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Research Article

Shear Wave Elastography ratio (E1/E2 ratio) in accordance with ACR-TIRADS in differentiating benign and malignant thyroid nodules (A single center cohort study)

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Abstract

Background: Shear ware Elastography is a new diagnostic tool for differentiating benign and malignant thyroid nodules with or without conventional ultrasound. The objective of this study was to evaluate the value of shear wave elastography (using the E1/E2 ratio) in differentiating benign thyroid nodules from malignant ones aiming to have a cutoff of values as compared with the results of FNAB/tissue pathology under the ACR-TIRADS guidelines. **Methods:** We evaluated 100 suspicious nodules found on 100 consecutive patients whom were referred from internal medicine and general surgery clinics between the periods of 8/2022 to 5/2023 for characterization of their clinically suspected nodular goiter. Patients had FNAB according to ACR-TIRADS guidelines to characterize their clinically proven single or multinodular goiter. Elastography ratio results were compared with the results of fine needle aspiration biopsy or tissue pathology **Results:** From the studied one hundred nodules, 68 of which were benign and 32 were malignant. The Median of E1 values were 61.6 with interquartile range from 26.6 to 90.4 for benign nodules and 144.2 with interquartile range from123.3 to 181.5 for malignant ones. The median of E1/E2 ratio was 0.34 with interquartile range from 0.22 to 0.65 for benign nodules and it was 0.09 with interquartile range from 0.07 to 0.16 for malignant nodules. ROC curve for E1/E2 ratio to predict benign and malignant thyroid lesions. Cut-off ≤ 0.15 predict malignant lesions. **Conclusions:** Shear wave Elastography ratio could be considered as reliable and valuable tool in differentiation between benign and malignant thyroid nodules with or without conventional ultrasound.

Keywords: Shear wave Elastography, Thyroid nodule, thyroid Malignancy, FNAB.

Introduction

Thyroid nodules reported to be found in 33% of adults between the age of 18 and 65 years and in 50% of the population over 65 years of age[(1)]. Although the majority of the thyroid nodules are benign, malignancy has a prevalence of 5% - 15%[(2)]. For number of years, there has an intense debate whether surgeries for thyroid nodules are unnecessarily performed[(3,4)], so the thyroid specialists seek for improvement in preoperative diagnosis. Only one from 15th suspected nodule is really malignant and unnecessarily thyroidectomy is performed for benign nodular goiter[(5-8)]. The role of sonographic assessment of thyroid nodules is to distinguish benign nodules which needs follow up and suspicious ones which needs further investigations [(9)].

Shear Wave Elastography is a new diagnostic tool of added value in differentiation between benign and malignant thyroid nodules [10-13]. Shear waves are transversely propagated waves created in stimulated tissues, with velocities increasing as the square root of the elastic modulus (stiffness) of the tissue. Shear wave elastography stimulates tissues with focused ultrasonic pulses, tracks shear waves with an ultra-fast US technique, and presents real-time output on elastograms in terms of shear wave velocity or estimated tissue stiffness [14, 15] ***(Figure 1)***

The aim of this study to evaluate the elasticity ratio values, specifically the E1/E2 ratio, to avoid the overlap in separate measured values in each nodule, and to find a cut of value in comparison with the pathological reports of FNAB/ tissue pathology according to ACR-TIRADS guidelines.

Methods:

One hundred consecutive patients were recruited from internal medicine and general surgery clinics after having an ethical approval from Faculty of Medicine, ethical board committee (476: 10/2022) A written consent was obtained from all patients for participation. Patients were examined with shear wave Elastography by GE LOGIQ S8 R4 OLED ultrasound machine 6/2021.

All patients were examined by a single operator of 5 years' experience by ACR-TIRADS guidelines

Inclusion criteria:

- All patients with thyroid nodules, either solitary or part of multinodular goiter
- Adult patients from 16-60 years' old
- Thyroid nodules with adjacent parenchymal thyroid tissue for measurement comparison
- Thyroid nodules of ACR-TIRADs III or more with size threshold to have FNAB, in accordance with ACR-TIRADS guidelines

Exclusion criteria:

- Patients out of age range
- Completely calcified nodules or with dense peripheral calcifications (can't tell nodules)
- Patients with coagulopathies contraindicating FNAB
- Completely cystic nodules

Patients underwent real-time SWE using a linear 9MHz transducer. SWE was displayed along-side grey-scale US (split screen mode) for lesion localization and SWE display scale (0 to 150 kPa, actual SWE measurements were independent of the display scale).

Collected measurements were

1- E1 value: Represent velocity within the examined nodule
2- E2 value: Represent velocity on the adjacent normal parenchyma
3- E1/E2 ratio.

Pending on TIRAD staging system, patients with suspected nodules, which are recommended for FNAB were included in our study

Technique of FNAB: [16]

- The Patient is laying on his back with neck extended and chin elevated.
- Skin was cleansed with alcohol preparation.
- A syringe 10 cm was used.
- With visual ultrasound method the needle penetrated the nodule with several advance-withdrawal motions then carefully maintained within the nodule for 2-5 seconds.
- Then withdrawal of the needle and apply the sample over slides.
- A sterile pad of cotton over the needle penetration site in the neck.

The collected slides were then examined with a single consultant pathologist of five years' experience and reported according to the Bethesda scoring system**[17,18]**.

Suspected follicular neoplasm nodules, underwent surgical excision with tissue speciment pathological examination

Statistical analysis:

The analysis of the data was carried out using the IBM SPSS version 26.0 statistical package software (IBM; Armonk, New York, USA). Normality of the data was tested using the Kolmogorov-Smirnov test.

Data were expressed as mean ± SD (Range) for parametric quantitative data and median (IQR) for non-parametric quantitative data in addition to both number and percentage for qualitative data.

Mann-Whitney test was done for non-parametric data between benign and malignant groups.
The Chi-square test or Fisher's exact test were used to compare categorical variables.
A ROC curve analysis was done for calculating sensitivity, specificity, PPV, NPV and overall accuracy of E1/E2 ratio to predict benign and malignant thyroid lesions.
A p-value less than 0.05 was considered significant.

Results

Our study included 100 patients, 92 females and 8 males in the age range from 22 y to 66 y with mean 42.1, fourteen from them not obese, 30 over weight and 56 not obese. Only 2 cases had autoimmune disease and 98 were negative, 94 from them were not smoker and 6 were smokers. None of the patients had history of radiation exposure Regarding the family history of thyroid diseases, 46 from them were positive and 54 were negative. (Table 1)
From the 100 patients,18 patients presented with solitary nodule, and 82 had multinodular goiter, only highly suspicious nodules according to ACR-TIRADS were furtherly evaluated.

The study was done on 100 nodules, 68 of them were benign and 32 were malignant. The Median of E1 values was 61.6 with interquartile range from 26.6 and to 90.4 for benign nodules and it was 144.2 with interquartile range from123.3 to 181.5 for malignant nodules. The median of E2 values was 18.9 with interquartile range from 9.2 to 32.6 for benign nodules and it was 14.4 with interquartile range from11.5 and to 22.9 for malignant nodules.
The median of E1/E2 ratio was 0.34 with interquartile range from 0.22 to 0.65 for benign nodules and it was 0.09 with interquartile range from 0.07 to 0.16 for malignant nodules. (Table 2)

ROC curve was used for E1/E2 ratio to predict benign and malignant thyroid lesions. Cut-off ≤ 0.15 predict malignant lesions. **(Figure 2)** In our study the cut off value for E1/E2 ratio was <0.15 which at this value predict malignant lesions P value was significant, with sensitivity 85.07%, specificity 75%, positive predictive value of 87.69%, negative predictive value of 70.59% and accuracy of 81.82%. **(Table 3)**.
An example of the cases is demonstrated in Figures 3,4 and 5

Table 1: demographic characters of cases

Demographic characters		Cases No.= 100
Age	Mean ± SD	42.1 ± 11.1
Gender: Male Female	No. (%)	 92 (92.0%) 8 (8.0%)
Obesity: Not obese Over weight Obese	No. (%)	 56 (56.0%) 30 (30.0%) 14 (14.0%)
History of autoimmune diseases: Positive Negative	No. (%)	 2 (2.0%) 98 (98.0%)
Smoking: Yes No	No. (%)	 6 (6.0%) 94 (94.0%)
Radiation exposure: Yes No	No. (%)	 0 100 (100%)
Family history of thyroid diseases: Positive Negative	No. (%)	 46 (46.0%) 54 (54.0%)

Table 2: Values of shear ware Elastography, comparison with FNAB results

Shear wave Elastography		TIRAD FNAB results No.= 100		p value
		Benign No.= 68	Malignant No.= 32	
E1	**Median (IQR)**	61.6 (26.6 – 90.4)	144.2 (123.3 – 181.5)	**<0.0001***
E2	Median (IQR)	18.9 (9.2 – 32.6)	14.4 (11.5 – 22.9)	0.615
E2/ E1	**Median (IQR)**	0.34 (0.22 – 0.65)	0.09 (0.07 – 0.16)	**<0.0001***

- ***Mann-Whitney test for non-parametric quantitative data between the two groups.***
- ****: significant level at p value <0.05***

Table 3: Cut off point and statistics of SWE

	E1/E2 ratio	
Cutoff point	≤ 0.15	
AUC	0.824	
P (95% CI)	**<0.0001*** (0.728 – 0.919)	
Statistics	**Value**	**95% CI**
Sensitivity	85.07%	74.62% – 92.6%
Specificity	75.0%	56.6% - 88.54%
Positive Predictive Value	87.69%	77.18% - 94.53%
Negative Predictive Value	70.59%	52.52% - 84.9%
Accuracy	81.82%	72.8% - 88.85%

Figure ligands:

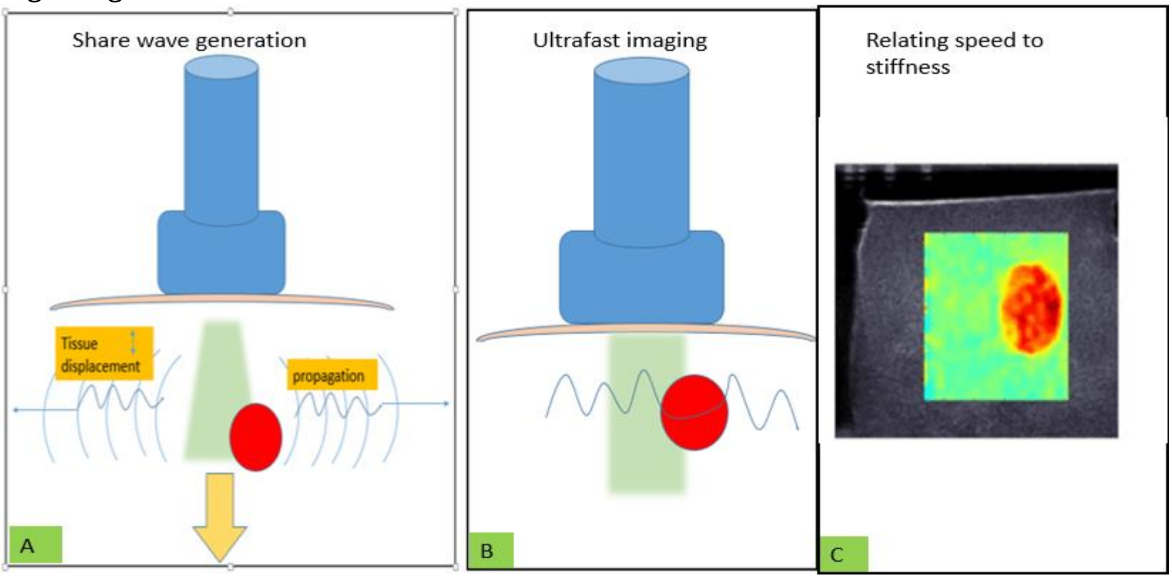
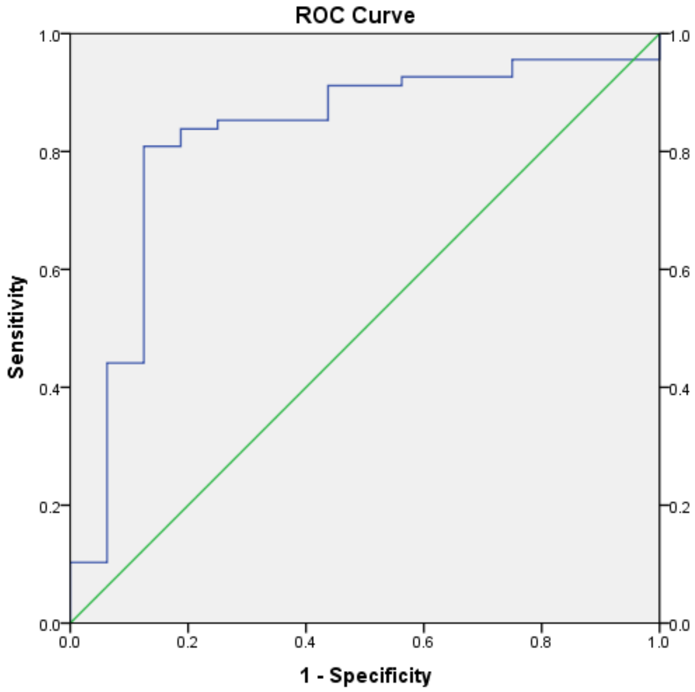


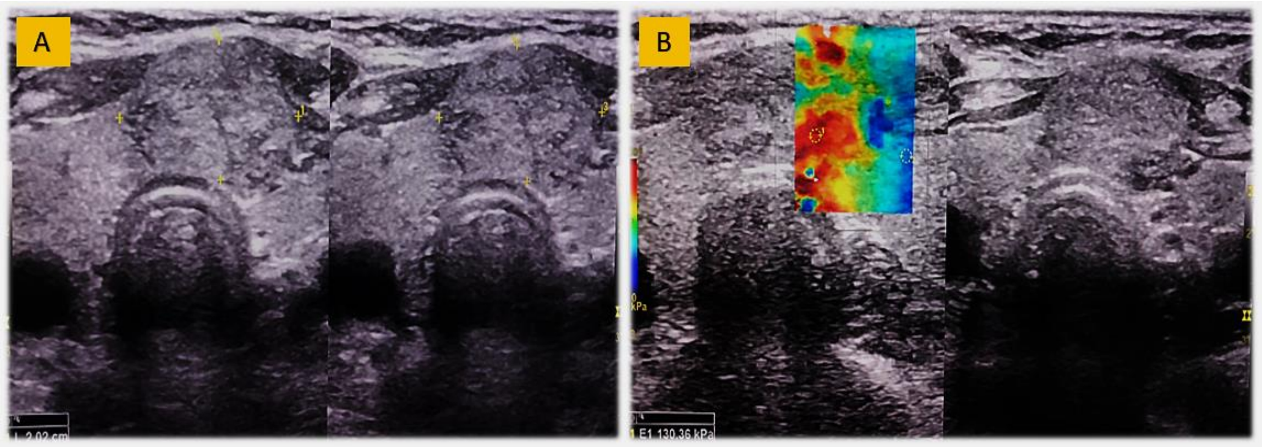
Fig (1) schematic representation of shear wave elastography main steps
a-The orange arrow indicates the direction of longitudinal wave of US which generate the transverse shear wave.
b- All crystals in the transducer are activated to generate plane waves which image the shear wave propagation.
c- A color map overlapped on the conventional US and the colors represent the stiffness which the red color indicates stiffer than the surrounding green soft tissues.

Figure 2:



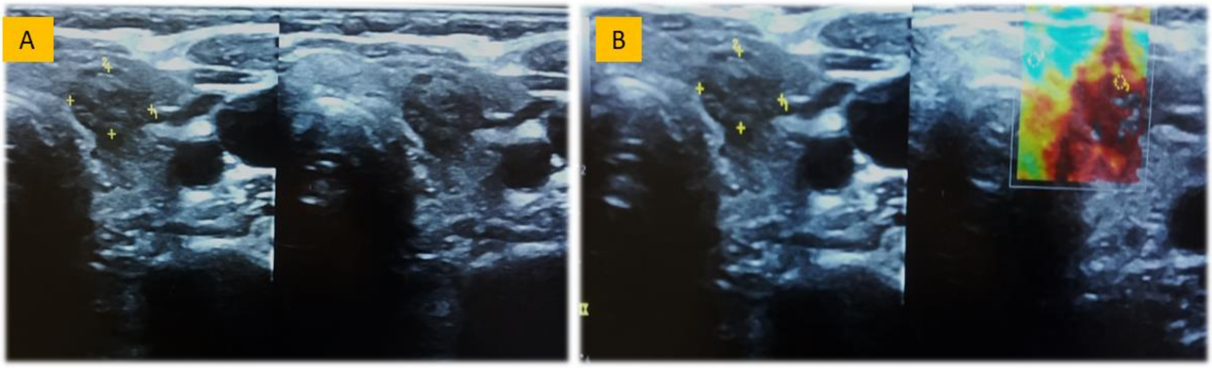
ROC curve for E2/E1 ratio to predict benign and malignant thyroid lesions.
Cut-off ≤ 0.15 predict malignant lesions.

Figure 3
Female patient 39 years old presented with palpable neck lump
On gray scale ultrasound assessment: there was a well-defined, isoechoic solid nodule involving isthmus and encroaching upon left thyroid lobe, wider than taller with no calcification within (TIRAD III).



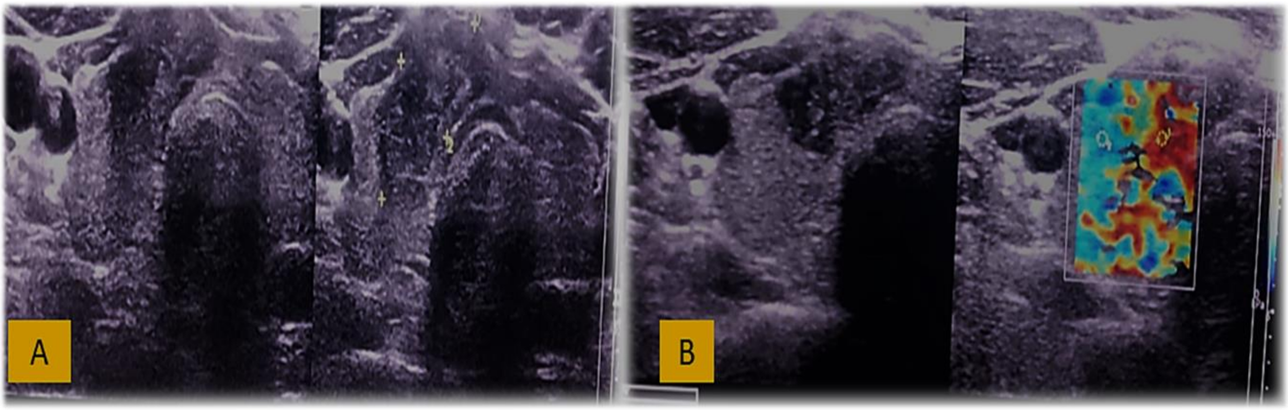
On SWE:
E1 (30.1)
E2 (10.13)
E2/E1 ratio (0.34)
FNAB result was benign thyroid nodule

Figure 4:
Female patient 55 years old presented to us with palpable neck lump
On grey scale assessment: there was a well-defined hypoechoic solid thyroid nodule in left lobe, wider than taller and no calcification within (TIRAD IV).



On SWE:
E1 (154.18)
E2 (25.73)
E2/E1 ratio (0.17)
FNAB result was follicular lesion consistent with adenomatous hyperplasia

Figure 5:
Female patient 26 years old presented to us with palpable neck lump
On grey scale ultrasound assessment: there was a rather defined hypoechoic solid thyroid nodule in right lobe, taller than wider and punctuate calcifications within (TIRADS V)



On SWE:
E1 (118.21)
E2 (16.78)
E2/E1 ratio (0.14)
FNAB result was suspicious for papillary carcinoma, that was confirmed after surgical excision and histopathological assessment

Discussion

Although the majority of the thyroid nodules are benign, malignancy has a prevalence of 5% - 15%[2]. Shear Wave Elastography uses dynamic method which represent the acoustic radiation force impulse imaging (ARFI)[19-21]. The 2D shear wave elastography and point shear wave elastography use acoustic impulses of the transducer of ultrasound to provoke a minute tissue movements which cause transverse shear waves that its speed is recorded and interpreted into an elasticity quantitative measurements.[19-21] Then a real time color coded map of elasticity of 2 × 3 cm is demonstrated overlying the image of the gray scale ultrasound[22] with corresponding values of elasticity repress-ented by kilopascal. The operator put a mobile and size modifiable region of interest then a quantitative elasticity index measurements are appeared [19].

The aim of our study was to evaluate the value of (E1/E2 ratio, Shear Wave Elastography) in assessment of thyroid nodules based on results of FNAB according to ACR-TIRADS guidelines. The use of this ratio avoid the wide range of measurements overlap when depending on the E1 ratio alone.

One hundred nodules from 100 consecutive patients were included, 92 females and 8 males (mean of age 42.1), all of them underwent shear wave-elastography exami-nation followed by FNAB if indicated by ACR-TIRADS guidelines.

The E1 indicates the elasticity index within nodule which was 61.6 for benign nodules and 144.2 for malignant ones. Having a lower elasticity index in benign nodules and high index in the malignant ones. This is similar to the study of (Sebag et al.,)[23] who found that the elasticity index within nodules was 36 for benign nodules and 150 for malignant ones and in agreement with the study of (Szczepanek-Parulska et al.,)[24] who found the elasticity index was 25 for benign nodules and 143 for malignant ones.

Other studies of (Park et al.,) [25], (Kim H et al.,)[26], (Farghadani M et al.,)[27], (Wang F et al.,)[28], (Liu B et al.,)[29], (Dobruch-sobczak K et al.,)[30], (Shang H et al.,)[31] found a lower values for elasticity indices within a nodules that were 88, 86, 83, 68, 64, 54 and 50 respectively for malignant nodules and were 51, 52, 44, 46, 28, 29 and 36 respectively for benign nodules. Despite these results discrepancy, they still having a lower elasticity index for the benign ones than the malignant ones and these differences can be explained by different techniques in elasticity measurements as on each study.

On the previous studies, the values of elasticity indices were only measured within the suspected nodules with wide variation on the found elasticity index. In our study we depend on the E1 (elasticity index within nodule), E2 (elasticity index within normal thyroid parenchyma) and E1/E2 ratio (the ratio between the two previous elasticity index) in evaluation of malignancy to improve of results and to narrow the differentiation zone. Statistical ROC curve in our study, concluded cut off value for E1/E2 ratio ≤ 0.15 which at this value predict malignant lesions. With significant P value, sensitivity of 85.07%, and specificity of 75%, positive predictive value was 87.69% and with accuracy of 81.82%.

As regard sensitivity and specificity, our results were similar to (Shang H et al.,)[31] who found that the sensitivity and specificity were 87% and 52% respectively and (Farghadani M et al.,) [27] who reported 86% and 66% respectively and also in agreement with (Szczepanek-Parulska et al.,)[24] with 86% and 81% respectively (Sebag et al.,)[23] who found 85% and 94% respectively .

Our results were higher than (Kim H et al.,)[26] (Liu B et al.,)[29] (Dobruch-sobczak K et al.,) [30] and (Park A Y et al.,)[25], whom reported average 60.25% for sensitivity and average 72% for specificity, this can be explained by different methods for measurements of elasticity and the measurement method, which differs according to the type of the machine.

With new generations of ultrasound machines, the added value of comparison of elasticity between the nodule and adjacent parenchyma and the auto calculation of E1/E2 ratio can facilitates/predict the type of nodule as a bed side test, avoiding the unnecessary FNAB in benign-looking nodules

Conclusions

Shear wave Elastography is a new diagnostic tool of added value in differentiation between benign and malignant thyroid nodules with or without conventional ultrasound SWE has a promising future in differentiation between benign and malignant thyroid nodules, further studies with more patients are necessary to generalize the results.

Limitation of the study

- The limited number of the studied population, more sample size needed in further studies
- The study only involved adult patients, generalization to pediatric population needs further studies - Still there is a debates, non-conclusive results regarding the can’t tell nodules.

List of Abbreviations:

ARFI: acoustic radiation force impulse.
E1: mean elasticity index in thyroid nodule.US: ultrasound.
E2: mean elasticity index in normal thyroid parenchyma MHz: megahertz.
FNAB: fine needle aspiration biopsy.
SWE: Shear wave elastography.
SWV: shear wave velocity.
US: Ultrasound

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