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Diagnostic accuracy of B-mode ultrasound, ultrasound elastography and diffusion weighted MRI in differentiation of thyroid nodules (prospective study)

Mahmoud Abdel Latif*, Magdy Mohamed El Rakhawy and Mohamed Fathy Saleh

Abstract

Background: The incidence of the thyroid nodules and its detection is increasing rapidly. The most precise method for diagnosis of the nodules of the thyroid is FNAC. But, about 10–20% of specimens of FNAC are indeterminate and non-diagnostic. Therefore, there is a demand for another diagnostic method for evaluating thyroid nodules. Thyroid ultrasound elastography may improve the ability to differentiate malignant from benign thyroid nodules. Few articles were published about the results of DW MRI in thyroid nodules, with its results confirmed that malignant nodules have lower mean ADC values than benign nodules. This study aims to investigate and compare the accuracy of B-mode ultrasound, ultrasound elastography and diffusion-weighted MRI in characterization of the nodules of the thyroid.

Results: The study included 56 patients with thyroid nodules (36 benign and 20 malignant). Thyroid ultrasound, ultrasound elastography and DWI were done for all patients. Ultrasound-guided FNA Cytological examination (as the gold standard) was done for 48 patients and surgical histopathology was done to 8 patients with non-diagnostic FNAC. The results showed: TIRADS score had sensitivity 90%, specificity 77.8% and accuracy of 82.14%. The elastography score had sensitivity 80%, specificity 88.9% and accuracy 85.7%. The use of the strain ratio had 80% sensitivity, 94.4% specificity and 89.3% accuracy. DWI and ADC value had 100% sensitivity and 94.4% specificity and the accuracy was 96.4% for differentiating malignant from benign thyroid nodules. Multi-parametric analysis by TIRADS and ADC had 100% accuracy.

Conclusion: Ultrasound elastography add valuable data over ultrasound TIRADS. But, diffusion weighted MRI and ADC value has more accuracy in differentiating malignant from benign thyroid nodules. The best performance was achieved by the combination of ACR-TIRADS and ADC value.

Keywords: Diffusion weighted, Ultrasound elastography, Thyroid nodules, FNAC, Malignant, Benign

Background

The incidence of the thyroid nodules and its detection is increasing rapidly; reaching up to 67% of the healthy population. About 5–15% of them are being cancerous [1, 2]. The real challenge is the diagnosis of the minority of patients with malignant nodules [3] (Fig. 1).

As malignant nodules require surgery and benign ones need follow up, hence, accurate and reliable diagnostic methods that can detect malignancy are essential in management of thyroid nodules [4] (Fig. 2).

The diagnosis of thyroid cancer depends on neck ultrasound and fine-needle aspiration (FNA) biopsy [5] (Fig. 3).

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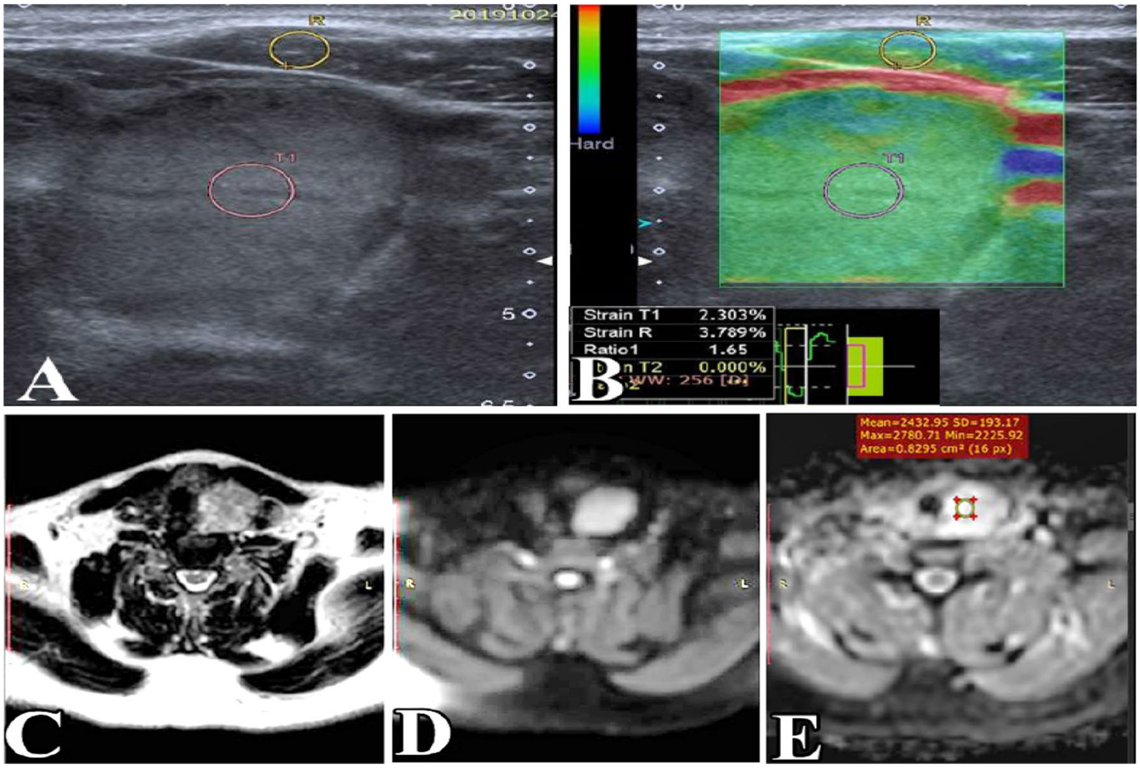

Fig. 1 Female patient aged 58 years presented with left thyroid lobe nodule. Ultrasound features of the nodule **A**: The left thyroid lobe shows a solid isoechoic nodule, wider more than taller with smooth outline. No calcifications. TIRADS categorization: TIRADS (3). On elastography color map **B**: no deep blue areas could be detected. Elastography score: (1). Strain ratio = 1.6. MRI study: T2 weighted signal **C**: left lobe nodule with intermediate signal intensity. Diffusion weighted images **D**: the nodule shows high signal intensity. ADC mapping **E**: it shows high signal with ADC value = 2.43×10^{-3}. Pathology: Hurthle cell adenoma

Ultrasound is the most common imaging modality used to diagnose lesions of the thyroid; however, still there are no dependable criteria to discriminate malignant from benign lesions. Also, in large and multiple nodules, it is not easy to assess the malignant possibility of the nodule [6] (Fig. 4).

It is believed that the most precise method for assessment of the nodules of the thyroid is fine needle aspiration cytology (FNAC). But, about 10–20% of specimens of FNAC are indeterminate and may be non-diagnostic [7]. In addition, the overlap of morphological signs between malignant and benign lesions may lead to difficulty in interpretation of cytology. Therefore, there is a need for another diagnostic method for evaluating thyroid nodules [8] (Fig. 5).

Thyroid ultrasound elastography (USE) is a noninvasive method of evaluating thyroid nodules that can provide complementary information to B-mode US and FNAC. Thyroid USE may improve the differentiation of malignant from benign thyroid nodules leading to decrease the number of needed fine needle aspiration biopsy (FNAB) [9].

There are available many studies discussing the use of ultrasound elastography in diagnosis of the nodules of the thyroid. However, the sensitivity and specificity of this method are sharply variable in the medical literature [10].

Diffusion weighted (DW)-MRI has been proved to have a role in assessment of tumors of the neck, with the quantitative parameter (ADC) value, could be used for differentiation of benign and malignant lesions [6].

Few articles were published about the results of DW MRI in thyroid nodules, with its results confirmed that malignant nodules have lower mean ADC values than benign nodules [11].

Aim of work

The aim of this study was to assess the value, compare the diagnostic accuracy and investigate the multi-parametric analysis of B- mode ultrasound, ultrasound elastography and diffusion-weighted MRI of the thyroid gland in characterization of the nodules of the thyroid (whether it is benign or malignant).

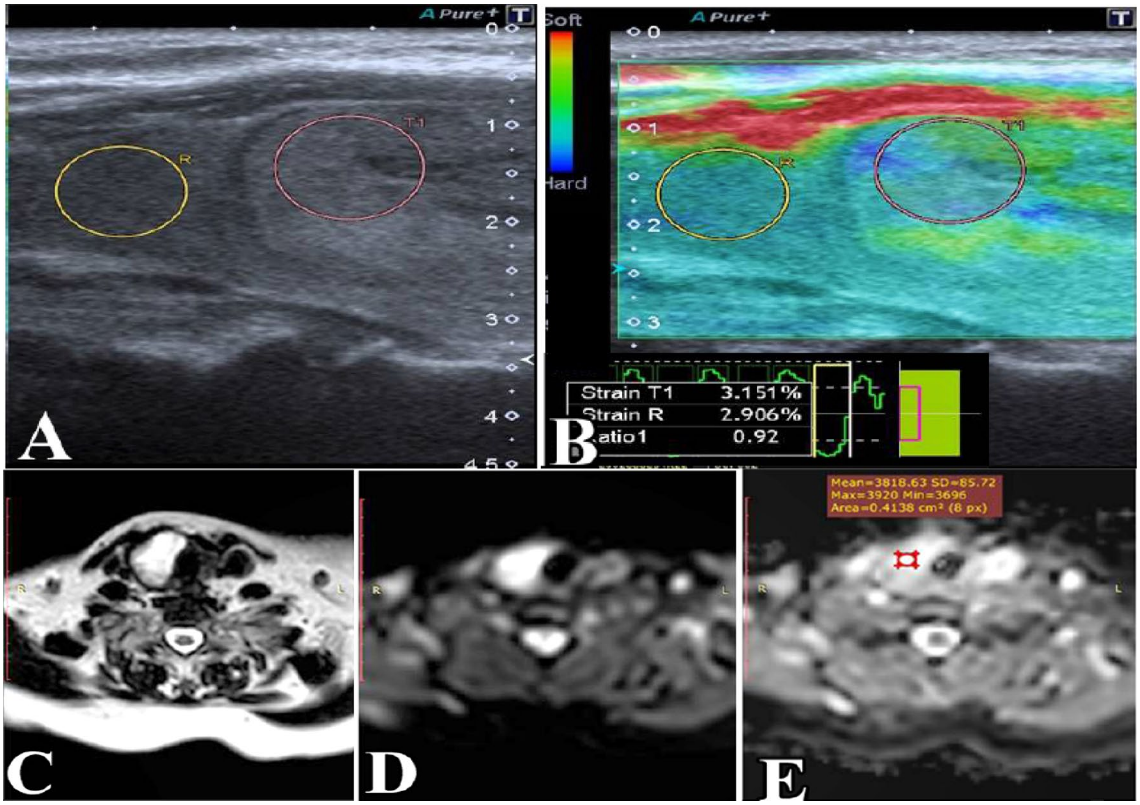

Fig. 2 Female patient aged 50 years presented with right thyroid lobe nodule. Ultrasound features of the module **A**: The right thyroid lobe shows a solid hyperechoic nodule, wider more than taller with smooth outline. No calcification or echogenic foci. TIRADS categorization: TIRADS (3). On elastography color map **B**: most of the nodule is shaded with green with small deep blue area. Elastography score: 2. Strain ratio = 0.9. MRI study: T2 weighted images **C**: right lobe nodule with mixed high and intermediate signal intensities. Diffusion weighted images **D**: the nodule shows high signal intensity. ADC mapping **E**: it shows high signal with ADC value = 3.81 × 10^{-3}. Pathology: colloid nodule

Methods

This prospective study was done during the period from November 2018 to March 2020. It included 60 patients, 4 patients refused to complete the MRI examination and were excluded. The final patient's number was 56 (20 males and 36 females), with 70 thyroid nodules. The age of the patients ranged from 17 to 65 years. The major concern of the referring physician was to distinguish malignant from benign nodules of the thyroid. The inclusion criteria were the presence of solitary or multiple nodules in the thyroid gland in patients at different age groups, the nodules were either solid or mixed (containing both solid and cystic parts). In case of patients having multiple nodules, the nodule having suspicious ultrasound features (having TI-RADS score 4 or 5) was selected for further analysis. In addition, patients should have normal bleeding profile.

Patients with contraindications of the FNAC procedure (e.g. thrombocytopenia or bleeding disorders), patients with complete shell-calcified nodules that may cause color mapping artifacts or pure cystic nodules without solid parts and patients with recurrent thyroid masses, history of operative procedure, chomo or radiotherapy on the thyroid gland, patients with contraindication to MRI or with bad general condition and patients had nodules with indeterminate or incomplete diagnosis were excluded.

The study had approved by our local committee of research and ethics and all participants signed informed consent before being included.

All patients were subjected to:

1. Thyroid ultrasound and ultrasound elastography using the machine (Toshiba Aplio-500 with linear probe 10–13 MHz).
2. Magnetic resonance imaging examination (mainly DWI) using Philips Ingenia 1.5 Tesla (T) MRI scanner
3. Ultrasound-guided FNA Cytological examination (as the gold standard) for 48 patients. Surgical histopathology was done to 8 patients with non-diagnostic FNAC to obtain final diagnosis.

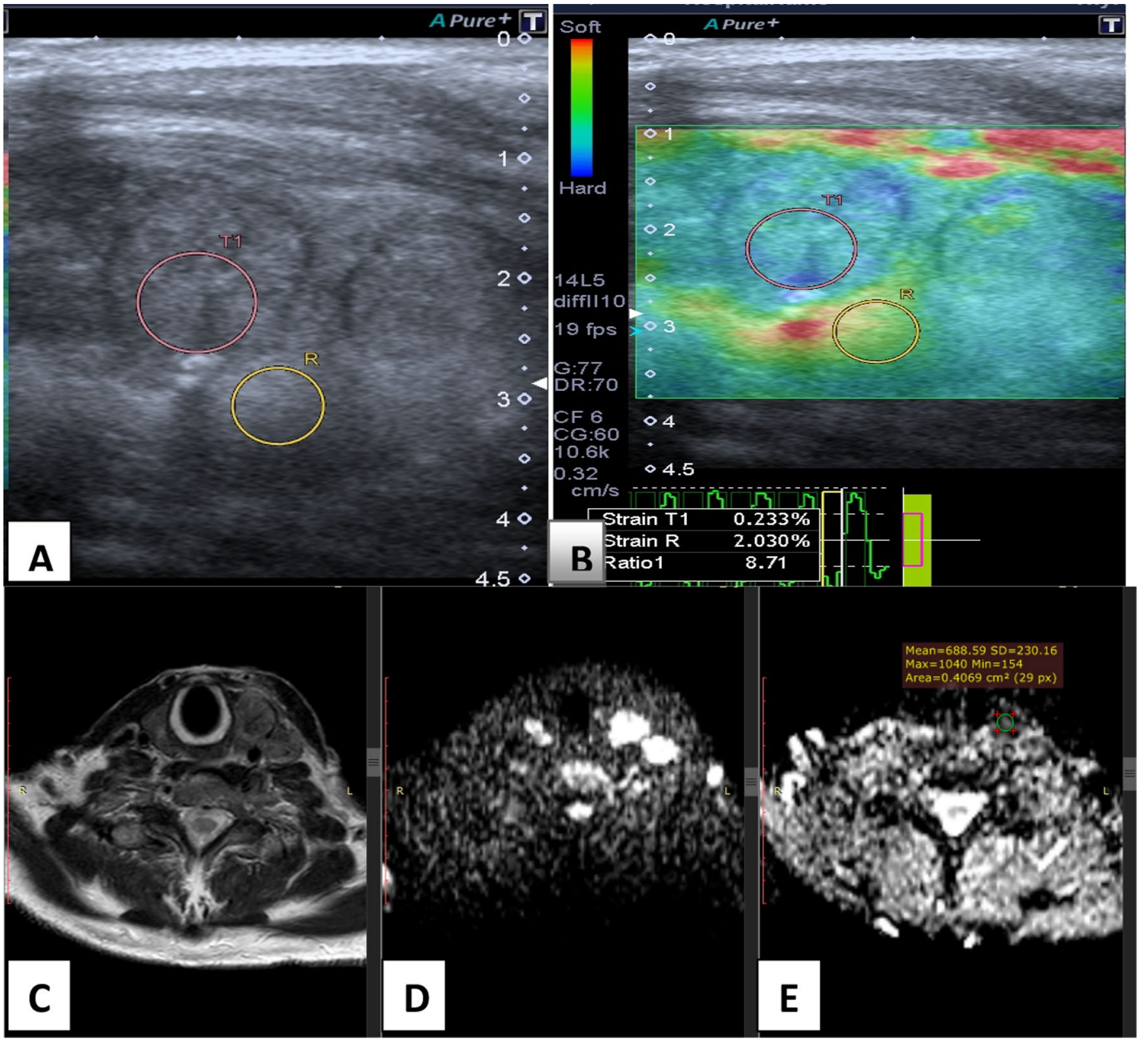

Fig. 3 Male patient aged 65 years presented with left lobe nodule. Ultrasound features of the nodule **A**: The left lobe shows solid nodule isoechoic to the surrounding thyroid tissue, wider more than taller with well-defined outline. Marginal macro-calcifications are noted. TIRADS categorization: TIRADS (5). On elastography color map **B**: most of the nodule is shaded with blue with small green areas are seen. Elastography score: (3) Strain ratio = 8.7. MRI study: T2 weighted image **C**: left lobe nodule isointense to the surrounding normal thyroid parenchyma. Diffusion weighted images **D**: the nodule shows high signal intensity. ADC mapping **E**: it shows low signal with ADC value = 0.68×10^{-3}. Pathology: papillary thyroid carcinoma

Imaging techniques

Thyroid ultrasound and elastography

The ultrasound examinations included two steps done during the same examination. First step: conventional ultrasound was carried out to define the nodule. Second step: ultrasound elastography with the same transducer using special software for sono-elastography.

Technique

The patient was lying supine with a pillow put under the neck to make his neck hyper-extended and his chin is elevated. Using adequate amount ultrasonic gel, the linear probe was applied to the front of the neck.

First, in B-mode US: thyroid gland nodules were localized and its Thyroid Imaging Reporting and Data System (TI-RADS) categorizations were identified according to ACR-TIRADS, 2017 Tessler et al. [12].

Second, in strain elastography: a region of interest (ROI) was applied, light pressure was done on the neck by the probe and a color box that includes the target nodule was highlighted by the examiner. Repeated compression followed by decompression was done in a vertical manner (perpendicular to the lesion plane). There is an available scale on the elastography machine to ensure that the applied compression was adequate. The strain ratio of the nodule in relation to remaining normal thyroid tissue or

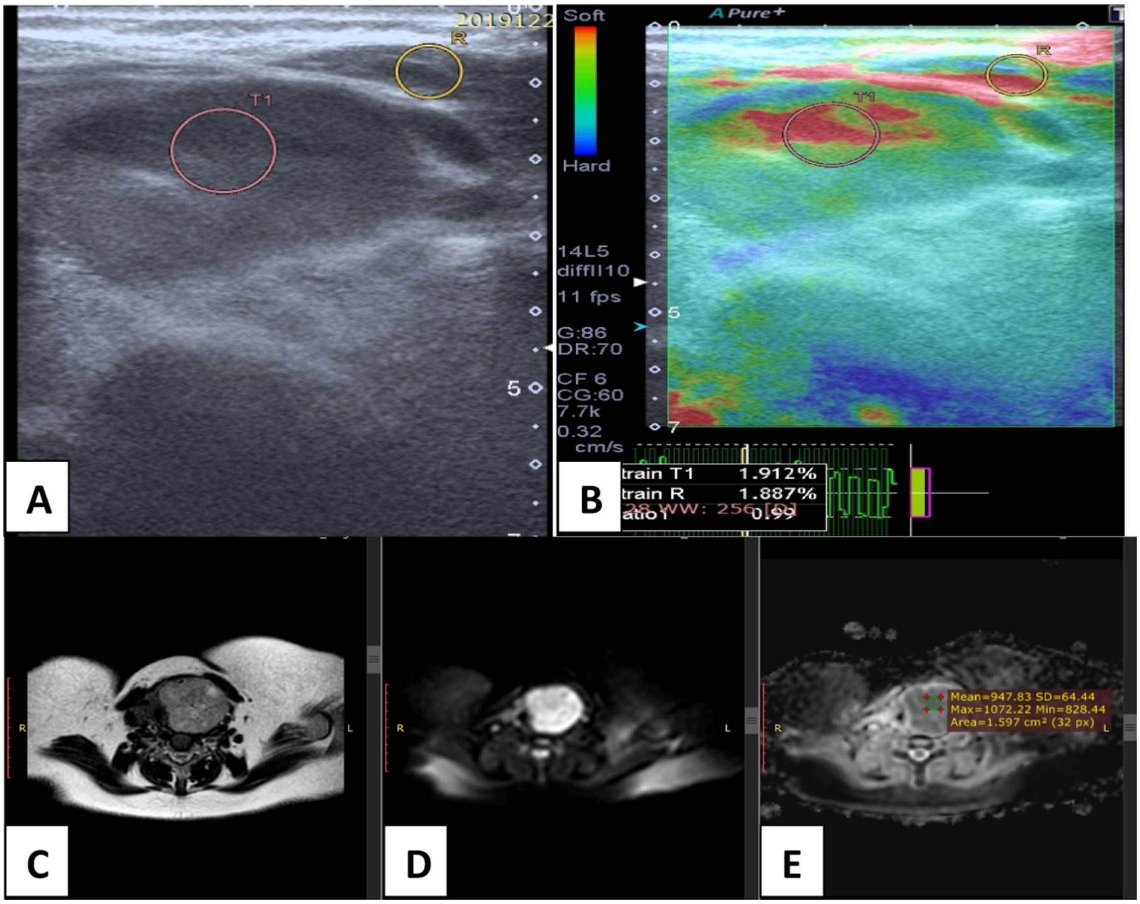

Fig. 4 Female patient aged 26 years presented with left lobe nodule. Ultrasound features of the nodule **A**: The left lobe shows solid hypoechoic nodule, wider more than taller with well-defined outline. No calcifications were noted. TIRADS categorization: TIRADS (4). On elastography color map **B**: most of the nodule is shaded with red and green (centrally) with small peripheral blue areas. Elastography score: (2) Strain ratio = 0.99. MRI study: T2 weighted image **C**: left lobe nodule with intermediate signal intensity is seen. Diffusion weighted images **D**: the nodule shows high signal intensity. ADC mapping **E**: it shows low signal with ADC value = 0.94×10^{-3}. Pathology: follicular thyroid carcinoma

to sternomastoid muscle (in case of large nodule with no available normal thyroid parenchyma) was measured and registered.

The available elastogram was presented on the gray-scale ultrasound image; in a color scale with the red color represents the softest tissue with great strain and the blue color represents the hardest tissue with no strain. The obtained elastographic images were divided and classified using the 5-points score by Rago's criteria (score1: low stiffness in the whole nodule; the whole nodule has even green color, and also the adjacent thyroid tissue. Score 2: low stiffness in a large part of the nodule; green color is almost completely present in the nodule, with only few spots of blue color. Score 3: most of the nodule has high stiffness; the dominant color of the nodule is blue color with only few spots of green color. Score 4: the whole nodule has high stiffness; the whole nodule has even blue color. Score 5: the whole nodule and adjacent thyroid tissue has high stiffness; blue color presents in the whole nodule and adjacent tissue Rago and Vitti [13].

The thyroid nodules were considered to be suspicious for malignancy, if it had Rago scores of 4 and 5.

The strain index (ratio)

The meaning of strain is the availability of the tissue for bending and deformation; so, soft tissue is expected to have more strain than hard tissue. The strain ratio is valuable in measuring the average stiffness of a lesion in comparison with its adjacent tissues.

The strain index (ratio) of the nodule of the thyroid compared to the normal thyroid tissue or that of the sternomastoid muscle (when no available surrounding normal thyroid tissue in the field for comparison) was measured and calculated. Three strain ratio measurements were taken and the average ratio was used as the representative strain ratio of the nodule.

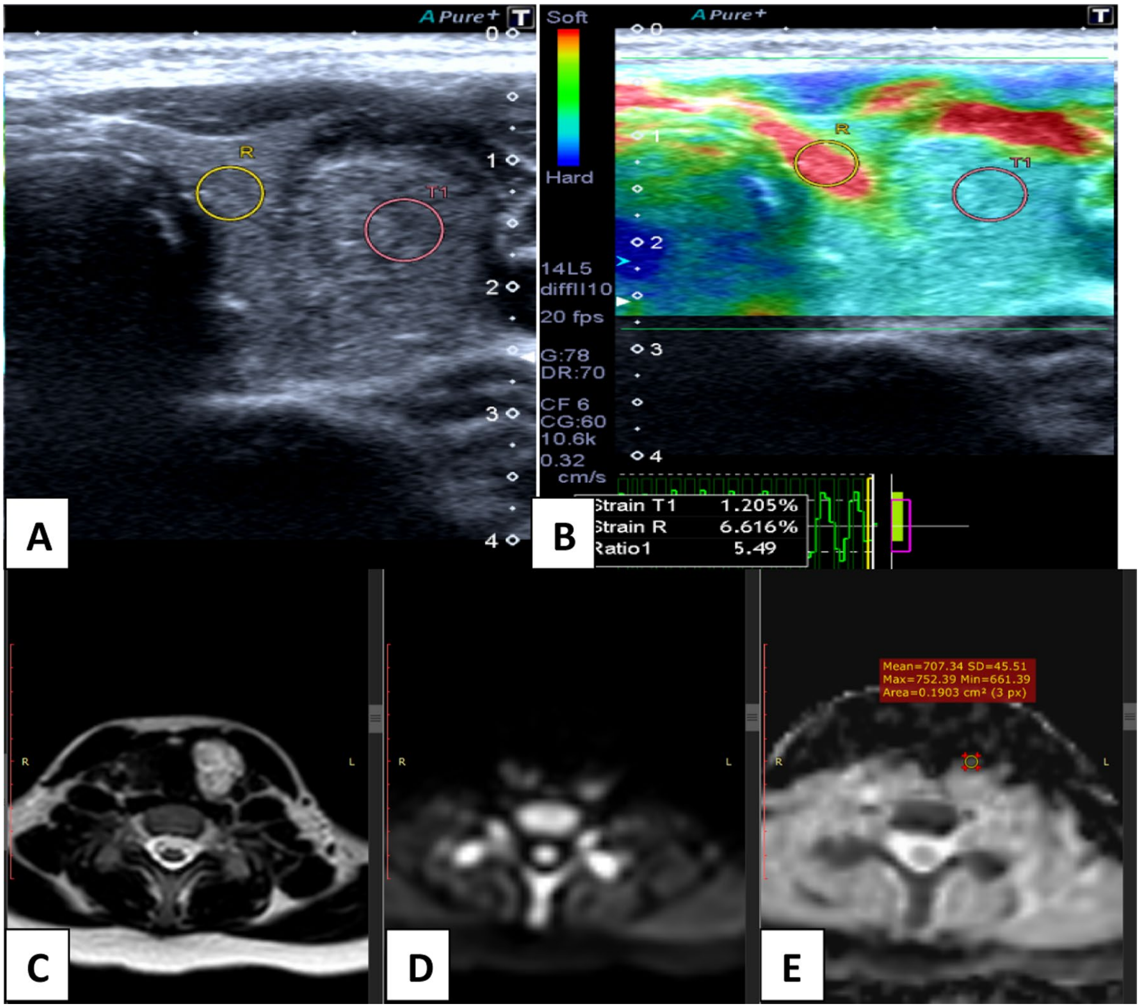

Fig. 5 Female patient aged 42 years presented with left lobe nodule. Ultrasound features of the nodule **A**: The left lobe shows a solid hypoechoic nodule, taller more than wider with well-defined outline. Micro calcifications are seen inside. TIRADS categorization: TIRADS (5). On elastography color map **B**: the entire nodule is evenly shaded blue. Elastography score: (4) Strain ratio = 5.49. MRI study: T2 weighted images **C**: left lobe nodule is seen showing mixed high and intermediate signal intensities. Diffusion weighted images **D**: areas of high signal intensity is seen within the nodule. ADC mapping **E**: it shows low signal with ADC value = 0.7 × 10^{-3}. Pathology: follicular thyroid carcinoma

Then the calculated average strain ratio for all examined nodules was correlated and compared to its cytological result, to confirm if it is benign or malignant.

MRI protocol

The MR examination was done using the MRI scanner (Philips Ingenia 1.5 T) for all patients with the same scanning parameters.

Patients were positioned supine, head first, with hips and knees extended, using a circular polarization array head and neck coil.

Axial T2-WI (TR/TE: 1250/200), FOV: 18 cm; matrix: 256 × 256, slice thickness: 2 mm, inter-slice gap: 1 mm).

Diffusion weighted imaging (DWI): single shot spin-echo planar imaging (SS-EPI) was used, with fat suppression in axial plane. TR: 1700 ms, TE: 100 ms, FOV: 25 cm, matrix: 192 × 144; number of slices: 30, section thickness = 5 mm, section gap: 2.5 mm, time of acquisition is approximately 1 min 45 s. Three b-factors images are obtained: 0, 500 and 1000 mm^2/s. The ADC maps were reconstructed.

The interpretation of the images

The MR images of all enrolled cases were presented on the MRI work station of Philips Ingenia 1.5 T MRI scanner. The ADC value for each of the thyroid nodules was measured in the ADC-map image, by drawing a suitable region of interest (ROI). Care should be taken to include the most hypo intense area inside the nodule and to exclude any cystic parts or areas causing artifacts inside the nodule. The average ADC value was calculated after taking three measurements and considered to represent the mean ADC value of the nodule. Then the calculated average ADC value for all examined nodules was correlated and compared to its cytological result, to confirm if it is benign or malignant.

All the ultrasound examinations were performed in succession by 2 independent radiologists (M. F. S. and M.A.L.) and all MRIs (mainly DWI) were done in attendance of both. The first radiologist had about 5 years and the second had more than 20 years' experiences in ultrasonic and MRI scanning. In case of controversy, the results were recorded by consensus of both and the aid of the third radiologist (M M EL) with experience more than 30 years in ultrasound and more than 25 years in MRI examinations.

The ultrasound-guided FNAB

The patients were referred to the interventional radiology unit to undergo ultrasound-guided FNAB from the thyroid nodules, provided that there are acceptable bleeding profile tests (INR ˂ 1.4 and platelet count ˃ 50.000/mL). The procedure was done by localization of the suspicious nodules and aspiration by a 20–22G needle under US guidance. The aspirated material was obtained and properly handled in the presence of a cyto-pathologist.

Surgical histopathology was done to the 8 patients with non-diagnostic FNAC to obtain final diagnosis.

Statistical analysis and data interpretation

Data were analyzed using IBM SPSS software, Version 22.0. The qualitative data were presented by number and percent. The quantitative data were presented by median (minimum and maximum) and mean, standard deviation. The threshold of significance was fixed at the (0.05) level.

Data analysis

Qualitative data

- Chi-Square test: to compare 2 or more groups
- Monte Carlo test as correction for Chi-Square test when more than 25% of cells have count less than 5 in tables ($>2 \times 2$).
- Fischer Exact test was used as correction for Chi-Square test when more than 25% of cells have count less than 5 in 2×2tables.

Quantitative data between groups

Parametric tests

- Student t-test: to compare 2 groups
- One Way ANOVA test: to compare more than 2 groups

Spearman's correlation

The Spearman's correlation: to find out the strength and direction of a linear relationship between two variables.

Diagnostic accuracy

The validity of the test is evaluated using Receiver Operating Characteristic (ROC) curve analysis, and then Sensitivity, Specificity, PPV, NPV and Accuracy were measured.

Results

There were 70 different thyroid nodules in 56 patients (with 10 patients had 2 or more nodules). In patients with multiple nodules, the nodule having TI-RADS score 4 or 5 was chosen for further analysis. So, the final number was 56 patients with 56 nodules, including 20 males and 36 females; with age ranging between (17 and 65 years) and the mean age was a 41.36 ± 14.23 years.

The fine needle aspiration was performed for the all 56 patients; it was diagnostic in 48 cases (34 benign and 14 malignant). While 8 cases (2 benign and 6 malignant) needed surgical histopathology for final diagnosis. Finally 36 nodules were benign and 20 were malignant.

Table 1 shows that in TIRADS 1 and 2: all nodules ($n=12$) were benign. TIRADS 3 score: out of (18)

Table 1 comparison of TIRADS and elastography score classification between benign and malignant lesions

		Total Benign $n=36$ (%)	Malignant $n=20$ (%)	Test of significance
TIRADS				
1	8	8 (22.2%)	0 (0.0)	MC
2	4	4 (11.1%)	0 (0.0)	$P<0.001$*
3	18	16 (44.4%)	2 (10.0)	
4	18	8 (16.7%)	10 (50.0%)	
5	8	0 (0.0%)	8 (40.0%)	
Elastography score				
1	18	18 (50.0%)	0 (0.0)	MC
2	18	14 (38.9%)	4 (20.0%)	$P<0.001$*
3	10	4 (11.1%)	6 (30.0%)	
4	8	0 (0.0%)	8 (40.0%)	
5	2	0 (0.0%)	2 (10.0%)	

MC, Monte Carlo test; *P*, Probability; *, statistically significant nodules, 16 were benign and 2 were malignant nodules. TIRADS 4 score: out of (18) nodules, 8 were benign and 10 malignant nodules. All TIRADS 5 nodules (8 nodules) were malignant.

Table 1 shows that in elastography score 1: all nodules ($n=18$) were benign. In elastography score 2 ($n=18$): 14 were benign nodules and 4 malignant nodules. In elastography score 3 ($n=10$): 4 benign and 6 malignant nodules. All nodules with elastography score 4 ($n=8$) and 5 ($n=2$) were malignant.

Regarding the TIRADS score: Nodules had TIRADS score 1, 2 and 3 ($n=30$); 28 of them were benign and 2 were malignant. Nodules with score 4 and 5 ($n=26$); 8 of them were benign and 18 were malignant with sensitivity and specificity = 90% and 77.8% respectively. The accuracy was 82.14% (Table 2).

Regarding the elastography score: Nodules had elastography score 1 and 2 ($n=36$); 32 of them were benign and 4 were malignant. Nodules with score 3, 4 and 5 ($n=20$); 4 of them were benign and 16 were malignant. Sensitivity and specificity were 80% and 88.9% respectively. The accuracy was 85.7% (Table 2).

Table 3 shows that strain ratio was significantly lower in benign lesions than in malignant ones (P-value < 0.001). For benign nodules, the strain ratio had a mean 1.2 ± 0.54, median 1.2 and a range (0.27–2.5). For malignant nodules, the strain ratio had a mean 3.79 ± 2.4, median 3.75 and a range (0.7–8.7).

As regard the strain index (ratio): Using the cut-off value = 1.85 had 80% sensitivity, 94.4% specificity and 89.3% accuracy for differentiating malignant and benign nodules (Table 3).

Table 4 shows that malignant lesions had lower ADC measurement than benign ones (P-value < 0.001). In benign nodules, the mean ADC value was (2.03 ± 0.64) with a range (1.3–3.8) and a median (1.9). In malignant nodules, the mean ADC value was (0.609 ± 0.298) with a range (0.16–0.9) and the median was (0.69).

As regard the ADC value: A cut-off value = 1.35 had sensitivity of 100%, specificity 94.4% and accuracy was 96.4% for differentiating benign and malignant nodules (Table 4).

Multi-parametric analysis: leading to increase the diagnostic performance as:

Combination of strain ratio to ACR TIRADS: there is increase in sensitivity = 90%, specificity = 94.4% and accuracy = 90% (Table 5).

Combination of TIRADS to ADC: leads to the best performance with sensitivity, specificity and accuracy = 100% (Table 5).

Discussion

To the best of our knowledge, this study is considered the first to use ultrasound ACR-TIRADS categorization, ultrasound elastography and MRI diffusion weighted imaging in a single work to examine the thyroid gland for characterization of malignant nodules, to compare the

Table 2 Validity of TRIADS and elastography scores in differentiating malignant and benign thyroid nodules

	Benign	Malignant	Sensitivity	Specificity	PPV	NPV	Accuracy
TIRADS score							
1–3	28	2					
4–5	8	18	90%	77.8%	69.2%	93.3%	82.14%
Elastography score							
1–2	32	4					
3–5	4	16	80%	88.9%	80%	88.9%	85.7%

PPV, Positive predictive value; NPV, Negative predictive value

Table 3 Validity of strain ratio in differentiating benign and malignant lesions

	Benign $n=36$	Malignant $n=20$	test of significance
Strain ratio			$z=4.32$
Mean ± SD	1.2 ± 0.54	3.79 ± 2.4	$P<0.001$*
Median (min–max)	1.2 (0.27–2.5)	3.75 (0.7–8.7)	

	AUC (95% CI)	*P* Value	Cut off point	Sensitivity	Specificity	PPV	NPV	Accuracy
Strain ratio	0.850 (0.664–1.0)	< 0.001*	1.85	80.0%	94.4%	88.9%	89.5%	89.3%

Z, Mann Whitney *U* test; *, statistically significant; AUC, Area under curve; PPV, Positive predictive value; NPV, Negative predictive value

Table 4 Validity of ADC for differentiation between benign and malignant thyroid nodules

	Benign $n=36$	Malignant $n=20$	test of significance
ADC value * 10^{-3}			$t=9.55$
Mean ± SD	2.03 ± 0.64	0.609 ± 0.298	$P<0.001$*
Median (range)	1.9 (1.3–3.8)	0.69 (0.16–0.9)	

	AUC (95% CI)	*P* Value	Cut off point	Sensitivity	Specificity	PPV	NPV	Accuracy
ADC (× 10^{-3})	1.0 (1.0–1.0)	< 0.001*	1.35	100.0	94.4%	100.0%	90.9%	96.4%

t, Student *t* test; *, statistically significant; *P*, Probability; AUC, Area under curve; PPV, Positive predictive value; NPV, Negative predictive value

Table 5 Validity of multi-parametric analysis (TIRADS + strain ratio) and (TIRADS + ADC Value) in differentiating benign and malignant thyroid nodules

	AUC (95%CI)	*P* value	Cut off point[#]	Sensitivity%	Specificity%	PPV%	NPV%	Accuracy%
US TIRADS + US elastography (strain ratio)	0.986 (0.963–1.0)	< 0.001*	.6355904	90.0	94.4	90.0	94.4	90.0
US TIRADS + Diffusion (ADC)	1.0 (1.0–1.0)	< 0.001*	0.5	100.0	100.0	100.0	100.0	100.0

[#] Detected through multivariate analysis

diagnostic accuracy of each and also to do multi-parametric analysis of these diagnostic methods in differentiation of malignant and benign thyroid nodules.

In the present study; fine needle aspiration (FNA) cytology results were diagnostic in 48/56 (85.7%) of cases, while 8 nodules needed surgical histopathology for final diagnosis. This is also shown in Azab et al. [14] study; where FNA was conclusive in 32/35 (91.4%) of cases and 3 cases required surgical histopathology for final diagnosis.

Benign nodules were more than malignant nodules as 36/56 (64.3%) were benign in nature, while 20/56 (35.7%) were malignant. Similar findings were reported by Ibrahim et al. [15] who found that 50/83 (60.3%) were benign and 33/83 (39.7%) were malignant. Lower ratios of malignant nodules were reported in studies done by Palani and Reshma [16], Chakraborty et al. [17] and Prasanth and Nallam [18] in which the ratios of malignant nodules were 20%, 14% and 7.5% respectively.

In the present study; the malignancy risk for TR1, TR2 and TR3 were 0.0%, 0.0% and 11% respectively. These results can cope with the study done by Jabar et al. [19] as malignancy risk for TR1; TR2 and TR3 were 0.0%, 0.0% and 6.9% respectively. Ruan et al. [20] found that malignancy risk for TR1, TR2 and TR3 nodules was 0.0%, 2.1% and 3.1% respectively. While Mohanty et al. [21] reported that none of the nodules with TIRADS score from TR1 to TR3 were malignant.

In the present study, the risk of malignancy for TR4 was 10/18 (56%) and TR5 nodules was 8/8 (100%). comparing to the study of Ruan et al. [20] in which the risk of malignancy for TR4 was (40.4%) and for TR5 nodules was (90.6%) and the study of Jabar et al. [19] in which the malignancy risk for TR4 was (29.2%) and for TR5 nodules was (80%).

In this study, the 5-points Rago criteria were used for detection of elastography score. The malignant nodules had higher elasticity scores than benign nodules (*P* value < 0.001) with 80% sensitivity, 88.9% specificity and 85.7% accuracy. Zhang et al. [22] reported that thyroid elastography score in detection of thyroid malignancy had lower sensitivity (73.0%) and nearly equal specificity (87.8%). Kyriakidou et al. [23] reported higher sensitivity (92%) and nearly equal specificity (90%) for the differentiation of nodules of the thyroid.

The results of this study found that using the cutoff strain ratio of 1.85 for characterization of malignant nodules of the thyroid had area under the curve (AUC) of 0.850 with sensitivity 80.0%, specificity 94.4% and diagnostic accuracy 89.3%. (*P* value = 0.001).

Idrees et al. [24] used the cutoff strain ratio (2.57) to distinguish between malignant and benign thyroid, it had sensitivity 90.0%, specificity 90.0%, and diagnostic accuracy 90.0%. Tian et al. [25] concluded that using the cutoff strain ratio of 2.52 for differentiation of malignant and benign nodules of the thyroid, had area under the curve (AUC) of 0.861 with 85.7% sensitivity, 90.5% specificity, 85.7% and 88.6% accuracy. Also, Cantisani et al. [26] found that using the cutoff strain ratio of 2.05 to discriminate between benign and malignant nodules of the thyroid, had area under the curve of

0.897 with 91.7% sensitivity, 80.0% specificity and diagnostic accuracy of 85.8%. (P value < 0.001).

The present study showed that the signal intensity in diffusion weighted images was not useful for differentiation of thyroid nodules ($P = 0.472$). Similarly, Aghaghazvini et al. [27] reported that the signal intensity of the nodule and its border were not valuable for differentiation of thyroid lesions (P-value > 0.05).

The present study showed that malignant lesions had lower mean ADC value than benign ones (P-value < 0.001). Using the ADC value 1.35×10^{-3} mm^2/s as a cutoff value for differentiation of malignant and benign nodules of the thyroid had sensitivity 100%, specificity 94.4% and accuracy of 96.4%.

Mohammad et al. [28] concluded that; benign nodules had mean ADC value ($1.39 \pm 0.11 \times 10^{-3}$mm^2/s). Malignant nodules had mean ADC value ($0.81 \pm 0.17 \times 10^{-3}$mm^2/s). Similar to the current study, they confirmed that using the cut-off ADC value 1.3×10^{-3} for the differentiation of the nodules of the thyroid had 100% sensitivity, 88.9% specificity and the overall accuracy was 95%.

Shokry et al. [29] confirmed that the use of cutoff ADC value 1.15×10^{-3}mm^2/s had sensitivity 88.2% and specificity 92.3% (P-value < 0.001). Also, Aghaghazvini et al. [27] reported that using the ADC cutoff value 1×10^{-3}mm^2/s had sensitivity 87% and specificity 96% for differentiation of thyroid nodules.

The study done by Pei et al. [4] concluded that US elastography may be a valuable tool when added to the US TIRADS in differentiation of benign and malignant thyroid nodules, as the combination of US elastography and TIRADS increased the diagnostic performance than elastography or TI-RADS alone. This matches with the results of the current study as strain ratio had more accuracy than ACR-TIRADS (89.3% vs. 82.14% respectively). Adding the strain ratio to the TIRADS leads to increase in sensitivity = 90% and accuracy 90%.

A comparative study between diffusion weighted imaging (ADC) and ultrasound TIRADS was done by Kong et al. [30], they found that the ADC had 92.2specificity and 87.6% accuracy. Ultrasound TIRADS had specificity 80.4 and accuracy of 86.9%.

This is also in accordance with the results of this study as ADC had more specificity (94.4%) and accuracy (96.4%) than either ACR-TIRADS (specificity was 77.8% and accuracy was 82.14%) or the strain ratio (specificity 94.4% and accuracy 89.3%.). The reason for the high percent in our study may be due to the small number of patients.

Sasaki et al. [31] used a special combination of MR time intensity curve and ADC analysis, their results showed sensitivity of 100%, specificity 71% and accuracy of 91% for differentiating benign from malignant thyroid nodules.

Wang et al. [32] studied the use of multiple MRI parameters for characterization of thyroid malignancy. ADC was the superior in differentiation of benign and malignant nodules, with 90% sensitivity and 91% specificity. When the results of ADC were combined with features associated with thyroid malignancy (such as irregular shape, ring sign and cystic degeneration), the outcome is improved with the sensitivity is increased to 97%, and the specificity was 95%.

The best performance was achieved in the current study by the multi-parametric analysis by adding ACR TIRADS to the diffusion ADC with sensitivity, specificity and accuracy = 100% in differentiation of benign and malignant thyroid nodules. Also, this study was done in a prospective manner in comparison with most of other studies which were retrospective.

Limitation and recommendation

Small number of patients.

Further large scale study is recommended for confirming the results.

In this study, strain elastography was used. Future studies using the shear wave elastography is needed.

Conclusion

Ultrasound elastography and measuring the strain ratio of thyroid nodules add valuable data over ACR-TIRADS categorization. It is recommended as adjunctive tool. However, the diffusion weighted MRI and ADC value had more accuracy in differentiation of malignant and benign thyroid nodules. Multi-parametric analysis leads to increase the diagnostic ability with the best performance achieved by the combination of ACR-TIRADS to diffusion weighted MRI and ADC value.

Abbreviations

FNA: Fine-needle aspiration; FNAC: Fine-needle aspiration cytology; FNAB: Fine-needle aspiration biopsy; USE: Ultrasound elastography; FOV: Field of view; DW-MRI: Diffusion weighted-magnetic resonance imaging; ADC: Apparent diffusion coefficient; DWI: Diffusion weighted imaging; TIRADS: Thyroid imaging reporting and data system; TR: Repetition time; TE: Echo time; ms: Millisecond; ROI: Region of interest; T: Tesla; SS-EPI: Single shot spin echo planar imaging; mm: Millimeter; cm: Centimeter; sec: Second; min: Minute; AUC: Area under the curve; ROC: Receiver operating characteristic curve; PPV: Positive predictive value; NPV: Negative predictive value; SD: Standard deviation; TR1: TIRADS 1; Vs: Versus.

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Authors' contributions

MAL: Idea of the research, writing of the manuscript, final revision of data and radiological images. Finalization of the research manuscript. MMEL: Supervision of the radiological examination of patients. Revision of the scientific and medical data and radiological images. MFS: collecting of the data, helping in writing of the manuscript and radiological examination of patients (under supervision). All authors read and approved the final manuscript.

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Availability of data and materials
Authors can confirm that all relevant data are included in the article and/or its supplementary information files.

Declarations

Ethics approval and consent to participate
This study was approved by Mansoura Faculty of Medicine—Institutional Research Board (MFM-IRB), and written informed consent to participate was obtained from all patients. Ethics committee reference number of acceptance is MS/16.02.42.

Consent for publication
Informed consent was taken from enrolled patients for publication.

Competing interests
Not applicable "The authors declare that they have no competing interests".

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