Role of Sonoelastography in Characterizing Cervical Lymph Nodes with Histopathological Correlation

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ABSTRACT:

INTRODUCTION: Cervical lymphadenopathy is common in clinical practice, arising from various causes like infections, vasculitis, and malignancies. In head and neck oncology, metastatic cervical lymphadenopathy is especially prevalent, often signaling a more aggressive disease. Accurate diagnosis and differentiation of these conditions are crucial for effective patient management and treatment planning.

OBJECTIVES

Primary objective

• To evaluate the accuracy and efficacy of sonoelastography in differentiating benign and malignant cervical lymph nodes using histopathological diagnosis as reference.

Secondary objective

• To determine the individual as well as combined role of ultrasonogram, Doppler and elastography in characterizing the benign and malignant nature of lymph nodes.

• To evaluate for replacing invasive methods like FNAC/ biopsy with non-invasive elastography for diagnosing malignant nodes.

MATERIALS AND METHODS: Eighty patients meeting the inclusion criteria were studied. Cervical lymph nodes were assessed using B-mode ultrasonography and Doppler to evaluate size, shape, margin, hilum, echogenicity, and intranodal vascular patterns. Real-time elastography classified the nodes as benign or malignant, with findings correlated to histopathology between September 2022 and February 2024 at Sri Manakula Vinayagar Medical College, Puducherry. Data was analyzed using MS Excel and SPSS version 24.

RESULTS: B-mode ultrasonography alone had a sensitivity of 80.7%, specificity of 77.7%, positive predictive value of 63.6%, and negative predictive value of 89.3%. Elastography alone showed a sensitivity of 69.2%, specificity of 85.1%, positive predictive value of 69.2%, and negative predictive value of 85.1%. When combined, sensitivity increased to 92.3%, specificity to 88.8%, positive predictive value to 80.0%, and negative predictive value to 96.0%. Thus, combining elastography with ultrasonography enhances diagnostic accuracy.

CONCLUSION: In conclusion, combining B-mode ultrasonography, Doppler, and elastography offers a comprehensive and highly accurate tool for diagnosing and characterizing cervical lymphadenopathy as benign or malignant. This integrated approach enhances diagnostic accuracy, crucial for effective patient management and treatment, reducing the need for invasive procedures in benign cases.

***KEYWORDS*:** Ultrasonography, elastography, B mode USG, Doppler ultrasound, cervical lymph node.

INTRODUCTION:

Cervical lymphadenopathy is a common clinical condition, posing a challenge for physicians due to its wide range of causes. In the realm of head and neck oncology, metastatic cervical lymphadenopathy is particularly prevalent. Depending on the primary tumor site, as many as 80% of patients diagnosed with upper aerodigestive mucosal malignancies exhibit cervical nodal metastasis at the time of presentation.(1) This differentiation is crucial not only for determining the patient's prognosis but also for guiding clinical decision-making and management strategies.(2) Malignant lymph nodes indicate a more aggressive disease course, necessitating a different therapeutic approach compared to benign causes. Thus, the ability to accurately diagnose and differentiate these conditions directly impacts the planning and success of patient management in clinical practice.

High-resolution ultrasound (US) is widely utilized for examining the morphology and internal structure of cervical lymph nodes (LNs). Additionally, color Doppler sonography is employed to evaluate the intranodal vessel patterns, blood flow velocity, and vascular resistance.(3) Real-time elastography (RTE) is a novel, non-invasive imaging technique that measures tissue elasticity by comparing the displacement of local tissues from US signals before and after applying compressive force.(4) In this context, stiff tissues deform less (exhibit less strain) compared to softer tissues when subjected to transducer compression. Given that malignant tissues are generally stiffer than benign ones, US elastography has been documented as useful in distinguishing malignant from benign lesions across various sites.(5-9)

There are two types of techniques in elastography: strain and shear wave-based elastography. Recent research has demonstrated the effectiveness of strain elastography in differentiating benign from malignant cervical LNs.(10,11,12) However, some researchers have raised questions regarding the added value of strain elastography over conventional US in predicting malignancy and selecting LNs for biopsy.(13,14,15) Shear wave elastography, which utilizes ARFI imaging, is an emerging sonographic method for evaluating malignant cervical nodes.(16,17) This study aims to assess the diagnostic effectiveness of strain elastography when used in combination with conventional B-mode and colour Doppler ultrasound (US) in differentiating between benign versus malignant lymph nodes in the cervical region and to provide a more comprehensive diagnostic tool that can aid in better prognosis and management decisions for patients with cervical lymphadenopathy.

MATERIALS AND METHOD:

This hospital based cross sectional study was conducted at Sri Manakula Vinayagar Medical College and Hospital (SMVMCH), which is located in a village 25 km west of Puducherry, South India. The study was conducted according to the good clinical practice guidelines and the Declaration of Helsinki. Written informed consent was obtained from the study participants. Considering the diagnostic accuracy of 94.8% of malignant cases identified by a sono-elastographic score of 3 or more in a study by Abdelgawad et al.(18) the sample size for the present study was found to be 76 at 95% confidence interval and 5% absolute precision. The sample size was rounded off to 80 for this study.

Inclusion Criteria

• Patients with unilateral or bilateral cervical lymphadenopathy who were referred for

ultrasonogram and ultrasonogram guided FNAC/biopsy.

• Patients with head and neck carcinoma with lymph nodal enlargement.

• Patients suspected with cervical lymph node secondaries of unknown primary.

• Patients suspected with pulmonary or extra pulmonary lymph nodal tuberculosis.

• Patients with reactive cervical lymphadenopathy, not responding to treatment.

Exclusion Criteria:

• Patients who underwent radiotherapy/ chemotherapy for cervical lymph node malignancy.

• Those who are on or completed treatment like anti tubercular drugs.

• Those who have undergone surgery like cervical lymph node excision.

• Those who have already underwent biopsy from the cervical lymph node.

Procedure:

Patients who fulfilled the inclusion criteria were considered for the study. Ultrasound examination was performed using a PHILIPS 70 G Affiniti with a 5-12 MHz linear transducer. A consistent scanning method was followed and the following parameters were evaluated: short axis diameter (cut off – 8mm), short to long axis diameter (cut off – 0.6), margin (regular/ irregular), fatty hilum (present/ absent), echogenicity (homogenous/ heterogenous), and intranodal vascular pattern (Pattern 1 – hilar/ no vascularity, Pattern 2 – peripheral vascularity, Pattern- mixed vascularity). Pattern 1 and 2 were considered benign and pattern 3 was considered malignant.

Then the setting was switched to Elastography mode. Real-time elastography was performed using a free-hand compression technique with quality control. In our machine, the color coding of the elastogram was set between blue and red: blue for softer tissues that deform more on compression, and red for stiffer tissues that deform less on compression, with green considered intermediate. The elastography pattern was stored and analyzed based on the scoring system proposed by Alam et al.[19] (explained in supplementary file 1), score 1 and 2 was considered benign and score 3 to 5 was considered malignant. After scoring, based on the obtained elastogram of the cervical lymph node, the strain ratio (cut off – 2.0) was calculated. The patient was then followed up for histopathological diagnosis either by FNAC or by biopsy.

(Sample case images in supplementary file 2)

Statistical analysis:

Data was entered into Epi Info software version 7.2.1.0 and was analyzed using SPSS software version 24. Continuous variables like age, short axis diameter and short to long axis diameter were expressed in mean and standard deviation. For the categorical variables like gender, clinical diagnosis, fatty hilum, echogenicity, margin, vascularity, elastography pattern, strain ratio and histopathological diagnosis, frequency and percentage analysis were used. Association between the study variables was assessed using Chi square test and independent t test.

All statistical tools were carried out at the level of significance of 5% and the probability- p value < 0.05 was considered statistically significant. B mode with Doppler ultrasound and elastography values were calculated to find the sensitivity, specificity, positive predictive value and negative predictive value and these values are compared with the histopathological examination.

Ethical consideration:

Institutional ethics committee approval was obtained (IEC no. EC/63/2022) and the study was conducted fulfilling the STARD checklist. Informed consent was obtained from study participants in their native language.

RESULTS:

The average age of the study participants was 40.50 ± 13.23 years and among the study participants, there were 41 females and 39 males, indicating a slight female preponderance at 51.2%, compared to 48.8% males.

In our study, cervical lymph nodes were evaluated using several criteria, including size, shape, echogenicity, margin characteristics, vascularity, elastography patterns, and strain ratio. **(Table 1, 2)**

Size and Shape: The mean short axis diameter was 11.83 ± 5.2 mm, with a range of 8-31 mm, using an 8 mm cutoff. The mean short to long axis diameter ratio was 0.67 ± 0.32, with a range of 0.4-1.8, and a 0.6 cutoff.

Fatty Hilum: Of 80 participants, 44 had a fatty hilum (3 malignant, 41 benign), while 36 did not (23 malignant, 13 benign). This difference was statistically significant.

Echogenicity: Homogenous echogenicity was observed in 50 participants (8 malignant, 42 benign), while 30 had heterogeneous echogenicity (18 malignant, 12 benign). This difference was statistically significant.

Margins: Regular margins were present in 70 participants (18 malignant, 52 benign), and irregular margins in 10 (8 malignant, 2 benign). The difference was statistically significant.

Vascularity: Pattern 1 was seen in 36 participants (5 malignant, 31 benign), pattern 2 in 24 (5 malignant, 19 benign), and pattern 3 in 20 (16 malignant, 4 benign). The differences were statistically significant.

Elastography Patterns: Pattern 1 was found in 14 participants (1 malignant, 13 benign), pattern 2 in 32 (4 malignant, 28 benign), pattern 3 in 18 (9 malignant, 9 benign), pattern 4 in 13 (9 malignant, 4 benign), and pattern 5 in 3 (all malignant). The variation was statistically significant.

Strain Ratio: The mean strain ratio was 1.83 ± 0.89. Benign cases had a mean of 1.41 ± 0.45, while malignant cases had a mean of 2.71 ± 1.06. This difference was statistically significant.

The findings indicate significant differences in the evaluated criteria between benign and malignant lymph nodes.

Table 1: B mode with colour Doppler USG, elastography and characterization of cervical lymph node among the study participants

Ultrasound parameters	
B mode Ultrasound parameters	
Short axis diameter (Mean ± SD)	11.83 ± 5.2
Short to long axis diameter (Mean ± SD)	0.67 ± 0.32
Fatty hilum	**Percentage (%)**
Present	55 (n = 44)
Absent	45 (n = 36)
Echogenicity	62.5 (n = 50)
Homogenous	37.5 (n = 30)
Heterogenous	
Margin	87.5 (n = 70)
Regular	12.5 (n = 10)
Irregular	
Vascularity	45 (n = 36)
Pattern 1	30 (n = 24)
Pattern 2	25 (n = 20)
Pattern 3	
Elastography findings parameters	
Elastography pattern	
Pattern 1	17.5 (n = 14)
Pattern 2	40 (n = 32)
Pattern 3	22.5 (n = 18)
Pattern 4	16.3 (n = 13)
Pattern 5	3.8 (n = 3)
Strain ratio (Mean ± SD)	1.83 ± 0.89
Histopathological examination	
	Percentage
Benign	67.5 (n = 54)
Malignant	32.5 (n = 26)

Table 2: Association between the study variables and malignancy among the study participants.

Association between the study variables		
	Independent t test	**P value**
Short axis diameter vs malignancy	5.43	0.001
Short to long axis vs malignancy	5.57	0.001
Strain ratio vs malignancy	7.70	0.001
	Chi square test	**P value**
Fatty hilum vs malignancy	29.39	0.001
Echogenicity vs malignancy	16.54	0.001
Margins vs malignancy	11.75	0.001
Vascularity vs malignancy	27.74	0.001
Elastography pattern vs malignancy	26.67	0.001

In our study, the diagnostic performance of B-mode and Doppler ultrasonography, elastography, and their combination were evaluated as follows: **(Table 3,4)**

B-Mode and Doppler Ultrasonography: Sensitivity was 80.7%, specificity 77.7%, PPV 63.6%, and NPV 89.3%.

Elastography: Sensitivity was 69.2%, specificity 85.1%, PPV 69.2%, and NPV 85.1%.

Combined Approach (B-Mode + Doppler + Elastography): Sensitivity improved to 92.3%, specificity to 88.8%, PPV to 80.0%, and NPV to 96.0%.

The combined method showed the highest diagnostic accuracy, significantly enhancing the ability to correctly identify malignant and benign cases.

Table 3: Distribution of benign and malignant lymph nodes versus histopathological examination.

	Benign	Malignant
B mode USG + Doppler	47	33
Elastography	54	26
B mode USG, Doppler and Elastography	50	30
Histopathological examination	54	26

Table 4: Sensitivity, Specificity, Positive predictive value and Negative predictive value of B mode with colour Doppler USG, elastography and combined B mode with colour Doppler USG and elastography in differentiating malignancy.

Value (95% CI)	**B mode with colour doppler ultrasonography**	**Elastography**	**B mode with colour doppler and elastography**
Sensitivity	80.77% (60.6-93.4%)	69.23% (48.2- 85.6%)	92.31% (74.8- 99.0%)
Specificity	77.78% (64.4-87.9%)	85.19% (72.8- 93.3%)	88.89% (77.3-95.8%)
Positive Predictive Value	63.64% (50.6-74.8%)	69.23% (53.0- 81.7%)	80.00% (65.1- 89.5%)
Negative Predictive Value	89.36% (79.0-94.9%)	85.19% (76.1- 91.1%)	96.00% (86.3- 98.9%)

DISCUSSION:

Approximately 800 lymph nodes exist in the human body, with roughly 300 situated in the head and neck area.[20] These nodes are susceptible to alterations in both physiological and pathological states. Cervical lymphadenopathy, observed across all age demographics, ranks among the prevalent clinical conditions in our country. It can stem from various sources including infection, inflammation, and malignancies. Given the diverse origins, the treatment approach for lymphadenopathy varies accordingly, underscoring the necessity of accurately determining the cause to ensure appropriate management.

When considering B mode and Doppler ultrasonography alone, the sensitivity of the method was calculated to be 80.7%, indicating its ability to correctly identify malignant cases. The specificity was found to be 77.7%, reflecting its accuracy in identifying benign cases. The positive predictive value (PPV), which represents the likelihood that participants identified as malignant truly have malignant conditions, was 63.6%. Conversely, the negative predictive value (NPV), indicating the likelihood that participants identified as benign are indeed benign, was 89.3%. Focusing solely on the performance of elastography, the sensitivity was calculated to be 69.2%. The specificity was found to be 85.1%. The positive predictive value (PPV) was found to be 69.2%. Additionally, the negative predictive value (NPV) was found to be 85.1%. When combining B mode with Doppler ultrasonography and elastography, the diagnostic performance improved significantly. The combined approach demonstrated a sensitivity of 92.3%, specificity of 88.8%, PPV of 80.0%. NPV of 96.0%. Similar study was performed by Tuncez. H.C et

al.[21] which showed a higher sensitivity of 90.4% and higher overall diagnostic accuracy of 73.9% when B mode USG, Doppler USG and USG elastography imaging were combined. Doppler ultrasound exhibited the highest specificity at 77.8%, while B-mode ultrasound was identified as having the lowest accuracy, at 56.7%.

The combination of B-mode ultrasonography, Doppler ultrasonography, and elastography significantly enhances diagnostic accuracy for assessing cervical lymphadenopathy, providing a more reliable tool for distinguishing between benign and malignant conditions. This integrated approach outperforms single modalities, leading to improved patient management and treatment planning. The combined use of these imaging techniques demonstrated high sensitivity (92.3%) and specificity (88.8%). This increases the confidence in diagnosing malignancies, potentially reducing the need for invasive procedures in benign cases. This study also showed improved positive predictive value (80.0%) and negative predictive value (96.0%), which is crucial for making accurate clinical decisions

As both ultrasound and elastography were conducted simultaneously, with ultrasound examination preceding elastography, the diagnostic determination was primarily made during ultrasound, potentially introducing observer bias into our study. Strain elastography provided solely qualitative assessments of tissue stiffness, lacking the capability for quantitative measurements. In cases where patients presented with multiple lymph nodes, only a single node was selected for study. However, studying very large lymph nodes posed challenges due to limitations in the region of interest box, which could accommodate only a small amount of adjacent reference tissue.

Based on our findings, we advise against relying solely on strain elastography for evaluating lymph node malignancy. However, incorporating strain elastography alongside ultrasound and Doppler criteria can enhance diagnostic accuracy and comprehensive assessment

CONCLUSION:

This study highlights the significant diagnostic value of combining B-mode ultrasonography, Doppler ultrasonography, and elastography in evaluating cervical lymphadenopathy. The multi-modal approach significantly improved sensitivity, specificity, PPV, and NPV compared to using each modality alone.

Overall, our findings suggest that this combined method offers a more accurate and comprehensive tool for distinguishing between benign and malignant cervical lymphadenopathy, enhancing diagnostic accuracy and reducing the need for invasive procedures in benign cases. Future research should validate these results in larger, more diverse populations to further confirm the benefits of multi-modal imaging.

LIST OF ABBREVIATIONS:

CI - Confidence interval

FP – False positive

FN – False Negative.

LN - Lymph node

NPV – Negative predictive value.

PPV- Positive predictive value.

RTE - Real time elastography

TP – True positive

TN – True negative

US - Ultrasound

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