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ORIGINAL ARTICLE

Role of Ultrasound Elastography in Evaluating Suspicious Thyroid Nodules

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Abstract

Ultrasound elastography is a promising new technique in the evaluation of the thyroid nodule. It allows for "virtual palpation" of the nodule, even smaller ones which may not be otherwise palpable clinically. Ultrasound elastography was developed to obtain information on tissue stiffness non-invasively. Due to the superficial location of the thyroid gland, lack of sonological interferences like bowel gas shadow, easy availability of USG, and no need for patient preparation, it is easy and feasible to obtain information regarding the stiffness in the organ or nodule objectively, even by beginners. Elastography is a technique that uses ultrasound to analyse the elasticity of a nodule by measuring the amount of distortion that occurs when the nodule is subjected to external pressure. Shear wave elastography (SWE) provides quantitative assessment in the form of elasticity indices ($E_{maximum}$, E_{mean}, $E_{minimum}$), and the stiffness of thyroid nodules can be evaluated with shear wave elastography. Malignant thyroid nodules tend to have higher shear wave elastography index. This was a prospective study. All patients with suspicious thyroid nodules who presented to head and neck oncology OPD with thyroid swelling with TIRADS score 3 or 4 and Bethesda III/IV were evaluated from December 2022 to February 2023. All the patients were screened with ultrasound, and reporting was done as per the ACR TIRADS reporting system following which elastography score was given based on the stiffness of the nodule. They further underwent FNAC from the suspicious thyroid nodule. Thyroidectomy was done as per department protocol. Twenty-four patients (38 nodules) were evaluated. There were seven males and 17 female patients included in the study. There were 23 malignant nodules in the final histopathology of the resected specimen. The sensitivity of TIRADS was 82.6%, specificity was 80%, for elastography specificity was 69.6%, sensitivity was 60%, for BETHESDA specificity was 66.7%, and sensitivity was 81.3%. The combined sensitivity and specificity for all three modalities combined were 93.33% and 95.6%. Receiver operator curve (ROC) analysis showed the area under the curve for USG TIRADS was 0.895, for elastography was 0.879, and for FNAC Bethesda was 0.902. AUC for combined tests ES + BETHESD was 0.800 ($p = 0.013$), TIRADS + BETHESDA was 0.833($p < .01$), and for TIRADS + ES + BETHSDA AUC was 0.967 ($p = 0.00$). Ultrasound elastography can be used as an adjunctive tool along with routine grey scale ultrasound for characterising suspicious thyroid nodules.

Keywords Elastography · Ultrasound · TIRADS · Thyroid · Bethesda cytology

Introduction

In general population, the prevalence of thyroid nodules is reported between 19 and 68%. Thyroid nodules with indeterminate characteristics pose a significant dilemma for the decision-making regarding the management [1]. The incidence of malignancy in indeterminate nodules ranges from 7 to 15% [2]. The risk of malignancy for TR3 nodule is 4.8% and for TR 4 is 9.1% [3]. There is no definite consensus on the management of indeterminate nodules, and various recommendations are available regarding the further imaging and invasive testing of such nodules.

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Ultrasound elastography is a non-invasive procedure that evaluates the degree of distortion of a tissue under application of an external force. It is based on the principle that the softer parts of tissues deform easier than the harder parts under compression, thus allowing an objective determination of tissue stiffness [4, 5]. Ultrasound elastography has proven valuable in discriminating benign from malignant thyroid nodules [6].

Shear wave elastography (SWE) is less operator-dependent and more reproducible than SE, and it provides quantitative assessment in the form of elasticity indices ($E_{maximum}$, E_{mean}, $E_{minimum}$). SWE uses focused ultrasound impulses at varying depths in tissue to induce tissue displacement and results in the generation of shear waves which propagate laterally. By evaluating the speed of shear waves in the tissue, the tissue stiffness can be determined. Malignant thyroid nodules have higher stiffness as compared to benign nodules so elastography can help in preoperative evaluation and diagnosis [7].

The aim of this study was to evaluate the efficacy of ultrasound elastography (USE) in characterising suspicious thyroid nodules and to correlate the USE findings with FNAC and final histopathology in patients undergoing thyroidectomy in a high-volume cancer centre.

Materials and Methods

This was a prospective study. All patients with suspicious thyroid nodules who presented to head and neck oncology OPD with thyroid swelling were evaluated from December 2022 to February 2023. All the patients were screened with ultrasound, and patients with TIRADS score 3 or 4 and Bethesda III/IV were included in the study for further evaluation. The ultrasound reporting was done by single senior radiologist as per the ACR TIRADS reporting system into TR1—benign, TR 2—not suspicious, TR3—mildy suspicious, TR4—moderately suspicious, and TR 5—highly suspicious. Real-time shear wave elastography was done following grey scale ultrasonography, and nodule stiffness was calculated in terms of kilopascals (kPA) and elastography ratio. Further guided fine-needle aspiration biopsy was done from the suspicious thyroid nodule, and the nodules were reported as per the Bethesda reporting system TSBRTC 2022 into six categories: I—nondiagnostic or unsatisfactory; II—benign; III—atypia of undetermined significance or follicular lesion of undetermined significance; IV—follicular neoplasm or suspicious for follicular neoplasm; V—suspicious for malignancy; VI—malignant. BSRTC V or VI nodules were diagnosed as suspicious for malignancy or malignant lesions, and nodules of level III or less were benign. Thyroidectomy was done as per department protocol.

Table 1 Elastography stiffness values

	E.MIN	E.MAX	E. MEAN	ER1	ER2
Mean	47.1	70.6	65.5	1.614	1.585
Median	27	40.8	33	1.60	1.50
Std. deviation	37.56	66.41	54.44	0.69864	0.96855
Range	90.70	183.90	136.70	2.30	3.10

Table 2 Accuracy of different modalities for III/IV category nodules

Category	Accuracy	
	III	IV
TIRADS + ES	69.2	73.68
TIRADS + BETHESDA	73.33	76.22
TIRADS + ES + BETHESDA	81.3	97.33

Statistical Analysis

The data was analysed using SPSS v29.0. The categorical variables like benign and malignant nodules were analysed using the chi-square test or Fisher's exact probability method. The diagnostic effects of USG TIRADS, ES, BSRTC, and the combinations USG TIRADS + ES, USG TIRADS + BSRTC, ES + BSRTC, and USG TIRADS + ES + BSRTC were analysed using the McNemar chi-square test. Receiver operating characteristic (ROC) curves were constructed, and the areas under the curve (AUCs) were calculated. The 95% confidence interval of the area under the curve was evaluated. The sensitivity and specificity were calculated by comparison with pathologic results. A p value < 0.05 was considered significant.

Results

A total of 38 nodules (24 patients) were evaluated. Seven male and 17 female patients were included in the study. There were 23 malignant nodules in the final histopathology of the resected specimen. The stiffness of the nodules was expressed in terms of kPA. The cutoff values for elasticity ratio calculated as thyroid nodule/thyroid parenchyma, E mean (kPa), for predicting malignant thyroid nodules were greater than or equal to 2.3, 65.53 kPA, respectively (Table 1).

The diagnostic accuracy of TIRADS + ES was 69.2% for III and 73.68% for IV nodules. Combined diagnostic accuracy was 81.3% for III and 97.3% for IV nodules (Table 2; Fig. 1).

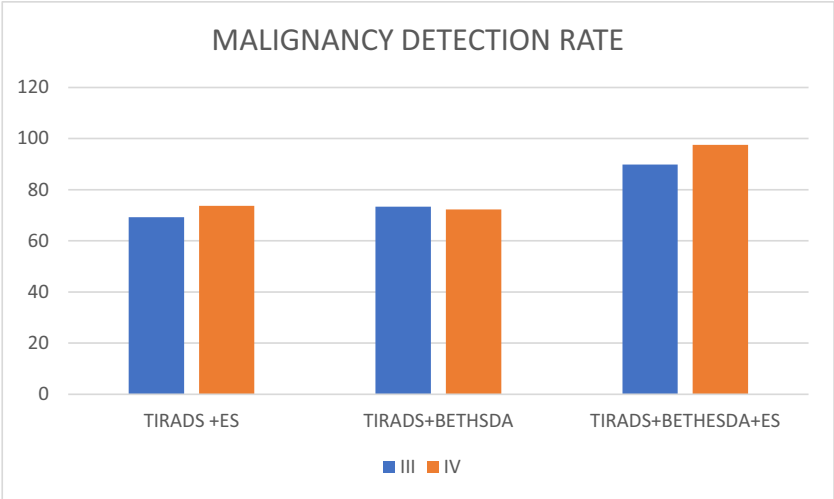

Fig. 1 Malignancy detection rates of different modalities

Table 3 Sensitivity and specificity of different modalities

Test	Specificity		*P* value
ACR TIRADS	80	82.6	0.01
ES	69.6	60	0.01
FNAC (BETHESDA)	66.67	81.3	0.01
ES+BETHSDA	60	78	<0.01
ACR TIRADS+BETHESDA	66.67	78.3	<0.01
ES+TIRADS	93.2	91	<0.01
TIRADS+ES+BETHESDA	93.333	95.6	<0.01

The sensitivity of ACR TIRADS was 82.6%, specificity was 80%, for elastography specificity was 69.6%, sensitivity was 60%, and for BETHESDA specificity was 66.7% and sensitivity was 81.3%. The combined sensitivity and specificity for all three modalities combined were 93.33% and 95.6% (Table 3).

On analysing the receiver operator curve (ROC), the area under the curve for USG ACR TIRADS was 0.895, for elastography was 0.879, and for FNAC Bethesda was 0.902. The area under the curve for combined modality was 0.967 (Table 4; Fig. 2).

The area under the curve (AUC) for elastography was 0.879, for USG was 0.895, and for FNAC Bethesda was 0.902. AUC for combined tests ES + BETHESDA was 0.800 ($p = 0.013$), ACR TIRADS + BETHESDA was 0.833 ($p < 0.01$), and for ACR TIRADS + ES + BETHSDA AUC was 0.967 ($p = 0.00$) (Table 5; Fig. 3).

Discussion

Ultrasonography is a widely used diagnostic tool for early diagnosis and screening. Thyroid nodules can be characterised into specific categories based on the sonographic features. However, there is significant inter observer variability in diagnosing the nodules based on the ultrasound characteristics. Intermediate nodules have 10–20% risk of malignancy [8]. Thus, American Thyroid Association (ATA 2015) recommends USE whenever available for preoperative risk assessment as a complementary tool with ultrasound [8].

Ultrasound elastography has been evaluated as a novel technique for evaluation of thyroid nodules. It measures the stiffness of the nodules by analysing the distortion in the nodule caused by applying external pressure [9].

In comparison to the normal thyroid parenchyma, most malignant thyroid nodules have firm stroma due to the presence of excessive collagen, excessive myofibroblast, and desmoplastic transformation; hence, resisting tissue strain upon stress malignant thyroid nodules are stiffer than benign nodules on SWE [7].

Among the available literature, the highest cut-off values of SWE indices for evaluating thyroid

Table 4 Area under the ROC for individual modalities

Test	Area	Std. error	Asymptotic Sig.b	Asymptotic 95%confidence interval	
				Lower bound	Upper bound
USG ACR TIRADS	.895	.053	.000	.791	.999
ELASTOGRAHPHY	.879	.059	.000	.762	.995
FNAC BETHESDA	.902	.042	.000	.819	.984

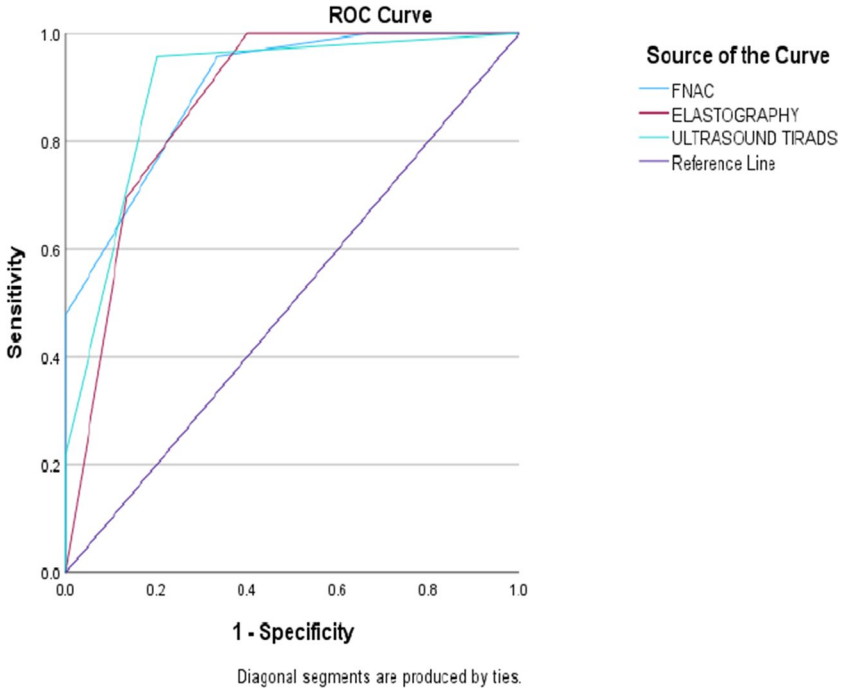

Fig. 2 ROC curve for FNAC, US, and USE

Table 5 Area under the ROC for combined modalities

Test	AUC	SE	Asymptotic Sig.b	Asymptotic 95% confidence interval	
				Lower bound	Upper bound
ES + BETHESDA	0.800	0.089	0.013	0.626	0.974
ACR TIRADS + BETHESDA	0.833	0.082	0.006	0.672	0.995
ACR TIRADS + ES + BETHESDA	0.967	0.039	0.000	0.890	1.000

malignancy were ≥ 95 kPa for $E_{maximum}$, ≥ 85.2 kPa for E_{mean}, and ≥ 54.2 kPa for $E_{minimum}$ [7].

In our study, the elastography value of E min was 47.1 kPa, E max was 70.6 kPa, and E mean was 65.6 kPa which is comparable to the available data for SWE indices to differentiate malignant and benign nodules.

In our study, the combined diagnostic accuracy of ACR TIRADS + ES for TIRADS CATEGORY III and IV nodules was 69.2 and 73.68%, ACR TIRADS + BETHESDA was 73.33and 76.22%, and all three modalities combined was 97.3%. The reasons attributed for the values for lower values of elastography and ACR TIRADS may be due to background thyroiditis present in the thyroid gland that may have masked the thyroid nodules in elastography resulting in comparatively lower scores; however, the definite effect of background thyroiditis on nodule elastography needs to be further evaluated.

Huang et al. [10] in their study reported the specificity of the strain wave ES for TI-RADS category 4 thyroid nodules (95.6%) which was comparable with other studies as per table, but the sensitivity was quite low (67.8%), Wang et al. [11] reported accuracy of USE of 90.2%, and Rubatelli et al. [12] reported specificity of 86.2%.

Lin et al. [15] reported sensitivity of 84.3% and specificity of 88.4% for shear wave elastography. Similarly, Xingdong Hu et al. [13] studied diagnostic potential shear wave elastography and found the sensitivity of 79% and specificity of 87%.

In our data, the area under the curve (AUC) for elastography was 0.879, for USG was 0.895, and 0.902 for Bethesda. AUC for combined tests ES + BETHESDA was 0.800 ($p = 0.013$), TIRADS + BETHESDA was 0.833($p < 0.01$), and for TIRADS + ES + BETHSDA area under the curve was 0.967 ($p = 0.00$), which was statistically significant for $p < 0.01$. Huang et al. reported area under the curve (AUC) for elastography as 0.847, KWAK TIRADS as 0.787, and Bethesda as 0.918. AUC for combined tests ES + BETHESDA was 0.913 ($p = 0.00$); for TIRADS + BETHESDA, it was 0.948 ($p = 0.012$); and for KWAK TIRADS + ES + BETHSDA, AUC was 0.967 ($p = 0.008$). [10].

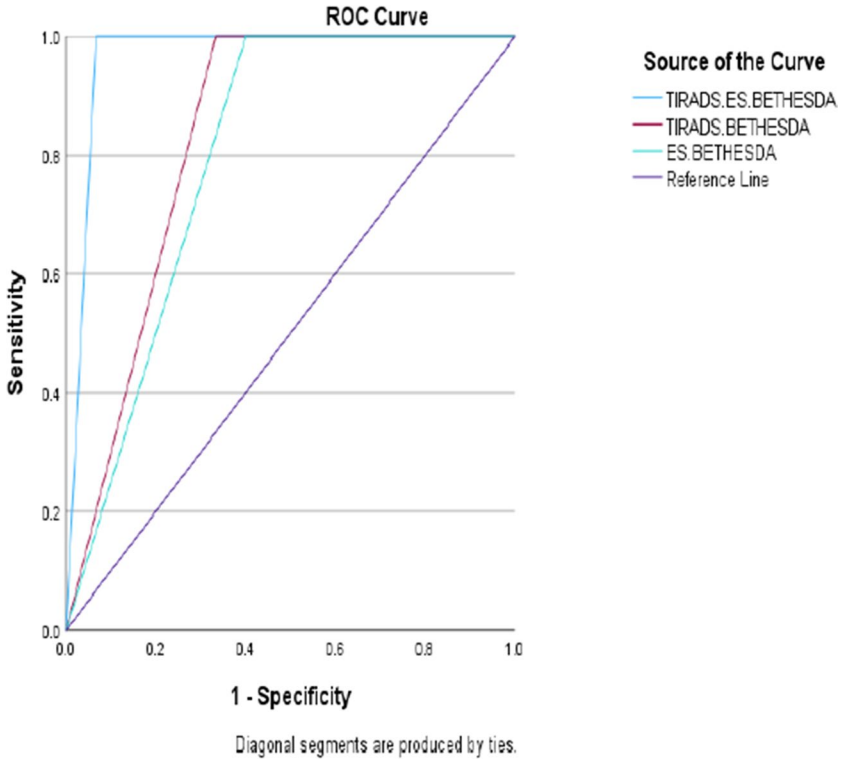

Fig. 3 Area under the ROC curve for combined modalities

Prajapati et al. in their study reported that the elasticity scores of 4–5 were highly predictive of malignancy with a sensitivity of 97.6%, a specificity of 66.6%, a positive predictive value of 88.8%, and a negative predictive value of 97.6% [6]. In our study, the diagnostic power of elastography was assessed quantitatively. The sensitivity USG TIRADS + FNAC BETHESDA + ELASTOGRAPGHY was 95.6%, specificity was 93.33%, accuracy was 97.3%, NPV was 95.7%, and PPV was 69.8%.

Our results show that combining the USG TIRADS, ES, and BSRTC can effectively improve the diagnostic accuracy of suspicious thyroid nodules. Therefore, non-invasive examination combined with invasive examination in form of fine-needle aspiration for the management of suspicious malignant nodules can avoid more expensive molecular tests.

Another role of elastography can be explored in active surveillance of the suspicious thyroid nodules to provide a more conservative approach of active surveillance management compared to invasive tools like fine-needle aspiration cytology. It can be used in selected patients with very low risk tumours like papillary microcarcinomas, patients with high surgical risk, and those with relatively shorter life expectancy in whom benefits of intervention may be unrealised. However, more concrete data needs to be seen for further role of elastography.

In 2013, European Federation of Societies [15] for Ultrasound in Medicine and Biology (EFSUMB) guidelines recommended US elastography as an additional too for thyroid lesion differentiation and a useful guide for following up lesions diagnosed as benign at FNA.

Our study has few limitations, one major limitation being the small sample size and single-centre data. Also, elastography is an operator-dependant tool that requires special skill and expertise for performing the test as well as interpreting the results. Perhaps a larger patient population, randomised study design and experience of other centres will give a better perspective.

Conclusion

Thyroid elastography can be used as an adjunctive tool along with routine ultrasound scan to increase the sensitivity and specificity for detecting suspicious thyroid nodules. The diagnostic potential of ultrasound elastography can be utilised as a "rule in" test for indeterminate lesions to exclude benign pathology, which may further help in decision-making for extent of surgery.

Declarations

Conflict of Interest The authors declare no competing interests.

Institutional Ethics Committee Clearance Granted with Human Ethics Committee number 72/22.

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