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Diagnostic Reliability of the American College of Radiology Thyroid Imaging Reporting and Data System in Royal Commission Hospital, Kingdom of Saudi Arabia

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Abstract

BACKGROUND: The American College of Radiology Thyroid Imaging Reporting and Data System (ACR TI-RADS) classified and predicted the risk of thyroid nodule malignancy with ultrasound scan scoring system.

AIM: Hence, we aimed to investigate the value of the combined use of ultrasound ACR TI-RADS scoring and ultrasound-guided thyroid fine needle aspiration cytology (FNAC) based on the Bethesda System for Reporting Thyroid Cytology (TBSRTC) for assessing the accuracy tests of diagnosing low and high-risk thyroid nodules of ACR TI-RADS.

METHODS: We enrolled 392 patients with thyroid nodules who underwent ultrasound scanning and scoring using the ACR TI-RADS classification along with ultrasound-guided thyroid FNAC and scoring with TBSRTC. The two methods were grouped as low and high risk of malignancy to evaluate the accuracy of ACR TI-RADS.

RESULTS: Three hundred and ninety-two patients were enrolled in the study. The mean (Standard deviation [SD]) age was 46.03 (13.96) years, 332 (84.7%) were females and the mean (SD) of body mass index was 31.90 (22.32) kg/m^2 and Vitamin D 17.65 (11.15) nmol/L. The mean (SD) for thyroid function test was 5.37 (44.16) mmol/L for thyroid-stimulating hormone, 1.48 (1.49) ng/dL for free thyroxine (FT4), and 2.69 (0.70) nmol/L for free triiodothyronine (FT3). Most of the participants were euthyroid (63.8%), but 28.6% had hypothyroidism and 7.7% had hyperthyroidism. The accuracy tests of ACR TI-RADS in relation to TBSRTC, were sensitivity (87.8%), specificity (65.2%), positive predictive value (29.8%), and negative predictive value (97%). The area under the curve = 0.590, 95% CI = 0.530–0.650, p < 0.006.

CONCLUSION: ACR TI-RADS is a simple, practical, and reliable scoring system for assessing thyroid nodule; it has a better overall diagnostic performance and the ability to exclude unnecessary FNAC with high negative predictive value.

Introduction

The incidence of thyroid tumors continues to increase worldwide [1] and represents the most prevalent endocrine cancer globally [2]. A similar increase in thyroid cancer was observed in the Kingdom of Saudi Arabia (KSA) and other Gulf countries [3], [4]. The presence of an abnormal lesion within the thyroid gland tissue is called a thyroid nodule [5]. Thyroid ultrasonography is the primary non-invasive modality used for evaluating thyroid nodules [6]. A thyroid ultrasound scan improves the diagnostic rate of thyroid nodules (50–60%) [7]. Classification and scoring systems are utilized to improve the diagnostic capacity of thyroid ultrasound scans. The American College of Radiology Thyroid Imaging Reporting and Data System (ACR TI-RADS) is one thyroid scoring system that is used to assess thyroid nodules and to predict those with malignant potential: the higher the score, the higher the malignancy risk [8]. The malignancy risk of thyroid nodules using ACR TI-RADS is predicted by ultrasound patterns: combining solidity, echogenicity, and suspicious ultrasound features [9]. The suspicious features of thyroid nodule ultrasound, such as micro-calcification, a nodule that is taller than it is wide and speculated or microlobulated margins, are considered to be independent predictors of malignancy in a solid or hypoechoic nodule [9]. However, thyroid fine-needle aspiration cytology (FNAC) remains the gold standard for evaluating thyroid nodular disorders [10]. Sonography-guided thyroid FNAC augments the accuracy and safety of the procedure for assessing thyroid nodules [11]. Additionally, the Bethesda System for Reporting Thyroid Cytology (TBSRTC) is an important and reliable scoring classification system that improves diagnostic accuracy [12]. Applying ACR TI-RADS criteria can minimize the number of ultrasound-guided FNACs performed on benign nodules [13]. Hence, many studies have assessed ACR TI-RADS to determine its sensitivity, specificity, positive predictive value, negative predictive value, accuracy rate and receiver operating characteristic (ROC) curves [14], [15], [16], [17], [18], [19], [20], [21], [22]. Thyroid ultrasound is a reliable non-invasive, practical method [6], [23]; it is accessible and has a low capital

cost [6]. Recently, published studies conducted in KSA have documented an increase in the thyroid cancer rate (9–11.7%) [4], [24] with a significant geographical variation across the different areas of KSA [4], [25], [26]. Despite the wide use and importance of thyroid ultrasound as an essential diagnostic tool, along with marked improvements in reporting systems globally and the trend of the increasing prevalence of thyroid cancer, few studies have published data assessing the accuracy of ACR TI-RADS in KSA. Hence, the current study aimed to investigate the accuracy of ACR TI-RADS and its associated factors among adult patients at the Royal Commission Hospital in eastern KSA.

Methods

A retrospective study was conducted at the Royal Commission Hospital from January 1, 2017, through September 31, 2021. The Royal Commission Hospital has 200 physicians in all major specialties and most subspecialties. It has a 217-bed capacity for inpatient care, as well as outpatient clinics and primary care services at many health centers throughout the city. We retrieved the medical records of patients (males and females), aged 18 years and older with documented thyroid nodules based on ultrasound findings who had undergone ultrasound-guided FNAC in the hospital. We excluded the medical records of patients with incomplete data, those who underwent partial thyroid surgery without prior thyroid FNAC, cases with known thyroid malignancy, patients diagnosed with thyroid cancer from a lymph node biopsy, and reports from other hospitals. The following data were collected in a questionnaire: age, gender, weight, and height to obtain the body mass index (BMI), thyroid status, and Vitamin D levels. High-resolution thyroid ultrasonography was performed in the radiology department by a specialist, then it was reviewed by a consultant radiologist before releasing the approved report. ACR TI-RADS was adopted for reporting the thyroid ultrasound scan, as seen in Table 1 [27]. The FNAC was done by an expert radiologist under ultrasound guidance. The procedure was performed after providing the patients with a proper explanation and obtaining their informed consent. Under aseptic conditions and application of a local anesthetic, a 22-gauge needle with a 10-mL syringe was used to target the areas presumed to contain the most cellular material of the thyroid nodule under ultrasound guidance. Then, continuous low negative pressure was applied concomitantly with a to-and-fro movement of the needle within the lesion to obtain material from the tissues of the thyroid nodule in the needle hub. Mild pressure was applied to prevent bleeding at the site of the needle puncture, then the patient was kept for 15 minutes before being reassured and discharged. The slides were prepared using a method similar to what is used for blood smears: one drop of aspirated material was forced onto each of several glass slides and the smears were prepared by using a second glass slide. The labeled slides were transferred to the histopathology department in the hospital after being fixed with 95% ethanol. A final cytopathology report was issued after each cell block was evaluated by an expert histopathologist. The outcome of the ultrasound-guided thyroid FNAC was reported using the 2017 TBSRTC [28], as seen in Table 2. All the thyroid nodules were evaluated by ultrasound and the nodules with an ACR TI-RADS classification were categorized into four groups (2, 3, 4, and 5). Patients with ACR TI-RADS 1 (normal thyroid gland) were excluded as there was no indication to subject them for FNAC. The results of the thyroid ultrasound scan were grouped in two categories according to diagnostic ability of the ACR TIRADS/The TBSRTC systems in distinguishing thyroid nodules that required or not FNAC and the potential risk of malignancy as reference standard (<ACR TIRADS 3/The TBSRTCIII vs. ≥ACR TIRADS 3/The TBSRTC III) [29]: low risk (ACR TI-RADS 2 [Not suspicious] and potential high-risk ACR TI-RADS 3 [Mildly suspicious]) (ACR TI-RADS 4 [Moderately suspicious] and ACR TI-RADS 5 [Highly suspicious]). The TBSRTC outcome of the thyroid FNAC was obtained for each group as illustrated in (Figure 1). Then, the remaining results of thyroid FNAC were assigned to two groups based on the potential risk of malignancy: low risk for malignancy (I–II) and high risk for malignancy (III–VI) to assess the accuracy of the ARC TI-RADS scoring system.

Table 1: TI-RADS

Category definitions	
TI-RADS -1	Normal thyroid gland
TI-RADS -2	Benign nodule
TI-RADS -3	Highly probable benign nodule
TI-RADS -4	Suspicion for malignancy
TI-RADS -5	Malignant nodule with more than two criteria of high suspicion

Table 2: The Bethesda system for reporting thyroid cytopathology

I. Non-diagnostic or Unsatisfactory	Cyst fluid only, virtually acellular specimen and other (obscuring blood, clotting artifact, etc)
II. Benign	Consistent with a benign follicular nodule (includes adenomatoid nodule, colloid nodule, etc), consistent with lymphocytic (Hashimoto) thyroiditis in the proper clinical context or consistent with granulomatous (subacute) thyroiditis
III. Atypia of Undetermined Significance	Follicular lesion of undetermined significance
IV. Follicular Neoplasm	Suspicious for a follicular neoplasm or specify if Hürthle cell (oncocytic) type
V. Suspicious for Malignancy	Suspicious for one of these cancer; papillary carcinoma or medullary carcinoma or metastatic carcinoma or lymphoma or other cancer
VI. Malignant	Diagnostic for one of these: Papillary thyroid carcinoma, poorly differentiated carcinoma, medullary thyroid carcinoma, undifferentiated (anaplastic) carcinoma, squamous cell carcinoma, carcinoma with mixed features (specify), metastatic carcinoma, non-Hodgkin lymphoma or other

Statistical Analysis

Data were analyzed using SPSS for Windows (version 22.0). Continuous data were checked for

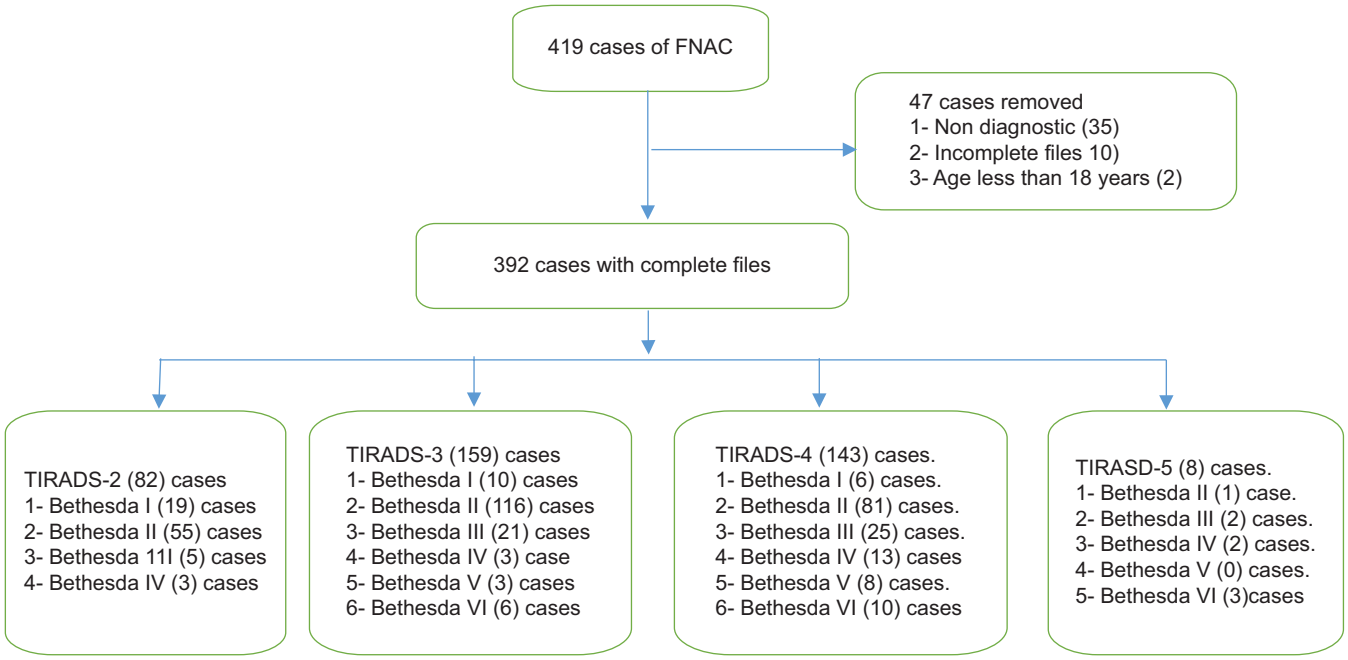

Figure 1: Inclusion and exclusion criteria

normality using the Shapiro-Wilk test, and none of the data were normally distributed. Data were expressed as proportions, the mean (Standard deviation [SD]), or as number (proportion), as applicable. The characteristic features were obtained: age, gender, thyroid status, thyroid function test, and Vitamin D level. Diagnostic accuracy tests were performed using a 4-grid cell to calculate the sensitivity, specificity, positive predictive value, negative predictive value, and ROC curves. The ROC curves were used to compare sensitivity and specificity. A larger area under the ROC curves was associated with a higher diagnostic accuracy.

Results

Three hundred and ninety-two patients who underwent a thyroid ultrasound scan and ultrasound-guided thyroid FNAC were enrolled in the study. The mean (SD) age was 46.03 (13.96) years, and 332 (84.7%) were females. The mean (SD) of BMI was 31.90 (22.32) kg/m^2 and vitamin D 17.65 (11.15) nmol/L. The mean (SD) for thyroid function test was 5.37 (44.16) mmol/L for thyroid-stimulating hormone, 1.48 (1.49) ng/dL for free thyroxine (FT4), and 2.69 (0.70) nmol/L for free triiodothyronine (FT3) (Table 3). Most of the participants were euthyroid (63.8%), but 28.6% had hypothyroidism and 7.7% had hyperthyroidism. The thyroid ultrasound reports for ACR TI-RADS groups 2, 3, 4, and 5 were (21.0%), (40.6%), (36.4%) and (2.0%), respectively. The outcome of the thyroid FNAC based on the TBSRTC reporting system was non-diagnostic (8.9%), benign in 64.4% of the cases, atypia of undetermined significance in 13.5% of the cases, follicular neoplasm in 5.4% of the cases, suspicious for malignancy in 2.8% of the cases and malignant in 4.8% of the cases. The accuracy tests results were sensitivity (92.3%), specificity (25.7%), positive predictive value (32.2%), and negative predictive value (87.5%), (Table 4).

Table 3: General characteristics of patients who underwent thyroid ultrasound and FNAC in eastern region 2017–2021

Variables	Mean	Standard deviation
Age, years	46.0306	13.96063
Body mass index, kg/m^2	31.9025	22.31620
Thyroid-stimulating hormone, mmol/L	5.3718	44.16181
Free triiodothyronine, nmol/L	2.6893	0.70443
Free thyroxine, ng/dL	1.4773	1.49466
Vitamin D, nmol/L	17.6470	11.14719
Gender	Number	Proportion
Female	332	84.7
Male	60	15.3
Thyroid status		
Euthyroid	250	63.8
Hypothyroidism	112	28.6
Hyperthyroidism	30	7.7

While ACRTI-RADS 2 demonstrated non-malignant changes on FNAC findings (Bethesda I (32.9%) vs. Bethesda II (67.1%), ACRTI-RADS 5 showed evidence of malignant changes in 87.5% of the group.

Table 4: Sensitivity and specificity of ACT TI-RADS for patients who underwent thyroid ultrasound and FNAC in eastern region 2017–2021

Test	Result%
Sensitivity	92.3
Specificity	25.7
Positive predictive value	32.2
Negative predictive value	87.5

FNAC: Fine needle aspiration cytology.

The sensitivity and specificity of the diagnosis for ARC TI-RADS were 87.7% and 65.2%, respectively (area under the curve [AUC] = 0.590, 95% CI = 0.530–0.650, p < 0.006), as seen in Figure 2.

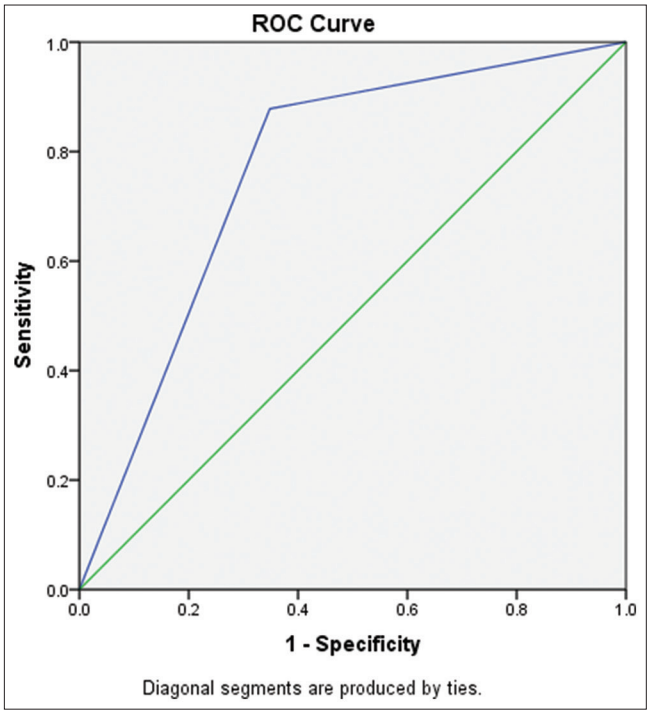

Figure 2: Receiver operating characteristic curve analysis of American College of Radiology Thyroid Imaging Reporting and Data System and the outcome of fine needle aspiration cytology (FNAC) (the Bethesda System for Reporting Thyroid Cytology) of patients who underwent thyroid ultrasound and FNAC in eastern region 2017–2021

Discussion

The main findings of our study regarding the accuracy of predicting malignancy risk based on a thyroid ultrasound reporting system (ACR TI-RADS) and the outcome of FNAC (TBSRTC classification) were: sensitivity (92.3%), specificity (25.7%), positive predictive value (31%), negative predictive value (87.5%) and AUC = 0.765, 95% CI = 0.590, 95% CI = 0.530–0.650, p < 0.006. Our results showed that ACR TI-RADS had a significantly superior diagnostic accuracy (sensitivity and positive predictive value) for the risk of malignancy in comparison to the results obtained from a study conducted recently in central of KSA (Qassim): sensitivity (75%) and positive predictive value (15.7%) [30]. On the other hand, we documented almost equal AUC = 0.60 (95% CI: 0.505–0.713) besides relatively lower specificity and negative predictive value than that obtained in KSA (Qassim), which were (62.35%) and (96.3%) respectively [30]. The sensitivity and specificity results obtained in our study were comparable to the results documented in a systematic review and meta-analysis study that evaluated 37,585 and 10,926 nodules, respectively; the sensitivity and specificity were 70% and 89%, respectively [31] and 98.3% and 55.2%, respectively [32]. The sensitivity of ACRTI-RADS for predicting the risk of malignancy was markedly higher than that seen in Brazil (90%) [15] Chile (88%) [14] China (77.3%) [19], Malaysia (85.7%) [22] Italy (67.6%) [29] and 58.9% [33], Israel 86% [13] and Turkey (76%) [34]. On the other hand a higher percentage of sensitivity was documented in different countries across the globe: Philippines (100%) [35], China (92.7%) [17] and (98.15%) [18], Korea (95.5%) [21] and (96.6%) [20] and Egypt (98.3%) [36]. In our study, the specificity of the ACRTI-RADS for predicting the risk of malignancy was lower than that reported in many different countries: obtained in Korea (58.6%) [21] and (52.9%) [20], Brazil (51.4%) [15], China (47.84%) [18] and (89.1%) [19], Philippines (52.2%) [36], Malaysia (51.1%) [22] and (70.7%) [17], Singapore (90.4%) [16], Italy (57.2 %) [29] and 58.9% [33], Egypt (90.9%) [36] and Turkey (97.5%) [34]. In the current study, the positive predictive value of the thyroid ACR TI-RADS was higher than that obtained in Italy (12.8 %) [29] and Philippines (16.5%) [35], but lower than that found in Chile (49%) [14], China (73.31%) [18] and, Korea (44.5%) [21] and Turkey (63.3%) [34]. In our study, the negative predictive value (87.5%) for risk of malignancy in thyroid nodular disease based on ACRTI-RADS was higher than that obtained in China (85.1%) [19]. Hence, this system may help reduce the rate of unnecessary thyroid FNAC. This was strengthened by markedly higher negative predictive value obtained in different studies conducted in different countries: Philippines (100%) [35], Korea (96.9%), Malaysia (98.6%) [22] Italy (95.0 %) [29], Brazil (94.7%) [15], Chile (88%), [14], China (94.65%) [18] and Singapore (93.8%) [16]. The AUC for ROC obtained in this study was almost similar to that obtained in a study conducted in Saudi Arabia (0.60) [30]. On the other hand, it was lower than the pooled AUC for ROC documented in a systematic review and meta-analysis study 0.938 [32] and in studies conducted in Korea (0.846) [20] and China (0.879) [19] and (0.817) [17]. The accuracy tests in our study and other studies indicated that ACR TI-RADS was a reliable non-invasive tool and a practical method for detecting the risk of malignancy in thyroid nodular disease, and it can prevent unnecessary FNAC and reduce the need for thyroid surgery when combined with the cytology result; it is also an appropriate method for screening and follow-up [21], [22], [23], [34], [36], [37]. The study documented non-malignant changes in ACRTI-RADS 2 on FNAC findings (Bethesda I (32.9%) versus Bethesda II (67.1%). Moreover, ACRTI-RADS 5 showed evidence of malignant changes in 87.5% of the group. The variability of accuracy tests in different studies may be explained by differences in the genetic backgrounds of the study groups and the influence of polygenetic factors, such as receptor tyrosine kinase/phenylthiocarbamide, the activation of oncogenes, such as Rat sarcoma, a human gene that encodes a protein called B-Raf and the overstimulation of the phosphatidylinositol 3-kinase/ protein kinase B pathway, which are involved in

thyroid tumorigenesis [38]. Furthermore, genetic mutations have been primarily attributed to unknown aetiologies (about 80%) [39]. Thus, these and other emerging molecular markers are used to provide additional approaches for classifying thyroid tumors and they may offer opportunities for developing novel approaches to tumor diagnosis, adding parameters for prognostic assessment, and stimulating potential biologic therapeutic strategies [39]. In fact, the recently updated TBSRTC has introduced molecular testing as a diagnostic adjunct to FNAC to avoid unnecessary surgery [28]. Moreover, malignant nodules with mixed echo patterns are scored lower in the ACR TI-RADS, resulting in misdiagnosis [8], which can affect the results of the accuracy tests. Additionally, thyroid ultrasound scans, the ultrasound-guided FNAC procedure, and cytology readings are operator dependent [40], which can impact the results. Moreover, differences in the methodologies adopted for these studies can influence the findings. Therefore, while thyroid ultrasound and FNAC are robust tools for evaluating thyroid nodular diseases, it is essential for physicians to continue to use their clinical judgment first and foremost when evaluating thyroid nodules [40].

This study had some limitations. First, it was a retrospective study, and the lack of ultrasound examination with the use of elastography and other factors were not assessed. In future studies, thyroid antibodies, iodine levels, nutritional pattern, genetic analysis, and environmental factors can be assessed.

Conclusion

ACR TI-RADS has a fair diagnostic accuracy value and higher negative predictive value, supporting its use as an important tool for assessing the risk of malignancy in thyroid nodules and reducing the need for unnecessary FNAC and thyroid surgery.

Author Contribution

Conceptualization: Hussain A Alyousif, Imad R Musa. Data curation: Mona A Sid Ahmed, Ayat Al Saeed, Abdulmuhsen Ali Ahmed Hussein. Formal analysis: Hussain A Alyousif Imad R Musa. Methodology: Hussain A Alyousif Imad R Musa. Project administration: Hussain A Alyousif Imad R Musa. Supervision: Imad R Musa. Validation: Mona A Sid Ahmed, Ayat Al Saeed, Abdulmuhsen Ali Ahmed Hussein. Visualization: Hussain A Alyousif Imad R Musa. Writing-original draft: Imad R Musa. Writing-review and editing: all investigators.

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