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Research Article

Diagnostic Accuracy of Axillary Ultrasound for Detecting Metastatic Lymph Nodes in Breast Cancer Patients

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Abstract

Background: Accurate assessment of axillary lymph node (ALN) involvement is critical for optimal management in breast cancer. Sentinel lymph node biopsy (SLNB) has reduced morbidity compared to complete axillary lymph node dissection (ALND), yet it remains an invasive procedure. Preoperative ultrasound (US) could help identify node-negative patients who may potentially avoid extensive surgery.

Objectives: In this study, we aimed to evaluate the diagnostic performance of US in predicting metastatic ALNs compared to surgical pathology in a cohort of Iranian breast cancer patients.

Methods: In this retrospective cross-sectional study, we evaluated 187 women with breast cancer (mean age 49.94 ± 11.32 years) treated from 2016 to 2021 at Shohada-e Tajrish Hospital, Tehran, Iran. All underwent preoperative US of the axilla followed by SLNB and/or ALND. We calculated US sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV). "Strict" criteria defined only definitively malignant nodes as positive, whereas "expanded" criteria considered suspicious nodes as positive.

Results: Of 187 patients, 158 (84.49%) underwent SLNB, with a mean of 3.61 ± 2.4 nodes examined (53/158 [33.54%] had metastases), and 55 (29.41%) underwent ALND, with a mean of 8.73 ± 5.00 nodes examined (21/55 [38.18%] positive). Using strict criteria, US sensitivity was 44.68%, specificity 81.11%, PPV 55.25%, NPV 73.74%. Expanded criteria improved sensitivity to 61.19% but reduced specificity to 60.83%. Neoadjuvant chemotherapy (NAC) [administered to 54 (28.9%)] further affected US accuracy.

Conclusions: Expanded US criteria yielded higher sensitivity but lower specificity, underscoring the trade-off between detecting more true positives and overcalling benign nodes. Prospective multi-center trials are warranted to clarify whether an expanded approach can safely reduce invasive staging.

Keywords: Breast Cancer, Axillary Lymph Nodes, Ultrasound, Sentinel Lymph Node Biopsy, Sensitivity, Specificity

1. Introduction

Breast cancer is the most commonly diagnosed malignancy among women worldwide and remains a leading cause of cancer-related morbidity and mortality. Axillary lymph node (ALN) status is pivotal for staging, guiding adjuvant therapy, and influencing prognosis.

Multiple clinical and molecular factors influence ALN involvement in breast cancer. Recent evidence using machine learning approaches has highlighted that tumor grade, histological subtype, tumor location, and biomarkers such as ER, PR, p53, and Ki67 significantly affect the likelihood of nodal metastasis (1). These findings underscore the complexity of axillary staging

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and support the need for reliable preoperative imaging, such as axillary ultrasound (US), to accurately identify node-positive patients and guide surgical management.

Historically, a complete axillary lymph node dissection (ALND) was standard, but it is associated with complications such as lymphedema and restricted shoulder mobility. Sentinel lymph node biopsy (SLNB) now offers a less morbid alternative, removing only a few nodes most likely to contain metastases if present (2, 3). Accurate assessment of ALNs is critical not only for staging and guiding therapy in breast cancer but also to minimize procedure-related complications. Although SLNB has reduced morbidity compared to complete ALND, studies have shown that removal of a higher number of negative nodes may increase the risk of lymphedema (4). This underscores the importance of reliable, noninvasive preoperative imaging methods such as axillary US to identify node-negative patients and potentially avoid unnecessary invasive procedure.

Nevertheless, SLNB itself is still invasive, and in patients who are truly node-negative, the procedure may be unnecessary. A reliable noninvasive imaging modality capable of accurately identifying nodal metastases could reduce the number of negative SLNB procedures. Among available imaging methods, US is widely accessible and cost-effective, making it a primary tool for preoperative axillary assessment in many centers (5, 6). However, its reported diagnostic accuracy varies greatly depending on the population studied, operator skill, and especially the definition of a "positive" node (7, 8).

Criteria for defining positive lymph nodes vary across studies , reflecting differences in sensitivity and specificity.

Despite numerous investigations into the utility of US for axillary staging, limited data exist in Middle Eastern populations comparing “strict” vs. “expanded” US criteria. This study addresses that gap, focusing on an Iranian breast cancer cohort and assessing how different diagnostic cutoffs for US can influence management decisions.

2. Materials and Methods

2.1. Study Design and Ethical Considerations

This retrospective cross-sectional study was conducted at the Cancer Research Center of Shohada-e Tajrish Hospital, affiliated with Shahid Beheshti University of Medical Sciences (Tehran, Iran), between 2016 and 2021. The study protocol was reviewed and approved by the Institutional Review Board (ethics code: IR.SBMU.CRC.REC.1401.032). All procedures adhered to the ethical principles outlined in the Declaration of Helsinki. Patient data were anonymized and handled confidentially prior to analysis to ensure privacy and ethical compliance. The requirement for informed consent was waived due to the retrospective nature of the study.

2.2. Patient Population

This study included 187 women with pathologically confirmed breast cancer who underwent a dedicated axillary US before surgery and received either SLNB, ALND, or both. Only patients with complete medical records, including final pathology results, were included, while those with missing imaging or pathology data were excluded. Demographic information, tumor characteristics (including location, stage, and subtype), and neoadjuvant chemotherapy (NAC) status were recorded. The mean age of the study population was 49.9 ± 11.3 years.

2.3. Imaging Protocol

All patients underwent targeted axillary US performed by experienced breast radiologists. Lymph nodes were evaluated based on standard morphological features, including cortical thickness, preservation of the fatty hilum, and nodal shape. Nodes without cortical thickening and with an intact fatty hilum were considered negative, whereas those showing mild cortical thickening and borderline morphology were classified as suspicious. Nodes with a markedly thickened cortex (> 3 mm), loss of fatty hilum, or abnormal shape were categorized as definitely malignant.

Two interpretive criteria were applied for diagnostic assessment. Under the strict criterion, only nodes deemed definitely malignant were classified as “positive.” Under the expanded criterion, both suspicious and malignant findings were considered “positive.”

2.4. Surgical Management and Pathology

Following imaging, each patient underwent SLNB and/or ALND at the discretion of the surgical team, based on tumor stage, clinical examination, and intraoperative findings. Sentinel lymph node biopsy was performed in 158 patients (84.49%), with a mean of 3.61 ± 2.40 nodes retrieved. Among these, 53 patients (33.54%) demonstrated metastatic involvement, with a mean of 2.06 ± 1.48 positive nodes. Axillary lymph node dissection was performed in 55 (29.41%) patients, yielding an average of 8.73 ± 5.00 nodes, of which 21 (38.18%) were metastatic, with a mean of 5.14 ± 4.70 involved nodes.

Pathological assessment served as the reference standard for lymph node status. All excised nodes were examined histologically using hematoxylin–eosin staining, and any metastasis greater than 0.2 mm in diameter was considered positive.

2.5. Data Analysis

Diagnostic performance metrics for US under both the strict and expanded criteria were calculated using standard definitions: sensitivity = true positives/(true positives+false negatives); specificity = true negatives/(true negatives+false positives); positive predictive value (PPV) = true positives/(true positives+false positives); and negative predictive value (NPV) = true negatives/(true negatives+false negatives).

The influence of NAC on nodal assessment was examined in a subgroup of 54 patients (28.9%). All statistical analyses were performed using SPSS software (version 25). A P-value < 0.05 was considered statistically significant.

3. Results

3.1. Patient and Tumor Characteristics

Among the 187 patients included in this study, 98 (52.4%) presented with right-sided tumors, while 89 (47.6%) had left-sided tumors. The upper-outer quadrant (UOQ) was the most common tumor location (45.5%), followed by the upper-inner quadrant (18.2%), lower-outer quadrant (17.1%), central region (12.4%), and lower-inner quadrant (7.5%).

Neoadjuvant chemotherapy was administered to 54 patients (28.9%). Breast-conserving surgery (BCS) was performed in 137 patients (73.7%), while 49 patients (26.3%) underwent mastectomy. Histologically, invasive ductal carcinoma (IDC) was the predominant subtype, accounting for 164 cases (87.7%), with invasive lobular carcinoma (ILC) representing 8 cases (4.3%). Lymphovascular invasion (LVI) was present in 56 patients (29.2%).

Regarding tumor biomarkers, 153 patients (81.8%) were estrogen receptor-positive (ER+), 110 (58.8%) were progesterone receptor-positive (PR+), and 44 (23.5%) were HER2-positive. Ki-67 proliferation index was ≥ 20% in 70 patients (37.4%). Tumor staging was distributed as follows: T0 (8, 4.3%), T1 (76, 40.6%), T2 (72, 38.5%), T3 (25, 13.4%), and T4 (6, 3.2%). Comprehensive baseline characteristics are presented in Table 1.

Table 1. Patient and Tumor Characteristics (N = 187)

Variables and Categories	No. (%)
Cancer side	
Left	89 (47.6)
Right	98 (52.4)
Tumor quadrant	
UOQ	85 (45.5)
UIQ	34 (18.2)
LOQ	32 (17.1)
LIQ	14 (7.5)
Central	23 (12.4)
Neoadjuvant therapy	
Received	54 (28.9)
Surgery	
BCS	137 (73.7)
Mastectomy	49 (26.3)
Histology (types of BC)	
IDC	164 (87.7)
ILC	8 (4.3)
LVI	
Present	56 (29.2)
Receptors	
ER+	153 (81.8)
PR+	110 (58.8)
HER2+	44 (23.5)
Ki-67	
≤ 20%	70 (37.4)
Stage	
T0	8 (4.3)
T1	76 (40.6)
T2	72 (38.5)
T3	25 (13.4)
T4	6 (3.2)

Abbreviations: UOQ, upper-outer quadrant; UIQ, upper-inner quadrant; LOQ, lower-outer quadrant; LIQ, lower-inner quadrant; BCS, breast-conserving surgery; IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma; LVI, lymph-vascular invasion; ER+, estrogen receptor-positive; PR+, progesterone receptor-positive.

Table 2. Comparison of Sentinel Lymph-Node Biopsy, Axillary Lymph-Node Dissection, and Sonography Findings by Clinical and Pathological Variables [a, b]

Variables and Categories	SLNB	ALND	Sono
Cancer location			
Left	5 (9.4)	10 (47.6)	13 (34.2)
Right	7 (13.2)	9 (17.6)	25 (65.8)
UOQ	29 (54.7)	10 (47.6)	19 (50)
UIQ	7 (13.2)	1 (4.7)	6 (15.8)
LOQ	9 (17)	4 (19.0)	6 (15.8)
LIQ	5 (9.4)	1 (4.7)	2 (5.3)
Central	6 (11.3)	3 (14.3)	4 (10.5)
Neoadjuvant	16 (30.2)	9 (42.8)	11 (28.9)
Surgery			
BCS	35 (66)	14 (66.6)	30 (78.9)
Mastectomy	18 (34)	5 (23.8)	8 (21.1)
Types of breast cancer			
ILC	5 (9.4)	1 (4.7)	0 (0)
IDC	48 (90.6)	18 (85.7)	37 (97.4)
LVI	30 (56.6)	11 (52.4)	13 (34.2)
Biomarker			
ER	53 (100)	19 (90.5)	30 (78.9)
PR	53 (100)	19 (90.5)	20 (52.6)
HER2	52 (98.1)	19 (90.5)	10 (26.3)
Ki67	18 (34)	7 (33.3)	13 (34.2)
Stage			
T0	2 (3.8)	1 (4.7)	1 (2.6)
T1	16 (30.2)	7 (33.3)	11 (28.9)
T2	26 (49.1)	7 (33.3)	17 (44.7)
T3	6 (11.3)	4 (19.0)	8 (21.1)
T4	3 (5.7)	0 (0)	1 (2.6)

Abbreviations: SLNB, sentinel lymph-node biopsy; ALND, axillary lymph-node dissection; UOQ, upper-outer quadrant; UIQ, upper-inner quadrant; LOQ, lower-outer quadrant; LIQ, lower-inner quadrant; BCS, breast-conserving surgery; ILC, invasive lobular carcinoma; IDC, invasive ductal carcinoma; LVI, lymph-vascular invasion; ER, estrogen receptor; PR, progesterone receptor.

[a] Values are expresses as No. (%).

[b] Diagnostic performance of ultrasound and SLNB compared with final histopathology, which is the reference standard.

3.2. Ultrasound Findings

Among the 187 patients, 38 nodes were classified as clearly malignant on preoperative US, 50 nodes were considered suspicious, and 99 were reported as negative. Using the strict criterion — where only definitively malignant features were considered positive — US demonstrated a sensitivity of 44.68%, specificity of 81.11%, PPV of 55.25%, and NPV of 73.74%.

When the interpretive threshold was expanded to include both suspicious and malignant nodes as positive, sensitivity increased to 61.19%, while specificity decreased to 60.83%. Correspondingly, PPV was 46.59% and NPV remained at 73.74%. This shift highlights the inherent trade-off between identifying additional true-positive cases and increasing the number of false-positive results.

3.3. Sentinel Lymph Node Biopsy and Axillary Lymph Node Dissection Results

Sentinel lymph node biopsy was performed in 158 patients (84.49%), with a mean of 3.61 ± 2.4 nodes retrieved per patient. Of these, 53 patients (33.54%) had at least one metastatic node. Axillary lymph node dissection was performed in 55 patients (29.41%), with a mean of 8.73 ± 5.00 nodes examined; 21 patients (38.18%) had histologically confirmed nodal metastases.

3.4. Impact of Neoadjuvant Chemotherapy

Among the 54 patients (28.9%) who received NAC, the sensitivity and specificity of US for axillary metastasis detection were 58.33% and 56.00%, respectively, based on the expanded criteria. Neoadjuvant chemotherapy appeared to alter nodal size and morphology, which may have contributed to the reduced diagnostic accuracy of US in this subgroup (Table 2).

4. Discussion

This retrospective analysis of 187 Iranian women with invasive breast cancer demonstrates that the diagnostic performance of axillary US is highly contingent on the interpretive threshold applied. When only unequivocally malignant nodes were deemed positive (strict criteria), sensitivity was 44.68% and specificity 81.11%. Broadening the definition to include morphologically suspicious nodes increased sensitivity to 61.19% but reduced specificity to 60.83%. This trade-off mirrors the fundamental tension between minimizing false negatives and avoiding overtreatment. (7).

Our figures align partly with Zhang et al. (7), who recorded 69.4% sensitivity and 81.8% specificity in a Chinese cohort, approximating our expanded-criteria sensitivity yet exceeding our specificity. Conversely, Riedel et al. (8) reported 53% sensitivity and 93% specificity using stringent criteria in early-stage disease, underscoring how greater interpretive rigor preferentially boosts specificity. Such inter-study differences likely reflect heterogeneity in equipment, operator expertise, and tumor biology.

Neoadjuvant chemotherapy introduced additional complexity: 28.9% of our patients received NAC, within whom US achieved 58.33% sensitivity and 56.00% specificity. Cytoreductive and stromal changes after NAC can obscure residual metastases or mimic benignity, suggesting that post-treatment nodal imaging may require modified sonographic hallmarks or adjunctive modalities.

Moreover, while our study focused on conventional axillary US, which demonstrated moderate sensitivity (44.7 - 61.2%) and specificity (60.8 - 80.3%), recent evidence suggests that adjunctive techniques such as ultrasound-guided fine needle aspiration (US-FNA) can substantially enhance diagnostic performance. Khoroushi et al. reported sensitivity and specificity exceeding 90% using US-FNA in a similar patient population, highlighting the potential of minimally invasive, image-guided methods to overcome limitations inherent to standard US. These findings underscore the importance of exploring combined imaging and cytological approaches in future studies to improve preoperative axillary staging and reduce false negatives (9).

From a clinical standpoint, classifying suspicious nodes as positive reduces the risk of understaging — critical where systemic therapy hinges on nodal status— yet incurs a higher rate of unnecessary sentinel-node biopsy (SLNB) or ALND, procedures associated with lymphoedema, neuropathy, and increased cost. In resource-constrained settings, US remains the most accessible staging tool; therefore, optimizing interpretive thresholds through standardized training and reporting frameworks could enhance care while containing expenditure.

4.1. Conclusions

In this cohort, expanded US criteria meaningfully increased sensitivity for detecting metastatic ALNs but decreased specificity, highlighting an inherent trade-off. Our findings suggest that employing an expanded threshold might help identify more true-positive nodal cases, but at the risk of overtreatment. Ultimately, the choice of US criteria should be guided by clinical context, patient preferences, and multidisciplinary discussion. Larger prospective trials could solidify these conclusions and potentially reduce the burden of unnecessary invasive staging procedures.

4.2. Limitations

Key limitations include the single-center, retrospective design, absence of centralized image re-review, and potential selection bias. Prospective multicenter studies that incorporate blinded assessment, elastography, contrast-enhanced US, or image-guided biopsy are necessary to refine thresholds and validate these findings. Machine-learning algorithms trained on large annotated datasets may also improve reproducibility and reduce operator dependence.

In summary, axillary US offers moderate accuracy whose balance between sensitivity and specificity can be deliberately shifted by adjusting interpretive criteria. Adopting an expanded threshold may be justified when missing nodal disease would materially alter adjuvant

management, whereas a strict threshold is preferable where surgical morbidity is the overriding concern. Tailoring the threshold to institutional resources, tumor biology, and patient preference is essential for truly individualized axillary care.

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Footnotes

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