

COMPARISON OF ULTRASOUND ELASTOGRAPHY VERSUS B-MODE ULTRASOUND IN DIFFERENTIATING MALIGNANT FROM BENIGN CERVICAL LYMPH NODES

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ABSTRACT

Objective: To compare the diagnostic accuracy of ultrasound elastography with B-mode ultrasonography in differentiating malignant from benign cervical lymph nodes, keeping histopathology as gold standard.

Study Design: Comparative cross-sectional study.

Place and Duration of Study: Radiology department of Combined Military Hospital, Rawalpindi, from May to Oct 2016.

Methodology: After approval from hospital ethical committee a total of 246 patients with palpable cervical lymph node and age 20-50 years of either gender were collected by non probability purposive sampling. Patients with already proven histopathology, any chronic disease, history of prior irradiation, malignancy and trauma were excluded. The demographic details including name, age, gender, location race was noted on a predesigned research proforma. First of all, the registered patients underwent B mode ultrasound of cervical lymph nodes as benign or malignant on the basis of ultrasound features. All these patients were subjected to ultrasound elastography and categorized from score 1-4 on the basis of elastographic tissue stiffness. Patients with score of 1 and 2 were labeled as benign, while 3 and 4 were labeled as malignant. The tissue diagnosis/ histopathology was taken as reference gold standard for both B-mode ultrasound and ultrasound elastography findings.

Results: A total number of 246 patients with a mean age of 36.63 ± 8.52 years were registered. Mean size of lymph node was 2.32 ± 1.07 cm. The positive predictive value was found to be 94.70%, negative predictive value 92.6%, sensitivity 95.33%, specificity 91.67% and diagnostic accuracy of 93.90% for ultrasound elastography while that of B-mode USG positive predictive value was found to be 92.05%, negative predictive value 80.0%, sensitivity 87.97%, specificity 86.36% and diagnostic accuracy of 87.40%.

Conclusion: The study results concluded that diagnostic accuracy of ultrasound elastography was higher compared to B-mode ultrasonography in non invasively differentiating benign from malignant cervical lymph nodes.

Keywords: Elastography, Lymph nodes, Malignant, Sensitivity, Ultrasonography.

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INTRODUCTION

Evaluation of lymph nodes (LNs) in patients with different underlying diseases is important to decide current status, proper treatment and prognosis of the patients¹. It is crucial to differentiate malignant lymph nodes from benign lymph nodes to follow appropriate treatment. Cervical lymph nodes are enlarged in infections of head and neck as well as from metastatic more sinister malignant lesions. Head and neck tumors are

most common primary tumors that metastasize to cervical lymph nodes leading to enlargement of these lymph nodes². Other than metastases and infections, head and neck is a common site of primary malignant tumor such as lymphoma^{3,4}. The differentiation of various causes of lymph node enlargement is difficult clinically. Therefore, various non invasive investigative modalities are developed to differentiate malignant from benign lesions. The treatment options as well as prognosis of disease is based on accurate diagnosis of the disease leading to cervical lymph nodes enlargement. Therefore, correct identification of the disease is very essential⁴. Ghajarzadeh *et al*

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in his research work has shown the prevalence of malignant cervical lymph nodes in 53.63% of patients with cervical lymphadenopathy⁵⁻⁷. The gold standard for evaluating enlarged LNs is pathologic examination of obtained tissue. Although fine-needle aspiration (FNA) is considered as the most efficient method for differentiating benign and malignant LNs, it is considered as an invasive method which is prone to sampling errors and analytic uncertainty⁸.

Currently various imaging techniques such as ultrasound, CT (computed tomography) and MRI (magnetic resonance imaging) are used to differentiate benign from malignant lymph nodes^{9,10}. In the current clinical practice, most common initial investigation of choice is high-frequency ultrasound imaging. It is used as initial noninvasive screening test for the diagnostic workup of superficial lymph nodes. B mode ultrasound, power doppler and color doppler ultrasonography are various high frequency ultrasound techniques, that are frequently used. These imaging modalities can display the location, size, shape and internal vascularity distribution of the lesion and these features of the lesion play a key role in the differentiating between varied differential diagnosis of enlarged lymph nodes.

As the available literature on accuracy of ultrasound elastography in diagnosing and differentiating benign cervical lymphadenopathy from malignant or metastatic cervical lymph nodes enlargement is limited in our local settings, therefore this study was conducted to find out the diagnostic accuracy of this imaging modality in comparison to B-mode ultrasonography. The rationale of conducting this study was to use a non invasive, less expensive, easily available modality of ultrasound elastography combined with B mode ultrasound in differentiating benign from malignant lymph nodes keeping histopathology as a gold standard. This would help us in designing a guideline/protocol for early screening and noninvasive diagnosis of cervical lymphadenopathy as benign or malignant and

decrease the requirement for invasive biopsies/ FNAC for histopathological assessment.

METHODOLOGY

The current comparative cross sectional study as conducted on 246 patients with palpable cervical lymph nodes referred by doctors to the Radiology department, Combined Military Hospital, Rawalpindi for ultrasonography. Patients with already proven histopathology, any chronic disease i.e., tuberculosis and diabetes mellitus, history of prior irradiation and history of trauma were excluded from the study. Sample was collected by non probability purposive sampling and sample size was collected by WHO calculator which appeared to be 240 patients. Informed written consent and relevant history was taken from all the registered patients. The demographic details including name, age, gender, location, racetrac were noted on a predesigned research proforma. First of all, the registered patients underwent B mode ultrasound of enlarged cervical lymph nodes by consultant radiologist (first author) and labeled as benign or malignant on the basis of ultrasonographic features. After this all these patients were subjected to ultrasound elastography using a linear array probe centered at 7.5 MHz of high-resolution ultrasound unit by the same radiologist. Patients were categorized from score 1-4 on the basis of elastographic tissue stiffness. Patients with score of 1 and 2 were labeled as benign, while 3 and 4 were labeled as malignant. B-mode ultrasound and USG elastography findings were correlated with histopathological report which was done in the institutional pathology laboratory and was done by consultant pathologist with post-fellowship experience of at least 5 years. All the data were recorded on a specially designed research proforma.

All the collected data were then analyzed in computer software SPSS-21. Standard deviation (SD) and mean were calculated for quantitative variables such as duration of disease, age and size of lymph node. Percentage and frequency were then calculated for qualitative variables i.e. benign and malignant cervical lymph node and

gender. 2x2 contingency table was used to calculate positive predictive value, negative predictive value, sensitivity and specificity along with diagnostic accuracy of ultrasound elastography and B-mode ultrasonography in differentiating malignant and benign cervical lymph node, taking histopathology as gold standard.

RESULTS

Out of total of 246 patients, 118 (47.97%) were male patients and 128 (52.03%) were female patients with ratio of 1:1.2. Age of the patients

confirmed malignant cervical lymph node in 151 (61.38%) cases. In USG elastography positive patients, 7 were false positive and 143 were true positive. Among 96, USG elastography negative patients, 88 were true negative and 8 were false negative ($p=0.926$) as shown below in table-II. B-mode USG findings supported the diagnosis of malignant cervical lymph node in 158 (64.23%) patients. Histopathology findings confirmed malignant cervical lymph node in 151 (61.38%) cases. In B-mode USG positive patients, 19 were

Table-I: Age, duration of disease and size of Lymphnodes of patients.

Variable	n=246		
	Minimum	Maximum	Mean ± SD
Age (years)	20	50	36.63 ± 8.52 years
Duration of disease (Months)	04	11	7.76 ± 3.29
Size of lymph node (centimeters)	02	3.5	2.32 ± 1.07

Table-II: Results of elastography and B mode ultrasound in comparison with histopathology.

	Positive result on histopathology	Negative result on histopathology	p-value
Positive on Ultrasound Elastography	143 (TP)*	07 (FP)***	0.0001
Negative on Ultrasound Elastography	08 (FN)**	88 (TN)****	
Positive on B Mode Ultrasound	139 (TP)*	19 (FP)***	0.0001
Negative on B Mode Ultrasound	12 (FN)**	76 (TN)****	

*-TP=True positive **-FP=False positive ***-FN=False negative ****-TN=True negative

varied from 20 to 50 years with estimated mean age of 36.63 ± 8.52 years. Mean duration of disease was 7.76 ± 3.29 months (table-I). Mean

false positive and 139 were true positive. Among the 88, B-mode USG negative patients, 68 were true negative and 12 were false negative ($p=0.514$)

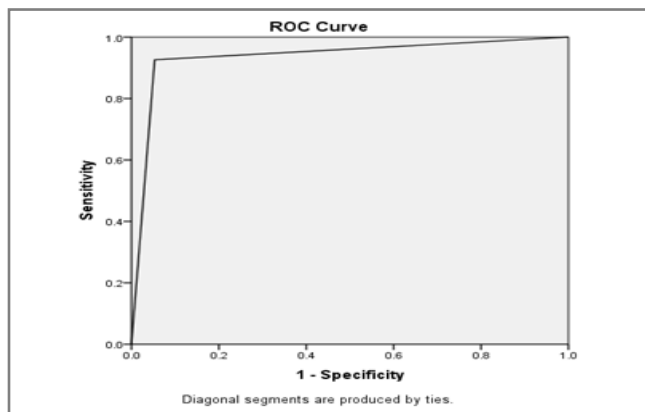


Figure-1: ROC curve of ultrasound elastography taking histopathology as gold standard.

size of lymph node was 2.32 ± 1.07 cm (table-I). USG elastography results supported the diagnosis of malignant cervical lymph node in 150 (60.98%) patients. Histopathological findings

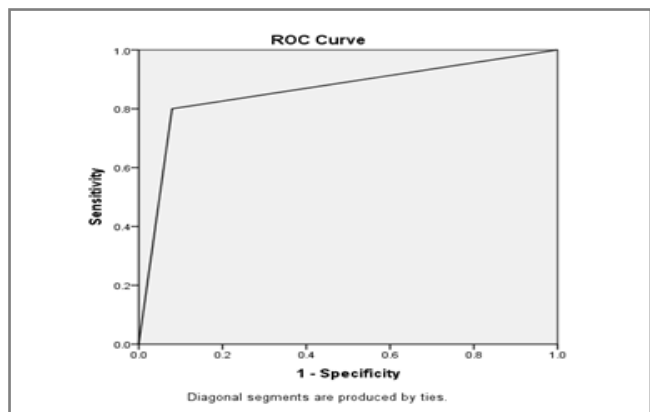


Figure-2: Shows ROC curve of B mode ultrasound taking histopathology as gold standard.

shown in table-II. Figure-1 & 2 shows ROC curve of ultrasound elastography and B mode ultrasound respectively.

DISCUSSION

Ultrasound elastography is the radiological investigation to determine the elastic properties of the soft tissues¹¹. Direct measurement of elastographic properties of biological structures and tissues is difficult to assess and therefore, indirect methods are devised to measure and approximately estimate stiffness of tissues. The elastogram is the image used to display the tissue compression results. In the elastogram, softer areas appear brighter while stiff areas appear dark¹²⁻¹⁴.

We did this study at our setup to determine the diagnostic accuracy of ultrasound elastography by comparing it with B-mode ultrasonography which was followed by histopathological confirmation. Histopathological diagnosis is the gold standard investigation for diagnosis of benign or malignant lesion and was taken as standard for comparison of results of both ultrasound elastography as well as B mode ultrasound. Out of these 246 patients, USG elastography supported the diagnosis of malignant cervical lymph node in 150 (60.98%) patients. Histopathology evaluation confirmed malignant cervical lymph node in 151 (61.38%) cases. In USG elastography, seven patients were false positive and 143 were true positive. Among 96 patients who were diagnosed as benign cases on USG elastography, 88 were true negative while only 8 were false negative ($p=0.926$). The overall specificity, sensitivity, positive predictive value, negative predictive value and diagnostic accuracy of ultrasound elastography was 92.63%, 94.70%, 91.67%, 95.33% and 93.90% respectively in segregating malignant from benign cervical lymph nodes.

On the other hand, B-mode USG findings supported the diagnosis of malignant cervical lymph node in 158 (64.23%) patients. Histopathological findings confirmed malignant cervical lymph node in 151 (61.38%) cases. In B-mode ultrasound positive patients, true positive were 139 while 19 patients were false positive. Out of total 88, B-mode USG negative patients, false

negative were 12 whereas 68 were true negative ($p=0.514$). The collective specificity, sensitivity, negative predictive value, positive predictive value and diagnostic accuracy of B-mode ultrasonography in differentiating malignant from benign cervical lymph nodes was 80.0%, 92.05%, 86.3%, 87.97% and 87.40% respectively. In a study, conducted by Bhatia *et al* and Choi *et al*, the sensitivity of elastographic ultrasound was found to be 93.8% and specificity was 89.5% in differentiating benign and malignant cervical lymph nodes. Sensitivity, specificity, and accuracy of B-mode sonography on the other hand were 98%, 59%, and 84%, respectively^{15,16}. ROC curve in fig-1 & 2 depicts that ultrasound elastography is significantly superior to B mode ultrasound in terms of both sensitivity and specificity.

According to a early meta-analysis carried out by Alam *et al*, where they analyzed dozen of studies on role of strain elastography in assessment of 50-155 axillary or cervical lymph nodes. This meta-analysis showed that mean specificity and sensitivity values were 90% (95% CI, 82% to 94%) and 74% (95% confidence interval [CI], 66% to 81%) for elastographic scale and 81% (95% CI, 49% to 95%) and 88% (95% CI, 79% to 93%) using strain ratios for each, respectively for detecting malignancies¹⁷. Roseline *et al* have also shown the sensitivity (78.57% - Confidence Interval 49.21% - 95.09%), specificity (84.62% - Confidence Interval 65.11% - 95.55%) and Diagnostic Accuracy (0.83) of B -mode Ultrasonography versus histopathology. They also assessed the sensitivity (71.43% - Confidence Interval 41.92% - 91.43%), specificity (92.31% - Confidence Interval 74.83% - 98.83%) and diagnostic Accuracy (0.85) ultrasound elastography versus Histopathology¹⁸.

In assessment of lymph nodes by ultrasound elastography, a four-point elastography scale is frequently employed for detection of malignancy in cervical lymph nodes. The stiffness is graded from 1-4, considering 4 being stiffest while grade 1 as very mildly stiff. A metastatic lymph node shows more stiffness as compared to benign lymph nodes, so elastographic scale scores of 1-2 indicate benign lymph nodes whereas

elastographic scale scores of 3-4 suggests malignant lymph nodes¹⁷.

CONCLUSION

After analyzing the results of this study and comparing it with already published international data, it can easily be concluded that the diagnostic accuracy of ultrasound elastography is higher than B-mode ultrasound in differentiating a benign cervical lymph node from malignant. This will improve patient care by early screening with resultant reduced time delay in starting the treatment and avoiding unnecessary invasive investigations, which consequently reduces patients' morbidity and mortality.

CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

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