The Performance of the American Thyroid Association (ATA) and American College of Radiology (ACR-TIRAD) Thyroid Nodule Risk-Stratification Systems in Determining High-Risk Nodules, and the Correlation of Site, Size, and Autoimmunity with High-Risk Features

Ibrahim H. Hussein, Mahmood T. Altemimi, Haider A. Alidrisi, Ammar M. Saeed Almomin, Nassar T. Alibrahim, Muqdam A. Hamza, Husam J. Imran, Ibrahim A. Zaboon, Ali H. Alhamza, Hussein A. Nwayyir, Abbas A. Mansour

Faiha Specialized Diabetes, Endocrine and Metabolism Center (FDEMC), College of Medicine, University of Basrah, Basrah, Iraq

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Abstract

Introduction: Neck ultrasonography (US) and fine-needle aspiration (FNA) biopsy are usually used to evaluate thyroid nodules. This study aimed to evaluate the performance of two popular thyroid imaging reporting systems in detecting thyroid malignancy and to evaluate the correlation between thyroid autoimmunity, nodule site, and size in the development of malignancy. **Methods:** This prospective study was conducted from January 2019 to July 2021 in Basrah, Iraq. The American Thyroid Association (ATA) and American College of Radiology-Thyroid Imaging Reporting and Data (ACR-TIRAD) systems were used to evaluate the malignant potential of 143 thyroid nodules in 131 patients. **Results:** The sensitivity and positive predictive value (PPV) of the ATA system for detecting malignancy were 96% and 20.8% for low-risk and 100% and 4.3% for high-risk nodules, respectively. ACR-TIRAD sensitivity and PPV were 84% and 22.1% for low-risk and 80% and 4.2% for high-risk nodules, respectively. The specificity and negative predictive value (NPV) of the ATA system for detecting malignancy were 11.6% and 92.3% for low-risk and 10.5% and 100% for high-risk nodules, respectively. The ACR-TIRAD specificity and NPV were 28% and 87.8% for low-risk and 26% and 96.9% for high-risk nodules, respectively. The strength of the correlation between FNA performed across different Bethesda categories and age, sex, nodule size, and positive thyroid peroxidase (TPO) antibodies were 0.25, 0.01, 0.22, and 0.4, respectively. **Conclusion:** Both systems are effective; however, adopting TI-RADS stratification results in fewer biopsies being performed for thyroid nodule assessment. Only sex was found to be significantly correlated with FNA performance in thyroid-nodule evaluation.

Keywords: American College of Radiology-Thyroid Imaging Reporting and Data, American Thyroid Association, fine-needle aspiration, thyroid nodule

Introduction

Ultrasonography (US) provides valuable information for predicting the risk of malignancy in each thyroid nodule.[1] However, no individual ultrasonographic feature can specifically diagnose a malignancy.[2] Therefore, multiple thyroid imaging reporting systems for risk stratification are available to determine nodules that require fine-needle aspiration (FNA).

In 2015, The American Thyroid Association (ATA) guidelines classified nodules into five classes from very low to

Address for correspondence: Dr. Mahmood T. Altemimi, Faiha Specialized Diabetes, Endocrine and Metabolism Center (FDEMC), College of Medicine, University of Basrah, Basrah, Iraq.
E-mail: mahmoodaltimimi83@gmail.com

Submitted: 01-Apr-2023 **Revised:** 27-Jul-2024
Accepted: 16-Oct-2024 **Published:** 30-Dec-2024

Supplementary material available online: https://journals.lww.com/indjem/

Access this article online

Quick Response Code:

Website: https://journals.lww.com/indjem/

DOI: 10.4103/ijem.ijem_154_23

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How to cite this article: Hussein IH, Altemimi MT, Alidrisi HA, Almomin AM, Alibrahim NT, Hamza MA, *et al*. The performance of the American Thyroid Association (ATA) and American College of Radiology (ACR-TIRAD) thyroid nodule risk-stratification systems in determining high-risk nodules, and the correlation of site, size, and autoimmunity with high-risk features. Indian J Endocr Metab 2024;28:622-8.

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high suspicion for malignancy with subsequent biopsy to intermediate-high risk one.[3] In 2017, the American College of Radiology published a paper for the American College of Radiology-Thyroid Imaging Reporting and Data System (ACR-TIRAD), which divided thyroid nodules into five tiers (TR1–TR5) based on specific US examination.[4] The ATA and ACR-TIRAD systems advocated a specified indication for performing FNA for each thyroid nodule while comparing variable accuracies and risk predictions.

This study aimed to evaluate the performance of two risk-stratification systems for differentiating between high- and low-risk thyroid nodules. The secondary aim was to assess the correlation between thyroid autoimmunity, nodule site, and size in the development of malignancy.

Materials and Methods

This a prospective cross-sectional observational study conducted from January 2019 to July 2021 at Faiha Specialized Diabetes, Endocrine, and Metabolism Center (FDEMC), a tertiary referring center in Basrah, Southern Iraq.

The sample size was calculated using the following equation:

$n = [Z_{1-\alpha/2}]^2 p\,(1-p)^2 \div d^2$, where $Z_{1-\alpha/2}$ = is the standard normal variate (at 5% type 1 error ($P < 0.05$), it is 1.96), p = expected proportion in population based on a local study for the evidence of nodular thyroid disease (5.2%),[5] and d = absolute/precision error of 5% and at type 1 error of 5% (0.05). The minimum sample size was 76, and the number of enrolled participants was 131.

US-guided FNA was performed on 143 thyroid nodules in 131 patients who underwent US. Ninety patients (63.4%) had solitary thyroid nodules for cytology, while 42 patients had MNG in whom 52 (36.6%) nodules of MNG harbouring multiple biopsied thyroid nodules were addressed in detail. After careful statistical analysis, we found that they did not significantly affect the results because of their lower number than pooled single nodules. We included every patient with palpable non-cystic thyroid nodules, or nodules detected by the US with a maximum diameter ≥10 mm. We considered any patient with at least two nodules to have multinodular thyroid disease (MNG).

The exclusion criteria included any nodule of size <10 mm, age <16 years, purely cystic nodules, patients with suppressed thyroid-stimulating hormone (TSH), FNA aspiration within the last 2 weeks, known bleeding diathesis, and known thyroid cancer.

Ultrasonography images and nodule characteristics

All patients underwent US imaging of the thyroid and neck by using a linear high-frequency broadband transducer (5–18 MHz). The US examination was performed in the Radiology unit of the centre, with the patient in a supine position and the neck slightly extended, using two different US machines: GE Logiq E9 (GE Healthcare, Milwaukee) and HD11XE (Philips Medical Systems Nederland B.V.). At least two well-qualified endocrinologists examined each patient separately with a representative grayscale view by using colour-flow Doppler to assess nodule features.

The obtained views were analysed to assess the site (whether it was located in the right or left lobe or the isthmus), size (measured in mm in three dimensions (anteroposterior, transverse, and longitudinal), taking into account the largest diameter in any dimension), texture (solid or solid cystic), echogenicity (anechoic, hypoechoic, isoechoic, or hyperechoic), vascularity pattern, margin (clearly well-defined and surrounded partially or completely by halo, irregular or lobulated, ill-defined, or extrathyroidally extended), and calcification (microcalcification, macrocalcification, or eggshell form).

After acquiring comprehensive US features, two qualified endocrinologists certified by the national institution's thyroid US training program independently determined each nodule's characteristics. A radiologist who did not participate in the study confirmed the characteristics of each nodule. Finally, to prevent the inter-rater reliability analysis from examining nodular thyroid criteria, the two endocrinologists and the independent radiologist judged the targeted nodules separately after matching the description criteria in a special form, and the higher matching rating score nodules were chosen for biopsy.

These targeted nodules were categorised according to risk-stratification systems. According to the 2015 ATA guidelines, US thyroid nodule categories are benign (<1%), very-low-suspicion (<3%), low-suspicion (5%–10%), intermediate-suspicion (10%–20%), and high-suspicion nodules (70%–90%). According to the ACR-TIRAD system, the US thyroid nodule categories are TR1 (benign), TR2 (not suspicious), TR3 (mildly suspicious), TR4 (moderately suspicious), and TR5 (highly suspicious).

Nodules were divided into three groups according to the following sizes: 10–20 mm, 21–30 mm, and >30 mm; thereafter, each nodule ≥10 mm was subjected to FNA.

Cytology by fine-needle aspiration under ultrasonography guidance

After performing risk stratification of each nodule by using both the ATA and ACR-TIRAD systems, US-guided FNA was performed from the indicated nodule by using a 21–23-G 10-mL syringe using a completely sterile aseptic technique, with the neck slightly extended. At least two aspiration attempts were performed to obtain a better yield.

The aspirating endocrinologist visualised the forward motion of the needle that carved tissue from the indicated nodule and accumulated in the needle shaft. The backward motion simply served to reposition the needle for the next stroke forward to collect additional material. The needle oscillation in the FNA biopsy process is approximately 3 per second with an intra-nodular dwell time of 3–5 seconds for the first biopsy. The intra-nodular dwell time begins when the needle enters the target lesion. This technique helped to optimise the cellular yield and decrease blood dilution.

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At least 2–4 slides for each nodule, with each slide having satisfied clusters of cells (not less than 100 cells per field), were prepared to smear the aspirated material, and these slides were fixed in 95% ethanol and transferred on the same day to a histopathologist. Each sample was subjected to histopathological examination, which yielded six groups of results according to the recommendations of the Bethesda system for reporting cytopathology (BSRTC): Bethesda 1: non-diagnostic or unsatisfactory, Bethesda 2: benign, Bethesda 3: atypia of undetermined significance/follicular lesions of undetermined significance (AUS/FLUS), Bethesda 4: follicular neoplasm/suspicious for follicular neoplasm (FN/sFN), Bethesda 5: suspicious for malignancy, and Bethesda 6: malignant.[6,7] Based on the Bethesda system, we classified the results as benign (Bethesda 2), neoplastic (Bethesda 3, 4, 5, and 6), and malignant (Bethesda 5 and 6) lesions.

Autoimmunity and biochemical tests

For all patients, we measured serum thyroid-stimulating hormone (TSH) by electrochemiluminescence (ECL) COBAS, and for most patients (108/131; 82.4%), we measured thyroid autoimmunity (TAA) by measuring thyroid peroxidase antibody (TPO) and thyroid-stimulating receptor antibody (Trab).

Statistical analysis

Data were analysed using IBM SPSS Statistics (version 26). We used the mean to express continuous data with either the standard deviation (SD) or standard error (SE). Categorical data were expressed as numbers and percentages (%). The correlation between the FNA results and (ACR-TIRAD and ATA system categories) was determined using Fisher's exact test. The performance of either system for diagnosing malignancy or neoplastic growth is presented in the form of sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV). The effects of other parameters such as sex, nodule, location, diameter, TSH, TPO, and TRAb on the FNA results were determined using Fisher's exact test. Finally, a one-way analysis of variance (ANOVA) was used to correlate patient age with FNA results. Statistical significance was set at $P < 0.05$.

Ethical aspects

Ethical approval was obtained from the ethical committee of the tertiary endocrine centre and the institutional review board (IRB) (57/36/22) for the study on 16th December 2018, according to the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards, and informed consent was obtained from all patients.

Results

The general characteristics of the cohorts included a mean age of 43.62 years, 12.6% participants of male sex, and an MNG of 36.4%. Autoimmunity was assessed by either positive TOP Ab or TRab at 30.2% and 45.5%, respectively. Most recruited participants were in the euthyroid state (95.3%), and 13 (9.9%) patients underwent surgery (lobectomy or total thyroidectomy) due to either high-risk suspicious nodules, compressive symptoms, cosmetic issues, or patients' preferences. The diameters of the nodules ranged from a minimum of 10 mm to a maximum of 53 mm [Table 1].

The distribution of the cytological results of FNA was benign (103 (72%)), non-diagnostic (15 (10.5%)), AUS/FLUS (14 (9.8%)), suspicious for follicular neoplasm (6 (4.2%)), suspicious for malignancy (4 (2.8%)), and malignant (1 (0.7%)) [Figure 1].

Correlation between the Bethesda results and the ACR-TIRAD system [Supplementary Figure 1]: The prevalence of abnormal neoplastic or malignant risk in the Bethesda system numerically, but non-significantly, increased as the TR categories moved from TR3 upwards ($P = 0.38$). For TR3, there were three (11.5%) cases with AUS/FLUS. Regarding TR4, 14.3% had neoplastic results, one (1.8%) was suspicious for malignancy, two (3.6%) were suspicious for follicular neoplasm, and five (8.9%) had AUS/FLUS. In the categories of TR5 and above, 35% had neoplastic results, one (2.5%) was malignant, three (7.5%) were suspicious for malignancy, four (10%) were suspicious for follicular neoplasm, and six (15%) had AUS/FLUS; however, all categories TR2 and less had benign results.

Correlation between the Bethesda results and the ATA system [Supplementary Figure 2]: A similar correlation between the Bethesda results and the ATA system is shown in Supplementary Figure 2, with a numeric and non-significant increase in neoplastic outcomes from low to high suspicion ($P = 0.06$). Among the low-suspicion nodules, three (8.3%) had AUS/FLUS. Among the intermediate-suspicion

Table 1: General characteristics of the 131 patients and 143 nodules

Variable	*n* (%)	Mean±SD
Age (years)		43.62±12.31
Gender (men)	16/131 (12.2)	
MNG	52 (36.4)	
Biopsied nodule		
Right	77 (53.8)	
Left	44 (30.8)	
Isthmus	22 (15.4)	
Diameter (mm) (range: 10–53)		21.16±9.36
TPO positive	26/86 (30.2)	
TRab positive	10/22 (45.5)	
TSH (mU/L)		1.56±1.51
Normal TSH	122 (95.3)	
High TSH	6 (4.7)	
Surgery		
Lobectomy	7 (5.3)	
Total thyroidectomy	6 (4.6)	

N: number; SD: standard deviation; MNG: multinodular goiter; TPO: thyroid peroxidase; Trab: thyroid-stimulating receptor; TSH: thyroid-stimulating hormone

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nodules, 12.5% had neoplastic potential, two (5%) were suspicious for follicular neoplasm, and three (7.5%) had AUS/FLUS. Of the high-suspicion nodules, 17% had neoplastic results distributed as one (2.3%) malignant, four (9.1%) suspicious for malignancy, four (9.1%) suspicious for follicular neoplasm, and eight (18.2%) with AUS/FLUS. However, the other nodules with very low suspicion were benign.

Although FNA cytology was conducted on all thyroid nodules depending on their size and US findings, cytology was indicated for 115 (89.8%) nodules using the ATA system, which was higher than the 95 (74.2%) nodules aspirated according to the ACR-TIRAD system. There were no statistically significant differences in the prevalence of neoplastic Bethesda lesions according to either scoring system [Figure 2]. When FNA was indicated for 24 (20.8%) nodules by the ATA system and 21 (22.1%) nodules by the ACR-TIRAD system, the neoplastic Bethesda results were quite comparable. When FNA was not indicated, the ATA system missed only one (7.7%) nodule with AUS/FLUS, and ACR-TIRAD missed four (12.1%) nodules (two with AUS/FLUS, one suspicious for follicular neoplasm, and one suspicion for malignancy).

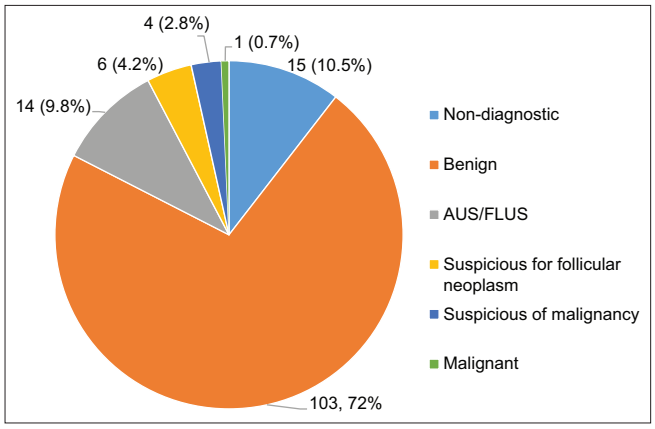

Figure 1: Distribution of fine-needle aspiration cytology results according to the Bethesda system

Tables 2 and 3 show that both the ATA and ACR-TIRAD systems had comparably low PPVs for diagnosing neoplastic lesions (20.8 and 22.1, respectively). Furthermore, both scoring systems showed lower PPVs for malignant lesions (4.3 and 4.2, each). However, the two systems had high NPVs, which seemed to be slightly higher in the ATA system than in the ACR-TIRAD system (neoplastic lesions: 92.3% vs 87.8%, respectively; malignant lesions: 100% vs 96.9%, respectively).

Men had a significantly higher risk of developing neoplastic lesions ($P = 0.01$) than women. Seven out of 15 men (46.7%) had neoplastic lesions compared to only 18 out of 113 (15.9%) in women. Other factors, such as patient age, nodule size and diameter, TSH level, and thyroid autoantibodies, did not correlate significantly with the Bethesda results [Table 4].

Discussion

Thyroid US is commonly used to stratify the potential malignancy risk in thyroid nodules and help in decision-making regarding the indication for FNA. In this study, thyroid US was done on a mean middle-aged population, and thyroid nodules were seen predominately among women (87%), with a female: male ratio of 7:1, which was in concordance with a prospective cohort study in North America where the prevalence of thyroid nodules in women was higher than in men (72% vs 41%; $P < 0.02$).[8] In addition, it was similar to a local cohort study in Iraq where nodular thyroid disease was present in 85.5% of women in a pool of conditions.[5] Similarly, there is a discrepancy in the prevalence of thyroid cancer between the sexes as women are predisposed to more thyroid cancer than men at a ratio of 3:1, which appears to be a global trend with some sort of aggressiveness of malignant thyroid lesions among men. These differences disappeared in a subset of thyroid malignancies, such as anaplastic and metastatic thyroid cancers.[9]

In this study, more than one-third of these nodules had an MNG background, whereas most others were solitary thyroid nodules. The effect of the number of nodules within the

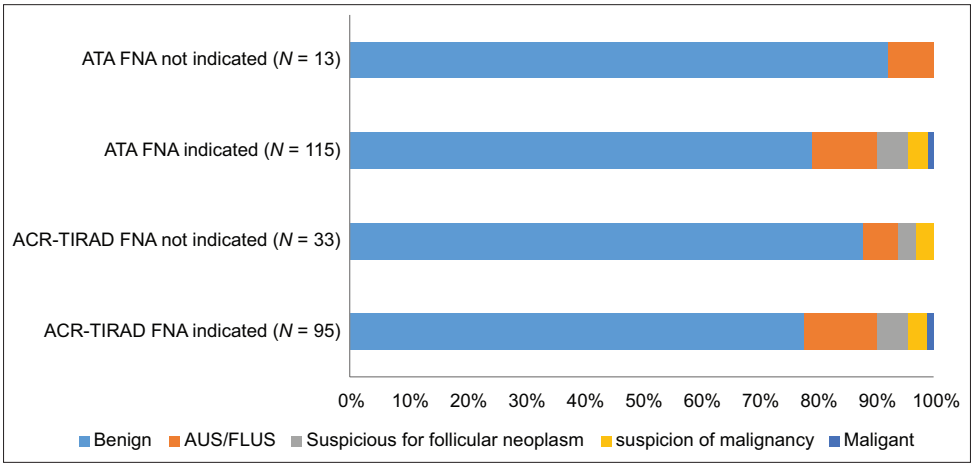

Figure 2: The distribution of the FNA Bethesda results within indicated and not indicated FNA on the ACR-TIRAD and ATA systems. (ACR-TIRAD Fisher's Exact Test=1.78, P=0.86, ATA Fisher's Exact Test=1.20, P=1.0)

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Table 2: Performance of two risk-stratification systems for diagnosis of thyroid neoplastic lesion (AUS/FLUS, suspicious for follicular neoplasm, suspicious for malignancy, and malignant)

	Sensitivity	Specificity	Positive predictive value	Negative predictive value
ACR-TIRAD	84	28	22.1	87.8
ATA	96	11.6	20.8	92.3

ACR-TIRAD: American College of Radiology Thyroid Imaging Reporting and Data System; ATA: American Thyroid Association; AUS/FLUS: atypia of undetermined significance/follicular lesions of undetermined significance (Bethesda 3)

Table 3: Performance of two risk-stratification systems for the diagnosis of thyroid malignant lesions (suspicious for malignancy, and malignant)

	Sensitivity	Specificity	Positive predictive value	Negative predictive value
ACR-TIRAD	80.0	26.0	4.2	96.9
ATA	100	10.5	4.3	100

ACR-TIRAD: American College of Radiology Thyroid Imaging Reporting and Data System; ATA: American Thyroid Association. The aims of splitting these two tables were to justify the neoplastic potential of thyroid nodules as defined in the text (Bethesda-III-V) by using the ATA and TIRAD-ACR systems in Table 2, while in Table 3, to clarify the malignant potential of thyroid nodule as defined in text (Bethesda IV-V) by using the same raters systems

Table 4: Correlations between different patient variables and the Bethesda results of fine-needle aspiration cytology

Variables	Benign	AUS/FLUS	Suspicious for follicular neoplasm	Suspicious for malignancy	Malignant	*P**
Age (years)	43.4±11.5	41.7±13.2	38.0±8.3	52.7±18.3	29±0	0.25**
Men	8 (53.3)	4 (26.7)	1 (6.7)	1 (6.7)	1 (6.7)	0.01
Women	95 (84.1)	10 (8.8)	5 (4.4)	3 (2.7)	0	
Nodule location						
Right	59 (84.3)	7 (10)	3 (4.3)	1 (1.4)	0	0.64
Left	31 (77.5)	4 (10)	2 (5)	2 (5)	1 (2.5)	
Isthmus	13 (72.2)	3 (16.7)	1 (5.6)	1 (5.6)	0	
Diameter (mm)	21.0±9.3	19.7±9.0	18.1±7.3	17.2±3.7	40.0±0	0.22
TSH						
Normal	98 (80.3)	14 (11.5)	5 (4.1)	4 (3.3)	1 (0.8)	0.51
High	5 (83.3)	0	1 (16.7)	0	0	
TPO						
Positive	22 (84.6)	2 (7.7)	1 (3.8)	1 (3.8)	-	0.40
Negative	47 (78.3)	10 (16.7)	3 (5)	0	-	
TRab						
Positive	10 (100)	0	0	-	-	0.48
Negative	9 (75)	2 (16.7)	1 (8.3)	-	-	

*Fisher's exact test. **The one-way analysis of variance (ANOVA). Abbreviations: AUS/FLUS: atypia of undetermined significance/follicular lesion of undetermined significance; TPO: thyroid peroxidase antibody; Trab: thyroid-stimulating receptor antibody; TSH: thyroid-stimulating hormone

thyroid lobes on the risk of malignancy is conflicting; some evidence suggests that more nodules within the thyroid lobes are associated with a higher risk of malignancy, as is mostly suspected in solitary thyroid nodules, while others suggest the reverse.[10] A meta-analysis and systematic review also confirmed the excess malignancy risk of a solitary nodule compared with a specified nodule in MNG.[11] Sippel *et al*. found a lower potential risk of thyroid malignancy among patients with follicular neoplasms who had another nodule in either thyroid lobe in the US preoperatively.[12]

Most thyroid nodules were discovered accidentally during a neck US and did not affect thyroid function in our patients (95%), though the others were in a hypothyroid state. In our cohort, there was no significant evidence of neoplastic thyroid lesions in patients with euthyroidism or hypothyroidism.

Assessment of thyroid status during the evaluation of thyroid nodules is of great value because of the different approaches requiring assessment of thyroid nodules arising in the hyperthyroid state than in euthyroidism or hypothyroidism. Thyroid scintigraphy is considered a cornerstone for differentiating autonomous hyperfunctioning thyroid nodules from the surrounding hyperactive thyroid tissue in patients with nodular hyperthyroidism because the management of these two conditions is entirely different.[13] In addition, evidence has shown that the prevalence of papillary thyroid cancer among individuals with Hashimoto's thyroiditis is variable, which may be attributed to sex differences and geographic and ethnic issues.[14]

Less than one-third of the examined participants were positive for TPO antibodies, and less than half were positive for TRab antibodies. The high positivity of TRab could be related to the small sample size, or some euthyroid populations may have

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positive TRab reaching a prevalence of 21.6% as observed by Chou *et al*., and the differences in the bioactivity and affinity of antibodies can explain this.[15] Autoimmunity has less of an effect on nodular thyroid diseases and thyroid malignancy because both malignant and benign diseases can be positive for thyroid autoantibodies (TAAs). The link between TAA and the risk of thyroid malignancies is controversial, but other evidence has been found, showing that positivity and high titres of serum TAA (both TPO and thyroglobulin antibodies) are considered significant and independent predictive risk factors for thyroid cancer regardless of sex.[14] In addition, the increment of TSH levels (>1.0 μU/mL) was an independent predictive risk factor for papillary thyroid cancer, which was higher in TAA-positive individuals than in TAA-negative individuals, confirming the known relationship between TAA titres and increased serum TSH levels.[16]

More than half of the biopsied thyroid nodules were in the right lobe, followed by the left lobe and the isthmus. The neoplastic behaviour of thyroid nodules was distributed in the right lobe (5.7%), left lobe (12.6%), and isthmus (11.1%) without significant differences. Although the isthmus harboured the least frequent thyroid nodules (15.4%), it usually contained a higher risk of neoplastic potential nodules than other locations. This was consistent with a large study conducted in the USA that confirmed the same results, even after adjusting for patient age, sex, family history of thyroid cancer, radiation exposure, maximum nodule size, and ACR TI-RADS score.[16]

More than two-thirds of the studied nodules in this cohort were benign (72%), which was consistent with a surgical series of nodular thyroid diseases that documented that 44%–77% of nodules were benign colloid nodules, 15%–40% were benign follicular adenomas, and 8%–17% were differentiated thyroid cancer.[17-19] The last one was higher than that in our registry of malignant thyroid lesions (Bethesda V–V1) (3.5%), and our malignant potential was consistent with a large cohort study of 21748 subjects with 3.9% of proven malignant thyroid nodules diagnosed in a single medical centre in Taiwan from January 1986 to December 1999.[8,9] This variability could be due to the sample size as the incidence of thyroid cancer has multifactorial causality depending on sex, age, radiation exposure history, family history, and other factors.[3]

Despite US-guided FNA cytology, more than 10% of biopsied thyroid nodules in our study were non-diagnostic (Bethesda I), which means the cells obtained to judge the diagnosis were unsatisfactory. They still have a 5%–10% risk of malignant potential, similar to non-biopsied thyroid nodules, and a second US-guided FNA can provide diagnostic smears in as many as 50% of cases.[20,21] Even under US guidance, sampling errors may occur in larger nodules. Concordance with a schedule of sampling different points of larger nodules with confirmation of the needle tip within the lesion, effective cytological specimen preparation, and compatibility with sample adequacy guidelines can eliminate this potential pitfall.[22,23]

By the ATA risk stratification, 115 (90%) nodules were indicated for FNA in this study, which was higher than those aspirated according to TI-RADS (74%). This higher rate of aspiration made the ATA risk more sensitive (96%), with a higher NPV (92%), but it had the least specificity (11%) to exclude thyroid neoplastic lesions. For diagnosing malignant thyroid lesions (Bethesda V–VI), ATA also had the highest sensitivity (100%) and NPV (100%) but still the lowest specificity (10.5%). The high sensitivity and low specificity of the ATA risk score for diagnosing neoplastic and malignant thyroid lesions may be attributed to the ATA-recommended FNA for any solid hypoechoic nodule >1 cm without concerning features (i.e. taller-than-wider shape, obviously invasive or irregularly shaped, and presence of microcalcifications) (intermediate suspicion nodule). The high sensitivity versus lower specificity for both systems is because they were developed as a first-step screening tool for thyroid neoplasm. However, they are associated with high false positive rates. The addition of more specific semi-conclusive sonographic features and more advanced US technology such as elastography may help to improve specificity. As a result, the ATA risk provides sufficient space for healthcare providers to make a clinical interpretation and judgment because it is a descriptive risk-stratification plan; unfortunately, some thyroid nodules cannot be classified precisely according to the ATA.[24]

Although TI-RADS had lower sensitivity and NPV with slightly higher specificity than ATA in diagnosing both neoplastic and malignant thyroid lesions in the current study, a restricted number of thyroid nodules were indicated for FNA, thus avoiding unnecessary aspiration in patients. Moreover, the TI-RADS was designed to standardise the sonographic features of each nodule in point values that determine FNA, which depends on a higher TI-RADS score.[4]

Yoon *et al*.[24] investigated the effectiveness of the diagnostic performance of six guidelines, including the ATA and TI-RADS assessments of thyroid nodule risk for malignancy. They found that all guidelines worked well, with good diagnostic performance when applied to small thyroid nodules, though the ATA guidelines were unable to classify 3.4% of 1293 nodules, of which 18.2% were malignant. Notably, this study only included nodules subjected to FNA or surgery. Most likely, a large proportion of nodules could not be classified, and other nodules were included because it is impractical to provide patterns that account for every potential constellation of features.[24]

The use of TI-RADS could lead to fewer biopsies of benign nodules, consequently reducing the number of biopsies of malignant nodules. Although both guidelines are valid, many healthcare providers are reluctant to adhere strictly to a single system at any time. Clinical judgment, individual risk assessment, and shared decision-making still play pivotal roles in deciding when to perform FNA for thyroid nodules. Therefore, guidelines remain a convenient tool for decision-making.

Both ATA and TIRAD have nearly comparable positive and negative predictive values for neoplastic thyroid nodules. However, TIRAD has higher specificity than ATA and may be associated with less FNA frequency (less cost). However, this

finding may be offset by the higher sensitivity and negative predictive value that was seen with the use of the ATA system.

This study has some limitations, including the lack of a definitive histopathological study of excisional biopsy for most nodules due to the unethical nature of performing surgery for low-risk nodules and the limited sample size. Finally, this series represents a single tertiary referral centre, and a thorough study is needed to generalize our results.

Conclusion

Both ATA and TIRAD systems are effective; however, adopting TI-RADS stratifications results in fewer biopsies being performed for thyroid nodule assessment. Only sex was significantly correlated with FNA performance in thyroid nodule evaluation while other parameters such as the site, size of thyroid nodule, and autoimmunity were not significantly correlated. Clinical judgment, individual risk assessment, and shared decision-making play pivotal roles in deciding when to perform FNAB for thyroid nodules. Therefore, guidelines remain a convenient tool for decision-making.

Acknowledgement

We would like to express our thanks to the participants for their cooperation and sincere gratitude to all our colleagues and paramedics, especially the radiologists "Nabeel Abdulateef, and Farah Saod Abdulaziz" and the laboratory personnel who are working in the Faiha Specialized Diabetes, Endocrine and Metabolism Centre (FDEMC), for their continuous supportive efforts in facilitating a highly scientific research environment.

Authors' contribution

IHH and MTA conceived the present idea of the study. NTA, HAA, MAH, and HJO contributed to the study design and execution, data analysis, manuscript drafting and critical discussion. MTA and OMK contributed to the study execution, data analysis, and manuscript drafting. AHA, ASB and AAM contributed to the critical discussion. All authors were involved in the preparation of the manuscript and approved the final manuscript.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

Data availability

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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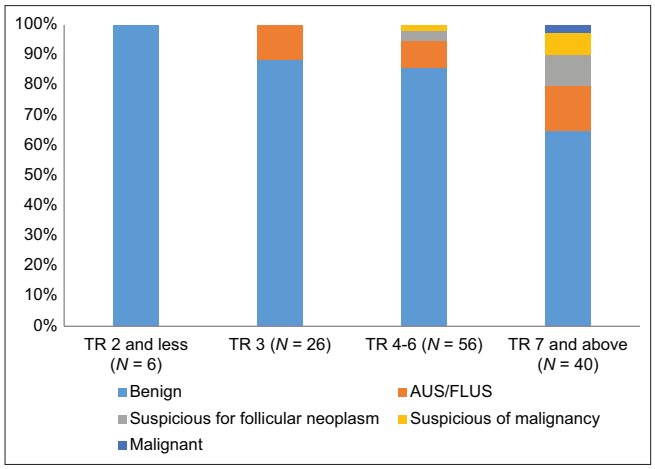
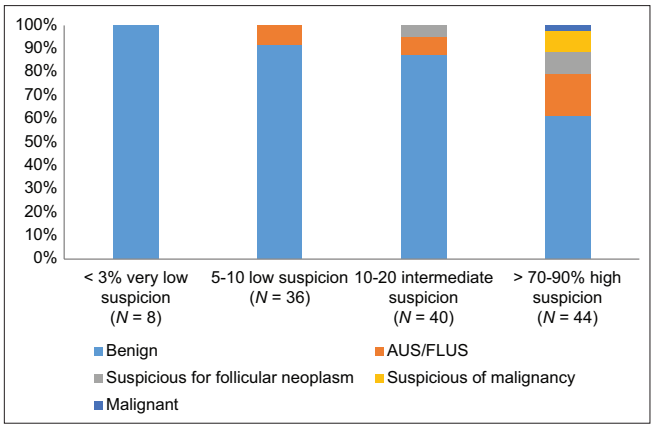


Supplementary Figure 1: Distribution of Bethesda results in different ACR-TIRAD system risk categories. (Fisher's exact test = 12.26, $P = 0.38$)



Supplementary Figure 2: Distribution of Bethesda results in different ATA system risk categories. (Fisher's exact test = 17.17, $P = 0.06$)

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