

Concordance between Axillary Ultrasound and Sentinel Biopsy in Clinically Node-Negative Early Breast Cancer

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ABSTRACT

Objective: To determine the sensitivity of axillary ultrasound in detecting axillary nodal metastasis in clinically and radiologically uninvolved axillary nodes in early carcinoma breast by comparing with sentinel node biopsy histopathology on frozen section.

Study Design: Comparative cross-sectional study

Place and Duration of Study: Breast Clinic, CMH, Rawalpindi Pakistan, from Aug 2020 to May 2021.

Methodology: Patients included in the study presented with breast cancer lesions with clinically impalpable axillary lymph nodes aged 18-75. Patients with clinically impalpable nodes underwent an ultrasound of the axilla; if suspicious nodes were found, the patient had subsequent axillary node dissection. Sentinel node biopsy (SLNB) was performed on axillary ultrasound in all patients with no suspicious or benign-looking nodes. Histopathological reporting was taken as standard. Lymph nodal status on axillary ultrasound, SLN biopsy and axillary lymph node clearance were documented and analyzed.

Results: Twenty-nine patients were included who had benign-looking lymph nodes on axillary ultrasound and underwent sentinel lymph node biopsy. The mean age of the patients was 54.03 ± 7.94 . Out of 29 patients, 24(82.8%) patients had negative Sentinel lymph node biopsy, and 5(17.2%) had positive Sentinel lymph node biopsy, who then underwent axillary lymph node dissection.

Conclusion: Sentinel lymph node biopsy is the gold standard to determine axillary lymph nodes involved in early carcinoma breast, which seem benign on pre-operative axillary ultrasound.

Keywords: Axillary lymph node dissection, Axillary ultrasound, Clinically impalpable nodes, Early breast cancer, Sentinel lymph node biopsy.

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INTRODUCTION

Lymph node involvement of the axilla in breast cancer is one of the most important predictors of outcome.¹ The diagnostic accuracy of radiology in staging the axilla could be much higher. Hence, pathological staging by performing a surgical excision of sentinel nodes has become the gold standard in modern times.²

Traditionally, axillary clearance was performed in all patients, which invariably resulted in post-operative complications, such as lymphedema, nerve injury, shoulder dysfunction, etc.³ ALND can be skipped in patients whose SLN biopsy is negative. This saves many patients from these dire complications. However, if SLNB is reported positive, ALND is undertaken to stage and for locoregional control.⁴

The diagnostic accuracy of axilla ultrasound has

been studied for a long time, but the results are difficult to interpret. One of the reasons for this is that the sensitivity and specificity of ultrasound are studied under variable clinical settings, and the equipment varies widely. Moreover, this investigation is heavily operator-dependent, too. This operator dependency and difference of equipment can change the results considerably.⁵ Several reports on axillary ultrasound have suggested sensitivity lying between 26 % to 94 %, and specificity ranges from 53% to 98%.^{6,7}

The objective of this study was to analyze the sensitivity of axillary ultrasound to accurately tell the involvement of axillary lymph nodes by cancer cells in patients with breast cancer by comparing it to sentinel lymph node biopsy. As sentinel lymph node biopsy histopathologically confirms axillary lymph node involvement.

METHODOLOGY

The comparative cross-sectional study was performed at Breast Clinic, CMH, Rawalpindi, from

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August 2020 to May 2021, after obtaining permission from the Institutional Ethical Review Board.

Inclusion Criteria: Clinically node-negative, curative intent, early breast cancer, pre-chemo disease, T1 and T2 stage.

Exclusion Criteria: Patients with positive nodes on axillary ultrasound, metastatic breast cancer, recurrent breast cancer, breast cancer in pregnancy, post-chemo disease, locally advanced breast cancer, and patients allergic to blue dye or technetium colloid were excluded from the study.

Study variables were documented and analyzed after the study. Informed consent was obtained from all the included patients. Sentinel lymph node biopsy was taken as a standard diagnosis for axilla involvement by disease. Patients having pre-operative clinically and radiologically negative axilla underwent per operative sentinel lymph node biopsy. Those cases having positive sentinel lymph nodes underwent axillary clearance. SLN sampling was performed by a dual method. The patient was injected with Technetium colloid dye injection one day before surgery, and blue dye was injected in the sub-areolar plexus operatively. Sentinel lymph nodes were picked by gamma probe and by seeing blue-coloured nodes. All hot, blue and clinically suspicious lymph nodes were taken as positive nodes. 3 to 4 sentinel lymph nodes were sent for the frozen section. Nodes positive on the frozen section were taken as involved, and the patient underwent axillary dissection if nodes were found positive.

Data was entered in Statistical Package for the Social Sciences (SPSS) version 25.00. Quantitative variables were summarized as Mean±SD. Qualitative variables were summarized as numbers and percentages. The Chi-square test was applied, and the *p*-value was calculated.

RESULTS

A total of 29 female patients were included; the mean age was 54.03±7.94, ranging from 38 to 75 years. The surgical plan was Breast-Conserving Surgery in 19(65.5%) and Mastectomy in 10(34.5%). Fourteen patients (48.3%) had right-sided disease, 15(51.7%) had left-sided disease, 6(20.7%) patients had T1 stage and 23(79.3%) patients had T2 stage, as shown in Table-I. Out of 29 patients, all had normal findings on axillary ultrasound; 24 patients (82.8%) had negative SLN biopsy, and no further axillary surgery was not done on them. Five patients (17.2%) had positive SLN biopsy

and subsequently had axillary clearance; a statistically significant association of Sentinel lymph node biopsy and axillary ultrasound *p*<0.001, as shown in Table-II.

Table-I: Demographic and Reproductive Variables (n=29)

Study Parameters	n(%)
Age(Mean±SD)	54.03±7.94 years
Surgical Plan	
Conserving Surgery	19(65.5)
Mastectomy Surgery	10(34.5)
Disease Side	
Right Side	14(48.3)
Left Side	15(51.7)
Stages	
T1 Stage	6(20.7)
T2 Stage	23(79.3)

Table-II: Comparison of Sentinel Lymph Node Biopsy and Axillary Ultrasound (n=29)

Axillary Ultrasound	Sentinel Lymph Node Biopsy		<i>p</i> -value
	Positive	Negative	
Yes	5(17.2)	-	<0.001
No	-	24(82.8)	

DISCUSSION

Our study shows that the gold standard axilla assessment method is sentinel lymph node biopsy, which can identify those involved axilla cases declared negative by pre-operative axillary ultrasound.

Regarding carcinoma breast, axillary lymph node involvement has a determining role in the prognosis. For this purpose, the axilla is staged by two methods pre-operatively: clinical examination and radiological proof. In cases with an impalpable axilla, axillary sentinel node sampling is the gold standard for axillary staging, done during the same operation to remove the breast tumour. As of now, any imaging technique has yet to be able to come close to sentinel sampling regarding diagnostic accuracy.

Sentinel lymph node biopsies are done using the dual tracer technique, which uses both blue dye and radioisotope; the results are highly accurate.^{8,9} A major anaphylaxis,¹⁰ disposing of radioactive waste, and a second potential surgery in up to 35% of patients with positive Sentinel lymph node biopsy.¹¹

Axillary ultrasound and sometimes axillary lymph node core cut biopsy, or FNAC has routinely undertaken pre-operatively clinical evaluation of patients presenting with early-stage carcinoma breast and is a part of current guidelines. However, the importance of tumour lymphatics and their involvement in tumour behaviour is controversial. Whether the metastasis in regional lymph nodes is due to only local

spread or a sign of systemic metastasis of the disease is still unknown.¹² However, axillary metastasis indicates poor prognosis, with the 5-year survival effectively decreased by 28% to 40% in patients with nodal spread.^{13,14} Therefore, axillary sampling is important to stage and locoregional control, which may increase overall survival.

Our study shows that if ultrasound shows that the axilla has non-suspicious lymph nodes, there is an 82.8% chance of negative lymph nodes on pathological reporting of sentinel lymph nodes. The result is similar to two prior studies, one by Valente *et al.*¹⁵ conducted at the University of Southern California between 2008 and 2010. The other by Khan *et al.*¹⁶ conducted at Agha Khan University Karachi in 2020, reports that negative findings of clinical examination and radiology in a patient mean an 86% chance of showing no metastasis in lymph nodes on SLNB histopathology.

False negative cases are the ones whose investigations do not show involvement of axillary metastasis on clinical examination and radiology, but the histopathology showed nodal metastasis.¹⁷ The false-negative percentage of ultrasound of axilla, as per our results, is 17.2%; this is in close agreement with previous studies by Afzal *et al.*¹⁸ and others by Curigliano *et al.*,¹⁹ that have reported a rate of 16.7% and 22.9%. So technically, 17.2% of patients with uninvolved axillas in clinical and radiology have axillary metastasis.

Our study has highlighted the importance of sentinel lymph node biopsy in detecting axillary metastasis in patients with normal clinical examination and radiology of the axilla.^{20,21}

LIMITATIONS OF STUDY

We have not included those cases that were positive for axillary metastasis radiology, as in our setup, such cases undergo axillary lymph node dissection. Another potential limitation can be the operator dependency of ultrasound, so improper observation of an abnormal lymph node might also be a reason for a false-negative result.

CONCLUSION

Sentinel lymph node biopsy is the best modality to rule out axillary lymph node metastasis in those cases of early breast cancer with benign-looking lymph nodes on radiology. If axillary lymph nodes are involved only, a formal axillary dissection is undertaken, which saves many patients from a more radical approach to axillary dissection in cases with uninvolved axillary lymph nodes. This method also decreases the number and severity of many complications seen with axillary lymph node clearance, such as lymphedema, pain, etc.

Conflict of Interest: None.

Authors Contribution

Following authors have made substantial contributions to the manuscript as under:

AM: & AAK: Data acquisition, data analysis, drafting the manuscript, critical review, approval of the final version to be published.

RB:, SRQN: & SN: Study design, drafting the manuscript, data interpretation, approval of the final version to be published.

FAK:, SM: & PK: Concept, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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