THE IMPLEMENTATION OF ACR TI-RADS IN CLINICAL PRACTICE

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ÖZGÜN ARAŞTIRMA ORIGINAL RESEARCH

Objective
To investigate the diagnostic accuracy of the Thyroid Imaging, Reporting and Data System of the American College of Radiology in thyroid nodules.

Material and Method
A total of 151 nodules were collected from 62 patients undergoing thyroid surgery in our center between August 2017 and September 2018. Ultrasonographic features of each nodule were recorded and classified according to the Thyroid, Imaging Reporting and Data System of the American College of Radiology by two radiologists and compared with a one-to-one basis on histopathology.

Abstract
Ince iğne aspirasyon biyopsisi için kesin bir boyut eşiği belirlemek yanlış yönlendirici olabilir, bunun yerine ultrasonoda malign özelliklerin belirlenerek cerrahi kararın kişî bazında verilmesi önerilmelidir.

Anahtar Kelimeler: Mikrokarsinoma, Sensitive, Spesifite, TIRADS, Tiroid nodülü

Sonuç
Ince iğne aspirasyon biyopsisi için kesin bir boyut eşiği belirlemek yanlış yönlendirici olabilir, bunun yerine ultrasonoda malign özelliklerin belirlenerek cerrahi kararın kişî bazında verilmesi önerilmelidir.

Keywords: Micronodule, Sensitivity, Specificity, TIRADS, Thyroid nodules
Introduction
Thyroid nodules are detected between 20 to 70% of the population and the prevalence is increased with iodine deficiency (1, 2). Ultrasonography (US) is currently the most used diagnostic tool for evaluating thyroid nodules (3). The decision of follow-up and/or surgery is made according to the ultrasonographic features of thyroid nodules and fine needle aspiration (FNA) results. However, mandating FNA for each nodule is not a practical option, since only less than 15% of FNAs are found to be malignant. Moreover, there is a risk of inconclusive results and overdiagnosis.

In order to decrease unnecessary FNAs, thyroid nodule risk stratification systems were developed based on certain ultrasonographic features such as irregular margins, hypoechogenicity, microcalcifications, and taller than wide appearance which are all strongly associated with malignancy (4-6).

Current data regarding these thyroid nodule risk stratification systems are contradictory depending on the country, region, and thyroid nodule prevalence in the population where the study was conducted (7-9). Among those, the Thyroid Imaging, Reporting and Data System of the American College of Radiology (ACR TI-RADS) stand upfront by creating standardized terms for thyroid US reports, signifying nodules with high risk for malignancy, and ultimately decreasing the number of unnecessary FNAs (10, 11).

This prospective study aimed to evaluate the diagnostic accuracy of ACR TI-RADS and to determine difficulties in the application of nodule risk stratification systems in routine clinical practice.

Material And Method
Study Design and Inclusion Criteria
This study was designed as a prospective study and was conducted in a single-tertiary center. It was approved by the Ethical Committee of Izmir Education and Research Hospital (17.08.2017/9/6) and all patients’ written consents were taken. The study was conducted in line with the principles of the Helsinki Declaration and was reported according to the STROBE guidelines (12). Patients were recruited among those who complained of any thyroid-related problems and underwent thyroid Doppler US in our institution between August 2017 and September 2018. The only exclusion criterion was the history of thyroid surgery.

Thyroid Doppler US was preoperatively performed in all patients by the same two radiologists. The sizes of each nodule were measured and ACR TI-RADS scores were calculated according to the five ultrasonographic features: composition, echogenicity, shape, margins, and echogenic foci as described by the original study (10). The maximum number of four nodules with the highest scores of ACR TI-RADS were chosen in patients with multinodular goiter.

Of 130 patients who met the eligibility criteria, 62 of them were offered surgical intervention which was given based on the ATA guidelines including suspicion or diagnosis of malignancy on FNA, cosmetic issues related to goiter, toxic solitary nodule, or multinodular goiter (4).

Study Variables
Demographic and clinical features including age, gender, preoperative diagnosis, the size, and number of nodules, ACR TI-RADS scores, FNA results, intraoperative and postoperative complications, and the length of hospital stay were noted.

Surgical specimens were investigated by a single pathologist who was blind to the preoperative ultrasonographic findings. Each nodule on the specimen was reported for its size, location, and...
histopathological result. The one-to-one matching of each nodule’s histopathological diagnoses with the corresponding nodule on the US was performed meticulously and evaluated for diagnostic accuracy by the principal investigator.

**Statistical Analysis**
The data was analyzed using SPSS 22.0. The median size of the thyroid nodules on the US and specimens were calculated and compared using non-parametric tests with Wilcoxon signed rank test. Overall sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) for ACR TI-RADS were analyzed by using the indications of FNA given for each nodule preoperatively. Thyroid nodules were also categorized according to their scores as TR1, TR2, TR3, TR4, and TR5 subgroups. Sensitivity, specificity, PPV, and NPV for ACR TI-RADS were also calculated for each of these subgroups.

**Results**
62 patients were included in this study and 151 nodules were investigated. The median age was found to be 47 (25-76) years. The median size of thyroid nodules measured on the US and in the pathology specimens were 19 (3-85) mm and 17 (0-97) mm, respectively (Table 1). There was found to be a statistically significant difference between the sizes of nodules measured on ultrasound and pathology specimens (p<0.05).

Total thyroidectomy and hemi-thyroidectomy were performed in 54 and 8 patients, respectively. Papillary carcinoma was demonstrated in 28 patients (45%), papillary microcarcinoma in 14 patients (22.5%), and Hurthle cell carcinoma in 1 (1.6%) patient. Single-focus of carcinoma was detected in 25 patients, whereas multifocal localization of carcinoma was detected in 18 patients.

<table>
<thead>
<tr>
<th>Variables</th>
<th>N of patients (%) or median</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gender</strong></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>14</td>
</tr>
<tr>
<td>Female</td>
<td>48</td>
</tr>
<tr>
<td><strong>Age (year)</strong></td>
<td>47 (25-76)</td>
</tr>
<tr>
<td><strong>Indications for surgery</strong></td>
<td></td>
</tr>
<tr>
<td>Multinodular goiter</td>
<td>38</td>
</tr>
<tr>
<td>Toxic nodular goiter</td>
<td>3</td>
</tr>
<tr>
<td>Graves disease</td>
<td>2</td>
</tr>
<tr>
<td>AUS</td>
<td>4</td>
</tr>
<tr>
<td>Follicular neoplasia</td>
<td>5</td>
</tr>
<tr>
<td>Suspicious for malignancy</td>
<td>4</td>
</tr>
<tr>
<td>Malignant cytology</td>
<td>6</td>
</tr>
<tr>
<td><strong>Size of nodules on thyroid US</strong></td>
<td>19 (3-85) mm</td>
</tr>
<tr>
<td><strong>Total thyroidectomy</strong></td>
<td>54</td>
</tr>
<tr>
<td><strong>Hemi-thyroidectomy</strong></td>
<td>8</td>
</tr>
<tr>
<td><strong>Size of nodules on pathology specimens</strong></td>
<td>17 (0-97) mm</td>
</tr>
<tr>
<td><strong>Pathology results</strong></td>
<td></td>
</tr>
<tr>
<td>Papillary carcinoma</td>
<td>28 (45%)</td>
</tr>
<tr>
<td>Papillary microcarcinoma</td>
<td>14 (22.5%)</td>
</tr>
<tr>
<td>Hurthle cell carcinoma</td>
<td>1 (1.6%)</td>
</tr>
</tbody>
</table>

Abbreviations: N, number; AUS, Atypia of undetermined significance; US, ultrasound.
Among 151 nodules, 21 nodules (13%) were categorized as TR1, 34 nodules (22.5%) as TR2, 46 nodules (30%) as TR3, 30 nodules (19%) as TR4, and 20 nodules (13%) as TR5. The median size of thyroid nodules was measured as 12 mm (4-50), 24.5 mm (5-75), 23 mm (6-62), 15 mm (3-85), 10.25 mm (5-46) in TR1, TR2, TR3, TR4, and TR5 respectively (Table 2).

Malignancy rates were calculated for each subgroup as 4.76% in TR1 (1/21), 23.5% in TR2 (8/34), 32.6% in TR3 (15/46), 40% in TR4 (12/30), 90% in TR5 (18/20). Overall sensitivity, specificity, PPV, and NPV were analyzed as 82.5%, 57%, 64.58%, and 77.67%, respectively.

**Discussion**

Thyroid US has been widely used in diagnosing thyroid pathologies in clinical practice. Although ultrasonographic features such as macrocalcifications, irregular margins, punctate echogenicity, and taller than wide shape suggest strong suspicion for malignancy, indications for FNA under US guidance are different based on the nodule risk stratification systems (6). The ACR TI-RADS was investigated in the present study regarding diagnostic performance to guide the clinical implementation of this risk model.

The ACR TI-RADS has a high size threshold for FNA: >2.5 cm in mildly suspicious nodules (TR3), >1.5 cm in moderately suspicious nodules (TR4), and >1 cm in highly suspicious nodules (TR5) which results in decreasing the number of unnecessary FNAs. This fact increases the importance of whether the nodules are designated to the right subgroup of TI-RADS, especially considering the interobserver variability among radiologists performing US (13,14). Moreover, ACR-TIRADS is a score-based system that is not simple and easy to apply clinically (15). It requires the initial assignment of a varying number of points in multiple distinct categories and then calculating the sum of these points across categories (16).

Furthermore, as we demonstrated in our study, the sizes of nodules measured on the US and actual pathology specimens can be quite different resulting in misleading the indication of the FNA threshold. The number of nodules that ACR TI-RADS recommended to follow without FNA was 103 out of 151 nodules, and 23 of those were found to be malignant on
histopathology. Nevertheless, 17 of those nodules were found to be papillary microcarcinomas.

Several studies regarding nodule risk stratification modules have been conducted in terms of demonstrating their specificity and sensitivity (17-20). In a multicenter study comparing ACR TI-RADS, European Thyroid Imaging and Reporting Data System (EU-TIRADS) and Korean Society of Thyroid Radiology (KSThR); the malignancy rates were found to be 7.5% in TR3, 40.1% in TR4, and 81.4% in TR5 for ACR TI-RADS. The ACR TI-RADS showed the best sensitivity (96.6%) but the lowest specificity (52.9%), while the KSThR had the highest specificity with 87.4% (19). On the other hand, Koc et al. reported that ACR TI-RADS had 48.89% sensitivity and 60.63% specificity, with the highest accuracy rate compared to EU-TIRADS and ATA guidelines (21).

Contrary to their findings, in the present study, we demonstrated that ACR-TIRADS had an overall 82.5% specificity and 57% sensitivity. This might be explained by the high number of microcarcinomas in a relatively small study population which is also the major limitation of our study. Moreover, it is known that nodules measuring under 10 mm are the major pitfalls for ACR TI-RADS and other nodule risk stratification systems, even though the necessity of operating on patients with microcarcinoma is still debated (22,23).

Another drawback of present study was the higher malignancy rates for TR3 and TR4 than the recommended range of ACR-TIRADS guidelines, that might be attributed to the deviation caused by sub-centimeter nodules and different observers. This had a significant effect on overall PPV(64.58%) and NPV(77.67%).

The use of thyroid nodule risk stratification systems should carefully be practiced and assessed in developing countries with endemic multinodular goiter. Even with experienced radiologists, the difficulties in assessing the nodules in patients with multinodular goiter cannot be overlooked. The presence of significant differences in the size of the nodules on US and pathology specimens should always be considered. Therefore, instead of setting a size threshold for FNA, signifying the malignant features on ultrasonography and making a decision for surgery on an individual base should be recommended.

Conflict of Interest Statement
The authors have no conflicts of interest to declare.

Ethical Approval
This study has been approved by the Ethical Committee of İzmir Education and Research Hospital (17.08.2017/9/6). It was conducted in line with the principles of the Helsinki Declaration. Written informed consent to participate and publish was obtained from all individual participants included in the study.

Consent to Participate and Publish
Written informed consent to participate and publish was obtained from all individual participants included in the study.

Funding
This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Availability of Data and Materials
Data are available on request due to privacy or other restrictions.

Authors Contributions
BB: Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Validation; Visualization; Writing-original draft.

MU: Conceptualization; Formal analysis; Funding acquisition; Investigation; Methodology.

MB: Investigation; Visualization; Writing-original draft.

AE: Investigation; Validation; Writing-original draft.

DS: Investigation Resources; Visualization.

CA: Project administration; Resources; Supervision; Validation; Writing-review & editing.

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