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Original Article

Evaluation of Benign and Malignant Cervical Lymphadenopathy: A Comparative Study of Shear Wave Elastography and Grayscale Ultrasound

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Abstract

Objectives The aim of the study was to evaluate role of shear wave elastography (SWE) using a novel methodology for differentiation of benign and malignant cervical lymph nodes.

Methods SWE was performed on 38 patients who presented with cervical lymph adenopathy. Color-coded elasticity maps were obtained, from which the stiffest region of interest (ROI) with a diameter of 2 mm was chosen. Maximum and mean Young's modulus values (Kpa) were calculated in selected 2-mm ROI. Finally, the results were correlated with the fine needle aspiration cytology findings in all patients to assess the diagnostic accuracy, sensitivity, and specificity at a defined cutoff value for distinguishing between benign and malignant lymphadenopathies.

Results There were 20 malignant cervical lymph nodes and 18 benign cervical lymph nodes. Malignant nodes showed significantly higher mean Young's modulus value (154.2 ± 46.19 kPa) compared with benign nodes (70.39 ± 30.76 kPa), with a *p*-value of less than 0.0001. Our findings indicate that the mean Young modulus value within a standardized 2-mm ROI outperformed grayscale ultrasound in terms of diagnostic accuracy (92.1 vs. 78.9%), sensitivity (100 vs. 80%), and specificity (83.3 vs. 77.7%), with the established cutoff values for high diagnostic accuracy indicating malignancy as greater than 92 for mean Young's modulus with an area under the curve of 0.964.

Conclusion SWE using a standardized 2-mm ROI provides improved sensitivity and diagnostic accuracy for differentiation of benign and malignant lymph node lesions.

Keywords
- benign
- cervical lymph node
- malignant
- shear wave elastography
- Young's modulus

Introduction

Cervical lymphadenopathy requires accurate differentiation between benign and malignant states, highlighting the need for sophisticated imaging. Ultrasonography, although effective for evaluation and differentiation between benign and malignant cervical lymphadenopathy, often leads to unnecessary biopsies.[1] Elastography, particularly shear wave elastography (SWE), has emerged as an advanced technique, enhancing ultrasonography by assessing tissue stiffness, a key indicator of malignancy.[2] Unlike strain elastography (SE), which relies on manual pressure application and provides

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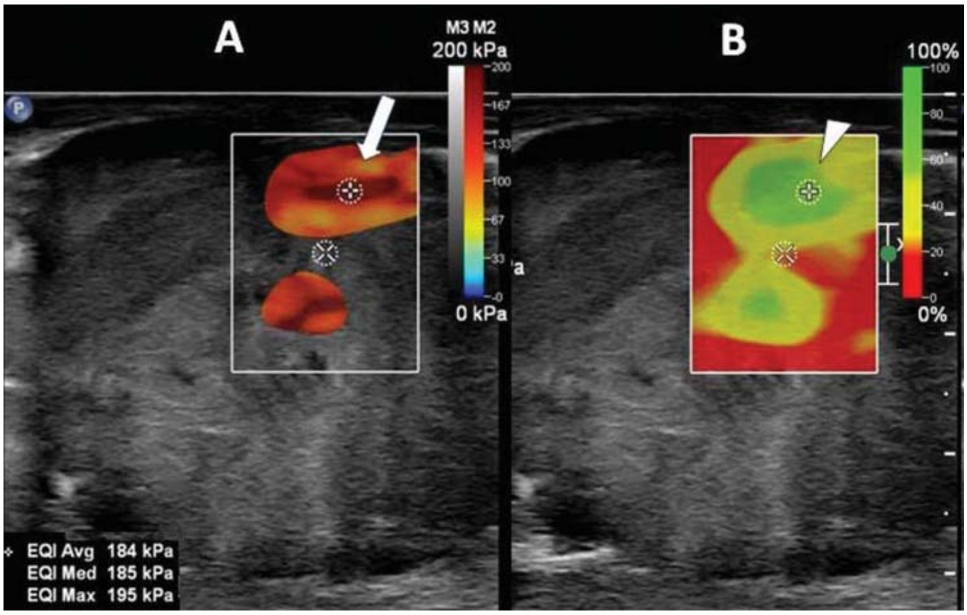

Fig. 1 Elastography methodology. (**A**) Shear wave elastography with a corresponding (**B**) color-coded confidence map of a metastatic node from squamous cell carcinoma. To measure Young's modulus in kilopascals (kPa), a region of interest with a standardized diameter of 2 mm is situated on the area deemed to be the stiffest (*arrow*), as determined through a visual evaluation of the color scale, which also correlates with a high confidence level on the confidence map (*arrowhead*). The mean elasticity quantification index (EQI mean) is noted at 184 kPa, and the maximum elasticity quantification index (EQI max) reaches 195 kPa.

relative stiffness measurements, SWE offers a quantifiable, more reliable assessment of tissue stiffness by measuring the speed of mechanically induced shear waves passing through the tissue.[3] This allows for objective, reproducible data on tissue elasticity, making SWE superior in terms of repeatability and accuracy. This study aims to assess the accuracy of SWE in distinguishing between benign and malignant lymph nodes. It evaluates a novel methodological enhancement, described by Bhatia et al,[4] where only the firmest region of the lymph node is sampled to calculate Young's modulus, which had not been further evaluated in any other study. This method has the potential to boost sensitivity and diagnostic precision compared with traditional elastography techniques, proposing it as a less invasive, more patient-centric alternative to traditional methods and SE, potentially improving the diagnostic process for cervical lymphadenopathy.

Methodology

Patient Selection

The study was conducted between August 2022 and February 2024 after receiving ethical clearance from the institutional ethical committee. It included 38 adult patients with clinically palpable cervical lymph nodes referred for ultrasonography from various departments.

The participants underwent a thorough clinical history review and physical examination. Grayscale ultrasonography and color Doppler were performed using a high-resolution eL18-4 transducer on a PHILIPS EPIQ 5 system, with patients in the supine position. Lymph node characteristics like location, size, margin, echogenicity, fatty hilum, and vascular patterns were meticulously recorded.

Elastography Technique

SWE was done and initially color-coded elasticity maps were obtained with a corresponding confidence map superimposed on the grayscale ultrasound image. From the stiffest area appearing dark red on the color-coded map, a 2-mm-diameter region of interest (ROI) was chosen, avoiding calcific, necrotic, or cystic areas. The rationale behind this was that there may be partial infiltration of the lymph node and a larger ROI may underestimate the overall stiffness. The maximum and mean Young's modulus values (Kpa) were calculated in the selected ROI (►**Fig. 1**). Finally, the results were correlated with the fine needle aspiration cytology (FNAC) findings in all patients to assess the diagnostic accuracy, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and the cutoff value for distinguishing between benign and malignant lymphadenopathies.

Statistical Analysis

Categorical variables were presented as frequencies and percentages, while quantitative data were depicted as means $\pm$ standard deviations or medians with interquartile ranges. The Shapiro–Wilk test assessed data normality. Statistical analysis involved independent *t*-tests for non-normally distributed quantitative variables and Fisher's exact test for qualitative variables with low expected counts. Receiver operating characteristic (ROC) curve analysis was employed to evaluate the diagnostic performance of the maximum and mean Young's modulus values and grayscale morphology for predicting malignancy and determining the sensitivity, specificity, PPV, and NPV. The analysis was conducted using SPSS software, version 25.0, by IBM, with the significance level set at $p < 0.05$ to identify meaningful differences.

Results

In our study examining cervical lymphadenopathy, significant variations were observed in morphological features between benign and malignant cases.

Among the 38 patients examined, the highest proportion was in the age range of 51- to 60-year age range (28.95%), with an average age of 45.97 years and a median of 50 years. Among these, 25 patients (65.79%) were males, while 13 (34.21%) were females. On the basis of the FNAC results, malignancy was suggested in 20 cases (52.63%), while benign outcomes were noted in 18 cases (47.37%).

On grayscale ultrasonography, the presence of well-defined margins was more common in benign instances (88.89%) than in malignant ones (55%; $p = 0.033$). Similarly, homogeneous echotexture was prevalent in benign cases (77.78%) compared with malignant ones (25%), with a *p*-value of 0.003. Although the distribution of short-to-long axis diameter (S/L) ratios (<0.5 at 38.89% for benign cases and 20% for malignant cases; ≥0.5 at 61.11% for benign cases and 80% for malignant cases) showed no significant difference ($p = 0.288$), the mean S/L ratio was significantly higher in malignant cases (0.68 ± 0.21) than in benign ones (0.51 ± 0.12), as evidenced by a *p*-value of 0.005. The presence of hilum differed markedly, being more frequent in benign cases (83.33%) than in malignant ones (15%), underscored by a *p*-value of less than 0.0001. Color flow patterns also varied, with a hilar pattern more common in benign cases (77.78%) and patchy flow in malignant cases (80%; $p = 0.0009$).

Further analysis using elastography revealed a stark contrast in the Young's modulus values between benign and malignant lymph nodes (►**Figs. 2–5**). Malignant nodes exhibited significantly higher maximum Young's modulus values (223.05 ± 46.99 kPa) compared with benign ones (103.78 ± 56.41 kPa), with a *p*-value of less than 0.0001. The mean Young's modulus also showed a similar pattern, with malignant nodes averaging at 154.2 ± 46.19 kPa, significantly higher than benign nodes at 70.39 ± 30.76 kPa, also with a *p*-value of less than 0.0001 (►**Table 1**).

The diagnostic performance of these elastography parameters was evaluated using the ROC curve analysis. The maximum Young's modulus demonstrated an area under the curve (AUC) of 0.942, mean Young's modulus an AUC of 0.964, and grayscale morphology an AUC of 0.789, all significant with $p < 0.0001$. The cutoff values for high diagnostic accuracy were greater than 171 for maximum Young's modulus and greater than 92 for mean Young's modulus, with the mean Young's modulus showing the highest sensitivity (100%) and a specificity of 83.33% (►**Table 2**).

When comparing the predictive power of these metrics, the mean Young's modulus stood out as a superior predictor

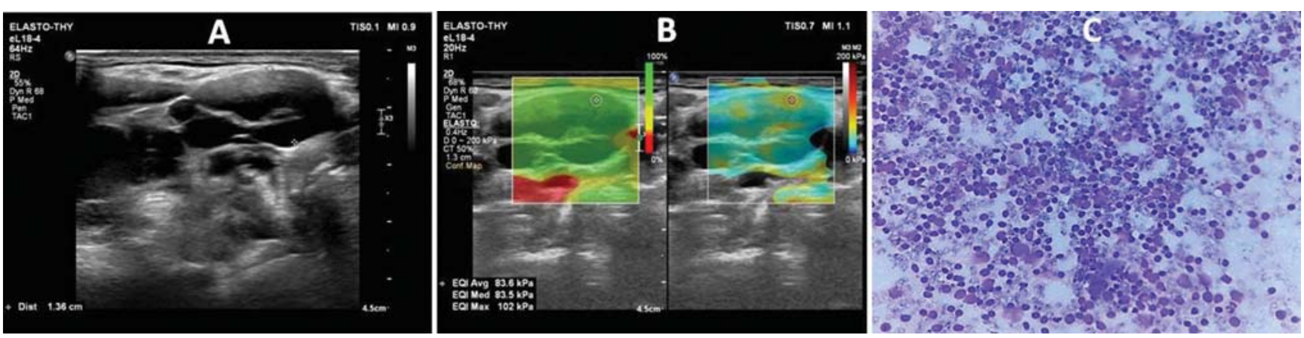

Fig. 2 Reactive hyperplasia (benign). (**A**) Grayscale ultrasound showing a well-defined homogenously hypoechoic lymph node (left level III) measuring 13 mm in short axis diameter and short-to-long axis diameter ratio of 0.52 with preserved fatty hilum, suggestive of benign lesion. (**B**) Shear wave elastography: the maximum elasticity quantification index (EQI max) is 102 kPa with a mean elasticity quantification index (EQI mean) of 83.1 kPa, consistent with benign lymph node. (**C**) Fine needle aspiration cytology indicated reactive hyperplasia.

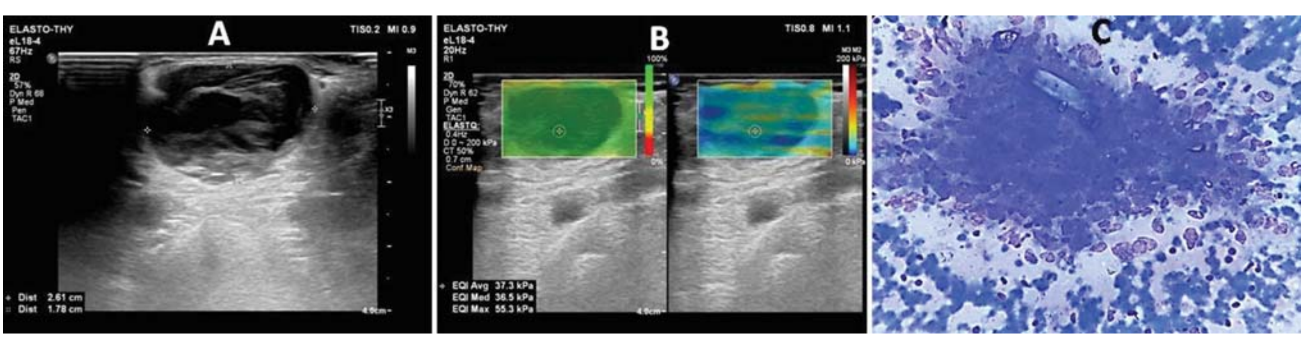

Fig. 3 Tubercular lymphadenopathy (benign). (**A**) Grayscale ultrasound showing a well-defined heterogeneous lymph node (right level IV) measuring 17 × 26 mm and short-to-long axis diameter ratio of 0.65 with loss of fatty hilum suggestive of malignant etiology. (**B**) Shear wave elastography: the maximum elasticity quantification index (EQI max) is 55 kPa with a mean elasticity quantification index (EQI mean) of 37.1 kPa, consistent with benign lymph node. (**C**) Fine needle aspiration cytology indicated tubercular lymphadenitis.

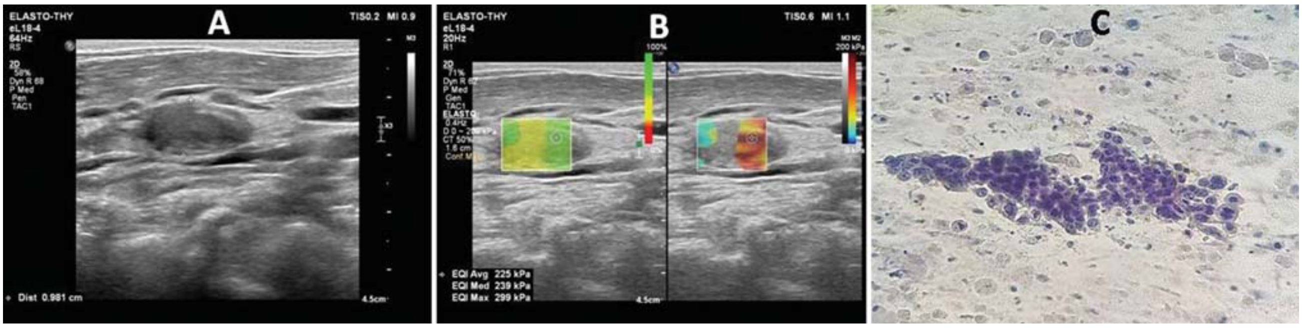

Fig. 4 Laryngeal carcinoma metastasis (malignant). (**A**) Grayscale ultrasound showing a well-defined homogenous lymph node (right level III) measuring 9.8 mm in short axis diameter and short-to-long axis diameter ratio of 0.51; however, the fatty hilum was lost, suggestive of benign lymph node. (**B**) Shear wave elastography: the maximum elasticity quantification index (EQI max) is 299 kPa with a mean elasticity quantification index (EQI mean) of 225 kPa, consistent with malignant etiology. (**C**) Fine needle aspiration cytology indicated a well-differentiated metastatic carcinoma.

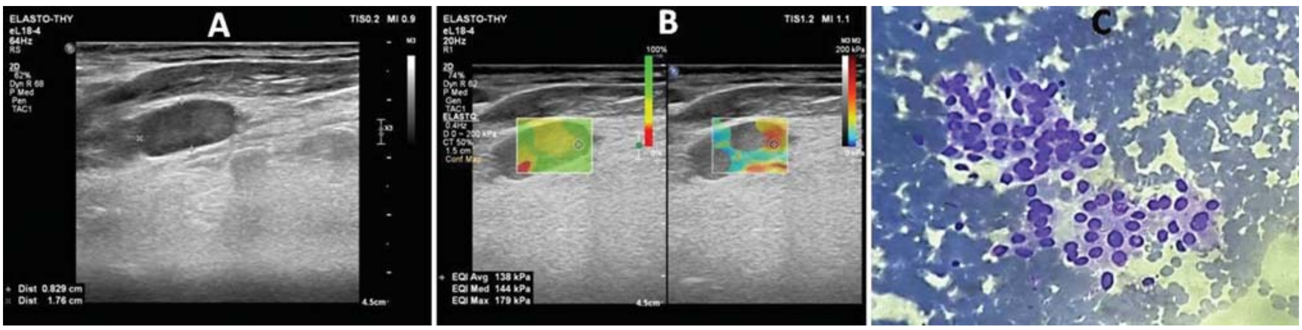

Fig. 5 Papillary carcinoma thyroid metastasis (malignant). (**A**) Grayscale ultrasound showing a well-defined homogenously hypoechoic lymph node (right level III) measuring 8.2 mm in short axis diameter and short-to-long axis diameter ratio of 0.46 with loss of fatty hilum, suggestive of benign lymph node. (**B**) Shear wave elastography: the maximum elasticity quantification index (EQI max) is 179 kPa with a mean elasticity quantification index (EQI mean) of 138 kPa, consistent with malignant etiology. (**C**) Fine needle aspiration cytology indicated metastatic papillary carcinoma of the thyroid.

Table 1 Association of Young's modulus (kPa) with benign and malignant lymph nodes

Young's modulus (kPa)	Benign ($n = 18$)	Malignant ($n = 20$)	Total	p-value
Maximum Young's modulus (kPa)				
Mean ± SD	103.78 ± 56.41	223.05 ± 46.99	166.55 ± 78.98	< 0.0001[a]
Median (25th–75th percentile)	97 (59.75–118)	202 (185.5–267.5)	180.5 (98.25–208)	
Range	31–241	159–299	31–299	
Mean Young's modulus (kPa)				
Mean ± SD	70.39 ± 30.76	154.2 ± 46.19	114.5 ± 57.7	< 0.0001[a]
Median (25th–75th percentile)	64 (50.75–81.75)	138.5 (131.75–160)	121 (68.5–138.75)	
Range	28–135	105–286	28–286	

Abbreviation: SD, standard deviation.
[a]Independent *t*-test.

of malignancy when contrasted with grayscale morphology, as evidenced by a significant difference in their AUC values (difference: 0.175, $p = 0.0143$). Despite some differences in their predictive capacities, these findings highlight the enhanced diagnostic potential of the mean Young's modulus for distinguishing between benign and malignant cervical lymph nodes, compared with traditional grayscale morphology. However, no statistically significant difference was seen between the mean and maximum Young's modulus values (►**Table 3**).

Discussion

SWE, an ultrasound-based technique, shows promise as an operator-independent method for assessing tissue stiffness without external compression, offering better reproducibility than SE. Our study aimed to evaluate the role of SWE using a novel methodology for differentiation between benign and malignant cervical lymph nodes.

We first observed the grayscale characteristics of lymph nodes, such as their margins, size, echotexture, presence of

Table 2 Receiver operating characteristic (ROC) curve of maximum Young's modulus (kPa), mean Young's modulus (kPa), and grayscale morphology for predicting malignancy

Variables	Maximum Young's modulus (kPa)	Mean Young's modulus (kPa)	Grayscale morphology
Area under the ROC curve (AUC)	0.942	0.964	0.789
Standard error	0.0408	0.0251	0.0682
95% confidence interval (CI)	0.814–0.992	0.847–0.998	0.626–0.904
p-value	<0.0001	<0.0001	<0.0001
Cutoff	>171	>92	–
Sensitivity (95% CI)	95% (75.1–99.9%)	100% (83.2–100.0%)	80% (56.3–94.3%)
Specificity (95% CI)	88.89% (65.3–98.6%)	83.33% (58.6–96.4%)	77.78% (52.4–93.6%)
PPV (95% CI)	90.5% (69.6–98.8%)	87% (66.4–97.2%)	80% (56.3–94.3%)
NPV (95% CI)	94.1% (71.3–99.9%)	100% (78.2-100.0%)	77.8% (52.4–93.6%)
Diagnostic accuracy	92.11%	92.11%	78.95%

Abbreviations: NPV, negative predictive value; PPV, positive predictive value.

Table 3 Comparison of area under the curve of maximum Young's modulus (kPa), mean Young's modulus (kPa), and grayscale morphology for predicting malignancy

Variables	Difference between areas	Standard error	95% confidence interval	*p*-value
Maximum Young's modulus (kPa) and mean Young's modulus (kPa)	0.022	0.032	−0.0412 to 0.0856	0.492
Maximum young's modulus (kPa) and grayscale morphology	0.153	0.085	−0.0141 to 0.320	0.0727
Mean Young's modulus (kPa) and grayscale morphology	0.175	0.071	0.0350–0.315	0.0143

Note: As per De Long et al test which is a statistical method used to compare whether there is a statistically significant difference between the AUCs of two correlated ROC curves.

hilum, and color flow pattern. Subsequently, elastography evaluation of the lymph node was done and the maximum and mean Young's modulus values were obtained.

Malignant nodes showed significantly higher maximum Young's modulus values (223.05 ± 46.99 kPa) compared with benign nodes (103.78 ± 56.41 kPa), with a *p*-value of less than 0.0001. Similarly, the mean Young's Modulus was significantly higher in malignant nodes (154.2 ± 46.19 kPa) compared with benign nodes (70.39 ± 30.76 kPa), with a *p*-value of less than 0.0001. We established the cutoff values for high diagnostic accuracy (>171 for maximum Young's modulus and >92 for mean Young's modulus).

Our findings indicate that the mean Young's modulus outperformed grayscale ultrasound in terms of diagnostic accuracy (92.1 vs. 78.9%), sensitivity (100 vs. 80%), and specificity (83.3 vs. 77.7%).

The study conducted by Lo et al[5] also reported that malignant lymph nodes had higher Young's modulus values (66.3 ± 24.3 kPa) compared with benign ones (41.4 ± 26.5 kPa), corroborating the relationship between tissue stiffness and malignancy, with a cutoff of 42 kPa yielding 83.3% sensitivity and 64.7% specificity. Similarly, in studies by Desmots et al[6] and Choi et al,[7] metastatic lymph nodes exhibited significantly higher maximum stiffness values compared with benign lymph nodes, with Desmots et al[6] reporting 72 ± 59 kPa (range: 14–300 kPa) for metastatic lymph nodes versus 23 ± 25 kPa (range: 7–146 kPa) for benign lymph nodes, and Choi et al[7] reporting 41.06 ± 36.34 kPa (range: 14.09–229.06 kPa) for metastatic lymph nodes and 14.22 ± 4.19 kPa (range: 6.12–28.57 kPa) for benign lymph nodes.

Moreover, the above-mentioned studies calculated Young's modulus using a larger ROI covering the entire cross-sectional area of the lymph node, which may affect the final mean Young's modulus value due to the presence of intralesional inhomogeneities such as necrosis, calcification, and hemorrhage.

Additionally, the research by Bhatia et al[4] found that a smaller standardized 2-mm ROI yielded comparable intrarater intraclass correlation coefficients when compared with a larger ROI that encompassed the entire lymph node for the quantitative analysis of tissue stiffness using Young's modulus.

The cutoff values identified in our study are significantly higher compared with those reported in the previous studies, primarily due to our methodological refinement. We utilized a standardized approach involving a 2-mm-diameter ROI precisely located on the stiffest portion of the lymph node, as visualized on color-coded elastography maps. This focused measurement strategy ensures that only the stiffest segment of the lymph node is sampled. Such a targeted approach is instrumental in elevating the cutoff values necessary for distinguishing malignant lymph nodes from benign lymph nodes, reflecting a more stringent and potentially more accurate method for assessing tissue stiffness and its correlation with malignancy. This enhancement in measurement technique underscores the importance of methodological precision in improving the diagnostic utility of Young's modulus measurements in clinical settings. Further, due to the precision in using a targeted ROI, there was no statistically significant difference between the mean and maximum Young's modulus values in predicting malignancy.

Thus, SWE, utilizing this enhanced methodology with increased sensitivity, can aid in the evaluation of lymph nodes. When combined with clinical and imaging data, it has the potential to reduce reliance on invasive procedures in select cases. However, SWE should not be used as a standalone tool to replace FNAC or biopsy; instead, it should serve as a complementary technique to enhance clinical decision-making and potentially decrease the need for unnecessary procedures in ambiguous cases. However, our study was conducted at a single center with a limited sample size and only one observer, raising concerns about interobserver variability in SWE procedures, which could affect result reproducibility. Additionally, difficulties in obtaining reliable elasticity quantification (EQ) values for lymph nodes of extreme stiffness limited the accurate assessment of tissue stiffness. These limitations emphasize the need for caution in interpreting the study's conclusions and underscore the importance of further research with larger, more diverse samples and multiple observers to validate the findings and assess SWE's diagnostic utility more comprehensively.

Conclusion

Ultrasound elastography, especially SWE, enhances traditional ultrasound by evaluating tissue stiffness with higher accuracy, thereby reducing the necessity for invasive biopsies. SWE, which quantifies tissue stiffness via shear wave speed, is particularly effective in distinguishing benign lymph nodes from malignant lymph nodes due to its quantitative nature, surpassing SE in reliability. Malignant nodes were notably stiffer, with the mean Young's modulus providing the greatest diagnostic precision (AUC: 0.964), demonstrating its potential as a precise and minimally invasive diagnostic tool. The strategic choice of a standardized 2-mm-diameter ROI in the stiffest part of the lymph node significantly contributes to the accuracy of these assessments, ensuring that measurements are consistently taken from the most relevant areas.

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Conflict of Interest
None declared.

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