ARE WE JUSTIFIED IN SUPPLEMENTING ELASTOGRAPHY WITH HIGH RESOLUTION ULTRASONOGRAPHY FOR DIFFERENTIATING BETWEEN BENIGN AND MALIGNANT CERVICAL LYMPH NODES?

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ABSTRACT

BACKGROUND
Cervical lymphadenopathy is a very common condition being referred for evaluation in the radiology department. It is very much necessary to differentiate these cervical lymph nodes into benign and malignant which will change the course of treatment. We aimed at differentiation of the enlarged cervical lymph nodes into benign and malignant by B-mode Ultrasound and Elastography, comparing with histopathology.

MATERIALS AND METHODS
Sixty four lymph nodes from 64 patients were examined by both B-mode sonography and elastography and compared with histopathological correlation in this accuracy. On B-mode sonography, the lymph nodes were classified as malignant and benign based on their score with 8 as the cut-off (Benign ≤8, Malignant >8). Scoring was based on size, shape, echogenicity, margins and hilar appearance. These lymph nodes on elastographic examination were diagnosed as benign and malignant based on the patterns of elasticity, with patterns 1/2/3 as benign and patterns 4/5 as malignant. The patterns 1, 2, 3, 4, and 5 were assigned scores of 2, 4, 6, 8, and 10 respectively. The combined score for each lymph node was the sum of the B-mode and elastographic scores. A statistically cut-off line between metastatic and reactive was set between scores 12 and 13. Scores 7–12 was determined to be reactive, and scores 13–20, metastatic. The final scores were compared with the histopathological findings.

RESULTS
Sensitivity, specificity and accuracy of B-mode sonography was 80%, 50% and 59% respectively; 86%, 61% and 71% for elastography; and 81%, 62% and 75% for the combined evaluation.

CONCLUSION
Elastography has better sensitivity, specificity and accuracy in detecting malignant cervical lymph nodes than B-mode sonography, and the combined sonographic evaluation (B-mode with elastography) improves the accuracy.

KEYWORDS
Elastography, B-Mode Sonography, Malignant Lymph Nodes.

BACKGROUND
Elasticity is a mechanical tissue character, which restrains the movement of tissues when pressure is applied. It varies in different types of tissues (fat, collagen and so forth) and in the same tissue in different pathologic states (inflammatory, malignant).[1] During the past few years, sonographic elastography, magnetic resonance elastography and some other techniques have performed digital measurements of tissue hardness.[2] In sonographic elastography, image representation of tissue hardness can be obtained using a conventional sonography machine with special software and a conventional ultrasound probe.[3,4]

Sonographic elastography has been used to examine several organs. The breast, thyroid, prostate, cervix, liver and so forth.[5] The head and neck contains 60 to 70 lymph nodes of the 400 to 450 in the human body.[6] Differentiation between reactive and metastatic lymphadenopathy is vital and one of the differentiating criteria is hardness (elasticity) of the lymph node.

MATERIALS AND METHODS
This was a prospective study from August to November 2016. 64 patients with cervical lymphadenopathy who were referred for sonography and ultrasound-guided fine needle aspiration cytology (FNAC) were the participants.

After obtaining written informed consent, patients underwent B-mode sonography, elastography and ultrasound-guided FNAC.

The study was conducted at Yenepoya Medical College Hospital. Lymph nodes from 64 patients were examined by both B-mode sonography and elastography and were later compared with histopathological correlation in this study.

After obtaining written consent from the patients, scans were done with a linear transducer 11L-D (4-10 MHz) in GE Voluson E8 Machine equipped with the real-time strain elastography. One radiologist with experience in conventional sonography and a novice in elastography performed the sonography.

The participants underwent B-mode sonography followed by elastography using same probe in the supine position with extended neck using a pillow below the shoulder. In case of multiple enlarged lymph nodes in same patient, the largest lymph node was studied. In case of no discrete lymph nodes being identified, smallest possible lymph node mass was selected for the study so that we could fit the lymph node in the elastography box. The scans were completed within a period of 5 to 10 minutes depending upon the case. In the same setting, FNAC of the lymph node was done and reports were collected within a period of 1 week.

B –Mode

For each lymph node studied, B-mode images were obtained and findings were documented in the below mentioned headings. The lymph nodes were classified according to the 1997 American Joint Committee on Cancer (AJCC) criteria for lymph nodes.[7,8,9]

1. Size (<1 cm -1, >1 cm-2).[9]
2. Longitudinal/Transverse diameter ratio (<0.6-1, >0.6-2).[7,10,11]
3. Shape (Oval -1, Round, -2).[7,10,11]
4. Echogenicity (Homogenous -1, Non-homogenous -2).[8,12]
5. Margins (Regular -1, Irregular -2).[7,13]
6. Hilar appearance (Present -1, Absent -2).[7,14]

Scores obtained by the B-mode ultrasound were summed up and the lymph nodes were classified as benign and malignant with 8 as the cut-off (Benign ≤8, Malignant >8).[5]

Strain Elastography

For strain elastography, linear transducer was placed over the lymph node and light manual pressure was applied with the transducer with gradual decompression until a stable image was obtained. ROI (Region of interest) of the Lymph node was compared with ROI of the adjacent muscle. Surrounding tissues like bone, blood vessels were avoided. The images were analysed and the lymph nodes were classified as benign and malignant based on their colour patterns as mentioned below. Ultrasonography elastogram was displayed over the B-mode image in a colour scale comprising, red for nodes with greatest elastic strain (soft), green for intermediate and blue for nodes with no strain (hardest) as shown in Figure 2.

Elastographic patterns were determined on the distribution and percentage of the lymph node areas with high elasticity-

1. Pattern 1, absent or a very small hard area (blue area)
2. Pattern 2, blue/hard area < 45% of the ROI
3. Pattern 3, blue/hard area ≥ 45% of the ROI
4. Pattern 4, peripheral hard/blue and central soft/red area
5. Pattern 5, hard area occupying entire lymph node with or without a soft rim.[5,6]

The patterns 1, 2, 3, 4, and 5 will be assigned scores of 2, 4, 6, 8, and 10 respectively.[5,6]

Scores obtained by the elastography were summed up and the lymph nodes were classified as benign and malignant with 8 as the cut-off (Benign ≤8, Malignant >8)[5] as shown in Table 1 and Figures 2-6.

The scores so obtained by B-mode ultrasound and Elastography were added up. A statistically supported cut-off line between metastatic and reactive was set. Scores 7–12 was determined to be reactive, and scores 13–20 Metastatic. Ultrasound-guided FNAC of all the enlarged cervical lymph nodes was performed under aseptic precaution using 21 gauge needles and sent for cytological study to the Department of Pathology (Radiological reports hidden), Yenepoya Medical College, Deralakatte. The Reports were collected within a period of 1 week to minimise errors. The final scores were compared with the histopathological findings.

Combined Evaluation of the Nodes

Combined score will be the total score of elastographic scores plus B-mode scores. A cut-off line between metastatic and reactive was set between scores 12 and 13, depending on the best accuracy. Scores 7–12 were determined to be reactive, and scores 13–20 metastatic.[15]

The lymph nodes were classified into benign and malignant based on the B-mode, Elastographic colour patterns and Strain ratios (Benign and malignant). The elastographic and B-mode analysis were carried out in 5 to 10 minutes time. After elastography evaluation, ultrasound-guided FNAC of all the enlarged cervical lymph nodes was performed under aseptic precaution using 21 gauge needles and sent for cytological study to the Department of Pathology (Radiological reports hidden), Yenepoya Medical College, Deralakatte. The Reports were collected within a period of 2 weeks to minimise errors.

Final Diagnosis

Lymph node was determined to be reactive or malignant on the basis of histopathology result which was our gold standard.

Ethical Considerations

In all patients, ultrasound and FNAC done on the request of their consulting physicians. Ethical clearance was obtained for the study by the ethical committee prior to the study.

RESULTS

Out of the 64 patients, 38 were male and 26 were female with a mean age of 42 years.

All the 64 patients underwent FNAC and their results are tabulated (Table 2).

B-mode Sonography

Several previous studies have been published before on diagnosis of malignant cervical lymph node by B-mode

sonography.[9-14] With short axis diameter cut-off of 10 mm, 20 of 64 lymph nodes were labelled as malignant (38 were actually malignant on HPE). Sensitivity and specificity of 71% and 50% noted respectively with insignificant p-value (0.08), whereas in a study by Lyschick et al[7] using a cut-off diameter of 8 mm the accuracy was 65%, seen to be slightly better when smaller sizes were used.

With the size/length ratio cut-off of 0.6, 24 of 64 lymph nodes were called as malignant. Sensitivity and specificity of 75% and 56% respectively with a significant p-value (0.011) was similar to previous studies supporting the round shape for malignant nodes.[7,10,11] Irregularity of margins in the lymph nodes as a criteria for malignancy had a poor sensitivity and specificity in our study. All the 64 lymph nodes examined showed absence of hila. But HPE showed 41% of these lymph nodes to be benign. Hence, the specificity of B-mode sonography was found to be less in this criterion. Heterogenous lymph nodes on B-mode were considered malignant in our study. With this criterion, we labelled 30 out of 38 lymph nodes as malignant with the sensitivity of 71% specificity of 63% and p-value being significant (0.007) as shown in Table 3.

With B-mode ultrasonography cut-off score of 8, we found sensitivity of 80%, specificity of 50% and NPV of 84%. P-value with this cut-off score was found to be significant (0.024) as shown in Table 5.

Elastography
With patterns 3, 4 and 5 considered as malignant, we found accuracy of 71% with sensitivity of 86% and specificity of 61%. The p-value of this was statistically significant (0.004) (Table 4 and Table 5), as compared to other studies as Lyshick et al[7], Alam et al[15] which had sensitivities of 85% and 83%, specificities of 98% and 100, accuracies of 92% and 89% respectively.

Combined Assessment
Elastography and B-mode sonography score were added up and a cut-off of 12 was set for benign nodes. With this criteria we achieved a sensitivity of 81% and specificity of 62% with a PPV of 68% and NPV 76%. The p-value for this cut-off was also significant (0.012).

Diagnostic Performance
The diagnostic performance of B-mode sonography, elastography and combined evaluation are shown in Table 5.

Pattern	Score	Description	Elastography
1	2	Absent or very small blue areas	Reactive
2	4	Small scattered blue areas ,total blue area <45%	Reactive
3	6	Large blue area ,total blue area ≥ 45%	Reactive
4	8	Peripheral blue area and central green area, suggesting central necrosis	Malignant
5	10	Blue area with or without a green rim	Malignant

Table 1. Pattern and Scoring of Elastography Findings

Type	No
Benign	28
Tubercular	4
Non-Granulomatous	24
Total	**28**
Malignant	36
Thyroid	18
Larynx	12
Lung	2
Breast	8
Others	6
Total	**36**

Table 2. Total Number of Benign and Malignant Lymph Node on Histopathology Evaluation

Sonographic Criteria	Lymph	Nodes	Accuracy (%)	P-value
	Reactive (%)	Metastatic (%)		
B-mode				
Short axis diameter			59	0.08
≤ 1 cm	18 (50)	18 (50)		
≥ 1 cm	8 (28)	20 (71)		
S/L ratio			65	0.011
≤ 0.6 mm	18 (56)	14 (43.8)		
≥ 0.6 mm	8 (25)	24 (75)		
Margin			53	0.029
Regular	22 (44)	28 (56)		
Irregular	4 (27)	10 (71)		
Hilum				
Present	0	0		
Absent	26 (41)	38 (59)		
Echogenicity			53	0.007
Homogenous	14 (63)	8 (36)		
Heterogenous	12 (28)	30 (71)		

Table 3. Results Based On B-Mode Criteria for Benign and Malignant Lymph Nodes

Total = 64		
Elastography	**Benign**	**Malignant**
1	10	4
2	16	8
3	0	20
4	2	4

Table 4. Results Based on Elastographic Criteria for Benign and Malignant Lymph Nodes

Diagnostic Performance	B-Mode Score	Elastography	Combined Score
Sensitivity (%)	80	86	81
Specificity (%)	50	61	62
Accuracy (%)	59	71	75
PPV	42	68	68
NPV	84	84	76
p-value	0.024	0.004	0.012

Table 5. Results of Diagnostic Capability of B-mode Sonography, Elastography, Combined Methods
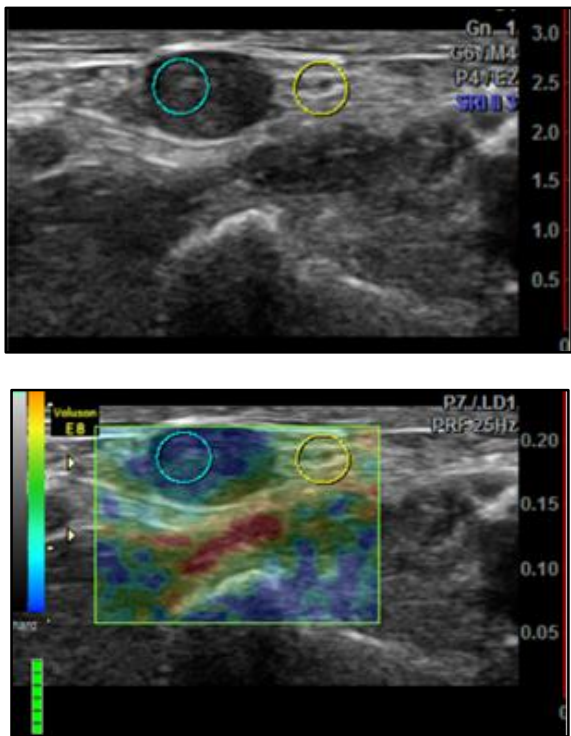
Figure 1. Elastography examination of level IV lymph node in a 50-year-old man. Elastogram appears on right of the box and is superimposed on a corresponding B-mode image .B-mode mage is displayed on the left side of monitor, Colour scale of tissue elasticity and frequency scale appear on the left upper and lower respectively. Final diagnosis was metastasis.
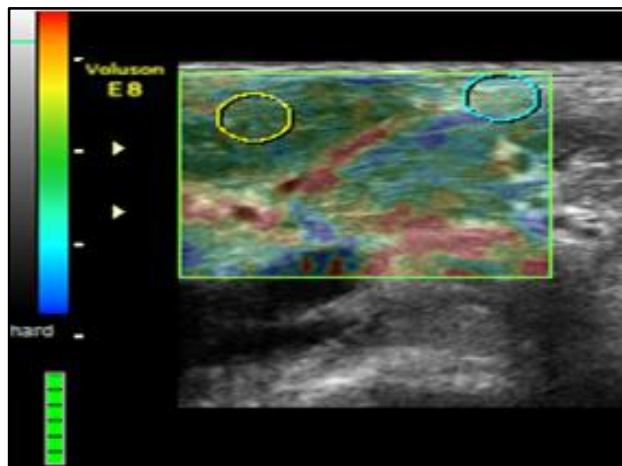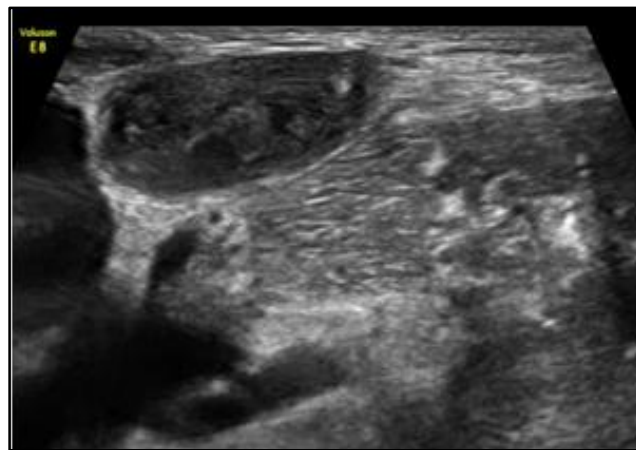

Figure 2. Diagrammatic appearance of five patterns of lymph nodes on Elastography

A.   Pattern 1: Absent or a very small hard area (blue area).
B.   Pattern 2: Blue/hard area < 45% of the ROI.
C.   Pattern 3: Hard area ≥45% blue/hard area ≥ 45% of the ROI.
D.   Pattern 4: Peripheral hard/blue and central soft/red area.
E.   Pattern 5: Hard area occupying entire lymph node with or without a soft rim.

Figure 3. Transverse sonogram of level V cervical lymph node in a 20-year-old man, B-mode on left shows score of 7, Elastography on left shows pattern 1 (score 2) benign lymph node.
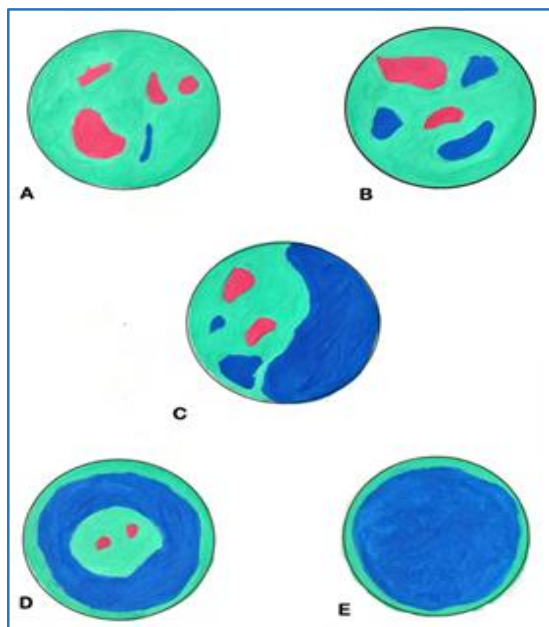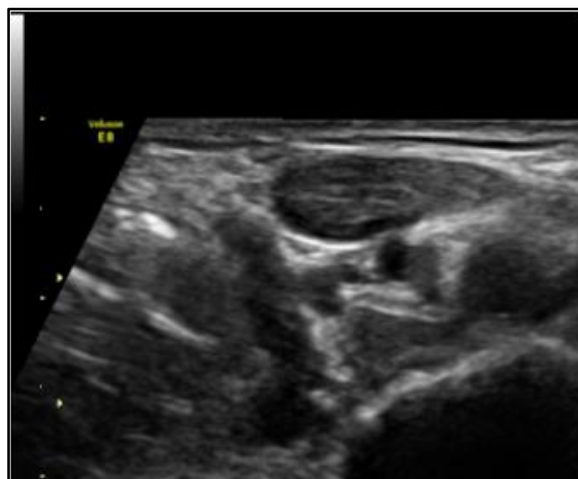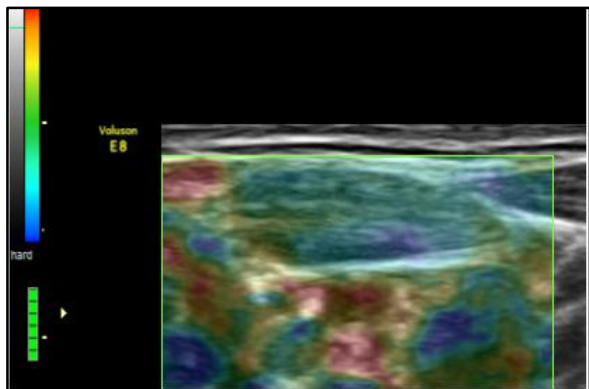
Figure 4. (a) Transverse sonogram of left level II cervical lymph node in a 53-year-old man, B-mode on the left showed score of 4, (b)Elastography showed pattern 2 (score 4) suggestive of benign lymph node.
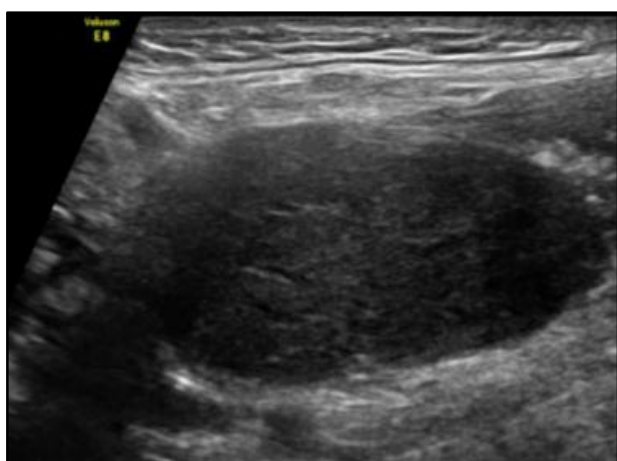

Figure 5. (a) Transverse sonogram of right level IV cervical lymph node in a 53-year-old man, B-mode sonography on the left showed B-mode score of 8, Elastography on the right showed pattern 3 (score 6).
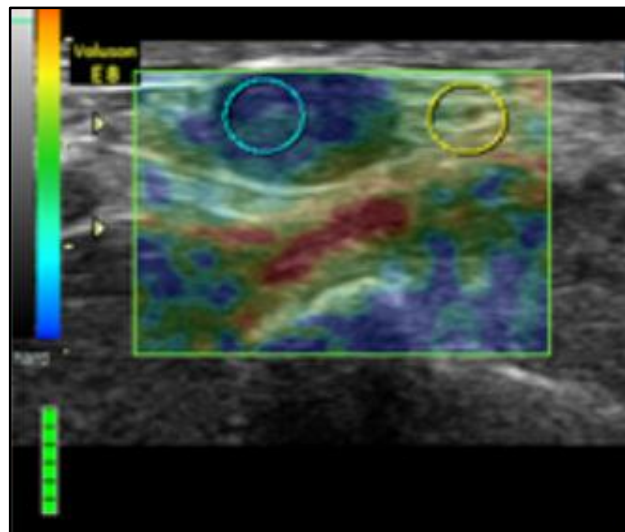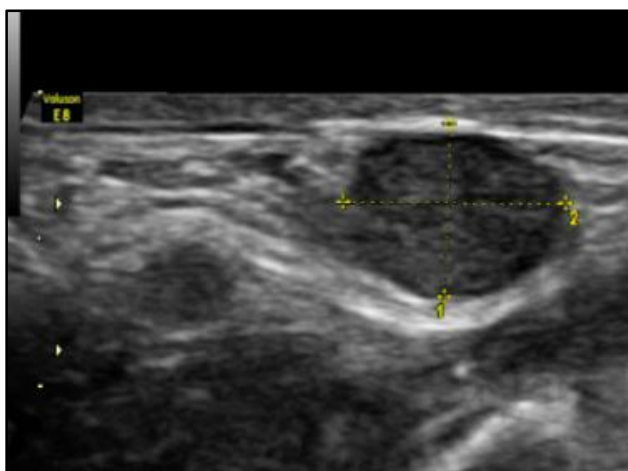

Figure 6. (a)Transverse B-mode sonogram of left level III cervical lymph node of a 55-year-old man showed score of 7, (b) Elastography showed pattern 4 (score 8).

Final HPE result was metastatic carcinoma from supraglottis

DISCUSSION
In this study, we have documented the accuracy of sonography and elastography individually and combined method in the differential diagnosis of benign versus malignant cervical lymph node.

B-Mode Sonography
Several previous studies have been published before on diagnosis of malignant cervical lymph node by B-mode sonography.[9-14] The accuracy of short axis diameter in our study was 59% and p value of 0.08 using cut-off diameter of 1 cm, whereas in a study by Lyschick et al[7] using a cut-off diameter of 8 mm the accuracy was 65%, seen to be slightly better when smaller sizes were used.

The S/L Ratio of ≤0.6 mm for benign nodes had accuracy of 65%, p value of 0.011 was similar to previous studies supporting the round shape for malignant nodes.[7,10,11]

Irregularity of margins in the lymph nodes as criteria for malignancy had a poor sensitivity and specificity in our study. In our study, the accuracy of lymph node margin as criteria to diagnose benign and malignant nodes was only about 53% with insignificant p value, suggesting that margins were no longer useful criteria. In our study, all the 64 LNs had absent hilum among which 26 lymph nodes (41%) were benign and 38 (59%) were malignant so the statistical data could not be calculated for this criterion.

Irregular margins of the lymph nodes and absence of hila as criteria for malignancy were found to be of no statistical significance in our study. Size of the lymph nodes more than 1 cm, S/L ratio of 0.6 cm, rounded lymph nodes and heterogeneity of the lymph nodes as criteria for malignant lymph nodes were statistically significant (p value <0.005).

Overall B-mode sonography had a sensitivity of 80% and specificity of 50%.

Elastography

Our study showed strain elastography had a sensitivity of 86%, specificity 61%, accuracy of 71% in diagnosing malignant lymph nodes as compared to other studies as Lyshick et al,[7] Alam et al[15] which had sensitivities of 85% and 83%, specificities of 98% and 100, accuracies of 92% and 89% respectively using both qualitative and quantitative criteria. Elastography had a better sensitivity and specificity than B-mode sonography.

Combined Evaluation

The accuracy and specificity of the combined evaluation was slightly higher than that of individual evaluations 75% and 62% respectively, suggesting that elastography can be added to B-mode sonography which will enhance the overall accuracy in diagnosing malignant lymph nodes.

Elastography and combined method provides better sensitivity and specificity than B-mode sonography alone. Elastography increases the accuracy of sonography in differentiating benign vs. malignant nodes.

Limitations

The study had some limitations.
1. Our data sample was small.
2. We compared lymph nodes from different regions of neck.
3. In case of no discrete lymph node, we used smallest lymph nodal mass for which no previous studies were available.
4. We used strain elastography for which the pressure was not defined and was subjective which would have led to alteration of the patterns with different radiologists.
5. Strain elastography is a less sensitive tool than shear wave elastography.
6. The study could not differentiate subtypes of benign and malignant lymph nodes (Differentiate reactive adenitis versus TB adenitis, Metastatic adenopathy versus Lymphoma).

CONCLUSION

Our study showed elastography has better sensitivity, specificity and accuracy in detecting malignant cervical lymph nodes than B-mode sonography and the combined sonographic evaluation improves the accuracy.

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