Role of TIRADS in nodular thyroid disease

Poster No.: B-0810
Congress: ECR 2014
Type: Scientific Paper
Authors: B. Raghavan, S. Paul; Chennai/IN
Keywords: Head and neck, Oncology, Thyroid / Parathyroids, Ultrasound, Efficacy studies, Pathology
DOI: 10.1594/ecr2014/B-0810

Any information contained in this pdf file is automatically generated from digital material submitted to EPOS by third parties in the form of scientific presentations. References to any names, marks, products, or services of third parties or hypertext links to third-party sites or information are provided solely as a convenience to you and do not in any way constitute or imply ECR's endorsement, sponsorship or recommendation of the third party, information, product or service. ECR is not responsible for the content of these pages and does not make any representations regarding the content or accuracy of material in this file.

As per copyright regulations, any unauthorised use of the material or parts thereof as well as commercial reproduction or multiple distribution by any traditional or electronically based reproduction/publication method is strictly prohibited.

You agree to defend, indemnify, and hold ECR harmless from and against any and all claims, damages, costs, and expenses, including attorneys' fees, arising from or related to your use of these pages.

Please note: Links to movies, ppt slideshows and any other multimedia files are not available in the pdf version of presentations.

www.myESR.org
Purpose

1. To classify nodular thyroid disease according to TIRADS classification.

2. To correlate TIRADS categories with the rates of malignancy in each category, in select study population.

3. To assess reliability of TIRADS classification.

Background

Nodular thyroid disease is very common, especially in females. Thyroid cancer is a relatively rare disorder as compared to the frequency of nodular thyroid disease detected on sonography. USG evaluation addresses the presence of nodular thyroid disease and characterises it and selects nodules which need image guided FNAC, the gold standard.\textsuperscript{1},\textsuperscript{2}.

However, no single determinant exists for categorisation of thyroid nodules into benign and malignant.

Horvath et.al\textsuperscript{3} envisaged the categorisation of thyroid nodules using multiple sonographic determinants so that an overall stratification of risk of malignancy can be done. This was based on BIRADS system of classification of breast lesions as proposed by American College of Radiology. The chance of malignancy in each group was adopted from those applied to each corresponding BIRADS subgroup. This new classification system was based on the sonographic features to streamline reporting of thyroid pathologies, thus reducing the degree of miscommunication between physicians and patients. This system was named as Thyroid Imaging Reporting and Data System (TIRADS); following the BI-RADS for breast lesions as a model\textsuperscript{3}.

The following categories were established:

TIRADS 1 - Normal thyroid gland
TIRADS 2 - Benign findings (0% chance of malignancy)
TIRADS 3 - Probably benign (< 5% chance of malignancy)
TIRADS 4 - Suspicious nodules. This category was subclassified into
4A (chance of malignancy 5 to 10%) and
4B (chance of malignancy 10 to 80%).
TIRADS 5 - Probably malignant nodules (chance of malignancy > 80%)
TIRADS 6 - This category includes biopsy proven malignant nodules.
Horvath et al. [3] classified nodular thyroid disease into TIRADS based on 10 patterns of nodules. This classification was further simplified by Kwak et al. who proposed categorisation of nodules into TIRADS based on the number of sonographic features suggestive of malignancy.

Kwak et al. [4] proposed that there is a significant increase in risk of malignancy as the number of suspicious sonographic features increased. Thus they reclassified the TIRADS according to the number of suspicious features:

TIRADS 5 - five suspicious sonographic features
TIRADS 4 - less than five suspicious sonographic features.

This was further subdivided into 4A, 4B and 4C.

TIRADS 3 - no suspicious sonographic features.

In their classification there was no categorical definition in segregating nodules into TIRADS 2 and TIRADS 3.

We have used a combination of both the systems for better co-relation.
Methods and materials

Patients

This study is a prospective, single blinded, single centre trial in patients presenting with thyroid nodules in Apollo Specialty Hospital, Chennai, India, between 2011 to 2013. 248 nodules (in 130 patients) were sequentially included, of which 229 thyroid nodules (in 111 patients) were analysed. 11 nodules had inadequate cytology due to haemorrhagic smear. In 8 nodules, cytology was not available as the patients were lost to follow up.

The nodules were evaluated in with Philips IU 22 machine with a 12-5 MHz linear probe and Siemens Acuson S 2000 machine using a VFX 9-4 MHz linear probe with an average frequency of 8 MHz and were characterised according to their sonographic features. Ultrasound variables were: size, nature, echo texture, echogenicity, margins, halo, shape (taller than wide), calcification, doppler, significant cervical adenopathy. The nodules were categorised into four categories and the number of nodules of in each category were counted. The categories are as follows: < 1 cm, 1 - 2 cm, 2 - 3 cm and > 3 cm.

We used a combination from Horvath et.al[3] and Kwak J Y, et. al.[4] to stratify nodules.

These nodules were characterised into TIRADS following the ten pattern correlation approach as proposed by Horvath et.al[3] for TIRADS 2 and 3; and according to the number of suspicious sonographic features proposed by Kwak J Y, et. al.[4] for TIRADS 4 and 5.

Counting the number of suspicious sonographic features is more practical than pattern matching in classification of TIRADS 4A, 4B and 5.

The parameters used for identifying suspicious nodules were:

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Feature suggestive of malignancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of nodules</td>
<td>Solitary</td>
</tr>
<tr>
<td>Echogenicity</td>
<td>Hypoechoic with relation to thyroid parenchyma</td>
</tr>
<tr>
<td>Margins</td>
<td>Irregular, spiculated[^5]</td>
</tr>
<tr>
<td>Calcification</td>
<td>Microcalcification[^6]</td>
</tr>
</tbody>
</table>
Doppler & Intranodular vascularity [7]
Cervical adenopathy & Significant

**TIRADS**

- Number of features suggesting malignant nodule
  - 4A: One
  - 4B: Two or three
  - 5: More than three

Colloid nodules were classified under TIRADS 2 (Fig. 1 on page ___)
pseudonodules in thyroiditis classified under TIRADS 3 (Fig. 2 on page 7);
sonographically suspicious nodules categorised as TIRADS 4 [subclassified into 4A (Fig. 3 on page 8) and 4B (Fig. 4 on page 9)];

and nodules with sonographic features consistent with malignancy were included in TIRADS 5 (Fig. 5 on page 9).

TIRADS 2 lesions are benign and do not require any FNAC correlation. TIRADS 3 nodules need follow up and are biopsied only if clinically indicated. TIRADS 4 lesions have one or more sonographic features of malignancy and need biopsy correlation. According to the study of Wienke J R, et. al. [8] 69% of histologically benign nodules have at least 1 sonographic feature suggestive of malignancy. Such nodules are classified as TIRADS 4A by Kwak J Y, et. al.[4].

TIRADS 5 lesions have obvious sonographic features of malignancy which should be confirmed by FNAC prior to surgical excision, if indicated.

Under real time ultrasound guidance FNAC was performed, a maximum of 3 separate needle passes were made in different locations especially in case of large nodules (> 2.5 cm).

**Statistical analysis:**

Details of each patient including the cytology report was entered in a proforma and the interpreted data stored in Microsoft Excel and the data processed using SSPS for Windows, Version 17.
Categorical data was presented by frequency or percentage and it was analyzed by using Chi-square and Fisher exact test. Univariate and multiple logistic regression analysis for concordance with malignancy were individually performed for each sonographic feature as well as each subgroup of TIRADS. All the analysis was done by using SSPS for Windows, Version 17. P-value of less than 0.054 was considered as significant.
Fig. 1: TIRADS 2: Upper nodule - spongiform or grid appearance, peripheral vascularity (FNAC: Colloid nodule); Lower nodule - anechoic (FNAC: Colloid cyst).

© RADIOLOGY, Apollo speciality hospital - Chennai/IN
Fig. 2: TIRADS 3: Psuedonodule in thyroiditis, almost involving the entire nodule. FNAC: Thyroiditis on the background of colloid nodule.

© RADIOLOGY, Apollo speciality hospital - Chennai/IN
**Fig. 3:** TIRADS 4A: Single sonographic feature of malignancy (intranodular vascularity). FNAC: Colloid nodule.

© RADIOLOGY, Apollo speciality hospital - Chennai/IN

**Fig. 4:** TIRADS 4B: Three features suggesting malignancy - Hypoechoic, ill-defined margins, internal vascularity. FNAC: Colloid nodule

© RADIOLOGY, Apollo speciality hospital - Chennai/IN
**Fig. 5:** TIRADS 5: More than three parameters suggesting malignancy - Hypoechoic, irregular margin, microcalcifications, internal vascularity. FNAC: Papillary carcinoma of thyroid.

© RADIOLOGY, Apollo speciality hospital - Chennai/IN
Results

The pathological distribution of nodules in our study group is shown in Fig. 6 on page 14.

Correlation of various sonographic characters with malignancy:

Univariate logistic regression analysis for concordance of each sonographic variable with malignancy shows significant correlation with the following parameters:

<table>
<thead>
<tr>
<th>Sonographic parameter</th>
<th>Odds ratio by univariate logistic regression analysis</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Solitary nodule</td>
<td>3.296</td>
<td>0.025</td>
</tr>
<tr>
<td>Hypoechoic nodule</td>
<td>6.883</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Irregular margin</td>
<td>89.310</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Microcalcification</td>
<td>58.667</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Intranodular vascularity</td>
<td>16.625</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Significant cervical adenopathy</td>
<td>15.214</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

Size distribution of nodules

<table>
<thead>
<tr>
<th>Size</th>
<th>Number of nodules</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 1 cm</td>
<td>83</td>
</tr>
<tr>
<td>1 - 2 cm</td>
<td>85</td>
</tr>
<tr>
<td>2 - 3 cm</td>
<td>51</td>
</tr>
<tr>
<td>3 - 4 cm</td>
<td>10</td>
</tr>
</tbody>
</table>

However no significant statistical correlation was obtained between size category with chance of malignancy.

In our study group, two sonographic features - irregular margins and microcalcification showed significant correlation with malignancy as calculated by
multiple regression analysis of the various sonographic features with probability of malignancy. Thus these can be considered as independent sonographic characteristics of malignancy. (Fig. 7 on page 14)

Concordance between b-mode and doppler with cytological results:

The provisionally radiological diagnosis was confirmed by cytological results in 87.34% cases. (Fig. 8 on page 14)

Within the 12.66% of nonconcordance of radiological and cytological observation in the study group, 55% (of 12.66%) were cytologically proven thyroiditis which had appeared as colloid nodules in various stages of degeneration.

Combined use of B-mode and doppler has a diagnostic reliability of 87.34%. Overlapping features seen in colloid nodules and thyroiditis reduce the reliability of differentiating between the two pathologies by B mode and doppler sonography.

TIRADS Classification:

1 out of 123 nodules (0.8%) classified as "TIRADS 2" were malignant. There was a 99.2% correlation of "TIRADS 2" being benign.

15 nodules (100%) classified in "TIRADS 3" were benign.

2 out of 59 nodules (3.4%) in "TIRADS 4A" were malignant.

2 out of 20 nodules (10%) classified as "TIRADS 4B" were malignant.

10 out of 11 (91%) nodules classified in "TIRADS 5" were malignant.

The distribution of malignancy among various TIRADS subgroups is shown in Fig. 9 on page 15.

Univariate logistic regression analysis of each TIRADS subgroup was done against chances of malignancy by "SSPS for Windows" software and the "Exp(B)" value or odds ratio was calculated.

<table>
<thead>
<tr>
<th>TIRADS subgroups</th>
<th>Exp (B) or odds ratio of malignancy</th>
<th>95% CI of Exp(B) Lower Upper</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>2.462</td>
<td>1.145 4.037</td>
</tr>
</tbody>
</table>
A significant statistical correlation with malignancy exists only in "TIRADS 5" subgroup. The other groups have a significant correlation with benignity.

TIRADS 4 (A and B) are suspicious of malignancy.

Similar univariate analysis with respect to **benign outcome** are as follows.

<table>
<thead>
<tr>
<th>TIRADS subgroup</th>
<th>Exp(B) or odds ratio of nodule being benign</th>
<th>95% CI of Exp(B) Lower</th>
<th>Upper</th>
</tr>
</thead>
<tbody>
<tr>
<td>4B</td>
<td>2.518</td>
<td>1.693</td>
<td>3.744</td>
</tr>
<tr>
<td>4A</td>
<td>2.358</td>
<td>1.681</td>
<td>3.307</td>
</tr>
</tbody>
</table>

Hence, nodules classified under TIRADS 4 are more likely to be benign and those classified under TIRADS 5 are more likely to be malignant. The other TIRADS categories have a very high correlation with cytological benign finding.
Fig. 6: Cytological distribution of thyroid nodules in our study.

© RADIOLOGY, Apollo speciality hospital - Chennai/IN

<table>
<thead>
<tr>
<th>Sonographic parameter</th>
<th>Odds ratio by multiple logistic regression analysis</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Irregular margin</td>
<td>47.129</td>
<td>0.05</td>
</tr>
<tr>
<td>Microcalcification</td>
<td>6.890</td>
<td>0.01</td>
</tr>
</tbody>
</table>

Fig. 7: Independent sonographic markers of malignancy

© RADIOLOGY, Apollo speciality hospital - Chennai/IN
**Fig. 8:** Concordance of B-mode and doppler features of thyroid nodules with cytological findings.

© RADIOLOGY, Apollo speciality hospital - Chennai/IN

**Fig. 9:** Distribution of malignancy among various TIRADS subgroups.
Conclusion

TIRADS based on several morphological features considered together, attempts to identify thyroid nodules which require cytological correlation. The risk of malignancy defined in each subgroup is similar to BIRADS classification for breast lesions \[3\].

Our study group included both palpable as well as non-palpable nodules ranging from 0.3 to 2.8 cm. However no significant correlation was obtained between nodule size and chances of malignancy.

The cytological inadequacy rates were approximately 5%. This is similar to that reported by Koo et.al. (6%) obtained for nodules ranging from 0.3 to 1.8 cm \[9\]. The overall rate of malignancy was 7.4% according to our study, which is marginally lower than the rate of incidence of 9.2% to 13% as observed by Frates M.C. et. al.\[6\]

In our study we followed the original idea put forward by Horvath et al.\[3\] in classifying our data set following pattern recognition approach, which was further modified by Kwak et al.\[4\] into a more objective simplified system.

The major advantages of this being objectivity in classifying nodules and identifying nodules according to preset baseline features, thereby eliminating observer bias.

In classifying nodules which did not comply with the patterns of TIRADS 2 and 3, the modified numerical approach of Kwak et al.\[4\] was used. Classifying nodules according to the number of suspicious features more than 3 in TIRADS 5, we obtained a high negative predictive value (92.96 %) of malignancy.

Univariate analysis of our study group revealed significant correlation of the following sonographic features with malignancy: solitary, hypoechoic nodule, irregular margins, microcalcification, taller than wide shape, similar to Kwak et al.\[4\] as tabulated in Fig. 10 on page 19.

A comparison of risk of malignancy in each TIRADS group obtained in the study of Horvath et al.\[3\] ; Kwak et al.\[4\] and in our study is shown in Fig. 11 on page 19. We observed a significant statistical correlation of TIRADS 5 with malignancy. The risk of malignancy (91%) was similar to those observed in the studies by Horvath et al (87%) and Kwak et al (87.5%).
The risks of malignancy of TIRADS 4B and TIRADS 4A were almost similar to that observed by Kwak et al.\cite{4}

The deviation from the results of Horvath et al may possibly arise from the reader-order bias\cite{10} that might be involved in the three stage study design used in their study: stage 1 - establishing sonographic patterns stage 2 - generating TIRADS classification stage 3 - validating TIRADS on additionally selected nodules;

So, there is a potential chance of more accurate interpretation in stage 3 of their study than would have been expected otherwise. However, we found that inclusion of separate subgroup (TIRADS 4C) by Kwak et al. has no significant statistical advantage over the proposed risk of malignancy as per the original work by Horvath et al.

**TIRADS 2 - An unusual feature :**

The rate of malignancy in TIRADS 2 is reported as 0%. We observed that of the 123 nodules which were classified as TIRADS 2, 1 nodule (0.8%) was cytologically proven to be follicular neoplasm, which on further excision biopsy turned out to be follicular carcinoma histopathologically.

This nodule was hypoechoic, with regular margins, increased through transmission, no intrinsic or peripheral vascularity and absence of microcalcifications or associated cervical adenopathy. (Fig. 12 on page 20)

Based on classification system proposed by Horvath et al\cite{3}, this nodule was classified as "colloid type 1" - TIRADS 2.

If our classification had been based on the system by Kwak et al.\cite{4} it would have been categorised as TIRADS 4A nodule, in view of its hypoechogenicity. Thus the categorisation by Kwak et al.\cite{4} is a more reliable and easy to use classification system with consistent results.

We propose that a bit more **stringent parameter be used for classifying TIRADS 5** (viz. classifying nodules with more than three sonographic features of malignancy as TIRADS 5) rather than five sonographic features as used by Kwak et al.\cite{4} to increase the negative predictive value of nodules classified into other groups. As in the recent BIRADS system there may be a **potential for including newer parameters** like elasticity (Shear wave velocity) in categorising thyroid nodules into TIRADS along with B mode features.
Fig. 10: Comparison of odds ratio of sonographic variables with chances of malignancy using univariate regression analysis, as obtained in our study and that of Kwak et al.[4]

© RADIOLOGY, Apollo speciality hospital - Chennai/IN
Fig. 11: Comparison of risk of malignancy in each TIRADS group obtained in the study of Horvath et al.[3] ; Kwak et al.[4] and in our study.

© RADIOLOGY, Apollo speciality hospital - Chennai/IN
Fig. 12: Upper images: Hypoechoic nodule initially classified as TIRADS 2; Shear wave velocity was very high (3.8 cm/s). FNAC - Follicular neoplasm. Lower images: Hypoechoic nodule initially classified as TIRADS 4A; Shear wave velocity was intermediately high (2.4 cm/s). FNAC - Colloid nodule.

© RADIOLOGY, Apollo speciality hospital - Chennai/IN
Personal information

Dr. Bagyam Raghavan, Head of department, Department of Radiology and Imaging Sciences, Apollo Specialty Hospital, Chennai, India.

Dr. Sounak Paul, Final year DNB resident, Department of Radiology and Imaging Sciences, Apollo Specialty Hospital, Chennai, India.
References:


7. Frates MC, Benson CB, Doubilet PM, Cibas ES, Marqusee E, "Can color Doppler sonography aid in the prediction of malignancy of thyroid nodules?", 2003, February 1, Volume 22(2), Page 127-31

