted on repeat FNAC where it was shown be benign hyperplastic nodule (Bethesda II) and other showed no increase in size on interval follow up on 3/6/9 months.

The risk of a malignant FNAC in TIRADS 3, 4 and 5 was 4.5, 38.4 and 70.4% respectively. Thus TIRADS 4 and 5 have 8.5 and 15.6 times chances of malignancy as compared to TIRADS 3 respectively.

Similarly the chances of a benign FNAC (Bethesda II) in TIRADS 2, 3, 4 and 5 was 98.3, 86.3, 38.5 and 18.5 % respectively.

TIRADS and BETHESDA results were cross-tabulated in a 2x2 table (Table 2) with TIRADS 4/5 and BETHESDA 4/5/6 considered positive for malignancy and the rest as negative.

Using this table, the sensitivity, specificity, PPV (positive predictive value) and NPV (negative predictive value) of ultrasound were calculated (considering FNAC as the gold standard) using the below formulas and were found to be as follows:
- Sensitivity (true positive rate) equivalent to a/ a+c = 92.3%.
- Specificity (true negative rate) equivalent to d/ b+d = 90.8%.
- PPV (proportion of people with a positive test result who actually have the disease) a/ a+b = 60%.
- NPV (proportion of those with a negative result who do not have the disease) d/ c+d = 98.75%.
- Also, there was significant association found between TIRADS and Bethesda (p value was <0.05 using Chi-square test).

**DISCUSSION**

The assessment of thyroid is a multipronged approach involving history with clinical examination, thyroid function tests, ultrasound thyroid and US-guided FNAC.

However until recently, the USG evaluation of thyroid lesions was less standardized. Then with the introduction of TIRADS and the endorsement of this classification system by the American College of Radiologists, we have a reproducible risk stratification system similar to BIRADS grading system for breast lesions. This system attempts to correlate sonographic features to cytological classification and gives an estimate of chances of malignancy in a particular 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 is to be emphasized here

Table 2. 2 x 2 table for diagnostic test results

<table>
<thead>
<tr>
<th>TIRADS (SCREENING TEST)</th>
<th>FNAC</th>
<th></th>
<th></th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>POSITIVE (malignancy positive)</td>
<td>NEGATIVE (malignancy negative)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>POSITIVE</td>
<td>24(a)</td>
<td>16(b)</td>
<td></td>
<td>40(a+b)</td>
</tr>
<tr>
<td>NEGATIVE</td>
<td>02(c)</td>
<td>158(d)</td>
<td></td>
<td>160(c+d)</td>
</tr>
<tr>
<td>TOTAL</td>
<td>26(a+c)</td>
<td>174(b+d)</td>
<td></td>
<td>200</td>
</tr>
</tbody>
</table>
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Table 3. Comparative evaluation of risk of malignancy amongst various TIRADS grades

<table>
<thead>
<tr>
<th>TIRADS</th>
<th>Our study (in %)</th>
<th>Singaporewalla et al (in %)</th>
<th>Periakaruppan et al (in %)</th>
<th>Horvath et al (in %)</th>
<th>Kwak et al (in %)</th>
<th>Moifo et al (in %)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>4.5</td>
<td>9.5</td>
<td>2.2</td>
<td>14.1</td>
<td>1.7</td>
<td>2.2</td>
</tr>
<tr>
<td>4</td>
<td>38.4</td>
<td>33.3</td>
<td>38.5</td>
<td>45</td>
<td>3.3-72.4</td>
<td>5.9-57.9</td>
</tr>
<tr>
<td>5</td>
<td>70.4</td>
<td>60</td>
<td>77.8</td>
<td>89.6</td>
<td>87.5</td>
<td>100</td>
</tr>
</tbody>
</table>

Table 4. Comparative evaluation of test characteristics in various studies

<table>
<thead>
<tr>
<th></th>
<th>OUR STUDY</th>
<th>Singaporewalla et al</th>
<th>Periakaruppan et al</th>
</tr>
</thead>
<tbody>
<tr>
<td>SENSITIVITY</td>
<td>92.3</td>
<td>70.6</td>
<td>92.3</td>
</tr>
<tr>
<td>SPECIFICITY</td>
<td>90.8</td>
<td>90.4</td>
<td>94.1</td>
</tr>
<tr>
<td>PPV</td>
<td>60</td>
<td>60</td>
<td>54.5</td>
</tr>
<tr>
<td>NPV</td>
<td>98.75</td>
<td>93.8</td>
<td>99.4</td>
</tr>
</tbody>
</table>

that it is not the presence or the absence of a single feature on ultrasound which is important. Rather the presence of at least two of the USG features is more accurate in differentiating a benign nodule and a high-risk nodule for malignancy.\(^{11,12}\)

In our study, we found that more than half of thyroid nodules (56%) belonged to TIRADS 2 having 0% chances of malignancy. So we can take a more informed decision about subsequent FNAC which although is a readily available and inexpensive test but also minimally invasive at the same time. But it is a prerequisite that the radiologist performing ultrasound and guided FNACs has had a good learning curve and has audited his/her results in comparison to FNAC.

Comparing our results with previous studies, female predisposition\(^{13}\) was similar to the studies of G. Periakaruppan et al.\(^{14}\) and K P Gupta et al.\(^{15}\) where 84% and 74% patients were females respectively. This might be explained by the effect of estrogen and progesterone, as pregnancy has been shown to be related to increased nodule size and new nodule development.\(^{16}\)

Comparative evaluation of risk of malignancy for each TIRADS grade was done with previous studies and is shown in Table 3.

The findings are similar in all except for slightly reduced percentage of malignancy in TIRADS 4 and 5 of Singaporewalla et al.\(^{17}\) as here only Bethesda 5 and 6 were included in malignant and not Bethesda 4 unlike others.

Table 4 compares the test characteristics (sensitivity, specificity, PPV and NPV) of our screening test (TIRADS) with those of prior studies by Singaporewalla et al.\(^{18}\) and Periakaruppan et al.\(^{15}\) and shows similar results.

One of the shortcomings of our study was that TIRADS 4 was considered as a single class and not classified into 4A, 4B and 4C which vary widely as far as malignant potential is considered.

**CONCLUSION**

TIRADS is an ultrasound-based effective risk stratification system correlating cytological and radiological features. It can predict the chances of a particular thyroid nodule for being malignant to a great extent. Especially keeping in mind its high negative predictive value and the fact that TIRADS 2 nodules have 0% chances of malignancy, FNAC can be deferred in these TIRADS 2 patients. It will also help reduce the burden on pathology department as these patients form the bulk of nodules reporting for thyroid FNAC.

**Compliance with ethics requirements:** The authors declare no conflict of interest regarding this article. The authors declare that all the procedures and experiments of this study respect the ethical standards in the Helsinki Declaration of 1975, as revised in 2008(5), as well as the national law. Informed consent was obtained from all the patients included in the study.
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References
