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Correlation of ultrasound features in the TIRADS scoring system with cytological findings in the FNAC of thyroid nodules and their association with the metabolic status

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Abstract

Background Thyroid nodules were widely encountered in the population, and the selection of thyroid nodules for fine needle aspiration cytology (FNAC) remains confusing. It is essential to investigate the risk factors associated with thyroid nodules.

Aim of work This study aimed to evaluate the accuracy of the American College of Radiology-Thyroid Imaging Reporting and Data System (ACR-TIRADS) scoring system in distinguishing malignant thyroid nodules from benign ones and its association with cytological examination of the FNAC of the thyroid nodules. Additionally, we seek to investigate any potential association between thyroid nodules and some metabolic derangements.

Patients and methods The study included 111 Egyptian patients with euthyroid nodules whom were subjected to history taking, clinical examination, and laboratory investigations including thyroid profile, fasting blood sugar (FBS), glycosylated hemoglobin A1c (HbA1c), and lipid profile. Thyroid ultrasound and FNAC were done for all patients. Categorization of each nodule was done according to the TIRADS. Cytopathological diagnosis was done by Bethesda system cytology classification.

Results There were 19 malignant and 92 benign nodules. There was a statistically significant difference between benign and malignant nodules regarding TIRADS classification, taller-than-wide shape, solidity, border, presence of peripheral calcifications, or punctuate echogenic foci ($p < 0.05$). Taller-than-wide shape had the highest specificity followed by irregular margin (94.6% and 92.6%, respectively). Sensitivity, specificity, PPV, and NPV for ACR-TIRADS versus cytopathology were 73.7%, 57.6%, 26.4%, and 91.4% respectively with overall accuracy of 60.4%. The high sensitivity and NPV of the US-based TIRADS classification system have excellent utility for correctly classifying nodules as positive for malignant disease. As regards risks for thyroid nodules, results showed that most of the study population were obese [Body Mass Index (BMI) = 31.6 ± 6.3, Waist circumference (WC) = 107.4 ± 13.9]. TSH and hypercholesterolemia did not show a significant association with thyroid malignancy.

Conclusion ACR-TIRADS classification is of high significant value in classifying nodules as positive for malignant disease and for predicting the absence of malignant disease, reducing unnecessary nodule FNAC. Hypercholesterolemia and TSH value were not significantly associated with malignant thyroid nodules.

Keywords Thyroid nodules, FNAC, TIRADs, Dyslipidemia, TSH

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Introduction

Thyroid nodules are a common disorder, with a prevalence of 2–6% through palpation and 19–35% through ultrasound inspection in the general population. They are characterized as focal thyroid regions with radiologically distinguishable altered echogenicity [1]. While most thyroid nodules are benign, malignancy was found in only 5–15% of cases [2]. High-definition ultrasonography is recommended for clinically detected nodules in euthyroid individuals. Horvath et al. proposed a thyroid imaging recording and data system (TIRADS) to assess the risk of malignancy in thyroid nodules [3]. Fine needle aspiration cytology (FNAC) of the thyroid nodules offers a reasonable strategy for treatment and provides the appropriate surgical method if indicated [4, 5]. Bethesda's cytological examination classification determines the patient's eligibility for surgery or medical treatment. Using ultrasound-guided FNA allows proper localization of the thyroid nodule during aspiration [6]. With both benign and malignant thyroid nodules becoming more prevalent, it is crucial to organize thyroid cancer prevention strategies. This can be achieved by avoiding the risk factors associated with thyroid nodules, such as obesity, diabetes, and insulin resistance [7–9].

Aim of work

Determine whether cytological examination of the FNAC of the thyroid nodules correlates with the accuracy of the American College of Radiology-Thyroid Imaging Reporting and Data System (ACR-TIRADS) scoring system in differentiating malignant from benign thyroid nodules. Further, determine whether thyroid nodules are associated with a metabolic derangement.

Materials and methods

It is a cross-sectional analytical prospective study which comprised 111 Egyptian patients (106 females and 5 males), their ages were from 25 to 70 years old, presenting by single or multiple thyroid nodules with a euthyroid state. They were referred to Endocrinology Clinic at Hospital of Cairo University, from January 2020 to December 2020. We excluded patients with hypothyroidism, hyperthyroidism, and previously known thyroid malignancy or with known bleeding diathesis. All patients underwent clinical examination including measuring waist circumference, body mass index (BMI), and blood pressure. The following tests were performed: serum thyroid stimulating hormone (TSH), free triiodothyronine (FT3), free thyroxine (FT4), fasting plasma glucose (FBG), 2-hour postprandial glucose (2HPP), glycosylated hemoglobin, total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and triglyceride (TG).

Thyroid ultrasound

Thyroid ultrasound examination was done, using a 7.5-MHZ transducer (Siemens, Erlangen, Germany scanner) including brightness B-mode, color-coded Doppler imaging, and transverse and longitudinal scanning of the thyroid gland for all cases. We use the TIRADS scoring to analyze the ultrasound findings of the nodules.

Image analysis

TIRADS scoring is determined from five distinct items of ultrasound findings. The cumulative score is proportional to the TR (TIRADS) category and malignancy rate. These radiologic items include composition of the thyroid nodule, the echogenicity, shape assessed on the transverse plane, margins, and echogenic foci with detected calcifications [10]. TIRADS scores 4 and 5 were considered positive for malignancy, while scores 1–3 were considered negative for malignancy.

One score is assigned from each of the following categories:

- Composition
  - Cystic or completely cystic *: 0 points
  - Spongiform *: 0 points
  - Mixed cystic and solid: 1 point
  - Solid or almost completely solid: 2 points
- Echogenicity
  - Anechoic: 0 points
  - Hyper- or isoechoic: 1 point
  - Hypoechoic: 2 points
  - Very hypoechoic: 3 points
- Shape: (assessed on the transverse plane)
  - Wider than tall: 0 points
  - Taller than wide: 3 points
- Margin
  - Smooth: 0 points
  - Ill-defined: 0 points
  - Lobulated/irregular: 2 points
  - Extra thyroidal extension: 3 points

- Echogenic foci: (choose one or more)
  - None: 0 points
  - Large comet tail artifact: 0 points
  - Macro-calcifications: 1 point
  - Peripheral/rim calcifications: 2 points
  - Punctate echogenic foci: 3 points

*Predominantly cystic or spongiform nodules are inherently benign. If these features are present no further points will be added (automatically TR1, excluded from this study).

Scoring and classification

TR 1	TR2	TR3	TR4	TR5
0 points, benign	2 points, not suspicious	3 points, mildly suspicious	4–6 points, moderately suspicious	≥ 7 points, highly suspicious

Ultrasound (U/S) guided FNAC of thyroid nodules

Patients underwent FNA of the thyroid nodules, after their consent. The ultrasound scanner utilized to find the nodule served as a guide for the FNA of the thyroid nodules. A 21-G needle connected to a plastic syringe was used during the procedure, which was carried out under strictly aseptic settings. At least two distinct passes sample the aimed nodule. Smears were fixed by 70% ethyl alcohol spray, then transported in slide containers to Cytopathology Unit, Pathology Department, Faculty of Medicine, Cairo University. For complex nodule, cyst content aspiration and any solid area samples were performed. The cyst content aspirate was sent for centrifuge in the cytopathology unit. FNAC were done for all the thyroid nodules from TIRADS score 2 to score 5, we excluded spongiform nodules and simple cysts.

Cytopathology

Smears of the FNAC were stained by modified Papanicolaou as well as hematoxylin and eosin (H&E) stains. The smears for each case were examined by a Leica microscope, then diagnosed using The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC) after fulfilling the adequacy criteria [6]. Bethesda IV, V, and VI groups were accepted as potentially malignant; on the other side, Bethesda II and III groups were accepted as benign samples. TIRADS sensitivity, specificity, negative predictive value (NPV), positive predictive value (PPV), and accuracy were calculated based on cytology results.

TBSRTC Category 1: Non-diagnostic or unsatisfactory (excluded in this study)

A smear was categorized as non-diagnostic if it did not fulfill the adequacy criteria laid down by the Bethesda system.

TBSRTC Category 2: Benign

Smears were interpreted as benign if they showed the cytomorphological features of colloid goiter/adenomatoid goiter or thyroiditis.

TBSRTC Category 3: Atypia of undetermined significance/follicular lesion of undetermined significance

Aspirates which had some features of atypia but could not be categorized definitely into either of the benign, SFN, SM, or malignancy categories.

TBSRTC Category 4: follicular neoplasm ((FN)/suspicious for a follicular neoplasm

Aspirates with cytomorphologic features of moderate to high cellularity, scant or absent colloid, with predominantly microfollicular or trabecular configuration of follicular cells in repetitive pattern. Aspirates with cytomorphologic features of Hurthle cell neoplasm were also placed in this category.

TBSRTC Category 5: Suspicious for malignancy

Aspirates that had cytological features suggestive of, but not definitive of, papillary carcinoma, medullary carcinoma, or others.

TBSRTC Category 6: Malignant

Aspirates that appeared unequivocally malignant were placed in this category.

Histopathology

Cases that undergone surgical resection of the thyroid gland were retrieved. Tissue sections of thyroidectomy were diagnosed according to WHO Classification of Tumors of Endocrine Organs, 5th Edition (Baloch et al., 2022). Required auxiliary immune stains were performed to assure diagnosis (BRAF v600E for NIFTP and chromogranin for medullary thyroid carcinoma). Serial sections of formalin-fixed paraffin-embedded tissue blocks were cut, then placed over adhesive-coated glass slides. Avidin-Biotin immunoperoxidase system was used. Sections were stained by using primary antibodies (rabbit monoclonal BRAF V600E, Ventana Medical Systems, Tucson, AZ, USA) and (monoclonal anti-chromogranin A clone DAK-A3, Dako, Santa Clara, CA) with positive and negative controls.

Statistics

Statistical Package for Social Sciences (SPSS) version 25 was used for data management and analysis. Proper

means, standard deviations, medians, and/or ranges summarize the numerical data. Numbers and percentages were used to represent a categorical set of data. The percentages and figures were used to estimate the frequency. Using the Shapiro-Wilk test and the Kolmogrov-Smirnov test, numerical data were examined for normality. To compare two independent percentages and determine the association between categorical variables, the chi-square test or the Fisher exact was used. For comparisons between the two groups, the Student's *t*-test and Mann-Whitney *U* test were used. Significance represented probability (*p*-value) of 0.05.

Results

Our case study embraced 111 patients with thyroid gland nodules. The age range was 25 to 70 years (mean = 44 ± 12). Females represent the majority of cases ($n = 106$, 95.5%). Figures 1, 2, and 3 and Table 1 illustrate the ultrasound results of cases.

Samples were categorized by The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC) of thyroid nodules. TBSRTC III is considered indeterminate and can carry a small proportion of malignant potentiality, but guidelines do not necessitate surgery in this case. TBSRTC IV represents neoplastic category with both benign tumors

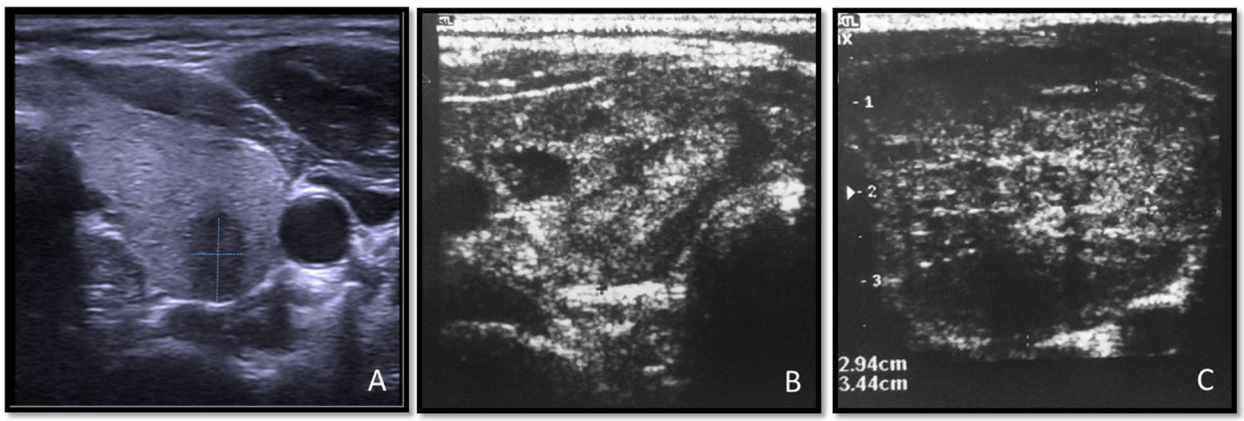

Fig. 1 Different sonographic patterns of thyroid nodules. TR5: **A** Completely solid nodule, hypoechoic, taller than wide. **B** Complex hypoechoic nodule with echogenic foci. **C** Very hypoechoic nodule with irregular border, punctate multiple echogenic foci

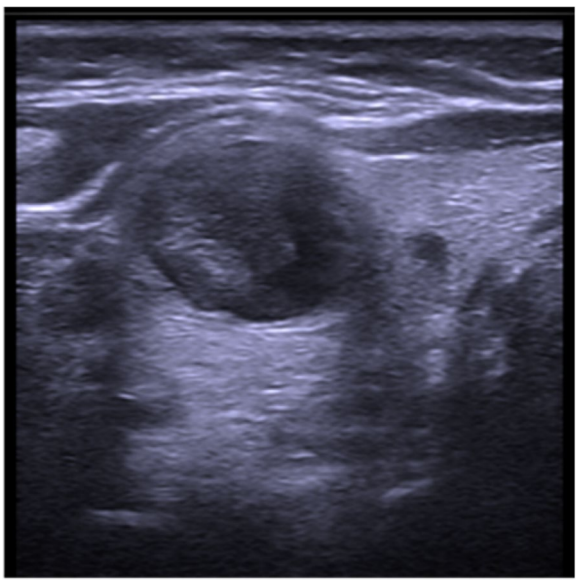

Fig. 2 Different sonographic patterns of thyroid nodules. TR4: Solid hypoechoic nodule

as follicular adenomas and malignant ones as follicular carcinomas (invasion could not be documented in FNAC). We had to discriminate nodules which are cytological malignant or suspicious for malignancy, with operational guidelines, from the other nodules. Therefore, Bethesda IV ($n = 7$), V ($n = 10$), and VI ($n = 2$) groups were accepted as potentially malignant ($n = 19$); on the other side, Bethesda II ($n = 75$) and III ($n = 17$) groups were accepted as benign samples ($n = 92$). Subsequently, cytological findings for studied nodules will be denoted by benign and malignant / potentially malignant terminology (Table 2). TBSRTC I nodules were dismissed ($n = 9$).

Follow-up of patients revealed only 27 cases who underwent thyroidectomy (24.32%), with detected seven malignant cases by histopathology. Six cases of them were categorized as TBSRTC V and VI (6/7 cases), with one FNA-missed incidental micro-carcinoma. There were 4 cases diagnosed as papillary thyroid carcinoma, one case diagnosed as medullary thyroid carcinoma (which was confirmed by positive chromogranin expression), and one case of follicular carcinoma. Non-invasive

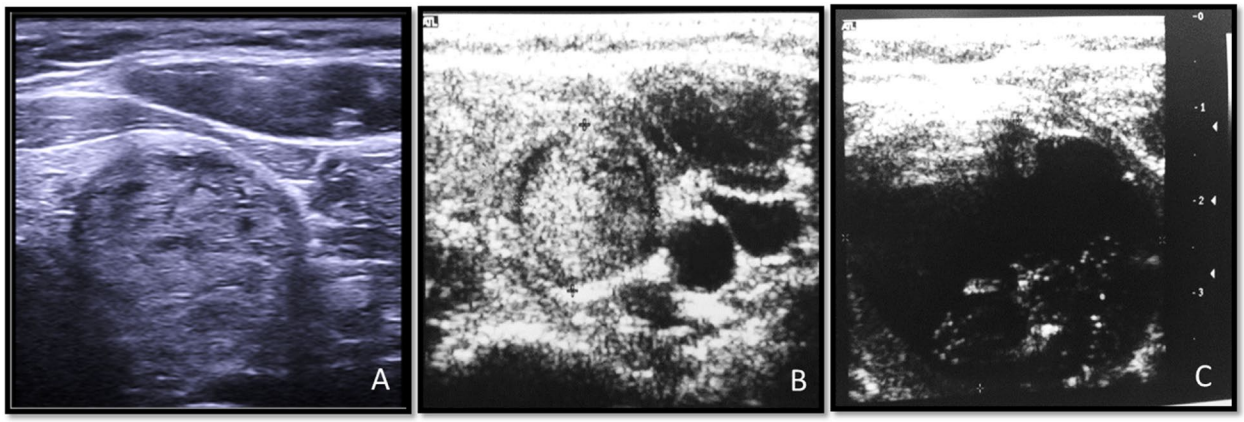

Fig. 3 Different sonographic patterns of thyroid nodules. TR2: **A** Mixed solid and cystic isoechoic nodule. **B** Isoechoic solid nodule with regular border. **C** Thyroid nodule, partially solid and cystic

Table 1 Nodules' characteristics by sonography

Factors	*n* = 111 (%)
Composition	
1 (mixed cystic and solid)	69 (62.2%)
2 (completely solid)	42 (37.8%)
Echogenicity	
0 (anechoic)	1 (0.9%)
1 (hyper -or isoechoic)	64 (57.7%)
2 (hypoechoic)	42 (37.8%)
3 (very hypoechoic)	4 (3.6%)
Shape	
0 (wider than tall)	102 (91.9%)
3 (taller than wide)	9 (8.1%)
Margin	
0 (smooth)	99 (89.2%)
2 (lobulated , irregular)	11 (9.9%)
3 (extra thyroidal extension)	1 (0.9%)
Echogenic foci	
0 (no detected foci)	60 (54.1%)
1 (macro-calcifications)	39 (35.1%)
2 (peripheral calcifications)	4 (3.6%)
3 (punctuate)	5 (4.5%)
4 (1 and 3)	3 (2.7%)
TIRADS	
2	23 (20.7%)
3	35 (31.5%)
4	40 (36.0%)
5	13 (11.7%)

follicular thyroid neoplasm with papillary-like nuclear features (NIFTP) has been documented in one thyroidectomy specimen, confirmed by negative expression to BRAF-600E to exclude non-invasive follicular variant of papillary thyroid carcinoma (Figs. 4, 5, 6, and 7).

Table 2 Cytological results in the study

Bethesda classification	*n* = 111 (%)
I (benign)	75 (67.6%)
III (FUS)	17 (15.3%)
IV(follicular neoplasm)	7 (6.3%)
V (Suspicious for malignancy)	10 (9.0%)
Suspicious for medullary carcinoma	1 (0.9%)
Suspicious for papillary carcinoma	9 (8.1%)
VI (malignant)	2 (1.8%)
FNAC Bethesda categories	
Potentially malignant	19 (17.1%)
Benign	92 (82.9%)

Table 3 summarizes the results of the analysis of ultrasound findings with thyroid potential malignancy. Our results show that solid composition, taller than wide, irregular nodules, peripheral calcifications, and punctuate echogenic foci showed significant associations with thyroid malignancy ($p < 0.05$). In contrast, echogenicity and macro-calcifications showed no significant association.

Correlating TIRADS with Bethesda system (Fig. 8), we find that:

- Out of the 23 TIRADS 2 nodules, none turned out to be Bethesda IV or higher (100% concordance).
- From the 35 nodules labeled as TIRADS 3, 30 nodules were Bethesda II and III (benign) and 4 nodules were Bethesda IV, only one nodule was Bethesda V and none was Bethesda VI (85.7% concordance).
- On the contrary, out of the 40 TIRADS 4 (moderately suspicious) nodules, only 8 nodules eventually were Bethesda IV or higher. Five nodules out of the

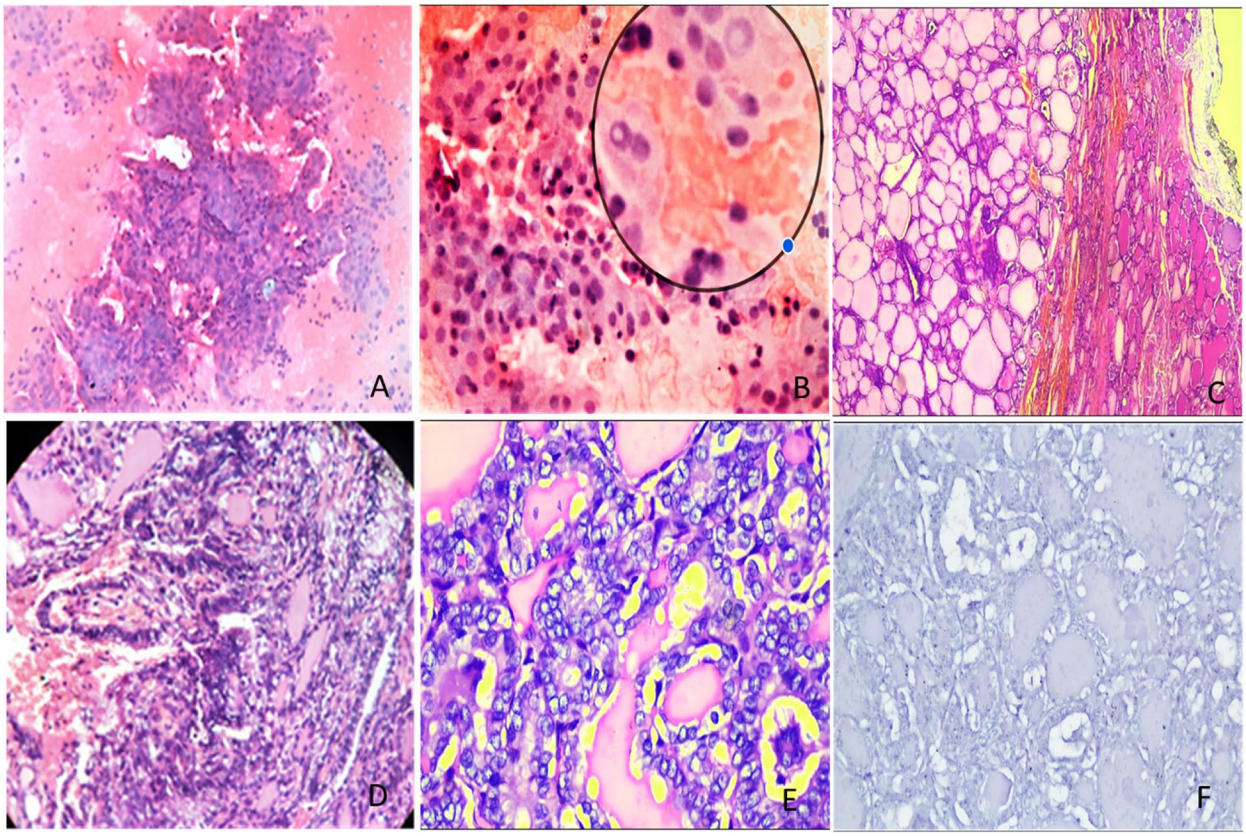

Fig. 4 NIFTP (non-invasive follicular thyroid neoplasm with papillary nuclear features). **A** and **B** Smears of follicular cells arranged in syncytia, showing copious cytoplasm, enlarged overlapping nuclei and focal nuclear pseudoinclusion (H&E stain, low and high powers). **C**, **D**, and **E** Tissue sections revealed defined fibrous nodule capsule, predominate follicular arrangement with focal abortive hyperplastic papillae. Nuclear score 3 (enlargement, crowding / overlapping, elongation, grooves, pseudoinclusions, and chromatin clearing). (H&E stain, low and high powers). **F** Negative BRAF-V600E immune stain

13 classified as TIRADS 5 (highly suspicious) came to be Bethesda IV or higher with low concordance 20% and 38.5%, respectively.

Table 4 shows calculated rates of malignancy in TIRADS categories compared with malignancy risk recommended by the ACR-TIRADS Committee. Along with the higher risk categories, the malignancy rates tended to rise.

The diagnostic accuracy of each evaluated ultrasound finding to identify malignancy is summarized in Table 5. "Taller-than-wide shape" category had the highest specificity (94.6%) but low sensitivity (21.1%). Irregular margin had high specificity (92.4%) and low sensitivity (26.3%). On the contrary, solid composition and the presence of echogenic foci had relatively higher sensitivity values (63.2% for both).

Regarding the clinical and laboratory data collected in this study, no difference was significantly found between benign and malignant groups (Table 6).

Discussion

A noticeable increase in thyroid carcinoma incidence has been observed, possibly due to the wide use of neck ultrasonography and the surveillance of sonar-guided FNAC of thyroid nodules [1]. While attempting to identify malignant nodules requiring surgery, it was a challenge to achieve the balance between avoiding overdiagnosis of unnecessary FNA and not missing the diagnosis of malignant thyroid nodules. The ACR-TIRADS system has standardized the language used to communicate thyroid ultrasound findings between clinicians and provided valuable insight into the management plan [3, 11, 12]. FNAC is crucial in triaging patients into operative and non-operative groups amid the increased awareness of thyroid diseases [13]. While radioactive exposure, improper iodine intake, and family history are recognized risk factors for thyroid cancer, they do not illustrate the whole picture. The prevalence of thyroid carcinoma is higher in the high-income lifestyles of the USA and China, where socioeconomic status significantly influences thyroid

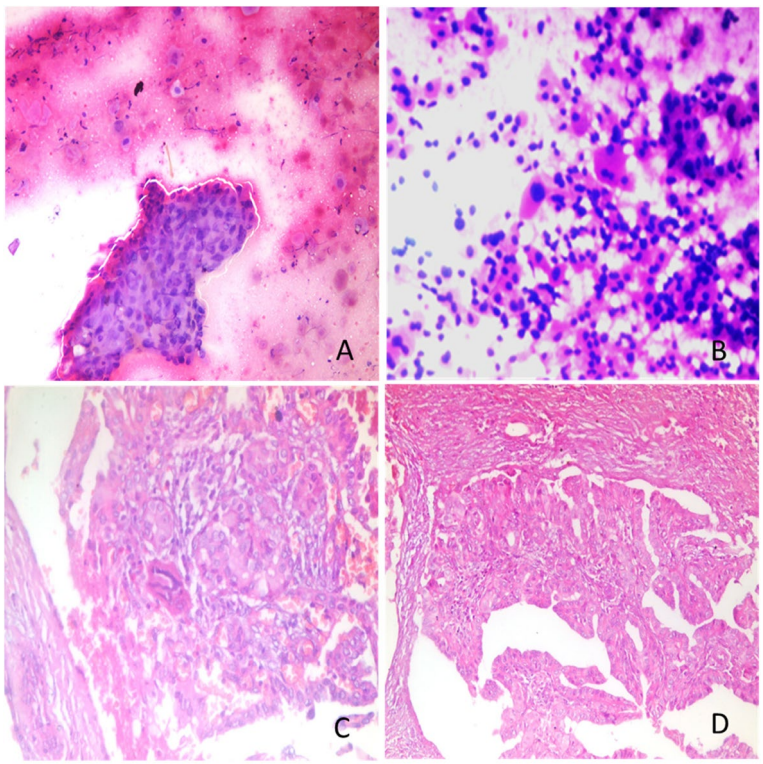

Fig. 5 Oncocytic cell adenoma. **A** and **B** Cells in microfollicular pattern showing abundant eosinophilic cytoplasm, round nuclei with focal enlargement. **C** and **D** Tissue section showing capsulated nodule with focal site aspiration changes. The cells showed abundant cytoplasm. The nuclei showed focal prominent nucleoli. (H&E stain, low and high powers)

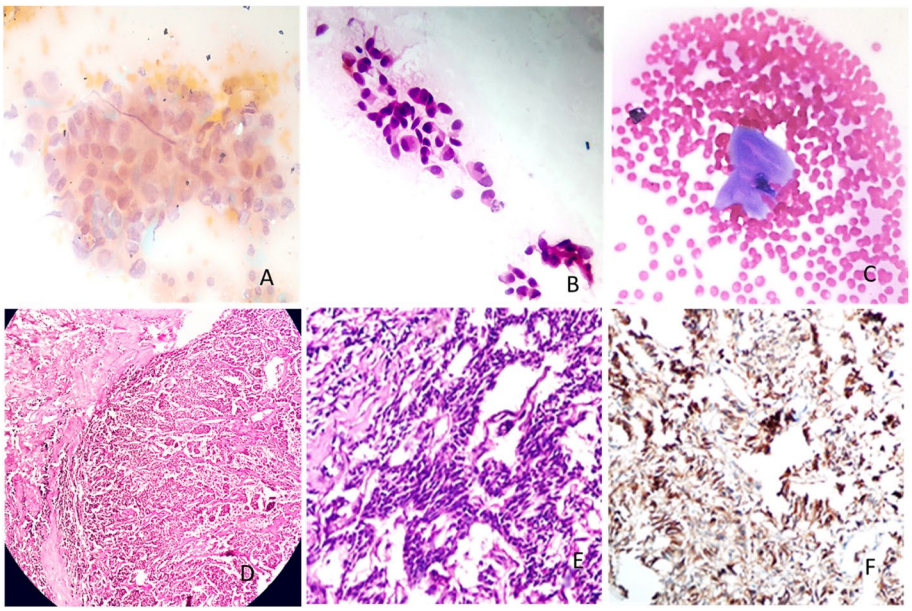

Fig. 6 Medullary carcinoma. **A** and **B** Follicular cells arranged singly and focal microfollicles. The cells exhibit eccentric nuclei, comet-shaped cytoplasmic extensions. **C** Amyloid deposit (H&E and pap stains, smear high powers). **D** and **E** Tissue sections showing neoplastic cells arranged in trabeculae with amyloid eosinophilic material (H&E, low & high powers). **F** Tumor cells showed positive chromogranin immune reaction (chromogranin immune stain, low power)

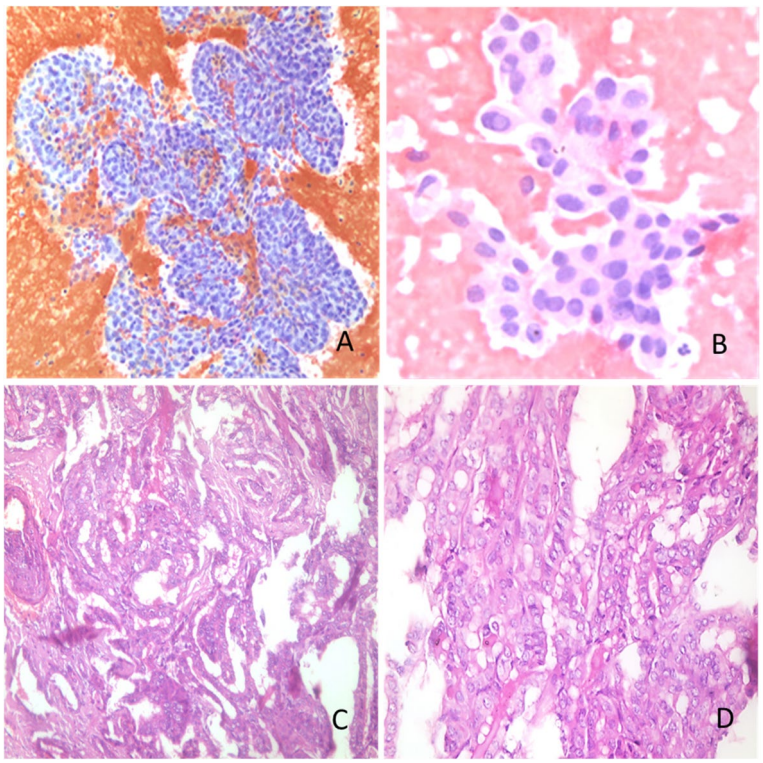

Fig. 7 Papillary thyroid carcinoma. **A** and **B** Follicular cells show malignant nuclear features: enlargement, overlapping, powdery chromatin, nuclear grooving, and inclusion (Pap stain, smears, low and high powers). **C** and **D** Tissue sections of papillary thyroid carcinoma. The cells showed malignant nuclear features (H&E stain, low and high powers)

status. Therefore, many studies focused on modifiable risk factors such as overnutrition, obesity, and dyslipidemia [14, 15]. Despite females having a higher incidence of thyroid nodules than males, men face a higher risk of malignancy [16]. In this study, females represented 95.5% of cases with thyroid nodules, consistent with findings in two other studies conducted in our endemic region [17, 18]. The risk of malignancy indicated is > 20% in the TR-5 group of ACR-TIRADS. In our study, we found a rate of 38.5% in TR-5 of ACR-TIRADS. However, rates for TR-3 and TR-4 groups were 14.3% and 22.5%, respectively, higher than the indicated risk in guidelines (5% for TR3 nodules, 5 to 20% for TR4) [10]. Barbosa reported a thyroid malignancy rate of 23.3% in patients with TR3 [19]. Another Indian study by De et al. found that TR-3 and TR-4 exhibited 22% and 29% rates of malignancy, respectively [20]. Discrepancies in these results may arise from the challenge of distinguishing between calcification and comet tail artifacts during sonographic examination, directly impacting the nodule's ultimate score. Additionally, macrocalcification and hyperechoicity did not indicate malignancy in earlier systems. Different tools were used in the cytology and histopathology diagnoses. Sonographic evaluation of thyroid nodules was aimed at ascertaining the likelihood of malignancy in conjunction with the results of the FNAC; this would pave the way for the best choice of further therapy. According to the sonographic features of the nodule, firmness, lobulation, or irregularity of the border, taller-than-wide shapes, peripheral calcifications, and punctate echogenic patches within the nodule were the most prevalent sonographic characteristics of malignant nodules. In agreement with our results, studies by Kwak and colleagues found that solid components, hypoechogenicity, margin irregularity, microcalcifications, and taller-than-wide shapes were significantly associated with malignancy [12]. Many studies acknowledged these features as potential signs of malignancy [18, 21–24].

As regards the ultrasound characteristics of the thyroid nodule, we found that a taller-than-wide shape had the highest specificity of 94.6% but a low sensitivity of 21%. Similarly, irregular margins had high specificity (92.4%) but a low sensitivity (26.3%). Our findings align with a meta-analysis study by Remonti, which found that a taller-than-wide shape and irregular margins had the highest specificities of 96% and 83%, respectively, but were not sensitive (26% and 50%) [25, 26]. Similarly, De D and his colleagues calculated

Table 3 Association between ultrasound characteristics and thyroid malignancy ($n = 111$)

Factors	TBSRTC		*P*-value
	Potentially malignant	Benign	
	$n = 19$ (%)[a]	$n = 92$ (%)[a]	
Composition			
Solid	12 (28.6)	30 (71.4)	0.019
Mixed cystic and solid	7 (10.1)	62 (89.9)	
Echogenicity			
Anechoic	0 (0)	1 (100.0)	NA
Hyper- or isoechoic	12 (18.8)	52 (81.3)	
Hypoechoic	6 (14.3)	36 (85.7)	
Very hypoechoic	1 (25.0)	3 (75.0)	
Echogenicity			
Hypoechoic	7 (15.2)	39 (84.8)	0.800
Iso and hyperechoic	12 (18.5)	53 (81.5)	
Shape			
Taller than wider	4 (44.4)	5 (55.6)	0.045
Wider than taller	15 (14.7)	87 (85.3)	
Margin			
Smooth	14 (14.1)	85 (85.9)	NA
Lobulated, irregular	4 (36.4)	7 (63.6)	
Extra thyroidal extension	1 (100)	0 (0)	
Margin			
Irregular	5 (41.7)	7 (58.3)	0.031
Regular	14 (14.1)	85 (85.9)	
Peripheral calcification			
Present	3 (75)	1 (25)	0.016
Absent	16 (15)	91 (85)	
Punctate echogenic foci			
Present	4 (50)	4 (50)	0.028
Absent	15 (14.6)	88 (85.4)	
Macro-calcifications			
Present	6 (14.3)	36 (85.7)	0.611
Absent	13 (18.8)	56 (81.2)	

[a] Percentages were calculated within row, *NA* not applicable

the specificity values for irregular margins and taller-than-wider shapes at 89% and 92%, respectively [20]. Regarding hypoechogenicity, our study showed a sensitivity of 36% and a specificity of 57%. However, the results of a meta-analysis showed better specificity (62.3%) and sensitivity (62.7%) [2]. In other studies, the sensitivity levels ranged from 26.5 to 87.2% [24, 27]. Peripheral calcifications and punctate echogenic foci in our study correlated with thyroid malignancy, consistent with previous studies [18, 23]. In our results, macrocalcification showed no significant association with the risk of malignant thyroid nodules, which agrees with some studies [22, 28, 29] but conflicts with other studies [27, 30]. So, macrocalcification played a controversial role in the risk of malignancy. Our study demonstrated 100% concordance between TIRADS 2 and TBSRTC, while TIRADS 3 had 85.7% concordance. TIRADS 4 and TIRADS 5 had concordance at 20% and 38.5%, respectively. Singaporewalla reported similar results for the TIRADS II and TIRADS III groups, with a concordance of 100% and 81% to cytology, respectively. However, the TIRADS 4 group nodules had a 33.3% higher concordance than in our study, and the TIRADS 5 group nodules showed even higher concordance between TIRADS and cytology at 60% [31]. In contrast, Pandya found that the TIRADS 2 and TIRADS 3 groups showed high concordance between TIRADS and cytology (93.7% and 95%, respectively) but low concordance in the TIRADS 4 and TIRADS 5 groups (11.2% and 23%, respectively).

In this study, sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) for ACR-TIRADS versus cytology were 73.7%, 57.6%, 26.4%, and 91.4%, respectively, with an accuracy of 60.4%. These findings agree with some studies [32, 33], although others showed higher specificity values [29, 31]. Mistry compared the TIRADS with the American Thyroid Association (ATA) guidelines and found that the TIRADS was superior in sensitivity, whereas the ATA guidelines were superior in specificity and PPV. TIRADS had a median sensitivity, specificity, PPV, and NPV of 90.0%, 57.4%, 49.0%, and 91.0%, respectively [34]. The present study observed no significant differences between benign and malignant groups in BMI, waist circumference, lipid profile, or HbA1C levels. These results align with De Siqueira's findings, in which thyroid nodules were more frequent in obese individuals, and parenchymal hypoechogenicity was more pronounced in obese than non-obese individuals. However, no significant differences were observed in terms of the risk of malignancy between obese and non-obese individuals [35]. Grimmichova did not observe an increased risk of thyroid cancer in diabetes or prediabetic patients compared to controls [36–38]. On the contrary, he found that BMI was positively correlated with the risk of thyroid cancer [39]. The association between hypercholesterolemia and thyroid cancer remains unclear. Our study found that serum cholesterol levels had no significant association with malignancy. The rate of malignancy in hypercholesterolemic patients (16.7%) nearly corresponded to those with normal levels (15%). These findings contrast with a Chinese study that concluded that hypercholesterolemia

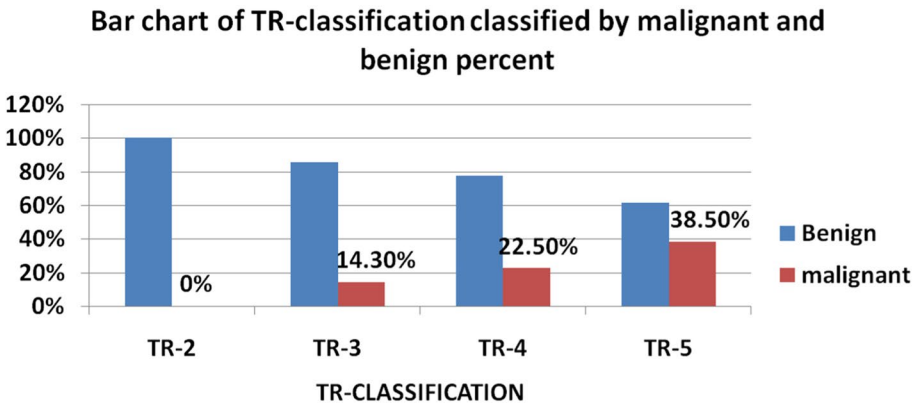

Fig. 8 Percentage of benign and malignant cases in different TIRADS classifications

Table 4 Malignancy rates in the categories of ACR-TIRADS

	TBSRTC		Recommended malignancy risk (%)	Calculated malignancy rate (%)
	Potentially malignant	Benign		
TIRADS				
TR 2	0	23	< 2%	0%
TR 3	5	30	2–4.9%	14.3%
TR 4	9	31	5–19.9%	22.5%
TR 5	5	8	> 20%	38.5%

Percentages were calculated within rows

was a risk factor for thyroid cancer [40]. Our study observed no significant difference in serum TSH levels between benign and malignant nodules, consistent with Hrafnkelsson's finding that serum levels of TSH and thyroxine did not differ between cases of thyroid malignancy and controls [41].

On the contrary, an extensive meta-analysis in China in 2020 revealed a significant association between higher TSH levels and the risk of thyroid malignancy [42, 43]. Finally, we concluded that the ACR-TIRADS classification, compared to the cytological findings of the ultrasound-guided FNAC of the thyroid nodules, holds significant value in discriminating between benign and malignant thyroid nodules. The TIRADS scoring system can be relied upon to avoid unnecessary FNAC or surgical treatment. Study limitations included the relatively small number of patients and the small number of males, potentially affecting the statistical power and

Table 5 Diagnostic accuracy of ACR-TIRADS

Diagnostic tool	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Overall accuracy (%)
TIRADS	73.7	57.6	26.4	91.4	60.4
Diagnostic accuracy of different components of ACR-TIRADS					
Composition	63.2	67.4	28.6	89.9	66.7
Echogenicity	36.8	57.6	15.2	81.5	54.1
Echogenic foci	63.2	57.6	23.5	88.3	58.6
Shape	21.1	94.6	44.4	85.3	82
Margin	26.3	92.4	41.7	85.9	81.2

PPV positive predictive value, *NPV* negative predictive value

Table 6 Correlation between laboratory / clinical data with TBSRTC

Factors	TBSRTC		*P*-value
	Potentially malignant	Benign	
	Mean ± SD	Mean ± SD	
BMI (kg/m^2)	32.5 ± 5.0	31.5 ± 6.6	0.543
Systolic blood pressure (mmHg)	116 ± 20.7	121.1 ± 19.7	0.330
Diastolic blood pressure (mmHg)	77.8 ± 9.9	76.5 ± 10.3	0.643
Waist circumference (cm)	110.9 ± 13.4	106.7 ± 13.9	0.239
Cholesterol (mg/dl)	173.6 ± 41.7	164.4 ± 48.7	0.470
LDL (mg/dl)	108.1 ± 52.1	98.4 ± 50.6	0.471
HDL (mg/dl)	55.9 ± 19.8	51.3 ± 14.3	0.260
Triglycerides (mg/dl)	97.7 ± 43.4	83.0 ± 38.8	0.163
HBA1C	5.7 ± 1.1	5.9 ± 1.3	0.680
FBG (mg/dl)	108 ± 56.9	99.9 ± 23.4	0.584
2HPP (mg/dl)	127.5 ± 25.5	133.3 ± 37.8	0.571
	Median (range)		
TSH (μU/mL)	1.25 (0.5–4.8)	1.1 (0.5–3.8)	0.553
Free T4 (ng/dL)	1.27 (0.5–2.0)	0.6 (0.6–1.1)	0.093
Free T3 (ng/dL)	2.8 (0.9–3.5)	3.25 (2.3–3.5)	0.067

SD standard deviation

reproducibility of the results. Moreover, the study performed the postoperative histopathological examination for a limited number of patients included in the study group. Further, extensive studies involving both genders in multiple centers across Egypt are recommended.

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Authors' contributions
Maha Assem was responsible for the writing of the manuscript and doing ultrasound for the participants. Yasmine Fathy was responsible for the pathology. Dina Esam collects the data. Shrook revised the scientific material

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Is not applicable.

Availability of data and materials
The data used to support the findings of this study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate
The study satisfied the requirements of the Revised Helsinki Declaration biomedical ethics, approved by the Research Ethics Committee, Faculty of Medicine, Cairo University.
Informed consent was obtained from all participants before inclusion.

Competing interests
The authors declare that they have no competing interests.

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