

Comparison of Muscle to Nodule Strain Ratio Elastography with Parenchyma to Nodule Strain Ratio Elastography in Suspicious Thyroid Nodules

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Abstract

Background: Ultrasound elastography (USE) is a non-invasive technique for distinguishing benign from malignant thyroid nodules. It uses strain ratio to determine thyroid nodular stiffness, however it has limitations when no normal thyroid tissue is present.

Objective: To assess the diagnostic performance of USE in the prediction of malignant thyroid nodules by assessing the strain ratio comparing the normal thyroid tissues as a reference and sternocleidomastoid muscle as a second reference.

Patients and Methods: The study was conducted on 33 patients with single TIRADS III or IV nodules at Al-Imamein Al-Kadhimein Medical City in Baghdad-Iraq for 5 months (August 25th, 2020 to January 15th, 2021), using both gray scale and real-time USE on a Voluson- E6 Ultrasound machine. Final diagnosis has been obtained by cytology and/or histopathology.

Results: The study involved a total of 33 patients, with 78.8% female and 21.2% male. Of these, 72.7% were benign, and 27.3% were malignant. The thyroid nodules were hypoechoic, taller, and micro calcified. The parenchymal-nodular SR of all thyroid nodules ranged from 0.55-6.0, while the muscle-nodular SR ranged from 0.42-5.25. The best (strain ratio) SR cutoff value was (\geq 3.63) for parenchymal-nodular SR, with sensitivity, specificity, and accuracy rates were 100%, 85%, and 89.2%, respectively.

Conclusion: The study found that sternocleidomastoid muscle has high sensitivity, specificity, and accuracy in predicting thyroid malignancy and differentiating benign from malignant nodules so making it safe for use in certain cases.

Keywords: Elastography, Thyroid nodules, Strain ratio, Muscle.

Introduction

Thyroid nodules are a prevalent concern in the general population, with an incidence of 5% in women and 1% in men in iodine-sufficient areas, and 19-68% detected using high-resolution ultrasound (1,2) Most thyroid nodules remain benign, with only 5% existence malignant (3). Diagnosing benign or malignant thyroid nodules is crucial for treatment. Fine needle aspiration biopsy (FNAB) is recommended for the diagnosis but has limitations (4). Ultrasound perceives thyroid nodules, their location, size, composition, and histopathology (5). It's crucial for identifying cancerous nodules due to their high prevalence (6). For solid thyroid nodules, parameters like echotexture, shape, borders, intramodular calcifications, and peri nodular halo should be evaluated (7). The American Thyroid Association [ACR] has developed the Thyroid Imaging Reporting and Data System [ACR-TIRADS], a sonographic technique for evaluating nodular features (8).

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The American Thyroid Association (ACR) strategies (9) declared that apart from worrisome cervical lymphadenopathy, single no sonographic characteristic or combination is sensitive enough to identify all malignant nodules. Elastography is an emerging sonographic technology that needs additional confirmation (10). Ultrasound elastography (USE) is an imaging method that detects tissue stiffness. It was first described in the 1990s and has since been further developed and enhanced to allow quantitative measurements of tissue stiffness (11). The elasticity of the thyroid gland depends on the structural features of the tissue matrix. Unlike conventional ultrasound (US) which determines reflectivity based on microscopic structure, elastography affords image contrast depending on histologic tissue structure, allowing discrimination between normal and parenchymal disorders (10). The normal thyroid has a soft advent, with variability in elastography appearance due to parenchymal hyperplasia and involution (12). Combining thyroid USE with B-mode US can enhance the capability to differentiate benign from malignant thyroid nodules and diminish the number of desired FNAs (13). Elastography methods can distinguish precious from normal tissue for investigative applications. Conservative ultrasound is a low-priced, adaptable, and commonly available modality, which also applies to USE (14). Elastography evaluates tissue elasticity, or the ability of tissue to resist deformation or regain its original shape after force is applied (11,15). Techniques include free-hand quasi-static or strain elastography [SE], which measures shape-deformation using a probe compression (10), and shear-wave elastography (SWE), a new technique that uses acoustic pressure from the probe to provide realtime elastic information (16). SE measures the shape-deformation and lesion stiffness compared to surrounding tissue, while SWE

detects the transverse component of particle displacement caused by an acoustic pulse from the probe (10). Strain elastography is a method used to measure the stiffness of thyroid nodules by analyzing changes in size and shape corresponding to the route of the investigative force (17),(18). The strain data are presented as a semitransparent color map termed an electrogram, which is placed on the B-mode picture (19). The strain ratio is a pseudoquantitative measurement that indicates the ratio of strain recorded in a neighboring reference tissue region of interest and strain measured in a target lesion ROI (20). Thyroid ultrasound strain imaging investigations can be classified based on the stimuli used and the grading systems employed. The most common stimulus utilized in thyroid ultrasound strain imaging is operator-applied external compression through the ultrasound transducer (14). Thyroid ultrasound strain imaging scoring systems include two qualitative elasticity scores (Asteria criterion, a 4-point score (21) or Rago criteria, a 5-point score) (22) and a semiquantitative thyroid stiffness index, which measures the strain in the background normal thyroid tissue versus the strain in the thyroid nodule (23). The Asteria criteria are based on four classes of tissue stiffness, whereas the Rago criteria range from score 1 (even elasticity throughout the nodule) to score 5 (no elasticity in the nodule or the area of posterior shadowing) (22). The real-time elastography (RTE) appearance of thyroid nodules is assessed subjectively using the elasticity score (ES) (23) and strain ratio (SR). The latter involves placing two similar ROIs at similar depths, resulting in a strain ratio that may be more accurate than elasticity imaging (24-26). Combining these measurements is assumed to be superior for malignancy assessment, as they provide independent measures (11).tissue as the first reference and



SCM muscle as the second reference. The current study's purpose was to assess the diagnostic performance of USE in the prediction of malignant thyroid nodules by assessing the strain ratio compared to sternocleidomastoid muscle and normal thyroid tissue as references.

Patients and Methods

This prospective study was conducted at the US unit of the Radiological Department at Al Imamein Al Kadhimein Medical City in Baghdad from August 25th, 2020, to January 15th, 2021. The study included 33 patients aged 18 years or older, with solitary thyroid nodules, including TIRADS III nodules of more than 25 mm and TIRADS IV nodules of more than 15 mm. The patients were examined using B-mode ultrasound and sonoelastography before undergoing fine-needle aspiration (FNA). Exclusion criteria included patients with inconclusive histopathology, TIRADS I and II, multiple thyroid nodules, abnormal thyroid parenchyma, neck surgery affecting the sternocleidomastoid muscle (SCM) or partial thyroidectomy, abnormal thyroid function tests, and thyroid nodules with eggshell calcification.

Imaging Methods:

Gray-scale US: The thyroid ultrasonic examination was carried out utilizing the Voluson-E6 Ultrasound machine (GE Healthcare, USA) with a 5 to 12 MHz linear array transducer. Thyroid nodule criteria were obtained with the patient resting supine with an exposed neck and a minor neck extension. The thyroid gland is scanned at axial, sagittal, and oblique planes. The size, margin, composition, echogenicity, orientation, and presence of calcification were all measured and documented. Real-time Elastographic US: Elastographic US of the nodules were carried out immediately after the B-mode US. The operator placed the linear probe perpendicular to the skin on the neck. A box was then highlighted that included

the selected thyroid nodule and an adequate surrounding normal thyroid tissue at the same depth as possible. This was followed by the inclusion of the same thyroid nodule and the other reference tissue (SCM muscle). To reduce motion artifacts, patients were instructed to hold their breath and refrain from swallowing during the examination. The probe exerted slight external compression until an ideal pressure was achieved, as indicated by the presence of a green color on the indicator bar in the upper left corner of the screen. The elastogram was displayed as a color scale over the grayscale image of the US. The color scale varied from red, which indicated components with the greatest elastic strain (softest which components), to blue. indicated without strain components (hardest components). Two SR were measured for each nodule by placing a selected ROI within the reference tissue and another ROI on the thyroid nodule as follows:

1. The parenchymal-nodular strain ratio (PNSR) measures the strain between the thyroid nodule and the surrounding normal thyroid tissue.

2. Muscle-nodular strain ratio (MNSR): the strain of the thyroid nodule with the second reference tissue the SCM muscle.

The average value for each selected nodule was calculated (at least three measurements were recorded), and the average was used to calculate the result.

Statistical analysis

The data were statistically analyzed using the Statistical Package for Social Sciences (SPSS) version 22 for Windows. Descriptive data are reported as mean \pm SD and frequencies as percentages. Chi-square and Fisher's exact tests were used for categorical variables when appropriate. The t-test was used for continuous variables. Sensitivity, specificity, accuracy, and

the cut-off value of each SR was calculated. In all statistical analyses, a P-value of < 0.05 was considered statistically significant.

Results

The histopathological distribution of the benign and malignant thyroid nodules according to age and gender: The results of showed this study that the final histopathological diagnosis of thyroid nodules was 24 (72.7%) benign and 9 (27.3%) malignant. The patient's age was ranging from (18 - 68) years, with mean \pm SD =43.4 \pm 10.7 years. In benign nodules, patients' ages ranged to 68 years., with mean \pm from 18 SD=41.29±12.89 years, whereas in malignant cases, the age ranged from 32 to 60 years, mean \pm SD= 44 \pm 8.32 years, with non-statistically significant result; P-value 0.88. The majority of patients with thyroid nodules were females 26 [78.8%], and most of the females had benign thyroid nodules 21 [87.5%]. However, the result was not significant. This is demonstrated in Table 1.

Table 1. Demographical characteristics of the studied sample distributed by the type of the thyroid nodules.

Parameters	Benign n=24	Malignant n=9	P-value			
Gender, n (%) Female Male	3(12.5) 21(87.5)	4 (44.4) 5(55.6)	0.68			
Age Mean ± SD Min Max	41.2±12.8 18 68	44±8.32 32 60	0.8			
*The result was non-significant at P- value < 0.05						

The sonographic characteristic of the thyroid nodules.

Echogenicity: The majority of the thyroid nodules were isoechoic 21(63.6%), 10 (30.3%)

and were hypoechoic, 2 (6.1%)were hyperechoic. Most of the benign thyroid nodules were isoechoic 18 (75%), and 4 (16.7%) of them were hypoechoic. While the malignant thyroid nodules, 6 (66.7%) of them were hypoechoic and 3 (33.3%) of them were isoechoic. The result was statistically significant P-value 0.019, as demonstrated in Table 2.

Composition: Most of the thyroid nodules were solid 26 (78.8%), most of the benign thyroid nodules were solid 19 (79.2%), and 5 [20.8%] of them were mixed. Most of the malignant thyroid nodules were solid 7 (77.8%), and only 2 (22.2%) of them were mixed. However, the result was not significant. This is demonstrated in Table 2.

Margin: Most of the thyroid nodules had welldefined margins 29 (87.9%). 23 (95.8%) of the benign thyroid nodule had well-defined margin. 6 (66.7%) of the malignant thyroid nodules had well defined margin. One third of the malignant thyroid nodules had ill- defined margin with significant result P- value = 0.047. These findings were demonstrated in Table 2.

Orientation: Most thyroid nodules were wider than taller 31 (93.9%). All the benign nodules were wider than taller 24 (100%). According to the study, most malignant nodules were wider than taller, and on the other hand, all nodules that were taller than wide (22.2%) had significant outcomes and were malignant. These findings were demonstrated in Table 2.

Calcification: 11 (45.8%) of the benign nodules showed no calcification, and 10 (41.7%) had macrocalcification. In the present study, most of the malignant nodules (8 from 9 cases =88.9%) had calcification. Microcalcification was most frequently encountered which is present in 5 cases (55.6%), while macro calcification is present in (3 from 9 cases=33.35). These findings were demonstrated in Table 2.

The TIRADS of selected thyroid nodules in relation to histopathological results: 12 of the benign thyroid nodules were TIRADS III, and 12 cases were of TIRADS IV.

All malignant nodules were of TIRADS IV with significant result, P-value < 0.05. These findings were demonstrated in Table 2.

Table 2. the association of the sonographic characteristic of the thyroid nodules with histopathological type of the nodules.

	Benign		Mali	P-value				
Parameters	No.	%	No.	%				
Echogenicity								
Hyperechoic	2	8.34	0	0				
Isoechoic	18	75	3	33.3	0.019*			
Hypoechoic	4	16.7	6	66.7				
Composition								
Solid	19	7.2	7	77.8	0.63			
mixed	5	20.8	2	22.2				
Margin								
Well-defined margin	23	95.8	6	66.7	0.047*			
Ill-defined margin	1	4.2	3	33.3				
Orientation								
Wider than taller [oval]	24	100	7	77.8	0.017*			
Taller than wider [oval]	0		2	22.2				
Calcifications								
No calcification	11	45.8	1	11.1	0.02*			
Microcalcification	3	12.5	5	55.6	0.02**			
Macrocalcification	10	41.7	3	33.3				
TIRADS								
TIRADS III	12	50	0	0	0.012*			
TIRADS IV	12	50	9	100				
*The result was significant at	*The result was significant at P-value <0.05, TIRADS: Thyroid Imaging Reporting and Data System							

The association of the histopathological type of thyroid nodules with their PNSR and MNSR: The PNSR of all thyroid nodules were ranging from (0.55-6.0) with mean \pm SD of 2.95 \pm 1.5. The mean \pm SD of benign nodules were 2.26 \pm 0.95, ranging from 0.55 to 4.33, while the mean \pm SD of malignant nodules were 4.87 \pm 1.11 ranging from (6-3.16). The MNSR of all thyroid nodules were ranging from (0.42-5.25) with mean \pm SD of 2.44 \pm 1.28. The mean \pm SD of benign nodules were 1.81 \pm 0.75, ranging from 0.42 to 3.13, while the mean \pm SD of malignant

nodules were 4.1 ± 0.8 ranging from 2.45-5.25 with significant P-value for both SR, as shown in Table 3.

Table 3	S. SR	ratios	of	thyroid	nodules	for	benign	and
maligna	nt les	ions ar	nor	ng the pa	tients.			

Par	ameter	N	Mean	SD	Min	Max	P- value
	Benign	24	2.26	0.95	0.55	4.33	
PNSR	Malignant	9	4.78	1.11	3.16	6.0	<0.001 *
	Benign	24	1.81	0.75	0.42	3.13	0.004
MNSR	Malignant	9	4.1	0.8	2.45	5.25	<0.001 *



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The cutoff value for PNSR and MNSR to differentiate between benign and malignant Nodule: The best strain ratio Cutoff value derived from analysis was (\geq 3.63) for PNSR (higher values were more indicative of malignant thyroid nodules, whereas values below this cut-off value, suggestive of benign nodule). The strain ratios of PNSR and MNS were represented by the ROC Curve in Figure 1.



Figure 1. The Strain ratio at ROC curve.

The best cut off value for parenchyma-nodule strain ratio is 3.63 with highest sensitivity, specificity and accuracy of 100%, 85.3% and 89.2% respectively, this indicates that all cases with pathological findings were accurately detected when the strain ratio exceeded 3.63. and suggests that 85.3% of non-pathological nodules were correctly classified as benign using this cutoff value. as seen in Table 4.

Table 4. PNSR Cutoff value to differentiate between benign and malignant thyroid nodules among the patients.

PNS	AU	AU P-value	Accura	Asymptotic 95% Confidence Interval		
R	С		су	Lower Bound	Upper Bound	
	0.9 46	<0.001 *	89.2%	0.874	1.000	
Po	sitive if			Sensitivity	Specifici ty	
	<u>≥</u> 2.88			100.0	82.7	
101	≥3.63			100.0	85.3	
≥3.73			98.8	87.5		
≥4.08			77.8	94.3		
≥ 4.50			66.7	100.0		

The best cutoff value for muscle –nodule strain ratio is 3.20 with highest sensitivity, specificity and accuracy of 100%, 91.1% and 93.3% respectively. This indicates that at MNSR \geq 3.20 all pathological nodules were accurately detected as malignant and 91.1% of nonpathological nodules were correctly classified as benign at this cutoff, as demonstrated in Table 5.

Table 5. MNSR Cutoff value to differentiate betweenbenign and malignant thyroid nodules among thepatients.

	AU C	P- value	Accurac	Asyn Confid	nptotic 95% lence Interval
	, v	, unue	,	Lower Bound	Upper Bound
MN SR	0.976	<0.00 1*	93.3%	0.927	1.000
	Positive if				Specificity
		≥2.8	100	83.3	
		≥3.20	100 .0	91.1	
		≥3.53	77. 8	100	
		≥4.09	66. 8	100	



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Discussion

In this study, there was no significant link between patient's age or gender and histological diagnosis. US examination can detect these nodules with irregular margins, microcalcification. and hypo echogenicity indicating biopsy these criteria may correlate with thyroid malignancy (27). FNA is necessary for distinguishing benign from malignant nodules, but it's invasive and may cause sampling errors. Approximately 15-20% of thyroid nodules yield non-diagnostic cytology or inadequate sampling (28), making it crucial to determine which nodules require follow-up and which necessitate re-aspiration.

Ultrasound elastography is a non-invasive technique used to differentiate benign and malignant thyroid nodules (29). However, it has limitations when there's no normal surrounding thyroid tissue, like multinodular goiter or Hashimoto's thyroiditis (29). A new reference tissue, SCM muscle, has been developed. There was no significant link between patient's age or gender and histological diagnosis, which is similar with other studies (30,32).

echogenicity, In terms of the current investigation found a statistically significant link between the echogenicity of thyroid nodules on US and histological diagnosis. This is consistent with recent research (33,34), which found a substantial association between the echogenicity of thyroid nodules and the prediction of malignancy. Furthermore. current study discovered a substantial relationship between the border of thyroid nodules and histological diagnosis, consistent with previous research (30,35) indicating that ill-defined or irregular predict malignancy. margins significantly Additionally, the orientation of thyroid nodules was found to have a highly significant correlation with malignancy prediction (35, 33). Moreover, the study found a significant

correlation between microcalcification and malignancy prediction, but these features alone are not accurate (36). The study also found a significant correlation between TIRADS (III and IV) and the distinction between benign and malignant thyroid nodules. Also, the study reveals a significant difference in the stiffness of benign and malignant thyroid nodules using US elastography for both PNSR and MNSR with P-value <0.001, similar to results documented in previous studies (30.37)revealing more rigidity in malignant nodules than in normal ones. Moreover, the study indicated that the best cut-off value for predicting malignant nodules is ≥ 3.63 , with 100% sensitivity, 85% specificity, and 89.2% accuracy, respectively. Previous studies have used the normal thyroid parenchyma's SR as a reference for discriminating between benign and malignant thyroid nodules, with a wide range of optimal cut-off values, from SR 1.1 in Rago et al. study [86% sensitivity and 90% specificity] to SR 4.2 in Ning et al. study with a sensitivity of 81.8% (22)

Additionally, the study indicated that the muscle-nodule strain ratio elastography (MNSR) for predicting malignant nodules was \geq 3.2, with a 100% sensitivity, 91.1 specificity, and 93.3% accuracy rate, respectively. This is higher than previous studies (30,38) which set **MNSRs** of over1.85 with sensitivity, specificity, and accuracy of 95.6%, 92.8%, and 93.4%, and above 2.31 for malignant thyroid nodules (39) Görgülü's (37) study set the highest MNSR cutoff value (>5.75), with the highest sensitivity and specificity (100% and 96.3%). The muscle-nodule SR was also variable compared to other studies. The variability in the cutoff value of SR (PNSR and MNSR) between previous studies and the current study can be attributed to differences in sampling criteria, examination techniques due to different machines and operators, and a lack



uniformity in procedures, such of as compression forces applied by operators. The current study found a statistically significant similarity between PNSR and MNSR in differentiation between benign and malignant thyroid nodules (p-value <0.001 for both) with better sensitivity, specificity, and accuracy rate of MNSR in comparison with PNSR. This result was concomitant with Görgülü study (37). Another study done by Aydin et al (30) shows no significant difference between PNSR and MNSR in the form of sensitivity, specificity, and accuracy rate in the prediction of malignant thyroid nodules, the sensitivity, specificity, and accuracy rate were 95.6%, 93.4%, and 94.3% respectively for PNSR and for MNSR, the sensitivity, specificity, and accuracy rate were 95.6%, 92.8%, 93.4% respectively with p-value < 0.001. This could be related to subtle inflammation of the thyroid parenchyma, which may be missed by the radiologist.

Conclusions

The study found that USE has high diagnostic accuracy in distinguishing benign from malignant thyroid nodules, while SCM muscle has high sensitivity, specificity, and accuracy in predicting nodular thyroid malignancy. MNSR had a better cutoff value of 3.2 compared to PNSR's 3.63 in the differentiation of

benign and malignant thyroid nodules, suggesting it could be used safely in cases where PNSR has limitations.

Recommendations

The study advocates for the use of elastography and Gray-scale US for assessing thyroid nodules and suggests using sternocleidomastoid muscle as a reference point in addition to normal thyroid parenchyma for better strain ratio measurement.

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Conflict of interest: None.

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مقارنة نسبة اجهاد انعضلات إلى العقيدات مع نسبة اجهاد نسيج الغذة الدرقية إلى العقيدات باستخدام فحص مرونة االنسجة بجهاز الموجات فوق الصوتية في عقيدات الغدة الدرقية المشبوهة

ا زينب فيصل عطية ، ٢ محمد محمد جواد

الملخص

الخلفية: ان التصوير بالموجات فةق الصوتية هة تقنية غير جراحية تم تطوير ها حديثا، وهي مفيدة في تمييز العقيدات الحميدة من عقيدات الغدة الدرقية الخبيثة. وقد أظهر قياس تصلب الغدة الدرقية بواسطة نسبة االجهاد نتائج واعدة. ومع ذلك توجد قيود كبيرة على نسبة االجهاد عندما يكون هناك نقص في أنسجة الغدة الدرقية الطبيعية المحيطة.

الأهداف: كان الهدف من الدراسة هو تقييم األداء التشخيصي في التنبؤ بالعقيدات الدرقية من خلا تقييم نسبة الأجهاد باستخدام انسجة الغدة الدرقية الطبيعية والعضلة القصية الترقوية الخائية كمراجع.

المرضى والطرق: أجريت دراسة استباقية على 33 مريضا مختارا من ذوي العقيدات الوحيدة من الثالث أو الرابع الذين حضروا وحدة الموجات فوق الصوتية في مدينة الامامين الكاظمين الطبية في بغداد – العراق في الفترة من 25 آب / أغسطس 2020 ألى 15 كانون الثاني /يناير 2021. تم فحص جميع المرضى بمقياس رمادي واستخدم الوقت الحقيقي بواسطة جهاز الموجات فوق الصوتية. Volution-E6 وقد تم الحصول على التشخيصات النهائية عن طريق علم الخلايا و/أو علم النتسج.

الاستنتاج :أظهرت العضلة القصية الترقوية الخشائية حساسية عالية وخصوصية ودقة في التنبؤ بأورام الغدة الدرقية. كان هناك تشابه بين نسبة أجهاد العقدي المتني و نسبة الجهاد العضلي الغدي في الدقة التشخيصية التمييز بين عقيدات الغدة الدرقية الحميدة والخبيثة. لذلك يمكن استخدام نسبة الاجهاد العضلي العقدي بأمان في الحالات التي يوجد فيها قيود على قياس الجهاد المتني العقدي

الكلمات المفتاحية: فحص مرونة االنسجة, عقيدات الغدة الدرقية, نسبة االجهاد.

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