Significance of TIRADS classification in detection of thyroid gland cancer

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ABSTRACT

Objective: Aim of this study was to retrospectively validate the effectiveness of TIRADS classification in diagnosis of thyroid cancer compared to cytological and pathohistological findings.

Methods: This observational, retrospective study included adult patients of both genders who were diagnosed with thyroid cancer and underwent thyroidectomy. The study was conducted at the Clinic for Nuclear medicine and Endocrinology of the Clinical Center University of Sarajevo in the period from June 2018. to November 2018. All patients had ultrasound (US) and TIRADS classification, fine needle aspiration (FNA) biopsy of the suspected nodules, thyroidectomy and pathohistological (PHD) analysis. TIRADS classification was compared to the results of FNA and PHD findings.

Results: A total of 100 nodules (from 76 patients) were included in the study. TIRADS classification showed that there was 1 (1.0%) nodule in TR2 class, 20 (20.0%) nodules in TR3 class, 72 (72.0%) nodules in TR4 class and 7 (7.0%) nodules in TR5 class. Comparing the results of FNA with TIRADS classification showed that there were no malignant nodules in TR2 class, in TR3 class there were 14 (70.0%) malignant nodules, in TR4 class there were 60 (83.3%) malignant nodules and in TR5 all nodules were malignant (7, 100.0%). Comparing the results of PHD with TIRADS classification showed that there were no malignant nodules in TR2 class, in TR3 class there were 17 (85.5%) malignant nodules, in TR4 class there were 71 (98.6%) malignant nodules and in TR5 class there were 7 (100.0%) malignant nodules.

Conclusion: TIRADS classification showed valid efficacy in identifying malignant thyroid nodules, although fine needle aspiration remains the most effective method. With continuous improvement of TIRADS classification system we can expect decrease in unnecessary thyroid biopsies and an overall improvement of thyroid cancer diagnostics.

Keywords: Thyroid Nodule, Ultrasound Imaging, Thyroid Cancer, TIRADS, Risk Classification

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INTRODUCTION

Thyroid nodules are very common in the general population, with most of them being asymptomatic and benign (1,2). Thyroid cancer is rare among human malignancies (<1%), but it is the most common endocrine cancer accounting for about 5% of thyroid nodules (3). A steady increase in the incidence rate of thyroid cancer has been noted in recent decades all over the world, mostly due to improved detection with rather than to a real increase in frequency(4,5)they can be associated with multiple pathologic conditions, including thyroid cancer.

Methods: This cross-sectional study determined the concordance of Ultrasound (TIRADS criteria).

Accurate discrimination between benign and malignant nodules is essential for guiding clinical management. High resolution ultrasonography and cytological evaluation remain the cornerstones of evaluation of thyroid nodules(2). Ultrasound (US) has been established as the first detection tool of choice in thyroid studies being an accurate method for detection of thyroid nodules (1). However, it is considered to have low accuracy in differentiating between benign and malignant thyroid nodules (4)they can be associated with multiple pathologic conditions, including thyroid cancer.

Methods: This cross-sectional study determined the concordance of Ultrasound (TIRADS criteria).

This is why fine needle aspiration (FNA) biopsy is widely considered to be the most accurate method for detection of malignancy and a fundamental part of current thyroid nodule evaluation

However, most nodules are benign, and even malignant nodules, particularly ones smaller than 1 cm, frequently exhibit indolent or nonaggressive behavior. Therefore, not all detected nodules require FNA and/or surgery(6)many nodules are biopsied to
identify the small number that are malignant or require surgery for a definitive diagnosis. Since 2009, many professional societies and investigators have proposed ultrasound-based risk stratification systems to identify nodules that warrant biopsy or sonographic follow-up. Because some of these systems were founded on the BI-RADS classification that is widely used in breast imaging, their authors chose to apply the acronym TIRADS, for Thyroid Imaging, Reporting and Data System. In 2012, the ACR convened committees to (1).

Due to different interpretations and indications for FNA, several US Thyroid Imaging Reporting and Data Systems (TIRADS) have been proposed for risk stratification of thyroid nodules (4) they can be associated with multiple pathologic conditions, including thyroid cancer.

Methods: This cross-sectional study determined the concordance of Ultrasound (TIRADS criteria. The TIRADS uses various combination of nodule characteristics, including composition, shape, margins and echogenicity to carry out a scale form very low to high risk of malignancy (2). The nodules are usually divided into different categories based on TIRADS and are then referred for FNA biopsy or follow-up, according to the variable risk of malignancy (4) they can be associated with multiple pathologic conditions, including thyroid cancer.

Methods: This cross-sectional study determined the concordance of Ultrasound (TIRADS criteria. The clinical use of TIRADS classification is still very limited and its practical application in clinical practice is questioned (4) they can be associated with multiple pathologic conditions, including thyroid cancer.

Methods: This cross-sectional study determined the concordance of Ultrasound (TIRADS criteria. The aim of this study was to retrospectively validate the effectiveness of TIRADS classification in the diagnosis of thyroid cancer compared to cytological and pathohistological findings.

Materials and methods

This observational, retrospective study included patients of both genders, older than 18 who were diagnosed with thyroid cancer and underwent thyroidectomy. The study was conducted at the Clinic for Nuclear medicine and Endocrinology of the Clinical Center University of Sarajevo in the period from August 2018 to March 2019. Patients with insufficient medical history and patients who had thyroidectomy at other medical facilities were not included in the study. All patients had US and TIRADS classification, FNA of the suspected nodules, thyroidectomy and pathohistological (PHD) analysis done. The study was approved by the Institutional Ethics Committee of the Clinical Center University of Sarajevo.

TIRADS scoring is determined from five categories of ultrasound findings of thyroid nodules: composition, echogenicity, shape, margins and echogenic foci. One score is assigned from each category. The higher the cumulative score, the higher the TR level and likelihood of malignancy. Biopsy is recommended for suspicious lesions (TR3 - TR5). If there are multiple nodules, the two with the highest TIRADS grades should be sampled (rather than the two largest). Table 1 shows classification and recommendations for TIRADS scoring (6). US guided FNA was performed by experienced nuclear medicine specialists and the sample was obtained through a single puncture under local anesthesia. The protocol at the Clinic for Nuclear Medicine and endocrinology is to perform FNA and cytology of the largest nodules and nodules that have calcifications. Findings of the FNA analysis are based on the standardized Bethesda terminology system for reporting thyroid cytopathology (7). All patients with malignancy suspicion undergo total thyroidectomy. PHD analysis of thyroidectomy specimen is performed by an experienced pathologist. Since benign nodules are also

<table>
<thead>
<tr>
<th>TIRADS</th>
<th>Scoring and classification</th>
<th>Recommendations</th>
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<tbody>
<tr>
<td>TR1</td>
<td>0</td>
<td>Benign</td>
</tr>
<tr>
<td>TR2</td>
<td>2</td>
<td>Not suspicious</td>
</tr>
<tr>
<td>TR3</td>
<td>3</td>
<td>Mildly suspicious malignant nodule</td>
</tr>
<tr>
<td>TR4</td>
<td>4-6</td>
<td>Moderately suspicious malignant nodule</td>
</tr>
<tr>
<td>TR5</td>
<td>≥ 7</td>
<td>Highly suspicious malignant nodule</td>
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FNA – fine needle aspiration
removed during surgery, we were able to compare TR2 and TR3 class with FNA and PHD findings. US of thyroid gland was performed on the standardized US models in the primary health care facilities by experienced radiologists. TIRADS score and class were determined retrospectively from the US images by nuclear medicine specialist, without previous knowledge of the cytological and PHD findings. The US features of the thyroid nodules were assessed for composition, shape, margins and echogenicity based on the published ARC TIRADS guidelines (6).

**Statistical analysis**

The data was compiled in MySQL and statistical analysis was performed using IBM SPSS v.21.0 for MacOS. For quantitative variables we used averages and standard deviation (SD) and we described qualitative variables in percentage distribution. Measurements of diagnostic accuracy (validity, predictive value, likelihood ratio) are shown by the ROC (Receiver Operating Characteristic) analysis. Confidence interval was set to 95% and statistical significance at 0.05.

**Results**

A total of 100 nodules (from 76 patients) were included in the study. The youngest patient diagnosed with thyroid cancer was 25 years old, while the oldest patient was 85. The mean patients age was 57.1 ± 13.7 years. Out of the total number of patients, 58 (76.5%) were women.

The results of TIRADS classification showed that there was 1 (1.0%) nodule in TR2 class, 20 (20.0%) nodules in TR3 class, 72 (72.0%) nodules in TR4 class and 7 (7.0%) nodules in TR5 class.

The results of FNA showed that there were 19 (19.0%) benign nodules, 16 (16.0%) nodules had suspicion of malignancy, while 65 (65%) nodules were found malignant.

Comparing the results of FNA with TIRADS classification showed that there were no malignant nodules in TR2 class, in TR3 class there were 17 (85.5%) malignant nodules, in TR4 class there were 71 (98.6%) malignant nodules and in TR5 class there were 7 (100.0%) malignant nodules.

The results of the PHD findings confirmed malignancy in 95 (95.0%) nodules, while the remaining 5 (5.0%) nodules were confirmed as benign. In fact, out of the total number of malignant nodules, the most common was papillary thyroid carcinoma found in 63 (66.3%) nodules, followed by follicular thyroid carcinoma found in 26 (27.4%) nodules, medullary thyroid carcinoma found in 3 (3.2%) nodules and poorly differentiated carcinoma found in 3 (3.2%) nodules.

Comparing the results of PHD with TIRADS classification showed that there were no malignant nodules in TR2 class, in TR3 class there were 17 (85.5%) malignant nodules, in TR4 class there were 71 (98.6%) malignant nodules and in TR5 class there were 7 (100.0%) malignant nodules.

The AUC (area under the curve) for TIRADS was above 86%, with sensitivity being 17.6% and specificity 96.4%. positive predictive value (PPV) was 50.0% and the negative predictive value (NPV) was 85.1%.

**Discussion**

Ultrasound features such as hypoechoic or very hypoechoic, taller-than-wide, microcalcifications, and irregular margins are associated with malignancy (8). In recent years, many distinct TIRADS guidelines have applied ultrasound features to classify thyroid nodules as malignant or benign, or to recommend US-FNA. Such diagnostic standards not only clarify the malignancy risk of thyroid nodules but also help guide treatment (8). TIRADS was originally developed as a modified BIRADS system (Breast Imaging-Reporting and Data System), which is generally used in breast cancer diagnoses. Since, several TIRADS classifications have been proposed (6,9–11)many nodules are biopsied to identify the small number that are malignant or require surgery for a definitive diagnosis. Since 2009, many professional societies and investigators have proposed ultrasound-based risk stratification systems to identify nodules that warrant biopsy or sonographic follow-up. Because some of these systems were founded on the BI-RADS® classification that is widely used in breast imaging, their authors chose to apply the acronym TI-RADS, for Thyroid Imaging, Reporting and Data System. In 2012, the ACR convened committees to (1, but
no TIRADS classification has been widely accepted(8). The ACR-TIRADS is suitable for all nodules, as it integrates all ultrasonographic characteristics, which are scored from 0 to 3 based on their malignant potential. The higher the score, the higher the malignancy risk. Therefore, the ACR-TIRADS is an objective and comprehensive method to evaluate the characteristics of each thyroid nodule and also to guide therapy. The disadvantage is that it is more complicated than the other guidelines. Moreover, malignant nodules with mixed echo patterns are scored lower in the ACR-TIRADS, resulting in misdiagnosis. The risk of malignancy for ACR-TIRADS 5 is ≥20% (8).

Thyroid nodule FNAs play key roles in ruling out the presence of thyroid cancer. However, the costs of sample collection and analysis are relatively high, and the aspiration itself can be a source of discomfort and anxiety for patients. Furthermore, in roughly one third of cases, cytomorphologic analysis of the aspirate yields inconclusive results that prompt repeat biopsies or additional, more expensive testing(12).

Finding a reliable way of classifying thyroid nodules, while decreasing stress on patients and possible procedure complications should be primary goal of any thyroid diagnostics procedure. With this study we wanted to assess the likelihood of using validated US classification in ruling out the nodules with low malignancy risk.

The cancer prevalence according to cytological findings in our study in each TIRADS class was 0.0% in TR2, 70% in TR3, 83.3% in TR4 and 100.0% in TR5 class. The cancer prevalence according to PHD findings in our study in each TIRADS class was 0.0% in TR2, 85.5% in TR3, 98.6% in TR4 and 100.0% in TR5 class. These results indicate that most of the nodules classified in TR3, TR4 and TR5 were in fact malignant and had an indication for FNA. Other study show smaller prevalence of malignant nodules in TR3 class, with TR4 class being the cut-off for malignancy (13,14). The reason for these differences could be in sample size, since a small sample in our study could indicate overrepresentation of malignant nodules. The PHD findings in our study showed papillary thyroid carcinoma as the most prevalent thyroid carcinoma which is consistent with findings in other studies (12,13). Overall TIRADS showed sensitivity of 17.6% and specificity of 96.4% and high NPV. Other studies showed similar results when it comes to specificity and NPV but higher sensitivity rates, compared to our study (8,13).

Despite the rapid increase in diagnosis, thyroid cancer death rates only increased slightly which could be suggestive of overdiagnosis among other things. Several population-based studies ascribed this to increasing utilization of US, FNA and an increase of thyroid nodules found on non-thyroid imaging studies (15). In some countries US is used for screening which has led to an epidemic of over-diagnosed thyroid cancer leading to overtreatment. In addition to the surgical risks of overtreatment, overdiagnosis of low-risk cancers also leads to psychological morbidity and increases health care costs. For these reasons, the role of thyroid US in thyroid cancer screening is limited(15).

There were several limitations to our study. The sample used in the study was small which could affect the prevalence of malignancy in each category. Since FNA and surgery were performed in all the cases, there could be overrepresentation of cancer compared to general population. The study was conducted retrospectively and the US were performed in primary health care facilities, with the images being evaluated for TIRADS afterwards. Also, this is a one institutional study conducted in a tertiary referral center.

TIRADS system is continuously improving and evolving, and is able to be modified according to new evidence as it becomes available. This might include in the future elastosonography findings, contrast-enhanced ultrasound, PET findings, or other imaging techniques(1).

In conclusion, TIRADS classification showed valid efficacy in identifying malignant thyroid nodules, although fine needle aspiration remains the most effective method. With continues improvement of TIRADS classification system we can expect decrease in unnecessary thyroid biopsies and an overall improvement of thyroid cancer diagnostics.
References


