Original Article

Single-center validation study of the American College of Radiology Thyroid Imaging Reporting and Data System in a Turkish adult population

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ABSTRACT

Objectives: This study aims to evaluate diagnostic performance of the American College of Radiology Thyroid Imaging Reporting and Data System (ACR-TIRADS) in the Turkish adult population.

Patients and Methods: A total of 422 thyroid nodules of 368 patients (103 males, 265 females; mean age 46.43 years; range, 18 to 81 years) diagnosed by fine needle aspiration biopsy (FNAB) or surgical pathology were retrospectively analyzed. The decisions for FNABs were mostly made by the experts of our hospital without using the ACR-TIRADS. The observers assessed five different aspects of thyroid nodules: echogenicity, shape, composition, margin, and echogenic foci. Nodules with 0 points were categorized as TR1, 2 points as TR2, 3 points as TR3, 4-6 points as TR4, and ≥7 points as TR5. The sensitivity, specificity, and diagnostic accuracy of ACR and the proportion of benign nodules and malignant nodules to be biopsied according to the ACR-TIRADS were calculated.

Results: The ACR-TIRADS identified 47 of 54 malignant nodules and identified 264 of 368 benign nodules yielding 73.6% diagnostic accuracy. Using the ACR-TIRADS would have spared 64.1% of benign nodules from FNAB. Of 54 malignant nodules, 23 were to be biopsied, 30 to be followed, and one malignant nodule was not planned to be biopsied or followed according to the ACR-TIRADS recommendations.

Conclusion: Despite its robustness in sparing a substantial number of benign nodules from FNAB, the use of ACR-TIRADS would prevent 55.5% of malignant nodules from FNAB. We suggest that FNAB threshold levels of the ACR-TIRADS should be extensively reviewed by the Turkish radiologists, endocrinologists, general surgeons, and ear, nose and throat surgeons before integrating the system to their daily practice.

Keywords: ACR-TIRADS, fine needle aspiration biopsy, risk stratification, thyroid nodules, ultrasound.

Thyroid nodules occur frequently with a prevalence reaching 67% in the adult population.[1-3] Approximately 90% of thyroid nodules are benign, and 10% are malignant. Differentiating between benign and malignant nodules is mandatory to establish appropriate management strategies.[1-3] Ultrasound (US) is the most common first-line modality for diagnosing and discriminating thyroid nodules.[1-3] Nodules which are highly suspected of malignancy

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are often referred for fine-needle aspiration biopsy (FNAB) or tissue biopsies.[1-3] Malignant nodules, which feature irregular margins, solid composition, hypoechogenicity, taller-than-wide shape, and microcalcifications, are well-known US features, although none of these features alone can differentiate malignant from benign nodules.[2-5] Hence, a composite risk scoring system is needed to elicit the nodules that should be further evaluated via FNAB. However, a lack of a general risk-scoring system precludes making valid comparisons between studies, identifying risk factors, and developing treatments. In 2009, Horvath et al.[6] described the first Thyroid Imaging Reporting and Data System (TIRADS), prompted primarily by the Breast Imaging Reporting and Data System (BIRADS). Until now, several reporting systems have been proposed to allow better risk stratification of thyroid nodules, improve communication between clinicians and radiologists, and enhance reliability between different thyroid US interpretations between institutes.[3,5,7,8]

In 2017, a committee including experts on thyroid pathologies proposed a new reporting system under the auspices of the American College of Radiology (ACR), known as the ACR-TIRADS.[4] The ACR-TIRADS is a point-based risk-scoring system, consisting of five categories from TR1 to TR5, in order of an increasing risk of malignancy ranging from 0.3 to 35% based on the US appearance of the thyroid nodules.[4] Since the introduction of the ACR-TIRADS, several authors have validated its diagnostic performance.[9-13] However, scarce data are available regarding the practical implications of ACR-TIRADS in the Turkish adults.

In the present study, we aimed to evaluate the diagnostic performance of the ACR-TIRADS by calculating the sensitivity, specificity, negative predictive value (NPV), positive predictive value (PPV), and diagnostic accuracy in differentiating malignant and benign nodules and to assess the interobserver reliability of the scoring system.

PATIENTS AND METHODS

This retrospective, cross-sectional study was conducted between January 2012 and January 2019. Consecutive patients with thyroid nodules who underwent thyroid US examinations at our institution were analyzed. Thyroid nodules of the patients diagnosed as benign or malignant via FNAB or surgical pathology results were included in the study. Nodules with undetermined cytology, nondiagnostic cytological analysis, or poor-quality US images were excluded. Finally, a total of 422 thyroid nodules of 368 patients (103 males, 265 females; mean age 46.43 years; range, 18 to 81 years) were included. A written informed consent was obtained from each patient. The study protocol was approved by the Vehbi Koç Vakfı Amerikan Hospital Ethics Committee. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Thyroid US examination and image analysis

All US and US-guided FNAB procedures were performed by a single radiologist with more than 20 years of thyroid US and US-guided FNAB experience. The operator performed all examinations using the same device (LOGIQ E9 with XDclear, General Electric [GE] Healthcare, Wauwatosa, WI, USA) with a linear array transducer (ML6-15) and frequency range of 12 to 15 MHz. First, the observer carefully viewed the right and left thyroid lobes from the superior to inferior poles. Longitudinal and transverse nodular images were captured and sent to our hospital's Picture and Archive Communicating System (PACS). The observer acquired multiple static images of the relevant thyroid nodule, and dynamic images were acquired at the discretion of the radiologist. Since this was a retrospective study with a cross-sectional design, the ACR-TIRADS and most of other systems were unavailable in much of our study period; hence, most biopsy indications from our tertiary center were not based on the ACR-TIRADS. The experts on our Institutional Endocrinology Board, which includes radiologists, general surgeons, ear, nose and throat surgeons, and endocrinologists, made most of the decisions regarding the FNABs.

Two readers retrospectively evaluated the US features of the thyroid nodules on our hospital PACS system and reached a consensus. The observers assessed five thyroid nodule aspects proposed by the ACR-TIRADS: composition, echogenicity, shape, margins, and echogenic foci.[4] Nodule compositions were interpreted as cystic, completely cystic, or spongiform (having

microcysts in >50% of the overall volume; 0 points), mixed cystic and solid (1 point), or solid or almost completely solid (2 points).[4] Echogenicity of the nodules was evaluated using the adjacent thyroid parenchyma as the reference tissue. The nodular echogenicity was interpreted as anechoic (0 points), hyper- or isoechoic (1 point), hypoechoic (2 points), or very/markedly hypoechoic (3 points). Very/markedly hypoechoic nodules were defined as being less reflective than the anterior neck muscles.[4] The nodule shape was classified as wider-than-tall (0 points) or taller-than-wide (3 points) on transverse images.[4] The nodule margins were classified as smooth (0 points), ill-defined (0 points), lobulated/irregular (2 points), or with extra-thyroidal invasion (3 points).[4] Echogenic foci were assessed as none or having a large comet-tail artifact (0 points), macrocalcifications (1 point), peripheral/rim calcifications (2 points), or punctate echogenic foci (3 points).[4] Different than the first four US features, nodules could be allocated points for more than one category. If a nodule had macrocalcifications (1 point) and peripheral/rim calcifications (2 points), the nodule was, then, allocated 3 points as recommended by the ACR-TIRADS. The patients with 0 points were categorized as TR1, 2 points as TR2, 3 points as TR3, 4-6 points as TR4, and ≥7 points as TR5.

Table 1. Ultrasound features and ACR-TIRADS categories of benign and malignant thyroid nodules

	Total		Benign		Malign		
Variables	Sayı	Yüzde	Sayı	Yüzde	Sayı	Yüzde	*p*
Number of nodules	422	100	368	87.2	54	12.8	-
ACR-TIRADS category							
TR1	11	2.6	11	3	0	0	<0.0001
TR2	38	9	37	10.1	1	1.9	
TR3	222	52.6	216	58.7	6	11.1	
TR4	100	23.7	86	23.4	14	25.9	
TR5	51	12.1	18	4.9	33	61.1	
Composition							
Cystic or completely cystic	11	2.7	11	3.1	0	0	<0.0001
Spongiform	13	3	12	3.2	1	1.9	
Mixed cystic and solid	93	22	85	23	8	14.8	
Solid or almost completely solid	305	72.3	260	54.3	45	83.3	
Echogenicity							
Anechoic	11	2.6	11	3	0	0	<0.0001
Hyper- or isoechoic	215	50.9	207	56.3	8	14.8	
Hypoechoic	163	38.6	145	39.4	21	38.8	
Markedly hypoechoic	30	7.1	5	1.3	25	46.2	
Shape							
wider-than-tall	390 (92.4)		356 (96.7)		34 (63)		<0.0001
taller-than-wide	32 (7.6)		12 (3.3)		20 (37)		
Margin							
Smooth	200	47.3	187	52.5	13	24.1	<0.0001
Ill-defined	188	44.5	169	45.9	19	35.1	
Lobulated/irregular	32	7.6	12	3.3	21	38.9	
Extra-thyroidal invasion	2	0.5	0	0	1	1.9	
Echogenic foci							
None	204	48.3	192	52.1	12	22	<0.0001
Large comet tail artifact	138	32.7	125	33.9	13	24	
Macrocalcifications	38	9	33	9	5	9.3	
Peripheral/rim calcifications	6	1.4	6	1.6	11	20.3	
Punctate echogenic foci	36	8.5	12	3.3	24	44.4	

ACR-TIRADS: American College of Radiology Thyroid Imaging Reporting and Data System.

Statistical analysis

Statistical analysis was performed using the IBM SPSS version 21.0 software (IBM Corp., Armonk, NY, USA). Descriptive data were presented in mean ± standard deviation (SD), median (min-max), or number and frequency. The US features of benign and malignant nodules were compared using the chi-square (χ^2) test. The TR2 and TR3 were considered benign, while TR4 and TR5 were considered malignant according to the ACR-TIRADS. The sensitivity, specificity, NPV, PPV, and diagnostic accuracy of the ACR-TIRADS system were calculated by accepting the surgical or FNAB results as the reference method. The ACR-TIRADS recommends no FNAB or follow-up for TR1 and TR2 nodules, recommends FNAB for TR3 nodules ≥2.5 cm and follow-up for TR3 nodules ≥1.5 cm, FNAB for TR4 nodules ≥1.5 cm and follow-up for TR4 nodules ≥1 cm, and FNAB for TR5 nodules ≥1 cm and follow-up for TR5 nodules ≥0.5 cm.[4] The proportions of benign and malignant nodules to be biopsied or not in accordance with the ACR-TIRADS criteria were also calculated to identify the percentage of benign nodules that would have been spared and the percentage of malignant nodules that would have been followed or excluded from further follow-up. The receiver operating curve (ROC) was used to analyze the area under the curve (AUC) value for the ACR-TIRADS in identifying malignant thyroid nodules. A p value of <0.05 was considered statistically significant.

RESULTS

Of 422 thyroid nodules, 368 were benign (87.2%) and 54 (12.8%) were malignant. Among 54 malignant nodules, FNAB results for 44 nodules were confirmed via a surgical pathology: 35 (79.5%) had a papillary thyroid carcinoma and nine (20.4%) had a follicular variant of papillary cancer. For the entire study cohort, 11 nodules (2.6%) were categorized as TR1, 38 (9%) as TR2, 222 (52.6%) as TR3, 100 (23.7%) as TR4, and 51 (12.1%) as TR5 according to the ACR-TIRADS (Table 1).

No nodules with cystic or completely cystic compositions were malignant; all of these were anechoic on US. Notably, of 30 markedly hypoechoic nodules, 25 were malignant (46.2% of all malignant nodules), and only five were benign (1.3% of all benign nodules; p<0.0001). Only 32 of 390 nodules (7.6%) had

Figure 1. *A 28-year-old-female patient with a thyroid nodule with a maximal diameter of 22 mm. The nodule's ACR-TIRADS appointments as follows: composition: solid (2 points), echogenicity: isoechoic (1 point), Shape: Wider than tall (0 points), margin: smooth (0 points), echogenic foci: none (0 points). Total points: 3, ACR-TIRADS category: TR3. ACR-TIRADS recommendation: Follow-up. The pathological result: Nodular goiter.*

ACR-TIRADS: American College of Radiology Thyroid Imaging Reporting and Data System.

Figure 2. *A 46-year-old-female patient with a thyroid nodule with a maximal diameter of 12.39 mm. The nodule's ACR-TIRADS appointments as follows: composition: solid (2 points), echogenicity: hypoechoic (2 point), Shape: Taller-than-wide (3 points), margin: ill-defined (0 points), echogenic foci: Peripheral/rim calcifications (2 points). Total points: 9, ACR-TIRADS category: TR5. ACR-TIRADS recommendation: FNAB. Pathological result: A malignant thyroid nodule; Surgical result: A papillary thyroid carcinoma.*

ACR-TIRADS: American College of Radiology Thyroid Imaging Reporting and Data System.

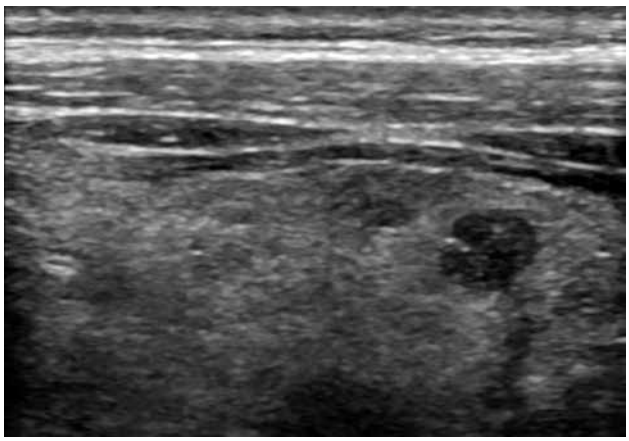

Figure 3. *A 38-year-old-male patient with a thyroid nodule with a maximal diameter of 6.7 mm. The nodule's ACR-TIRADS appointments as follows: composition: solid (2 points), echogenicity: hypoechoic (2 point), Shape: wider-than-tall (0 points), margin: smooth (0 points), echogenic foci: Punctate calcifications (3 points). Total points: 7, ACR-TIRADS category: TR5. ACR-TIRADS recommendation: Follow-up. Pathological result: A malignant thyroid nodule; Surgical result: A papillary thyroid carcinoma.*

ACR-TIRADS: American College of Radiology Thyroid Imaging Reporting and Data System.

Figure 4. *A 55-year-old-male patient with a thyroid nodule with a maximal diameter of 12 mm. The nodule's ACR-TIRADS appointments as follows: composition: solid (2 points), echogenicity: hypoechoic (2 point), Shape: wider-than-tall (0 points), margin: ill-defined (0 points), echogenic foci: none (0 points). Total points: 4, ACR-TIRADS category: TR4. ACR-TIRADS recommendation: Follow-up. Pathological result: A malignant thyroid nodule; Surgical result: A papillary thyroid carcinoma.*

ACR-TIRADS: American College of Radiology Thyroid Imaging Reporting and Data System.

taller-than-wide shape configurations and, of these, 20 had a taller-than-wide shape on both the transverse and longitudinal planes, seven had a taller-than-wide shape on only the transverse images, and five had this shape on only the longitudinal images. Of 54 malignant nodules, 20 (37%) had a taller-than-wide shape and only 12 of 356 benign nodules (3.3%) had a longer anteroposterior diameter than the transverse diameter. Of 54 malignant nodules, 24 had punctate echogenic foci and 11 had peripheral/rim calcifications. Two nodules had both punctate echogenic foci and peripheral/rim calcifications. Among 368 benign nodules, only 12 had punctate echogenic foci and six had peripheral/rim calcifications. Table 1 further details the US characteristics of the thyroid nodules. Figures 1-4 show the representative US features for thyroid nodules in the different ACR-TIRADS categories.

When TR4 and TR5 showed malignancy, the ACR-TIRADS correctly identified 47 of 54 malignant nodules (87%) and 264 of 368 benign nodules (71.7%). Overall, the ACR-TIRADS

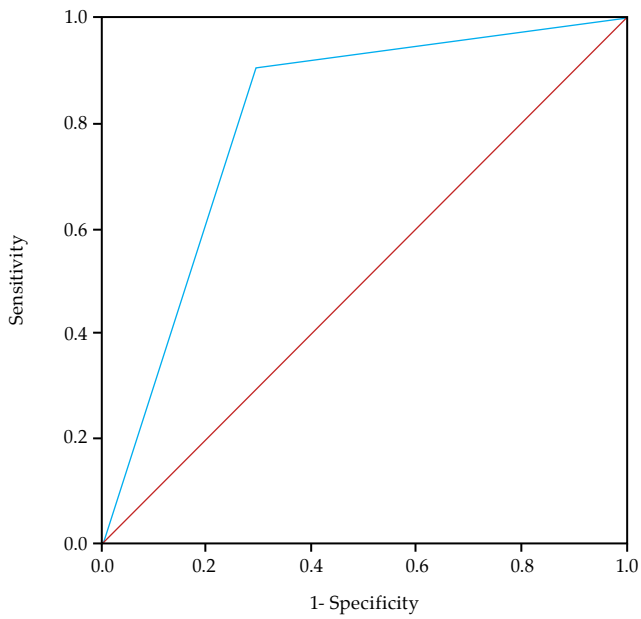

Figure 5. *Receiver operating characteristic (ROC) curve analysis of ACR-TIRADS in identifying malignant nodules using TR4 as a cut-off point. Area under the curve (AUC)= 0.80, p<0.0001, 95% CI= 0.74 to 0.86.*

ACR-TIRADS: American College of Radiology Thyroid Imaging Reporting and Data System.

Table 2. Decisions for thyroid nodules according to ACR-TIRADS

	Histopathological status			
	Benign		Malign	
Decision	n	%	n	%
Biopsy	132	35.9	23	42.5
Follow-up	187	50.8	30	55.5
No further evaluation	49	13.3	1	1.8

ACR-TIRADS: American College of Radiology Thyroid Imaging Reporting and Data System.

yielded 87% sensitivity, 71.7% specificity, 97.4% NPV, 31.1% PPV, and 73.6% diagnostic accuracy. Figure 5 shows a ROC for ACR-TIRADS to determine malignant nodules using TR4 as the cut-off value. Using the ACR-TIRADS would have spared 236/368 (64.1%) benign nodules from FNAB. Of these 236 nodules, 49 (13.3%) would not have been further followed, while 187 (50.8%) would have been scheduled for follow-up. Among 54 malignant nodules, one (1.9%) was classified as TR2, six (11.1%) were TR3, 14 (25.9%) were TR4, and 33 (6.1%) were TR5. Of these, 23 (42.5%) were compatible with the biopsy criteria of the ACR-TIRADS recommendations, 30 (55.5%) with follow-up, and one with a malignant nodule (1.8%) required no biopsy or follow-up (Table 2). Among 51 nodules classified as TR5, 18 (32.5%) were benign and 33 (64.7%) were malignant. Of 100 nodules categorized as TR4, 86 (86%) were benign and 14 (14%) were malignant.

DISCUSSION

In the present study, we retrospectively evaluated 368 benign and 54 malignant thyroid nodules as confirmed by FNAB or surgical specimen. The results showed that the ACR-TIRADS had an excellent diagnostic sensitivity, reaching 87% in identifying malignant thyroid nodules. However, it showed a relatively low specificity in discriminating malignant and benign nodules (71.7%). The overall diagnostic accuracy of the reporting system was found to be 73.6%. Previous ACR-TIRADS validation studies reported similar diagnostic metrics. Xu et al.[12] reported 96.6% sensitivity, 52.9% specificity, and an AUC of 0.84 using the ACR-TIRADS to discriminate benign from malignant thyroid nodules. Zheng et al.[13] evaluated 1,033 nodules from 1,013 patients and found that the ACR-TIRADS had a high sensitivity reaching 99.0%, despite low specificity (43.4%).

The ACR-TIRADS is a point-based US risk-scoring system which was originally developed to select and categorize thyroid nodules by whether they should be biopsied, followed, or require no further evaluation.[4] The main advantage of the ACR-TIRADS over pattern-based risk stratification systems, such as the American Thyroid Association (ATA) Guidelines and the Korean Society of Thyroid Radiology (KSThR), is its ability to classify almost all thyroid nodules via imaging.[5,6] Using the ATA and KSThR, up to 13.9 and 9.7% of malignant thyroid nodules may remain unclassified, respectively, since several patterns which are not suggested in either set of guidelines can be observed in malignant nodules.[10] Furthermore, nodule composition, echogenicity, and margins may be unclear, particularly when retrospectively reviewing US images for research purposes.[4] Therefore, the ACR-TIRADS filled this potential gap by recommending adding 2, 1, and 0 points, respectively, for nodules in which these categories could not be confirmed.[4] Consistent with previous studies, we successfully categorized all nodules in the present study using the ACR-TIRADS.[10-13]

One of the main theoretical frameworks of these classification systems, including ACR-TIRADS, is to reduce the number of unnecessary biopsies, particularly for benign nodules. Hoang et al.[14] evaluated the number of biopsy decisions made by eight radiologists based on their own practice patterns and according

to the ACR-TIRADS criteria for 100 thyroid nodules (15 malignant and 85 benign). Overall, the radiologists suggested performing biopsies for 80 of 100 nodules (80%) with 95% sensitivity and 20% specificity. The use of the ACR-TIRADS reduced the biopsy decisions by 27%, slightly reduced the sensitivity (87%), and prominently increased the specificity (51%). In another study, Middleton et al.[10] studied 352 malignant nodules and 3070 benign nodules and found that the ACR-TIRADS spared 52.9% of the benign nodules from FNAB, which was nearly twice the number spared, while using the ATA guidelines or KSThR TIRADS. In our cohort, the use of the ACR-TIRADS to patients spared 64.1% of benign nodules from FNAB, which was comparable to the rates reported in previous works.

Despite the success of the ACR-TIRADS in sparing a significant number of benign nodules from FNAB and possibly from surgical interventions due to non-diagnostic results, the ability of the ACR-TIRADS to spare a significant number of benign nodules could also prevent malignant nodules from being biopsied. In the present study, 30 of 54 nodules (55.5%) would have been followed according to the ACR-TIRADS, despite 87% of these nodules being categorized as moderately suspicious (TR4) or very suspicious (TR5). Additionally, 22% of these nodules which would have been scheduled for an active surveillance had cervical lymph node metastasis. Other authors also reported similar results using the ACR-TIRADS. Zheng et al.[13] found that approximately 69% of 230 malignant nodules categorized as TR5 would not have been recommended for FNAB according to the ACR-TIRADS, although 55 of these had cervical lymph node metastases at the time of diagnosis. Middleton et al.[10] reported that the ACR-TIRADS would not have referred 31.8% of malignant nodules for biopsy, and up to 11.1% of 288 malignant nodules with a diameter of ≥1 cm would have been followed, rather than undergoing FNAB. We acknowledge that most malignant nodules which are not considered for FNAB according to the ACR-TIRADS are indolent, which is unlikely to affect the prognosis of the disease.[15]

More importantly, no imaging or biochemical parameters exist that can definitively determine whether a malignant nodule would be indolent. Additionally, not recommending a biopsy for a nodule highly suspicious for malignancy may impair a patient's confidence in the radiologist's practice, particularly for the Turkish population. Furthermore, actively surveilling a nodule without knowing its exact pathological status may cause unnecessary anxiety in patients. In addition to the patients' quality of life, thyroid surgeons may prefer to forego an active surveillance for a suspicious thyroid nodule. In the present study, nodules categorized as TR5 using the ACR-TIRADS had an approximate 64% risk of being malignant. This rate was comparable to that found in several studies, but substantially higher than the risk ratio proposed by the ACR committee.[4] Thus, it is not straightforward for a thyroid surgeon to implement an active surveillance and explain its rationale to patients, while informing patients that their nodules may reach a 64% risk of malignancy. Nevertheless, we suggest that, despite the ACR-TIRADS criteria not recommending FNAB for particular cases of TR4 and TR5 thyroid nodules, surgeons' and patients' concerns should be considered and FNAB should be offered and used, when necessary.

Nonetheless, the present study has several limitations. First and foremost, selection bias was unavoidable, as we were only able to include thyroid nodules having FNAB or surgical pathology results. The US characteristics of thyroid nodules which underwent thyroid US examinations without indications of FNAB may differ from those of the study population. Second, we retrospectively reviewed patients' US images, which could not substitute real-time US examinations in interpretation quality; however, we believe that we eliminated this disadvantage using high-quality cine-images, which are routinely obtained for nodules scheduled for FNAB at our institution. Finally, we were unable to evaluate other thyroid-reporting systems or compare their diagnostic value with that of ACR-TIRADS, as this was beyond the scope of the present study. We believe this would be worthwhile to investigate in future works.

In conclusion, the ACR-TIRADS showed an excellent diagnostic sensitivity, reaching 87% in identifying malignant thyroid nodules, with an acceptable specificity (71.7%). The main

robustness of the ACR-TIRADS in the present study was its ability to spare a significant number of benign nodules from FNAB. The use of the ACR-TIRADS would also prevent 55.5% of malignant nodules from FNAB. Despite the diagnostic accuracy of the ACR-TIRADS validated by the current study and previous studies, this critical flaw should be remembered by radiologists and thyroid surgeons. We suggest that the FNAB threshold levels set by the ACR-TIRADS be extensively reviewed by the Turkish radiologists, endocrinologists, general surgeons, and ear, nose and throat surgeons before integrating the system into their daily practice.

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