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COMPARATIVE PERFORMANCE OF TWO-DIMENSIONAL ULTRASONOGRAPHY AND ELASTOGRAPHY FOR SUSPECTED AXILLARY LYMPH NODE METASTASIS OF BREAST CANCER, KEEPING HISTOPATHOLOGY AS GOLD STANDARD

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ABSTRACT

Background: Evaluating axillary lymph node (ALN) status remains a key step in staging and managing breast cancer. We aimed to compare the diagnostic performance of two-dimensional ultrasonography and elastosonography in identifying suspected ALN metastasis, using histopathology as the gold standard.
Methods: We enrolled 175 patients with clinically suspected ALN involvement. Each patient underwent both ultrasonography and elastosonography, followed by histopathological confirmation. We calculated sensitivity, specificity, positive and negative predictive values, and overall accuracy for each imaging method.
Results: Histopathology confirmed metastatic involvement in 81 patients (46.3%). Ultrasonography identified malignant nodes with 41.9% sensitivity and 60.6% specificity. Elastosonography showed higher sensitivity (58.0%) but lower specificity (45.7%). Diagnostic accuracy remained similar for

IRB- 3715/DUHS/Approval/2024/34 **Submitted Date: 15/05/2025** **Accepted Date: 28/05/2025** **Published Date: 04/06/2025** **Journal of Medical & Health Sciences Review**	both modalities—52.0% for ultrasonography and 51.4% for elastosonography. **Conclusion:** Both ultrasonography and elastosonography offer moderate diagnostic value in assessing ALN metastasis. Elastosonography increases sensitivity but leads to more false positives. Clinicians should use these tools to support, rather than replace, histopathological evaluation in treatment planning.

INTRODUCTION

Breast carcinoma is the most common malignant tumor in women that leads to highest rate of mortality in females including both young and old age groups. The important parameters of the tumor, that determine the prognosis of patients include dimensions, grade, human epidermal growth factor receptor 2 (HER-2) status, axillary lymph node involvement and metastasis.[1-2]

The axillary lymph node involvement in breast cancer patients, is one of the most important prognostic factors that influences the management of such patients. The study regarding prevalence of axillary lymph node metastasis in patients with pure tubular carcinoma of breast is reported as 27%.[3] The five-year survival rate decreases by 40% in breast cancer patients with axillary lymph node metastasis as compared to breast cancer patients without axillary lymph node involvement.[4] Ultrasonography, elastography, mammography, CT scan, MRI and PET-CT are non-invasive imaging modalities to assess the axillary lymph node metastasis. Mammography is the best imaging tool for breast cancer screening and diagnosis; but it has limited role in evaluation of axillary lymph node as it does not cover the entire axilla. MRI breast provides exceptional images due to better soft-tissue resolution, but it is not possible to include each group of axillary lymph nodes due to the fact that breast coil has restricted range.[5] Furthermore, the cost of breast MRI is very high and it is not available in every setup. Ultrasonography is commonly used imaging modality due to easy availability, non-invasive, low cost and radiation free quality. This modality can provide comprehensive details in context of metastasis involving all groups of axillary lymph nodes and it is commonly used in clinical practice as compared to various above mentioned imaging modalities. Ultrasound elastography is a new emerging non-invasive modality that determines the deformation degrees of tissues that have different hardness co-efficient after being compressed by external forces.[6] The stiffness of the lymph node is an important factor that is not assessed by two dimensional gray scale ultrasound. Elastography technique provides coded maps which are colored specifying the elasticity of various portions of targeted tissue and determines an elasticity score to differentiate between benign and malignant lymph node. A study was conducted by Zhao et al,[7] and its report included the details regarding the Sensitivity, Specificity and Accuracy of two-dimensional ultrasonography and elastography for the purpose of involvement of axillary lymph node in breast cancer patients and the results were as follows: 77.3% versus 86.4%, 76.5% versus 85.3% and 76.9% versus 85.9% respectively. Furthermore, according to another study reported, Sensitivity, Specificity, Positive and Negative predictive value of the two dimensional ultrasound and elastography were as follows: 75%, 71% , 58% and 89%, and 71%, 72%, 50% and 86% respectively.[8] For the management of breast cancer patients , the status of lymph node is paramount in order to provide assistance to medical practitioners for

making the preoperative and surgical decisions. The current study aimed to evaluate the diagnostic value of the distinct applications of the conventional ultrasound and elastography.

MATERIALS AND METHODS

This descriptive cross-sectional study was conducted in the Radiology Department of Dr. Ruth K.M. Pfau Civil Hospital, Karachi, over the course of one year following ethical approval by the Institutional Review Board (IRB) of Dow University of Health Sciences (DUHS), Karachi. The study aimed to assess the diagnostic performance of two-dimensional ultrasonography and elastography in detecting axillary lymph node metastasis among breast cancer patients, using histopathology as the reference standard. The sample size was calculated using Dr. Lin Naing's sample size calculator based on a sensitivity of 77.3%, specificity of 76.5%, and a prevalence rate of axillary lymph node metastasis of 27%. With a 10% margin of error and 95% confidence interval, a total of 175 participants were required. A non-probability consecutive sampling technique was employed for recruitment.

Female patients aged between 18 and 70 years, presenting with clinically suspected axillary lymph nodes and referred for biopsy by the attending clinician, were eligible for inclusion. Patients were excluded if they had a prior history of neoadjuvant therapy, were previously diagnosed with axillary metastases, or declined to provide consent. Once IRB approval was granted, eligible patients were identified and invited to participate. All participants were provided with a detailed explanation of the study's objectives and procedures, after which informed written consent was obtained. Baseline demographic and clinical data were recorded using a structured proforma.

Each enrolled participant underwent gray-scale two-dimensional ultrasonography followed by elastography. The gray-scale ultrasound was performed by a radiologist with five years of experience using a Toshiba Diagnostic Ultrasound System (TUS-X100S, Japan) equipped with a 7.5 MHz linear array transducer. Diagnostic criteria for malignancy included one or more of the following features: round shape, irregular hypoechoic texture, absence or displacement of the fatty hilum with cortical thickness greater than 2.5 mm, and high-resistance Doppler flow with a resistance index exceeding 0.7. Subsequently, elastography was conducted by a second radiologist with five years of sonographic experience using the SuperSonic Imagine system (SSIP92001, France). Elastograms were graded on a scale from 1 to 5 based on tissue stiffness, with scores of 1 or 2 considered indicative of benign lymph nodes, and scores of 3, 4, or 5 suggestive of malignant/metastatic nodes. Lymph nodes were further categorized based on the presence or absence of visible hila.

Following imaging, patients were referred to their respective clinicians for multidisciplinary evaluation. Decisions regarding biopsy were jointly made by the clinical and radiology teams. Ultrasound-guided biopsy was performed by a consultant radiologist with specialized experience in women's imaging and interventions. Tissue samples were sent to the pathology laboratory for histological confirmation of axillary lymph node metastasis. Data management involved secure storage of both hard and electronic copies of patient information, labeled only with unique participant IDs. Data entry was conducted by trained personnel and stored on password-protected systems to ensure confidentiality and data integrity.

All collected data were analyzed using SPSS version 26. Descriptive statistics were presented as mean ± standard deviation or median with interquartile range (IQR) for continuous variables, and frequencies with percentages for categorical variables. The Shapiro-Wilk test was used to assess the normality of continuous data. Diagnostic

performance parameters—including sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall diagnostic accuracy—were calculated using 2x2 contingency tables. Potential confounding variables such as age, duration of lymphadenopathy, and family history of malignancy were controlled through stratification, with post-stratification analysis performed using additional 2x2 tables.

RESULTS

A total of 175 patients suspected of having axillary lymph node metastasis of breast cancer who met the inclusion criteria were enrolled in the study. The mean age was 44.51±15.19 years. Out of 175, 73 (41.7%) patients belonged to age group 18-45 years and 102 (58.3%) belonged to age group 46-70 years. Amongst the patients 48 (27.4%) and 127 (72.6) had lymph node for ≤ 15 and > 15 days respectively. Overall, 81 (46.3%), 71 (40.6%) and 98 (56%) had positive metastatic axillary lymph node on histopathology, ultrasound and elastosonography. (Table 1)

Using ultrasound and taking histopathology as gold standard for diagnosis of metastatic axillary lymph node, true positives (TP) were recorded as 34, false positives (FP) 37, false negatives (FN) 47 and true negatives (TN) as 57. Sensitivity was 41.9%, specificity was 60.6%, positive predictive value (PPV) was 47.8%, negative predictive value (NPV) was 54.8% and diagnostic accuracy (DA) was 52.0%. (Table 2-4)

Moreover, elastosonography and taking histopathology as gold standard for diagnosis of metastatic axillary lymph node, true positives (TP) were recorded as 47, false positives (FP) 51, false negatives (FN) 34 and true negatives (TN) as 43. Sensitivity was 58.0%, specificity was 45.7%, positive predictive value (PPV) was 47.9%, negative predictive value (NPV) was 55.8% and diagnostic accuracy (DA) was 51.4%. (Table 3-4)

DISCUSSION

The accurate evaluation of axillary lymph node (ALN) metastasis is a cornerstone in the staging and management of breast cancer, influencing surgical planning, systemic therapy, and prognostication. This study aimed to compare the diagnostic performance of two-dimensional ultrasonography (2D US) and elastosonography in detecting suspected ALN metastases, using histopathology as the reference standard.

The results demonstrated that while elastosonography had a higher sensitivity (58.0%) compared to 2D US (41.9%), it exhibited a lower specificity (45.7% vs. 60.6%). The overall diagnostic accuracy of both modalities was comparable, with values of 52.0% for 2D US and 51.4% for elastosonography. These findings suggest that each modality possesses distinct strengths and limitations, and that neither alone is sufficiently reliable to replace histopathological confirmation.

Ultrasonography remains a widely used, non-invasive, and cost-effective modality for initial assessment of ALNs. It can identify morphological abnormalities suggestive of malignancy, such as cortical thickening, round shape, and loss of fatty hilum.[9-11] However, these criteria are operator-dependent and may be limited in detecting micrometastases or in differentiating reactive from malignant nodes. [12-13] In the present study, 2D US demonstrated moderate specificity but poor sensitivity, resulting in a high false negative rate (47/81 cases), which may lead to underestimation of nodal involvement.

Elastosonography, an imaging technique that evaluates tissue stiffness, showed improved sensitivity, likely due to the higher rigidity of metastatic nodes caused by increased cellularity and stromal desmoplasia. [14-16] However, its specificity was reduced, potentially due to false positives in inflammatory or fibrotic nodes, which also exhibit increased stiffness. [17] These limitations align with previous literature, where elastography has been noted to overestimate malignancy in benign reactive or granulomatous lymphadenopathies. [18]

Our findings align with other studies that have highlighted the value of combining imaging modalities for better diagnostic performance. For example, one study. reported that the integration of elastography with conventional ultrasound improved sensitivity and diagnostic confidence in assessing ALNs. [19] Similarly, other studies emphasized that elastography alone should not be used in isolation due to its variability and dependency on lymph node type and tissue composition. [20-21]

Although elastography demonstrated higher sensitivity, its modest accuracy and specificity limit its standalone utility in clinical decision-making. Moreover, our results emphasize that even when advanced imaging is employed, false negatives and false positives remain clinically significant. This reinforces the role of histopathological confirmation, which remains the gold standard for definitive diagnosis of ALN status, especially prior to surgical or systemic treatment decisions. [22]

Given the modest diagnostic performance of both modalities individually, a multimodal approach, where morphological evaluation by 2D US is complemented by functional stiffness analysis through elastosonography, may offer a more comprehensive preoperative assessment. Such integration can potentially reduce unnecessary biopsies or avoid undertreatment, particularly in resource-limited settings where MRI or PET/CT may not be feasible.

LIMITATIONS

This single-center study may limit generalizability. We did not assess interobserver variability or evaluate the combined use of imaging modalities. Histopathological confirmation relied partly on core needle biopsies, which may miss micrometastases. Long-term follow-up and advanced imaging comparisons were not included.

CONCLUSION

Our findings show that both two-dimensional ultrasonography and elastosonography provide diagnostic information for evaluating axillary lymph node metastasis among breast cancer patients. Elastosonography improved sensitivity but at the cost of specificity. Clinicians should view these tools as supportive rather than standalone diagnostics. Histopathology remains critical for confirming lymph node involvement and guiding treatment decisions.

CONFLICT OF INTEREST

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

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TABLE 1: CHARACTERISTICS OF PATIENTS

DEMOGRAPHY		NUMBER	PERCENTAGE
AGE	**18-45 YEARS**	73	41.7%
	46-70 YEARS	102	58.3%
DURATION OF LYMPH NODE	**≤ 15 DAYS**	48	27.4%
	> 15 DAYS	127	72.6%
FAMILY HISTORY OF MALIGNANCY	**YES**	91	52.0%
	NO	84	48.0%
MALIGNANT AXILLARY LYMPH NODE ON HISTOPATHOLOGY	**POSITIVE**	81	46.3%
	NEGATIVE	94	53.7%
MALIGNANT AXILLARY LYMPH NODE ON ULTRASOUND	**POSITIVE**	71	40.6%
	NEGATIVE	104	59.4%
MALIGNANT AXILLARY LYMPH NODE ON ELASTOSONOGRAPHY	**POSITIVE**	98	56.0%
	NEGATIVE	77	44.0%

TABLE 2: DIAGNOSTIC ACCURACY OF ULTRASOUND USING HISTOPATHOLOGY AS GOLD STANDARD FOR THE DIAGNOSIS OF MALIGNANT AXILLARY LYMPH NODE

VARIABLE		HISTOPATHOLOGY		TOTAL
		POSITIVE	NEGATIVE	
ULTRASOUND	**POSITIVE**	34(TP)	37(FP)	71
	NEGATIVE	47(FN)	57(TN)	104
TOTAL		81	94	175

TABLE 3: DIAGNOSTIC ACCURACY OF ELASTOSONOGRAPHY USING HISTOPATHOLOGY AS GOLD STANDARD FOR THE DIAGNOSIS OF MALIGNANT AXILLARY LYMPH NODE

VARIABLE		HISTOPATHOLOGY		TOTAL
		POSITIVE	NEGATIVE	
ELASTOSONOGRAPHY	POSITIVE	47(TP)	51(FP)	98
	NEGATIVE	34(FN)	43(TN)	77
TOTAL		81	94	175

TABLE 4: SENSITIVITY, SPECIFICITY, POSITIVE AND NEGATIVE PREDICTIVE VALUES AND DIAGNOSTIC ACCURACY OF THE ULTRASOUND & ELASTOSONOGRAPHY USING HISTOPATHOLOGY AS GOLD STANDARD FOR THE DIAGNOSIS OF MALIGNANT AXILLARY LYMPH NODE

VARIABLE	SENSITIVITY	SPECIFICITY	POSITIVE PREDICTIVE VALUE	NEGATIVE PREDICTIVE VALUE	DIAGNOSTIC ACCURACY
ULTRASOUND	41.9%	60.6%	47.8%	54.8%	52.0%
ELASTOSONOGRAPHY	58.0%	45.7%	47.9%	55.8%	51.4%