

Role of Elastography In Differentiating Malignant and Benign Thyroid Nodules Using Fine Needle Aspiration Cytology (Fnac) As Gold Standard

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ABSTRACT

Objective: to determine the efficacy of elastography in differentiation of malignant and benign thyroid nodules using fine needle aspiration cytology (FNAC) as gold standard.

Study Design: Analytical cross-sectional study.

Place and Duration of Study: Department of Radiology, Combined Military Hospital (CMH), Rawalakot, Pakistan, from Oct 2022 to Mar 2023.

Methodology: A total of 150 patients having one or more solid thyroid nodules diagnosed on conventional ultrasound were enrolled in the study. After obtaining informed consent, all patients underwent strain elastography under standard protocol and findings of strain elastography were compared with cytological findings.

Results: There were 69(85.2%) patients who had malignant lesions on elastography as well as FNAC positive (true positive) while 59(85.5%) patients had non-malignant lesion on elastography as well as negative FNAC (true negative). The sensitivity and specificity was 85.2% and 85.5%, respectively. Positive and negative predictive values were 87.3% and 83.1%, respectively while overall accuracy was 85.3%.

Conclusion: Elastography or strain elastography have high efficacy to differentiate malignant thyroid nodules and benign thyroid nodules and can be used in replacement of fine needle aspiration cytology (FNAC).

Keywords: Elastography, Fine-Needle, Thyroid Nodule, Ultrasonography

How to Cite This Article: Hussain R, Ashraf M, Pervaiz S. Role of Elastography In Differentiating Malignant and Benign Thyroid Nodules Using Fine Needle Aspiration Cytology (Fnac) As Gold Standard. Pak Armed Forces Med J 2025; 75(5): 969-972. DOI: <https://doi.org/10.51253/pafmj.v75i4.10893>

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INTRODUCTION

Nodular thyroid disease is a common endocrine disorder.¹ which refers to the presence of nodules or abnormal growths in the thyroid gland.² The prevalence of nodular thyroid disease is influenced by geographical location, iodine deficiency, and exposure to goitrogens.³ In the case of South Asian populations, including Pakistan, iodine deficiency and the use of goitrogens contribute to the higher prevalence of thyroid diseases.⁴ Ultrasonography (USG) is commonly used to detect thyroid nodules, but it may not be sufficient to differentiate between benign and malignant nodules.⁵ Fine Needle Aspiration Cytology (FNAC) is performed on suspicious nodules to obtain cells for analysis⁶ with a specificity range of 60-98% and a sensitivity range of 54-90%. However, FNAC has limitations, as around 10-15% of aspirates may be non-diagnostic.⁷ Ultrasound elastography, also known as sonoelastography, is an imaging technique that provides information about the stiffness or hardness of tissues.⁸ It is considered a useful adjunctive tool to

conventional ultrasound (USG) in assessing thyroid lesions and improving diagnostic accuracy. This technique can help differentiate between benign and malignant thyroid nodules.⁹ The primary advantage of ultrasound elastography is that it provides additional information without the need for an invasive procedure like biopsy. FNAC can be cumbersome for patients and can pose a financial burden on both patients and healthcare systems, especially in countries with limited resources.¹⁰

METHODOLOGY

This analytical cross-sectional study was started after gaining approval from Hospital Ethics board (IERB No. 1319). It was conducted at Department of Radiology, Combined Military Hospital (CMH), Rawalakot, Pakistan, from October 2022 to March 2023. Non-probability consecutive sampling technique was used for sample collection. Informed, written consent was also obtained from all patients after ensuring confidentiality.

Inclusion Criteria: Patients of between the age of 18-80 years, of either gender, having one or more solid nodules in a thyroid lobe (as determined by conventional ultrasound examination) were included.

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Received: 14 Sep 2023; revision received: 06 Jan 2024; accepted: 08 Jan 2024

Exclusion Criteria: Patients with nodules which were purely cystic without any solid component, occupied more than 75% of the volume of the thyroid lobe, lack of sufficient surrounding thyroid tissue for reference comparison during sonoelastography and strain ratio analysis or thyroid nodules exhibiting peripheral calcification were excluded.

The ultrasound was performed in a dimly lit room with a comfortable temperature ranging from 22°C to 24°C. The patient was positioned in a supine (lying on the back) position with a hyperextended neck. Prior to the ultrasound examination, age, gender, medical record number, address, and clinical history were obtained from each patient. Grayscale USG was conducted to visualize the number, size, and location of thyroid nodules. After performing grayscale USG and identifying a region of interest (ROI) within the thyroid, sonoelastography was carried out. The study utilized a 5-pattern scoring system for thyroid elastography, assigning a numerical score or category to the elastographic patterns observed in the thyroid nodules. A data collection form was used to record the sonoelastography score and strain ratio for each thyroid nodule. FNAC report was obtained for each nodule, and this information was used to compare the findings from the sonoelastography and strain ratio measurements. Statistical Package for Social Sciences (SPSS) version 23.0 was used for data analysis, quantitative variables were presented in the form of mean $\pm$ standard deviation (SD). Proportions (frequency) were calculated for categorical value. To evaluate the performance of sonoelastography in relation to cytology, a 2 x 2 table was constructed. This table compared the results of sonoelastography (positive/negative) against the results of cytology (true positive, true negative, false positive, and false negative). Chi square test was used. The p value $\leq$ 0.05 was considered as significant.

RESULTS

Overall, 150 patients were included in this study. There were 79(52.7%) males and 71(47.3%) females. The mean age of the patients was 26.28 $\pm$ 9.13 years. Most of the patients 103(68.7%) $\leq$ 50 years of age. The mean number of nodules among patients was 2.01 $\pm$ 1.32. Most patients 97(64.7%) had $\leq$ 2 number of nodules. The mean size of nodules of the patients was 24.32 $\pm$ 8.63 mm. Most of the patients (104, 69.3%) had nodules on right side. Sonoelastography found malignant lesions in 79(52.6%) patients and Fine

Needle Aspiration Cytology (FNAC) was positive in 81(54.0%) patients. More details are listed in Table-I.

There were 69(85.2%) patients who had malignant lesions as well as FNAC positive, called true positive while 59(85.5%) patients had non-malignant lesions as well as negative FNAC, called true negative, ($p < 0.001$). The sensitivity and specificity was 85.2% and 85.5%, respectively. Positive and negative predictive values were 87.3% and 83.1%, respectively while, overall accuracy was 85.3% as shown in Table-II.

Table-I: Demographic Characteristics of Participants, (n=150)

Variable	n (%)
Sex	
Male	79(52.7%)
Female	71(47.3%)
Age (years)	
$\leq$ 50	103(68.7%)
>50	47(31.3%)
Number of nodules	
$\leq$ 2	97(64.7%)
>2	53(35.3%)
Size of nodule (mm)	
10-20	81(54.0%)
>20	69(46.0%)
Location of nodules	
Right	104(69.3%)
Left	46(30.7%)
Sonoelastography	
Malignant lesions	79(52.6%)
Non-malignant lesions	71(47.3%)
Fine needle aspiration cytology	
Positive	81(54.0%)
Negative	69(46.0%)

Table-II: Association of Fine Needle Aspiration Cytology and Sonoelastography, (n=150)

Variable	Fine needle aspiration cytology	
	Positive	Negative
Sonoelastography positive	True Positive 69(85.2%)	False positive 10(14.5%)
Sonoelastography negative	False negative 12(14.8%)	True negative 59(85.5%)

$$\text{Sensitivity} = TP / (TP + FN) = 69 / (69 + 12) * 100 = 85.2\%$$

$$\text{Specificity} = TN / (TN + FP) = 59 / (59 + 10) * 100 = 85.5\%$$

$$\text{Positive Predictive Value} = TP / (TP + FP) * 100 = 69 / (69 + 10) = 87.3\%$$

$$\text{Negative Predictive Value} = TN / (TN + FN) * 100 = 59 / (59 + 12) = 83.1\%$$

$$\text{Diagnostic Accuracy} = (TP + TN) / \text{All patients} * 100 = (69 + 59) / 150 = 85.3\%$$

DISCUSSION

Elastography can help by providing additional information about the stiffness or elasticity of the tissue as malignant thyroid nodules often exhibit increased stiffness compared to benign nodules.¹¹ This non-invasive and painless method can easily be performed during a regular ultrasound examination,

however, elastography is typically used as an adjunctive tool and should not be relied upon as the sole method for diagnosing thyroid nodules as it is usually combined with other diagnostic techniques, such as FNAC, to obtain a comprehensive evaluation of the nodule and determine the appropriate course of action.¹² In this study, sonoelastography noted malignant lesions in 52.6% patients and FNAC was positive in 54.0% patients. A study,¹³ reported diagnostic performance of sonoelastography in benign and malignant nodules identification, using cytology as the gold standard with sensitivity 90.0%, specificity: 90.0%, positive predictive value 91.53%, negative predictive value 88.24% and diagnostic accuracy 90.0%. In our study, sensitivity and specificity were 85.2% and 85.5%, respectively while positive and negative predictive value was 87.3% and 83.1%, respectively, and overall accuracy was 69.4%. One author,¹⁴ reported that a strain ratio of 2.52 can serve as a cutoff value to differentiate between malignant and benign thyroid nodules, with an area under the curve (AUC) of 0.861, with a sensitivity of 85.7%, and specificity reported as 90.5%. Another study,¹⁵ determined effectiveness of elastography in place of FNAC and reported that FNAC can be omitted safely in determination of thyroid nodules when diagnosis performed under elastography. One study,¹⁶ reported 80% sensitivity and 100% specificity ($p < 0.001$) and suggested that use of both sonography and elastosonography is more efficacious. In one study,¹⁷ strain elastography was identified as a potential tool for distinguishing between benign and malignant thyroid nodules with reported performance metrics including a sensitivity of 100%, specificity of 80.2%, positive predictive value (PPV) of 61.7%, negative predictive value (NPV) of 100%, and overall accuracy of 100%, demonstrating its efficacy in differentiating between benign and malignant nodules. While the utilization of elastography as a diagnostic technique for thyroid cancers was first reported in 2007,¹⁸ since then, numerous retrospective and prospective studies have been conducted to evaluate thyroid nodules using elastographic methods. These studies have employed various scoring systems and have compared the elastographic findings with pathology results or results from FNAC across different patient groups,^{19,20} indicating greater usage.

LIMITATIONS OF STUDY

The interpretability and external validity of our results are subject to certain limitations. The primary constraints include the modest cohort size and its derivation from a

single center. Furthermore, the enrollment process was hampered by a significant number of declinations, particularly from participants residing in remote communities, where socio-cultural and religious factors influenced the willingness to engage in the research, thereby posing a potential for selection bias.

CONCLUSION

Elastography or strain elastography has high efficacy to differentiate malignant thyroid nodules from benign thyroid nodules and can be used in replacement of FNAC.

Conflict of Interest: None.

Funding Source: None.

Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

RH & MA: Data acquisition, data analysis, critical review, approval of the final version to be published.

SP: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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