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Original Research

Prospective Assessment of Ultrasound Elastography in Characterization of Thyroid Nodules

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ABSTRACT:
Background: Thyroid nodules are common clinical entities with a rising detection rate due to the widespread use of imaging techniques. Although most nodules are benign, accurate differentiation from malignant lesions is essential to avoid unnecessary invasive procedures. Conventional ultrasound, while useful, often lacks specificity, and fine-needle aspiration cytology (FNAC) may yield indeterminate results. Ultrasound elastography, a technique assessing tissue stiffness, has emerged as a promising adjunct to improve diagnostic precision. **Aim:** To prospectively evaluate the effectiveness of ultrasound elastography, using both qualitative (Tsukuba scoring) and quantitative (strain ratio) approaches, in distinguishing benign from malignant thyroid nodules, with cytology and histopathology as reference standards. **Material and Methods:** A prospective observational study was conducted on 90 patients with thyroid nodules at a tertiary care hospital. All patients underwent conventional B-mode ultrasound, real-time strain elastography, and US-guided FNAC. Nodules were graded using the 5-point Tsukuba elasticity score and strain ratio (SR) was calculated. Cytological evaluation followed the Bethesda System. Statistical analysis was performed to determine the sensitivity, specificity, and diagnostic accuracy of elastography. A p-value <0.05 was considered statistically significant. **Results:** Among the 90 patients, 75.6% were female and 24.4% male. Most nodules were located in the right lobe (47.8%). All nodules with Tsukuba score 1 and 95.5% with score 2 were benign. Malignancy was confirmed in 66.7% and 85.7% of nodules with scores 4 and 5, respectively. Mean SR for benign nodules was 1.72 ± 0.55, while for malignant nodules it was 3.84 ± 0.88 ($p < 0.001$). Elastography demonstrated a sensitivity of 85.7%, specificity of 87.1%, positive predictive value of 75.0%, negative predictive value of 93.5%, and overall accuracy of 86.7%. The optimal SR cut-off was 2.5, with an AUC of 0.91. **Conclusion:** Ultrasound elastography is a highly effective non-invasive technique for characterizing thyroid nodules. Both Tsukuba scoring and strain ratio showed strong correlation with cytological findings. The high sensitivity and specificity highlight elastography's utility in improving risk stratification and potentially reducing unnecessary FNAC procedures.

Keywords: Ultrasound elastography, Thyroid nodules, Tsukuba score, Strain ratio, Fine-needle aspiration cytology

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INTRODUCTION

Thyroid nodules are a common clinical finding, with their prevalence increasing significantly due to the widespread use of high-resolution imaging modalities. Most nodules are benign and asymptomatic, yet the crucial clinical challenge lies in accurately distinguishing malignant nodules that require surgical intervention from benign ones that can be conservatively managed. The incidence of palpable thyroid nodules in the general population ranges from 4% to 7%, but ultrasonography has revealed a much higher prevalence, up to 67%, particularly in iodine-deficient areas and among the elderly population[1].

Traditional evaluation of thyroid nodules relies heavily on clinical examination, ultrasound, and fine-needle aspiration cytology (FNAC). However, physical palpation is limited in its sensitivity, especially in detecting smaller or deep-seated nodules, often missing lesions under 1 cm². High-resolution B-mode ultrasound has become the cornerstone of thyroid imaging, offering detailed morphological analysis that guides risk stratification. Features such as hypoechogenicity, irregular margins, microcalcifications, and taller-than-wide shape are associated with an increased risk of malignancy[2]. Nonetheless, these criteria may overlap between benign and malignant lesions, leading to diagnostic uncertainty in a substantial number of cases.

To overcome the limitations of grayscale sonography and FNAC, newer sonographic techniques have been developed to enhance diagnostic accuracy. Among these, ultrasound elastography has emerged as a valuable tool that provides additional functional information by evaluating tissue stiffness. Since malignant tissues are generally firmer due to increased cellularity and desmoplastic reaction, elastography allows differentiation based on mechanical properties rather than just morphology[3]. Two main types of elastography are used in clinical practice: strain elastography and shear wave elastography. Strain elastography, the more widely used technique, assesses relative tissue displacement in response to manual compression, displaying it as a color-coded elastogram[4].

The role of elastography in characterizing thyroid nodules is grounded in the principle that malignant nodules typically demonstrate reduced elasticity and increased stiffness compared to benign ones. In strain elastography, stiffness is semi-quantitatively expressed using visual scoring systems such as the Tsukuba score, which ranges from 1 (very soft) to 5 (very hard). Additionally, the strain ratio (SR), a quantitative parameter comparing the strain of surrounding normal tissue to that of the nodule, serves as an objective marker to differentiate benign from malignant nodules[5].

Studies in other organs, such as the breast, have already established elastography's diagnostic potential. The application of similar techniques to thyroid imaging has gained momentum, showing promise in refining the risk stratification of thyroid nodules, especially those that yield indeterminate or non-diagnostic cytology[6]. The integration of elastography into thyroid ultrasound protocols has shown improved sensitivity and specificity in identifying malignancies, and some authors have proposed its use in combination with grayscale ultrasound to enhance decision-making and reduce unnecessary FNACs.

Despite encouraging results, variability in operator technique, equipment settings, and lack of standardized interpretation have limited the widespread adoption of elastography. The learning curve associated with proper acquisition of elastographic images and variability in interpreting elastograms can affect the reproducibility of findings. Moreover, certain types of nodules—such as those with large cystic components, isthmic location, or those adjacent to pulsatile vessels—may produce suboptimal elastographic results[7]. Therefore, continuous validation through prospective clinical studies is essential to establish consistent cut-off values for SR and to define the diagnostic thresholds for routine use.

Another challenge arises in cases where nodules show indeterminate cytology, such as those classified as Bethesda III or IV, for which the malignancy risk can vary widely. These cases pose a diagnostic dilemma for clinicians, often leading to either repeated FNACs or diagnostic surgery. In such scenarios, elastography has been suggested as a supplementary tool to improve confidence in clinical decisions[8]. Moreover, integrating elastography findings with other sonographic parameters and risk assessment systems, such as TI-RADS (Thyroid Imaging Reporting and Data System), can further refine the evaluation algorithm for thyroid nodules.

Recent technological advancements, including acoustic radiation force impulse (ARFI) imaging and virtual touch tissue imaging, have offered additional options for stiffness measurement. These methods offer more reproducible and operator-independent assessments, though their availability may be limited to certain high-end machines. Nevertheless, strain elastography remains more accessible and widely used in routine clinical practice due to its compatibility with most conventional ultrasound equipment[9].

Given the growing burden of thyroid nodules, especially in iodine-deficient regions and with increasing incidental detection through cross-sectional imaging, there is an urgent need to establish cost-effective, non-invasive, and accurate diagnostic strategies. Ultrasound elastography fits this need by offering real-time functional imaging without ionizing radiation. It holds the potential to significantly reduce the number of unnecessary biopsies and surgeries by accurately identifying benign nodules that can be managed conservatively.

MATERIALS AND METHODS

This prospective observational study was conducted at the Department of Radiology of a tertiary care hospital, following approval from the Institutional Ethics Committee. Written informed consent was obtained from all participants prior to inclusion. A total of 90 consecutive patients referred for evaluation of thyroid nodules were enrolled in the study. Inclusion criteria were: patients aged 18 years or older, presence of one or more thyroid nodules detected either clinically or on prior imaging, and willingness to undergo ultrasound (US), ultrasound elastography (USE), and fine-needle aspiration cytology (FNAC). Patients with diffuse thyroid disease such as Hashimoto's thyroiditis, those with a history of thyroid surgery or radioiodine therapy, nodules with predominant cystic components (more than 50%), or inadequate image quality or poor compliance were excluded from the study.

All patients underwent conventional B-mode ultrasound followed by ultrasound elastography using a high-resolution ultrasound system equipped with elastography capabilities (such as Hitachi HI VISION Avius or GE Logiq E9) and a high-frequency linear transducer (7–15 MHz). Conventional ultrasound parameters such as size, shape, margin characteristics, echogenicity, presence of microcalcifications, and vascularity were documented. Thereafter, real-time strain elastography was performed with the patient positioned supine and the neck extended. Gentle repetitive manual compression was applied to acquire elastographic images, with each nodule evaluated in both longitudinal and transverse planes.

An elastography score (ES) was assigned to each nodule using the standard 5-point Tsukuba scoring system. In this system, score 1 indicates even strain throughout the nodule (soft), score 2 indicates strain in most of the nodule with some areas of no strain, score 3 indicates strain only at the periphery, score 4 indicates no strain in the nodule, and score 5 indicates no strain in both the nodule and surrounding tissue. In addition to qualitative scoring, a strain ratio (SR) was calculated by comparing the strain of adjacent normal thyroid tissue to that within the nodule using region-of-interest (ROI) software tools.

All patients underwent US-guided FNAC of the target nodule(s) either on the same day or within one week of imaging. Cytological diagnoses were made according to the Bethesda System for Reporting Thyroid Cytopathology. For patients who underwent surgery, histopathology reports were used as the definitive diagnostic reference standard.

Statistical analysis was performed to evaluate the diagnostic accuracy of ultrasound elastography. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall diagnostic accuracy were calculated. Differences in elastography scores and strain ratios between benign and malignant nodules were analyzed using the chi-square test and independent t-test, respectively. Receiver Operating Characteristic (ROC) curves were generated to determine the optimal cutoff value for the strain ratio. A p-value of less than 0.05 was considered statistically significant. All statistical analyses were performed using SPSS version 16.0.

RESULTS

Patient Demographics and Nodule Characteristics (Table 1)

Among the 90 patients enrolled in the study, a substantial majority were female, accounting for 75.6% (n = 68), while only 24.4% (n = 22) were male. This female predominance is consistent with the known higher prevalence of thyroid nodules and thyroid diseases in women. In terms of age distribution, the most common age group was 31–45 years, comprising 37.8% (n = 34) of the study population, followed by patients aged 46–60 years (32.2%, n = 29). Younger patients aged 18–30 years made up 13.3% (n = 12), while those above 60 years constituted 16.7% (n = 15). Regarding anatomical distribution, nodules were most frequently located in the right thyroid lobe (47.8%, n = 43), followed by the left lobe (43.3%, n = 39). A smaller subset (8.9%, n = 8) had nodules located in the isthmus.

Correlation of Elastography Score with Cytological Diagnosis (Table 2)

A significant relationship was observed between elastography scores and cytological outcomes. Nodules with lower elastography scores (Score 1 and 2) were predominantly benign. All 16 nodules with a score of 1 were benign (100%), while 95.5% (n = 21/22) of nodules with a score of 2 were also benign. Score 3 nodules showed a slightly higher malignancy rate, with 15% (n = 3/20) diagnosed as malignant. Notably, the risk of malignancy increased significantly with higher elastography scores. Among nodules scored as 4, 66.7% (n = 12/18) were malignant, and for those with a score of 5, malignancy was confirmed in 85.7% (n = 12/14). These findings strongly support the diagnostic utility of the Tsukuba scoring system in distinguishing benign from malignant thyroid nodules, with high scores indicating increased stiffness and greater likelihood of malignancy.

Comparison of Strain Ratio in Benign vs Malignant Nodules (Table 3)

The mean strain ratio (SR) was significantly different between benign and malignant nodules. Benign nodules (n = 62) had a mean SR of 1.72 ± 0.55, with a range of 0.9 to 2.8. In contrast, malignant nodules (n = 28) exhibited a much higher mean SR of 3.84 ± 0.88, ranging from 2.3 to 5.6. This difference was statistically significant with a p-value of < 0.001, indicating that malignant nodules are significantly stiffer than benign ones. The clear separation of SR values between the two groups reinforces the clinical relevance of SR as a quantitative parameter in elastography for thyroid nodule characterization.

Diagnostic Performance of Elastography Parameters (Table 4)

When assessed for diagnostic efficacy, ultrasound elastography—based on both Tsukuba scores and strain ratios—demonstrated high diagnostic accuracy. The sensitivity and specificity were 85.7% and 87.1%, respectively, indicating that the technique is both reliable in detecting malignancies and effective in ruling out benign cases. The positive predictive value (PPV) was 75.0%, while the negative predictive value (NPV) was notably high at 93.5%, reflecting a strong ability to correctly exclude malignancy in negative cases. The overall diagnostic accuracy stood at 86.7%. Receiver Operating Characteristic (ROC) analysis identified an optimal strain ratio cut-off value of 2.5, with an impressive area under the curve (AUC) of 0.91, indicating excellent diagnostic performance.

Table 1: Demographic and Clinical Profile of Patients (n = 90)

Parameter	Number of Patients	Percentage (%)
Gender		
Male	22	24.4%
Female	68	75.6%
Age Group (years)		
18–30	12	13.3%
31–45	34	37.8%
46–60	29	32.2%
>60	15	16.7%
Nodule Location		
Right Lobe	43	47.8%
Left Lobe	39	43.3%
Isthmus	8	8.9%

Table 2: Distribution of Elastography Score (Tsukuba Scoring) and Cytological Outcome

Elastography Score	Number of Nodules	Benign (Bethesda II)	Malignant (Bethesda V/VI)
Score 1	16	16 (100%)	0 (0%)
Score 2	22	21 (95.5%)	1 (4.5%)
Score 3	20	17 (85%)	3 (15%)
Score 4	18	6 (33.3%)	12 (66.7%)
Score 5	14	2 (14.3%)	12 (85.7%)
Total	90	62 (68.9%)	28 (31.1%)

Table 3: Comparison of Strain Ratio (SR) Between Benign and Malignant Nodules

Diagnosis	Mean SR ± SD	Range
Benign (n = 62)	1.72 ± 0.55	0.9 – 2.8
Malignant (n = 28)	3.84 ± 0.88	2.3 – 5.6
p-value	**< 0.001**	

Table 4: Diagnostic Performance of Elastography Score and Strain Ratio

Parameter	Value
Sensitivity	85.7%
Specificity	87.1%
Positive Predictive Value	75.0%
Negative Predictive Value	93.5%
Accuracy	86.7%
Optimal SR Cut-off (from ROC)	2.5
Area Under ROC Curve (AUC)	0.91

DISCUSSION

The demographic findings in this study, with a predominance of female patients (75.6%), align with previously reported patterns in thyroid nodule epidemiology. This gender distribution reflects the well-documented hormonal and autoimmune influences contributing to thyroid pathology in women. Similar trends were observed in a study by Papini et al. (2002), where 80% of the thyroid nodule population were female[10]. The age group most affected in our study was 31–45 years (37.8%), comparable to the mean age of 42 years reported in their series, indicating that thyroid nodules commonly affect middle-aged individuals.

The elastography score distribution in our study showed a significant correlation with cytological diagnosis. High Tsukuba scores (4 and 5) were strongly associated with malignancy (66.7% and 85.7%, respectively), while lower scores (1 and 2) corresponded to benign lesions (100% and 95.5%, respectively). These results are consistent with the findings of Rago et al. (2007), who demonstrated that nodules with scores 4 and 5 had a malignancy rate of 81%, whereas scores 1 and 2 had a rate of less than 5%[11]. This reinforces the utility of qualitative elastography scoring in predicting malignancy.

Quantitative analysis using strain ratio (SR) further supported differentiation between benign and malignant nodules. In our study, malignant nodules had a significantly higher mean SR (3.84 ± 0.88) compared to benign ones (1.72 ± 0.55), with a p-value of <0.001. These findings are in concordance with the study by Lyshchik et al. (2005), who reported a mean SR of 3.7 ± 1.5 in malignant nodules versus 1.5 ± 0.8 in benign nodules[12]. The statistically significant difference in SR between groups validates its role as a reliable quantitative marker for malignancy.

In terms of diagnostic performance, elastography in our study yielded a sensitivity of 85.7%, specificity of 87.1%, and overall accuracy of 86.7%, with an AUC of 0.91. These results are in agreement with the work of Moon et al. (2008), who reported a sensitivity of 88%, specificity of 85%, and an AUC of 0.89 for elastography when used in combination with B-mode ultrasound features[13]. Such consistency highlights the robustness of elastography as an adjunctive diagnostic tool in thyroid imaging.

The optimal strain ratio cut-off value derived from ROC analysis in our study was 2.5. This threshold closely mirrors that reported by Azizi et al. (2013), who identified a cut-off of 2.3 with comparable sensitivity (80%) and specificity (85%) for differentiating malignant nodules[14]. The slight variation in cut-off points across studies may be attributed to differences in equipment, technique, and study population, but generally supports a similar diagnostic threshold in clinical practice.

The combination of qualitative (Tsukuba score) and quantitative (SR) elastographic parameters in our study provided complementary strengths, achieving high NPV (93.5%), which is critical for excluding malignancy and potentially reducing unnecessary biopsies. A similar conclusion was drawn by Cantisani et al. (2012), who found that integrating both modalities increased diagnostic accuracy and clinician confidence, particularly in indeterminate nodules[15].

CONCLUSION

Ultrasound elastography, both qualitative and quantitative, is a valuable non-invasive adjunct to conventional ultrasound in the evaluation of thyroid nodules. The Tsukuba scoring system and strain ratio showed strong correlation with cytological outcomes, with higher scores and ratios significantly associated with malignancy. Elastography demonstrated high sensitivity, specificity, and diagnostic accuracy, reinforcing its role in improving risk stratification and potentially reducing unnecessary biopsies.

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