Endocrine (2018) 61:398–402
https://doi.org/10.1007/s12020-018-1620-6

ENDOCRINE METHODS AND TECHNIQUES

Does the ACR TI-RADS scoring allow us to safely avoid unnecessary thyroid biopsy? single center analysis in a large cohort

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Received: 3 January 2018 / Accepted: 26 April 2018 / Published online: 9 May 2018

Abstract

Introduction The American College of Radiology (ACR) has recently proposed a guideline that recommends clinicians to perform thyroid fine-needle aspiration biopsy (FNAB) on the basis of ultrasound features. In this study, we focused on nodules for which no biopsy is recommended by the ACR Thyroid Imaging, Reporting and Data System (TI-RADS) guideline.

Subjects and methods Two-thousand eight-hundred and forty-seven consecutive patients with thyroid nodules who underwent FNAB according to the 2009 American Thyroid Association (ATA) guideline were included. The nodules were re-classified according to the ACR TI-RADS guideline as benign (TR1), not suspicious (TR2), mildly suspicious (TR3), moderately suspicious (TR4) and highly suspicious (TR5). The TR3 category was stratified into two subcategories as regard to the nodule size (TR3; <25 mm and TR3; ≥25 mm).

Results Two-hundred and thirty-three (8.2%) patients with non-diagnostic FNABs were excluded. When the TR2 and TR3; <25 mm categories were merged, FNAB was suggestive of thyroid cancer in 17 of 1382 patients (1.2%). FNAB revealed Bethesda IV–VI in 5 of 273 patients with the TR3; ≥25 mm category (1.8%), in 61 of 896 patients with the TR4 category (6.8%), and in 18 of 63 of patients with the TR5 category (28.6%). The ACR TI-RADS scoring was 98.8% (95% CI: 98 to 99.3) specific for identification of a benign nodule.

Conclusion Our data suggest that ACR TI-RADS scoring is an applicable and potentially cost-effective approach to determine thyroid nodules to be biopsied, although a small proportion of thyroid cancers would be missed.

Keywords Thyroid nodules · Fine-needle aspiration biopsy · Thyroid cancer · Thyroid ultrasound

Introduction

Thyroid nodules are a common clinical problem and although the majority are benign, approximately 5% can harbor malignancy mainly with differentiated thyroid cancer [1]. With the increased utilization of ultrasound (US) for evaluation of non-thyroid lesions of the neck, the incidental finding of thyroid nodules has dramatically increased [2, 3].

The American College of Radiology (ACR)'s recently implemented guideline endorses a clinical approach for the management of patients with thyroid nodules that are driven by US findings, which helps clinicians to decide whether a fine-needle aspiration biopsy (FNAB) is required. In this approach, nodules with overall ACR Thyroid Imaging, Reporting and Data System (TI-RADS) score <3 are classified as benign (TR1)/ non-suspicious (TR2) and no biopsy is recommended. Also, no biopsy is recommended for mildly suspicious nodules with an ACR TI-RADS score

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3 (TR3) if they are smaller than 25 mm, however, follow-up is recommended for nodules larger than 15 mm, which fall into this category [4].

This approach may avoid unnecessary thyroid biopsies, and would be cost-saving. However, it is possible that some malign nodules may be left undiagnosed if a biopsy is not performed. To address this question, we retrospectively analyzed our FNAB data primarily by focusing on nodules for which no biopsy is recommended based on the ACR TI-RADS guideline.

Materials and methods

The data are collected in 2847 consecutive patients with thyroid nodules who underwent a FNAB between 2010 and 2014 in Tepecik Training and Research Hospital.

US was performed by using high-spatial resolution US machines equipped with a 5.5–12.5-MHz linear probe. Routine FNAB was performed in accordance with the 2009 ATA guideline. Basically, FNAB was recommended all patients with solid nodules ≥1 cm, patients with mixed cystic–solid nodules ≥1.5-2 cm and spongiform nodules ≥2 cm, and patients with high-risk history who had nodules ≥5 mm. Clinical notes were revised in patients with nodules 5–10 mm in size who underwent a FNAB because the nodule was classified in the high-risk group. These suspicious features were microcalcifications, marked hypoechoic appearance, increased nodular vascularity, infiltrative margins, and being taller than wide on transverse view. Also, FNAB was performed in several patients although they did not meet the 2009 ATA criteria for routine FNAB, which was even so ordered, based on the personal clinical judgment of the clinicians. No FNAB was performed for purely cystic nodules.

The nodules were then re-classified according to the ACR TI-RADS guideline. To do so, scoring was done for composition, echogenicity, shape, and margin characteristics of the nodules, and extra points were added if the nodules contained any echogenic foci. After all, nodules were classified as benign (TR1), not suspicious (TR2), mildly suspicious (TR3), moderately suspicious (TR4), and highly suspicious (TR5). The TR3 category was stratified into two subgroups regarding the nodule size (TR3; <25 mm and TR3; ≥ 25 mm). The TR1, TR2, and TR3; <25 mm categories consisted of nodules, which are not recommended to be biopsied based on the ACR TI-RADS recommendations.

Cytopathological interpretation of FNAB samples was done using the Bethesda System for Reporting Thyroid Cytopathology [5]. In patients who underwent thyroidectomy, specimens were submitted to surgical pathology for gross and microscopic examination. Retrospective re-classification of all nodules according to ACR TI-RADS system was blind regarding FNAB results.

Statistical analysis was performed using Statistical Package of Social Science (SPSS, Chicago, IL), version 22 for Windows. Variables were assessed for normal distribution using the one sample Kolmogorov–Smirnov test. Categorical variables were compared by the chi-square test. One-way ANOVA followed by Bonferroni correction post-hoc test was used for comparison of variables. The specificity of ACR TI-RADS scoring to avoid unnecessary FNAB was calculated from the chi-square test of contingency with cytopathological interpretation taken as the reference standard. Specificity was defined as the probability that the test result will be negative when the disease is not present, which was expressed as percentages. The 95% confidence intervals (CI) were calculated from binomial expression. A p-value <0.05 was accepted as statistically significant.

Results

Table 1 shows characteristics of patients. Two-hundred and thirty-three patients (8.2%) with non-diagnostic FNABs (Bethesda I) were excluded from the analysis. Of the remaining patients ($n = 2614$), 508 patients (19.4%) were classified in the TR2, 874 patients (33.4%) in the TR3; <25 mm, 273 patients (10.5%), in the TR3; ≥25 mm, 896 patients (34.3 %) in the TR4, and 63 patients (2.4%) in the TR5 categories. There was no patient in the TR1 category.

There was no significant difference, although patients in the TR3; ≥25 mm category were slightly older compared to that classified in the TR2 category. Female predominance was remarkable, while there were even more females in the TR3; <25 mm category compared to the TR2 and TR3; ≥ 25 mm categories. Nodule sizes were variable as shown. TSH levels were similar. Among patients classified in the TR2 category, FNAB was suggestive of thyroid cancer in four patients (0.8 %). Of those; one patient had Bethesda category VI, two had V and one had IV FNAB reports. Papillary carcinoma was confirmed in three patients, and medullary carcinoma was detected in another patient on thyroidectomy specimens. FNAB was helpful to detect thyroid cancer in 13 of 874 (1.5 %) patients classified in the TR3; <25 mm category. Among those, 12 patients had nodules sized between 15–25 mm. Thyroid nodules fell within Bethesda category VI in five patients, V in four patients and IV in four patients. Among those, 11 patients had papillary cancer, one had follicular thyroid cancer, and one had medullary thyroid cancer on thyroidectomy specimens. When the TR2 and TR3; <25 mm groups were merged, thyroid malignancy was detected in 17 of 1382 patients (1.2%) based on FNAB. FNAB was suggestive of

Table 1 Comparison of patients in different ACR TI-RADS categories

	TR2 ($n = 508$)	TR3; <25 mm ($n = 874$)	TR3; ≥25 mm ($n = 273$)	TR4 ($n = 896$)	TR5 ($n = 63$)
Age (years)	50.1 ± 14.2 †vs.TR3; ≥25 mm	51.2 ± 13.4	53.8 ± 13.7 †vs.TR2	50.7 ± 13.9	48.0 ± 15.7
Female/Male (n)	418/90 ‡vs.TR3; <25 mm	793/91 ‡vs.TR2 ‡vs.TR3; ≥25 mm	221/52 ‡vs.TR3; <25 mm	779/117	52/11
Nodule size (mm)	24.9 ± 16.6 ‡vs.TR3; <25 mm ‡vs.TR3; ≥ 25 mm ‡vs.TR4	15.5 ± 4.3 ‡vs.TR2 ‡vs.TR3; ≥ 25 mm ‡vs.TR4 ‡vs.TR5	33.0 ± 7.6 ‡vs.TR2 ‡vs.TR3; <25 mm ‡vs.TR4 ‡vs.TR5	18.5 ± 9.4 ‡vs.TR2 ‡vs.TR3; <25 mm ‡vs.TR3; ≥ 25 mm	20.8 ± 10.1 ‡vs.TR3; <25 mm ‡vs.TR3; ≥ 25 mm
TSH (IU/L)	1.7 ± 2.8	2.1 ± 2.8	1.6 ± 6.2	2.0 ± 4.8	1.5 ± 1.7
Thyroid cancer (n, %)	[a]11 (2.2%) [b]4 (0.8%) ‡vs. TR4 ‡vs. TR5	[a]16 (1.8%) [b]13 (1.5%) ‡vs. TR4 ‡vs. TR5	[a]7 (2.6%) [b]5 (1.8%) †vs. TR4 ‡vs. TR5	[a]68 (7.6%) [b]61 (6.8%) ‡vs.TR2 ‡vs.TR3; <25 mm ‡vs.TR3; ≥ 25 mm ‡vs.TR5	[a]19 (30.2%) [b]18 (28.6%) ‡vs.TR2 ‡vs.TR3; <25 mm ‡vs.TR3; ≥ 25 mm ‡vs.TR4

Categorical variables are shown as frequencies and percentages. Numerical data are presented as mean ± standard deviation (SD). Categorical variables were compared by the chi-square test, which also included additional chi-squared tests for pairwise differences. One-way ANOVA followed by Bonferroni correction post-hoc test was used for comparison of variables

†$p < 0.05$; ‡$p < 0.001$

[a]Incidental microcarcinomas included

[b]Incidental microcarcinomas excluded

thyroid cancer in 5 of 273 patients (1.8 %) with the TR3; ≥25 mm category, 61 of 896 patients (6.8%) with the TR4 category, and 18 of 63 patients (28.6 %) classified in the TR5 category.

The clinical usefulness of ACR TI-RADS scoring to avoid unnecessary FNAB was also assessed by specificity analysis, which showed that the scoring was 98.8% (95% CI: 98 to 99.3) specific for identification of a benign nodule. To note, incidental low-risk papillary microcarcinomas were detected in several patients as shown in Table 1 who underwent thyroidectomy because of cosmetic reasons despite having benign FNAB results. None of these patients required postoperative radioiodine ablation, and they were not included in the specificity analysis.

Discussion

Thyroid US, in conjunction with FNAB, plays an important role in the evaluation of patients with a thyroid nodule and detecting candidates for surgery [6, 7]. The ACR TI-RADS scoring has propounded an approach to define a risk stratification system for thyroid nodules to guide decisions regarding FNAB and follow-up [4].

In this study, we included patients who underwent FNAB based on the previous ATA guidelines on thyroid nodules and differentiated thyroid cancer, which was published back in 2009 [8]. After re-classification of these patients according to the ACR TI-RADS guideline [4], we were able to generate a group of patients in whom no FNAB is recommended according to the ACR TI-RADS recommendations; however, FNAB had already been performed. This gave us the unique opportunity to analyze the outcome of these "no FNAB required" patients according to the ACR TI-RADS; and to assess the clinical utility of this new set of recommendations for the management of thyroid nodules in a large single center cohort of subjects.

We were able to detect few patients with thyroid cancer within the TR2 and TR3 categories. The rates of thyroid cancer detected in the TR2 and TR3 categories were similar.

There was also no significant difference in thyroid cancer risk between patients in the TR3; <25 mm and TR3; ≥25 mm categories. In the ACR TI-RADS "no FNAB required" categories, there were 17 patients (1.2%) who were diagnosed with thyroid cancer on FNAB. Also considering ten additional patients with incidental microcarcinomas discovered after thyroidectomy, there was a 1–2% probability of missing a thyroid cancer (mostly low-risk differentiated thyroid cancers) if no FNAB had been performed in these nodules as suggested by the ACR TI-RADS. Based on the large number of patients in these categories, we have to note that about 6% of the thyroid cancers diagnosed in our series would have been missed that way. On the other hand, thyroid cancer risk was obviously increased in patients who fell in the TR4 and TR5 categories, which suggests that US features are more informative than the size of the thyroid nodule. Although previous studies suggested that nodule size may assist in cancer risk assessment [9, 10], recent data suggest no linear relationship between the nodule size and malignancy risk [11–13].

There were several limitations of our study. Our data are from a single institution and retrospective in nature. We should acknowledge that the data is partly confounded by the incidental papillary microcarcinomas discovered in the histopathology in addition to thyroid cancers diagnosed based on FNAB. More importantly, although all patients with Bethesda IV, V, and VI FNAB results were referred to surgery, the big majority of patients with benign FNAB did not undergo thyroidectomy. Nevertheless, data concerning the results of long-term surveillance of cytologically benign nodules may confirm high accuracy for benign FNAB cytology [14, 15].

In conclusion, our findings suggest that the ACR TI-RADS scoring is an applicable and potentially cost-effective approach to determine thyroid nodules to be biopsied. However, a small proportion of low-risk thyroid cancers would be missed if ACR TI-RADS recommendations are firmly followed.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval The study was approved by Clinical Research Ethical Committee of Izmir Katip Celebi University Hospital (29.11.2013-No: 226). All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all participants before the FNAB and other procedures in consistency with the regulations of the national authorities. IRB approval was obtained to use the data.

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