

Strain Elastography for Differentiation between Benign and Malignant Thyroid Nodules

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ABSTRACT:

Objective: To find out the diagnostic accuracy of strain elastography in differentiating between benign and malignant thyroid nodules taking cytology as a gold standard.

Study Design: Descriptive study.

Place and Duration of study: Radiology Department, Institute of Nuclear Medicine and Oncology (INMOL), Lahore, Pakistan, from February to July 2019.

Methodology: A total of 110 patients aged 18-80 years of either gender having one or more solid nodules, in thyroid lobe on conventional ultrasound examination, were included. Patients with cystic nodules, nodules that constitute more than 75% volume of thyroid lobe and thyroid nodules with peripheral calcification were excluded. All the patients then underwent strain ultrasound elastography with high-resolution unit equipped with a linear array probe which was centered at 7.5 MHz. Sonoelastographic findings were correlated with cytology.

Results: Overall sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of sonoelastography in differentiating between benign and malignant thyroid nodules taking cytology as gold standard was 90.0%, 90.0%, 91.53%, 88.24% and 90.0%, respectively. Optimal cutoff to differentiate between malignant and benign nodules for elasticity strain using ROC curve was 2.57. Area under the curve (AUC) was found to be 0.933 (0.879-0.987) $p < 0.001$.

Conclusion: Sonoelastography is the non-invasive modality of choice with high diagnostic accuracy in differentiating between malignant and benign nodules.

Key Words: Sonoelastography, Strain elastography, Thyroid nodule, Benign, Malignant, Sensitivity, Specificity.

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INTRODUCTION

Nodular thyroid disease is one of the most common endocrine disorders affecting both genders and all age groups.^{1,2} It is more prevalent in South Asian population due to iodine deficiency and use of goitrogens.^{2,3} In Pakistan, thyroid disease has become an important public health issue in areas of iodine-deficient diet. Approximately 70% of population in Pakistanis at risk of developing thyroid diseases.⁴

Ultrasonography (USG) is accurate for the detection of thyroid nodules. However the accuracy is not appreciable for benign/malignant differentiation.⁵⁻⁷ Fine needle aspiration cytology (FNAC) is used for suspicious nodules having specificity of 60-98% and a sensitivity of 54%-90%.⁷ FNAC has limitations in its ability to exclude malignancy, as up to 10-15% of FNAC aspirates are nondiagnostic and repeat biopsy is done.³

Repeat biopsy is a cumbersome procedure and is also a financial burden for patient and the healthcare system keeping in mind the country's limited resources. Ultrasound elastography (Sonoelastography) is a good adjunctive tool to conventional USG that can be used to assess the hardness of the thyroid lesions and improves the diagnostic performances.^{8,9} Globally, a lot of researches have been published on ultrasound elastography in differentiating benign from malignant thyroid nodules. However, local data is lacking and large-scale prospective studies are desirable to ascertain the role of this new technique in Pakistani population. Hence, if research finds similar diagnostic accuracy here as reported elsewhere in the world then ultrasound elastography can be used as a powerful adjunct tool in future with other ultrasound modalities for early detection of benign or malignant conditions and avoid unnecessary invasive work-up and anxiety for patients. It will also decrease the financial burden on patient and healthcare system in an already resource-limited country.

Therefore, the objective of this study was to find out the diagnostic accuracy of strain elastography in differentiation between benign and malignant thyroid nodules taking cytology as a gold standard.

METHODOLOGY

It was a descriptive study conducted at the Radiology Department, Institute of Nuclear Medicine and Oncology (INMOL), Lahore from February to July 2019. Sample size was 110 with confidence

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level of 95% along with the expected prevalence of thyroid nodules, i.e. 33% with 11% desired precision for sensitivity of 84% and 7% desired precision for specificity 84.7% of strain elastography to differentiate between benign or malignant thyroid nodules.^{3,7} Non-probability, consecutive sampling was done.

Patients aged 18-80 years of either gender having one or more solid nodules, in thyroid lobe on conventional ultrasound examination, were included. Patients with cystic nodules without any solid component were excluded from this study. Patients having nodules that constitute more than 75% volume of thyroid lobe were also excluded as sufficient thyroid tissue was not available in surroundings for reference comparison of sonoelastography and strain ratio. Thyroid nodules with peripheral calcification were also excluded, because of artifact associated with calcification interference with elastography.

After receiving approval from institutional review board, data were collected for the period of 6 months. A total 110 patients, based on above mentioned criterion, were selected. Informed consent was taken from every patient. Toshiba Aplio 500 Ultrasound Machine was used for thyroid USG and sonoelastography using 5 MHz probe. Ultrasound was done in a dim light room in a comfortable temperature (22°C-24°C), patient was in supine position with hyper extended neck. After getting basic bio-data (e.g. age, gender, medical record number, address, clinical history), Grayscale USG was done to see number, size and location of thyroid nodule. Region of interest was selected and once grayscale USG is done, sonoelastography was done in region of interest and scoring was done according to 5 pattern scoring system of thyroid elastography.

Table 1: Patient characteristics.

Variable	Frequency	Percentage (%)
Age (years):		
<50	81	73.64
>50	29	26.36
Mean \pm SD = 41.01 \pm 13.71 (14-76) years		
Gender:		
Male	39	35.45
Female	71	64.55
Number of nodules:		
≤ 2	78	70.91
>2	32	29.09
Mean \pm SD = 1.95 \pm 1.02		
Size of nodule (mm):		
10-20 mm	54	49.09
>20 mm	56	50.91
Mean \pm SD = 22.95 \pm 11.27 mm		
Location of nodules:		
Right	78	70.91
Left	32	29.09
Diagnostic accuracy of sonoelastography:		
True positive	54	91.52
False positive	05	8.47
True negative	45	88.23
False negative	06	11.76

Sonoelastographic strain ratio was also calculated. Sonoelastography score and strain ratio was noted in data collection form. Then finally FNAC was done of the thyroid nodule as a gold standard, using 22-25 gauge needles. Report of FNAC was obtained for comparison with elastography, according to operational definition. Selection bias was addressed by designing effective ques-

tionnaire, while measurement bias was addressed by using same USG machine and same operator on every patient.

All statistical analysis was done using SPSS version 20. Quantitative variables (e.g. age, number of nodules, size of nodule, sonoelastographic score, sonoelastographic strain ratio) were presented in the form of mean \pm SD. Qualitative variables (e.g. gender, location of nodule, histopathological diagnosis on FNAC) were presented in the form of frequencies and percentages. A 2 x 2 table was constructed to determine the sensitivity, specificity, PPV and NPV of sonoelastography taking cytology as gold standard. The optimal cutoff for differentiating benign nodules from malignant ones was determined using receiver operating characteristic (ROC) curve.

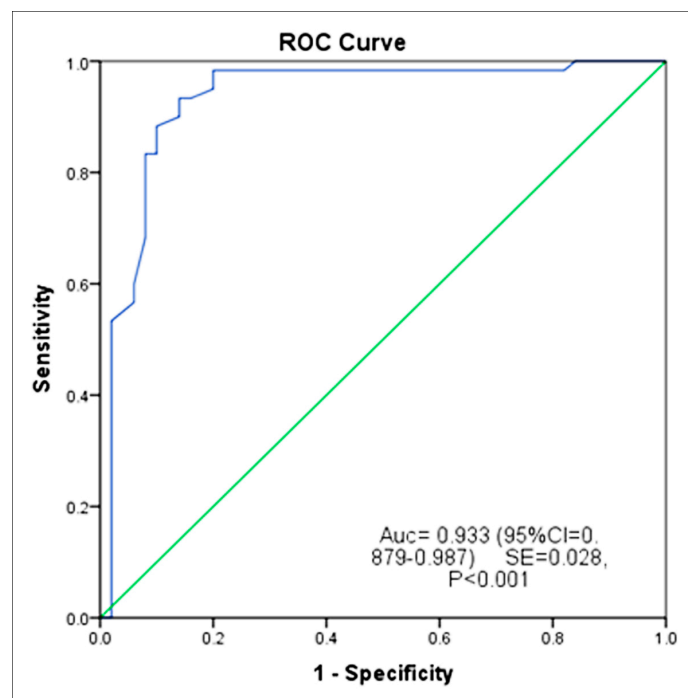


Figure 1: Receiver operating characteristic (ROC) curve describing diagnostic accuracy of sonoelastography strain ratio in differentiation of benign and malignant thyroid nodules taking cytology as gold standard providing 2.57 as optimal cutoff ratio.

RESULTS

The mean age of patients was 41.01 \pm 13.71 years ranging from 14-76 years. Majority of the patients (n=81, 73.64%) were < 50 years of age (Table 1). Out of these 110 patients, 71 (64.55%) were females and 39 (35.45%) were males. Male to female ratio was 1.8:1 (Table I).

Mean number of nodules were 1.95 \pm 1.021 (Table 1). The mean size of nodule was 22.95 \pm 11.270 mm (Table I). Distribution of patients according to location of nodules is shown in Table I.

Mean sonoelastography strain ratio for benign vs. malignant lesions was 1.60 \pm 0.79 (95% CI: 1.38-1.83) and 3.08 \pm 0.60 (95% CI: 2.93-3.24), respectively. Most appropriate cutoff for differentiating malignant and benign thyroid nodules for elasticity strain using ROC curve was 2.57. Area under the curve (AUC) was found to be 0.933 (0.879-0.987, p<0.001, Figure 1).

Sonoelastography identified malignant lesions in 59 (53.64%) subjects while benign lesions were found in 51 (46.36%) patients. Overall, 60 (54.55%) cases were FNAC positive while 50 (45.45%)

had negative findings. In sonoelastography positive patients, 54 (true positive) had malignant lesions and 05 (false positive) had benign lesions on cytology. Among the 51 sonoelastography negative patients, 06 (false negative) had malignant lesions on cytology whereas, 45 (true negative) had benign lesions on cytology (Table I).

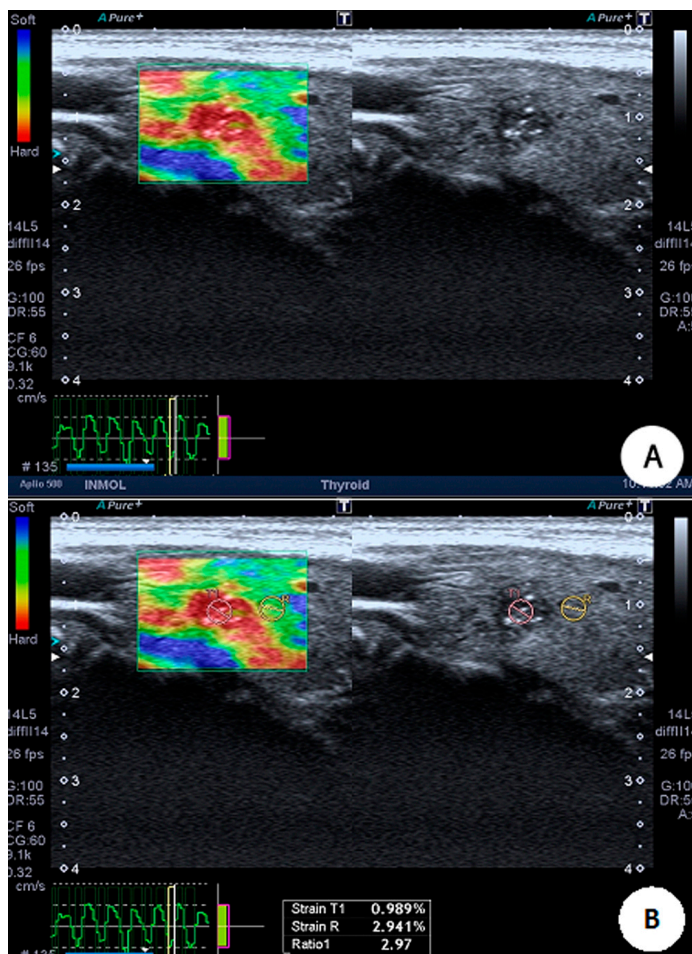


Figure 2: Sonoelastographic images in a 42-year female who underwent routine checkup. (A) An 8 mm hypoechoic nodule was noted in left lobe of thyroid with poorly defined margins and microcalcifications at gray-scale US and assessed as suspicious. On real time elastography nodule was entirely red and assigned a score of 4 according to 5 pattern scoring system of thyroid elastography. (B) Strain ratio was calculated by placing ROI in the lesion and other in surrounding tissue at the same level. Strain ratio was high (2.97) suggesting it to be malignant.

On FNAC this thyroid nodule was diagnosed as papillary thyroid carcinoma.

Overall sensitivity, specificity, positive and negative predictive value and diagnostic accuracy of sonoelastography in differentiation of benign and malignant thyroid nodules taking cytology as gold standard was 90.0%, 90.0%, 91.53%, 88.24% and 90.0%, respectively.

Sonoelastographic images of a patient with hypoechoic nodule in left lobe of thyroid is shown in Figure 2. The nodule was assessed as suspicious at grey scale US (Figure 2A) while, strain ratio of 2.97 suggested it to be malignant (Figure 2B). The cytology of nodule confirmed thyroid carcinoma.

DISCUSSION

Sonoelastography is a dynamic ultrasound technique that can estimate tissue stiffness and provides a qualitative assessment of the target tissue.^{10,11} Elastography has emerged as an adjunctive tool

for diagnosis of malignant thyroid nodules.¹² It is noninvasive and painless method which can easily be performed and able to highlight fine details of thyroid nodule.¹²

Strain elastography has found its place in characterising thyroid nodules. According to the recent consensus, a firm hard nodule upon palpation is likely to be malignant.¹³ Fine needle aspiration cytology (FNAC) is the diagnostic of choice for the purpose but it is an invasive procedure. Moreover, 10-15% of the nodules remain indeterminate. As malignant nodules are generally hard and firm, so strain elastography can be used to determine which nodule must be subjected to FNAC.¹²

The present study was conducted to find the accuracy of strain elastography in differentiation of benign and malignant thyroid lesions taking cytology as gold standard. In the present study, mean strain ratio for malignant lesions was significantly high ($p < 0.001$) as compared to the benign lesions being 3.08 and 1.60, respectively. The most suitable cutoff strain ratio for distinguishing benign from malignant thyroid nodules was found to be 2.57 (Figure 1).

These results are in concordance with Wuguo *et al.*, reporting that strain ratio of 2.52 can be used as a cutoff to distinguish between malignant and benign thyroid nodules. Area under the curve in their study was 0.861 with sensitivity of 85.7%, specificity of 90.5%, PPV of 85.7%, NPV of 90.5% and diagnostic accuracy of 88.6%.¹⁴ The sensitivity and specificity of 90.0%, PPV of 91.53% and NPV of 88.24% determined in this study is promising. Diagnostic accuracy remained 90.0%. Area under the curve was 0.933 (0.879-0.987, $p < 0.001$, Figure 1).

Strain ratio values between 2.5-4.5 have been reported in literature for differentiation of thyroid nodules. Good sensitivity and specificity of the method for thyroid nodule characterisation has been observed.¹⁴⁻¹⁸ The only concern with the use of strain elastography for diagnostic purpose is the absence of an agreement about the threshold value.¹⁸

A number of related studies have also reported the high diagnostic accuracy of strain elastography for characterising benign and malignant thyroid nodules. Appreciable sensitivity and specificity of strain elastography was observed ranging from 97-85% and 91-80%, respectively.¹⁹⁻²³

Null *et al.* in a recent meta-analysis have evaluated the efficacy of strain elastography to replace FNAC in soft thyroid nodules. The results of study supported the idea to safely omit FNAC in completely soft thyroid nodules (Asteria 1), where fairly high specificity of strain elastography was observed in detecting benign thyroid lesions.²³

So, strain elastography has potential to minimize redundant FNAC procedures.

The results of this study also favour the use of strain elastography for characterisation of thyroid nodules. The threshold determined in this study is concordant with literature reported values.

CONCLUSION

This study concluded that strain elastography has fairly high accuracy to differentiate between benign /malignant thyroid nodules. It has not only perceptibly improved the ability of differentiating

thyroid nodules preoperatively; but is also helpful for the surgeons in proper decision-making. So, the authors recommend that sonoelastography should be done routinely in all thyroid lesions for accurate diagnosis of malignant thyroid nodules preoperatively and opting proper surgical approach.

ETHICAL APPROVAL:

Ethical approval for the study was taken from institutional review board in January 2019.

PATIENTS' CONSENT:

Informed consent was taken from every patient.

CONFLICT OF INTEREST:

Authors declared no conflict of interest.

AUTHORS' CONTRIBUTION:

AI: Data acquisition and analysis, drafting, final approval.

RS: Conception and design, data acquisition, drafting, critical revision, final approval.

IF: Analysis and interpretation, drafting, final approval.

AS: Conception, critical Revision, final approval.

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