

EVALUATION OF AXILLARY LYMPH NODES STATUS IN BREAST CANCER: ROLE OF ULTRASOUND GUIDED CORE NEEDLE BIOPSY AND ULTRASONOGRAPHIC PARAMETERS IN PREOPERATIVE STAGING

Dr. Maryam Ikram^{*1}, Dr. Zeeshan Rashid Mirza², Dr. Rafia Shazad³, Dr. Farwa Malik⁴,
Dr. Hamza Ikram⁵, Dr. Usman Sani⁶

¹ Post Graduate Trainee (FCPS Radiology), INMOL Cancer Hospital, Lahore

² Consultant Radiologist / HOD (Study Supervisor), INMOL Cancer Hospital, Lahore

³ Consultant Radiologist, INMOL Cancer Hospital, Lahore

⁴ Post Graduate Trainee (FCPS Radiology), INMOL Cancer Hospital, Lahore

⁵ House Officer, Services Hospital, Lahore

⁶ Medical Officer, Mayo Hospital, Lahore

^{*1}maryamikram47@gmail.com

DOI: <https://doi.org/10.5281/zenodo.19229525>

Keywords

Breast Neoplasms, Lymphatic Metastasis, Lymph Nodes, Ultrasonography, Biopsy, Preoperative Care.

Article History

Received: 08 January 2025

Accepted: 30 January 2025

Published: 15 February 2025

Copyright @Author

Corresponding Author: *
Dr. Maryam Ikram

Abstract

Background: Accurate preoperative assessment of axillary lymph nodes in breast cancer is challenging. This study evaluated ultrasonographic parameters and ultrasound-guided core needle biopsy to improve detection of nodal metastases, guide surgical planning, and potentially reduce unnecessary axillary dissections.

Objectives: To evaluate the diagnostic accuracy of ultrasonographic parameters and ultrasound-guided core needle biopsy in detecting malignant axillary lymph nodes in breast cancer, using histopathology as the gold standard.

Duration: Six months w.e.f 01-05-2023 to 31-10-2023

Methodology: After informed consent, all patients underwent high-resolution axillary ultrasonography, followed by ultrasound-guided core needle biopsy of all lymph nodes. Multiple core samples were sent for histopathology, and all patients received definitive surgical management. This allowed direct comparison of ultrasonography and core biopsy findings with histopathology, enabling accurate assessment of false positives, false negatives, and diagnostic performance.

Results: A total of 270 participants with a mean age of 51.4 ± 12.35 years were included, with 61% of axillary lymph nodes confirmed malignant on histopathology, consistent across age groups. Ultrasonographic parameters showed a sensitivity of 86.7%, specificity of 70.5%, and accuracy of 80.4%, while ultrasound-guided core needle biopsy demonstrated superior performance with 93.9% sensitivity, 89.5% specificity, and 92.2% accuracy.

Conclusion: Ultrasonography and ultrasound-guided core needle biopsy provide reliable preoperative assessment of axillary lymph nodes in breast cancer. Core needle biopsy demonstrates higher sensitivity, specificity, and accuracy. Their use improves staging accuracy, informs surgical planning, and may reduce unnecessary axillary dissections, ultimately enhancing patient management and treatment outcomes.

INTRODUCTION

Breast cancer is a global health concern with a significant impact on women's well-being.¹ It remains a major challenge due to its complex pathogenesis and diverse clinical manifestations, which hinder effective treatment and prevention.² The etiology of breast cancer is multifactorial, with demographic, social, and biomedical risk factors. Age, early menarche, delayed first childbirth, menopause, nulliparity, short-duration lactation, use of hormonal contraceptives, obesity, high-fat diet, hormone replacement therapy, and family history significantly increase risk.³ Early signs include a breast or axillary lump, skin changes, nipple alterations, pain, or unusual discharge. Skin dimpling resembling an orange peel and breast enlargement are important indicators even in the absence of a palpable mass.^{3,4}

Breast cancer is the most frequently diagnosed cancer and the leading cause of cancer-related death among women. Worldwide, over 2.3 million new cases were estimated in 2020, accounting for one-fourth of female cancer diagnoses and one-sixth of cancer-related deaths. The National Cancer Institute reported 266,120 new cases and 40,920 deaths in 2018.⁵ Nearly half of cases occur in Asia, where disease burden and mortality are rising, particularly in low- and middle-income countries.⁶ Pakistan has the highest incidence in Asia, ranking second in incidence and first in mortality, with one in nine women affected during her lifetime.⁷

Although breast cancer cannot be fully prevented, early detection significantly improves prognosis and reduces the need for invasive treatment.⁸ Axillary lymph node metastasis (ALNM) is the most common site of spread and a key prognostic factor.⁹ Ultrasonography is widely used to assess lymph node characteristics due to its noninvasiveness, convenience, and patient acceptance.¹⁰ However, pathological confirmation requires biopsy, and ultrasound-guided core needle biopsy (US-CNB) provides gold-standard histological results with sensitivity of 97–99%.^{11,12} Preoperative axillary ultrasound and US-CNB are now recommended guidelines for accurate staging and treatment planning, providing safe and reliable evaluation without major complications.^{13,14}

Accurate preoperative assessment of axillary lymph nodes in breast cancer is crucial for staging and surgical planning, yet remains challenging. Mansoor et al.¹⁵ reported high sensitivity (83.5%) and negative predictive value (95%) for axillary ultrasound, while Sidhwani et al.¹⁶ and Afzal et al.¹⁷ demonstrated that ultrasound-guided core needle biopsy achieves sensitivities of 87.9–94% with excellent specificity. However, no study has directly compared ultrasonographic parameters and core needle biopsy against histopathology in the same cohort, highlighting the need to evaluate both modalities for precise detection of nodal metastases and improved surgical decision-making.

METHODOLOGY

This study was a cross-sectional diagnostic accuracy study conducted in the Department of Radiology in collaboration with the Department of Oncology at INMOL Cancer Hospital, Lahore. The study was carried out over six months following approval of the synopsis. The sample size was calculated using the WHO sample size calculator, taking the expected sensitivity of ultrasound-guided core needle biopsy as 83.51%, specificity as 51.58%, confidence level of 95%, margin of error of 10%, and prevalence of axillary lymph node metastasis in breast cancer as 64%. Non-probability consecutive sampling was used to enroll all eligible patients, and all participants underwent assessment using each modality: ultrasonography, ultrasound-guided core needle biopsy, and histopathology.¹⁵

Operational definitions were established for all study variables. An axillary lymph node was considered suspected malignant if it demonstrated measurable abnormal features on clinical examination. Nodes were classified as malignant on ultrasonography if they met one or more of the following criteria: cortical thickness exceeding 3 millimeters, absent or displaced fatty hilum, rounded shape, irregular margins, or abnormal vascularity on Doppler imaging. Nodes were considered malignant on ultrasound-guided core needle biopsy if histopathological examination of tissue obtained under ultrasound guidance revealed metastatic carcinoma. Histopathology served as the gold standard, and nodes were

classified as malignant if metastatic tumor deposits were observed microscopically.

After informed consent, all enrolled patients underwent high-resolution ultrasonography of the axilla using a linear high-frequency transducer. All lymph nodes, whether appearing suspicious or not on ultrasonography, were evaluated and underwent ultrasound-guided core needle biopsy using an 18-gauge automated biopsy needle, with multiple core samples obtained for histopathological examination. Subsequently, all patients underwent definitive surgical management, including sentinel lymph node biopsy and/or axillary lymph node dissection. This ensured that ultrasonographic findings and core needle biopsy results could be directly compared to histopathology for each patient, allowing accurate determination of false negatives, false positives, and overall diagnostic performance of each modality.

Data were analyzed using SPSS version 25.0. Age, sensitivity, specificity, positive predictive value, negative predictive value, and overall diagnostic accuracy were calculated for ultrasonography versus histopathology and for core needle biopsy versus histopathology. Comparative analysis between the two modalities was performed using chi-square test, and a p-value ≤ 0.05 was considered statistically significant.

RESULTS

A total of 270 participants were included, with a mean age of 51.40 ± 12.35 years. Among them, 87 patients (32.2%) were aged 50 years or younger, while the majority, 183 patients (67.8%), were over 50 years of age as shown in Table 1.

Ultrasonography identified 174 nodes (64.4%) as malignant, while 96 nodes (35.6%) were considered non-malignant. Core needle biopsy detected malignancy in 166 nodes (61.5%) and reported 104 nodes (38.5%) as benign. Histopathological examination, serving as the reference standard, confirmed malignancy in 165

nodes (61.1%) and benign status in 105 nodes (38.9%). These findings indicate a high concordance among the three modalities in preoperative evaluation of axillary lymph node involvement in breast cancer. Data is given in Table 2. The frequency of malignant axillary lymph nodes on histopathology was similar across age subgroups, with 60.9% in patients ≤ 50 years and 61.2% in those >50 years, showing no statistically significant difference ($P = 0.964$). Data is given in Table 3.

Using histopathology as the gold standard, ultrasonography correctly detected 143 true positives and 74 true negatives, with 31 false positives and 22 false negatives. This corresponded to a sensitivity of 86.67%, specificity of 70.48%, and an overall accuracy of 80.37%. The disease prevalence was 61.10%, with a positive predictive value of 82.18% and a negative predictive value of 77.09%, demonstrating that ultrasonographic assessment is a reliable tool for preoperative evaluation of lymph node involvement in breast cancer, as shown in Table 4.

Using histopathology as the gold standard, ultrasound-guided core needle biopsy correctly identified 155 true positives and 94 true negatives, with 11 false positives and 10 false negatives. This corresponded to a sensitivity of 93.94%, specificity of 89.52%, and an overall accuracy of 92.22%. The disease prevalence was 61.10%, with a positive predictive value of 93.37% and a negative predictive value of 90.39%, as given in Table 5.

Against histopathology as the gold standard, ultrasonographic parameters demonstrated a sensitivity of 86.67%, specificity of 70.48%, positive predictive value (PPV) of 82.18%, negative predictive value (NPV) of 77.09%, and overall diagnostic accuracy of 80.37%. Ultrasound-guided core needle biopsy showed superior performance with a sensitivity of 93.94%, specificity of 89.52%, PPV of 93.37%, NPV of 90.39%, and diagnostic accuracy of 92.22%. Data is given in Table 6.

Table 1: Demographic Characteristics of Patients with Suspicion of Malignancy in Axillary Lymph Nodes

| Characteristics | Participants (n=270) |
|-----------------|----------------------|
| Age (years) | 51.40±12.35 |
| • Upto 50 years | 87 (32.2%) |
| • >50 years | 183 (67.8%) |

Table 2: Frequency of Malignancy of Axillary Lymph Nodes on Each Modality

| Modality | Malignant | Frequency (n) | Percent (%) |
|-----------------------------|-----------|---------------|-------------|
| Ultrasonographic Parameters | Yes | 174 | 64.4 % |
| | No | 96 | 35.6 % |
| | Total | 270 | 100.0 % |
| Core Need biopsy | Yes | 166 | 61.5 % |
| | No | 104 | 38.5 % |
| | Total | 270 | 100.0 % |
| Histopathology | Yes | 165 | 61.1 % |
| | No | 105 | 38.9 % |
| | Total | 270 | 100.0 % |

Table 3: Comparison of Frequency of Malignant Axillary Lymph Nodes on Histopathology Stratified for Subgroups of Age

| Subgroups | n | Malignancy n (%) | P-value |
|-----------------|-----|------------------|---------|
| Age (years) | | | |
| • Upto 50 years | 87 | 53 (60.9%) | 0.964 |
| • >50 years | 183 | 112 (61.2%) | |

Chi-square test, observed difference was statistically insignificant

Table 4: 2x2 Contingency Table to Determine Diagnostic Performance of Ultrasonographic Parameters against Histopathology as Gold Standard

| Ultrasonographic Parameters | Histopathology | | Total |
|-----------------------------|-------------------------|-----------------|-------|
| | Malignant Axillary Node | No | |
| Malignant Axillary Node | 143 ^a | 31 ^c | 174 |
| No | 22 ^b | 74 ^d | 96 |
| Total | 165 | 105 | 270 |

^aTrue Positive = 143, ^cFalse Positive = 31, ^bFalse Negative = 22, ^dTrue Negative = 74

| Statistic | Formula | Value |
|-------------|-------------------|--------|
| Sensitivity | $\frac{a}{a + b}$ | 86.67% |

| | | |
|---------------------------|-------------------------------|--------|
| Specificity | $\frac{d}{c + d}$ | 70.48% |
| Accuracy | $\frac{a + d}{a + b + c + d}$ | 80.37% |
| Disease prevalence | $\frac{a + b}{a + b + c + d}$ | 61.10% |
| Positive Predictive Value | $\frac{a}{a + c}$ | 82.18% |
| Negative Predictive Value | $\frac{d}{b + d}$ | 77.09% |

Table 5: 2x2 Contingency Table to Determine Diagnostic Performance of US Guided Core Needle Biopsy against Histopathology as Gold Standard

| US Guided Core Needle Biopsy | Histopathology | | Total |
|------------------------------|-------------------------|-----------------|-------|
| | Malignant Axillary Node | No | |
| Malignant Axillary Node | 155 ^a | 11 ^c | 166 |
| No | 10 ^b | 94 ^d | 104 |
| Total | 165 | 105 | 270 |

^aTrue Positive = 155, ^cFalse Positive = 11, ^bFalse Negative = 10, ^dTrue Negative = 94

| Statistic | Formula | Value |
|---------------------------|-------------------------------|--------|
| Sensitivity | $\frac{a}{a + b}$ | 93.94% |
| Specificity | $\frac{d}{c + d}$ | 89.52% |
| Accuracy | $\frac{a + d}{a + b + c + d}$ | 92.22% |
| Disease prevalence | $\frac{a + b}{a + b + c + d}$ | 61.10% |
| Positive Predictive Value | $\frac{a}{a + c}$ | 93.37% |

| | | |
|---------------------------|-------------------|--------|
| Negative Predictive Value | $\frac{d}{b + d}$ | 90.39% |
|---------------------------|-------------------|--------|

Table 6: Comparison of Parameters of Diagnostic Accuracy between Ultrasound Guided Core Needle Biopsy and Ultrasonographic Parameters Taking Histopathology as Gold Standard

| Against Histopathology as Gold Standard | Sensitivity | Specificity | PPV | NPV | Diagnostic Accuracy * |
|---|-------------|-------------|--------|--------|-----------------------|
| Ultrasonographic Parameters | 86.67% | 70.48% | 82.18% | 77.09% | 80.37% |
| US Guided Core Needle Biopsy | 93.94% | 89.52% | 93.37 | 90.39% | 92.22% |

* p-value <0.05.

DISCUSSION

Accurate assessment of axillary lymph node status is crucial in breast cancer for staging, prognosis, and surgical planning, yet preoperative evaluation remains challenging.^{11,12} While ultrasonography and core needle biopsy are widely used, comparative data on their diagnostic performance remains limited, particularly in correlating imaging findings with histopathology. Emerging evidence suggests that ultrasound-guided core needle biopsy may improve preoperative detection of nodal metastasis, allowing more precise surgical decisions and potentially reducing unnecessary axillary dissections.¹⁵⁻¹⁹ To address this gap, the present study was designed to evaluate the role of ultrasonographic parameters and ultrasound-guided core needle biopsy in accurately staging axillary lymph nodes in breast cancer.

Comparison of the findings of this study with existing literature highlights both consistencies and variations in the preoperative assessment of axillary lymph nodes in breast cancer. Sidhwani et al. evaluated 132 patients with invasive breast cancer, reporting a mean age of 57.67 ± 13.03 years. The majority of tumors were invasive ductal carcinoma, and hormone receptor positivity was highly prevalent, with estrogen receptor positive cases in 90.2% and progesterone receptor positive cases in 87.9%. The most common immunohistochemical subtype was Luminal B in 50% of patients. Tumors were predominantly of moderate grade and early-stage (pT1). Ultrasound-guided core needle biopsy showed a sensitivity of 87.9% and specificity of 100%, with positive and

negative predictive values of 100% and 89.2%, respectively, leading to a diagnostic accuracy of 93.9%. These results align closely with our study, which also demonstrated high diagnostic accuracy of core needle biopsy in preoperative staging.¹⁶

Statch et al. conducted a study of 470 patients, of whom 166 were node positive, with 79 exhibiting suspicious findings on axillary ultrasound. Their analysis identified that the primary factor contributing to false-negative ultrasonographic results was the small size of nodal metastases. Within the sentinel lymph node biopsy subgroup, 45% of patients had metastatic deposits smaller than or equal to 5 mm. The authors concluded that axillary ultrasound is limited in detecting small metastatic deposits, emphasizing the need for further studies to determine whether leaving these small metastases untreated impacts disease-free and overall survival. These observations highlight a limitation that aligns with our findings regarding the sensitivity of ultrasonography.¹⁸

Mansoor et al. reported on 217 patients who underwent axillary ultrasound, with 139 showing suspicious lymph nodes subjected to core needle biopsy and 80 with normal-appearing nodes undergoing sentinel lymph node biopsy. The calculated sensitivity, specificity, positive predictive value, negative predictive value, and overall accuracy were 83.51%, 51.58%, 55.47%, 95%, and 65%, respectively. They concluded that axillary ultrasound offers high sensitivity and negative predictive value, while core needle biopsy is a safe, simple, and accurate technique to avoid unnecessary axillary dissection. These findings

reinforce the results of the present study, demonstrating the reliability of core needle biopsy in preoperative evaluation.¹⁵

Jain et al. evaluated preoperative contrast-enhanced ultrasonography (CEUS) of axillary lymph nodes and correlated findings with histopathology after modified radical mastectomy or sentinel lymph node biopsy. They reported that heterogeneous enhancement with microbubbles was the most distinguishing feature of malignant nodes, further supporting the value of advanced ultrasonographic parameters in identifying nodal metastases, consistent with our observations.¹³

Afzal et al. demonstrated that ultrasound-guided core needle biopsy achieved a sensitivity of 88%, specificity of 100%, positive predictive value of 100%, negative predictive value of 89.28%, and diagnostic accuracy of 94% in clinically node-negative breast cancer patients. Their study concluded that positive core biopsy results could obviate the need for sentinel lymph node biopsy, allowing surgeons to proceed directly to axillary dissection. These findings closely mirror the high sensitivity, specificity, and accuracy observed in the current study.¹⁷

CONCLUSION

Ultrasonography and ultrasound-guided core needle biopsy provide reliable preoperative assessment of axillary lymph nodes in breast cancer. Core needle biopsy demonstrates higher sensitivity, specificity, and accuracy. Their use improves staging accuracy, informs surgical planning, and may reduce unnecessary axillary dissections, ultimately enhancing patient management and treatment outcomes.

LIMITATIONS & RECOMMENDATIONS

This study's strengths lie in its large cohort, systematic assessment of ultrasonography and core needle biopsy, and comparison with histopathology as the gold standard. Limitations include its single-center design and potential under-detection of micro-metastases in small lymph nodes. Future prospects involve multicenter validation, incorporation of advanced imaging modalities, and longitudinal follow-up to evaluate the impact of preoperative lymph node assessment on surgical decision-making, recurrence rates, and

overall patient outcomes in breast cancer management.

Conflict of Interest: None

Source of Funding: None

Authors Contribution

Author 1: Designed the study; acquired, analyzed, and interpreted data; drafted the manuscript; approved the final version; and agreed to be accountable for all aspects of the work.

Authors 2-4: Contributed to study conception and design; performed data analysis; drafted and critically revised the manuscript for important intellectual content; approved the final version; and agreed to be accountable for all aspects of the work.

Authors 5-6: Contributed substantially to data analysis and interpretation; critically revised the manuscript for important intellectual content; approved the final version; and agreed to be accountable for all aspects of the work.

REFERENCES

- Xu H, Xu B. Breast cancer: epidemiology, risk factors and screening. *Chin J Cancer Res.* 2023;35(6):565-83.
- Zheng H, Zhao R, Wang W, Liu X, Wang X, Wen C, et al. The accuracy of ultrasound-guided fine-needle aspiration and core needle biopsy in diagnosing axillary lymph nodes in women with breast cancer: a systematic review and meta-analysis. *Front Oncol.* 2023;13:1166035.
- Prusty RK, Begum S, Patil A, Naik DD, Pimple S, Mishra G. Knowledge of symptoms and risk factors of breast cancer among women: a community based study in a low socio-economic area of Mumbai, India. *BMC Womens Health* 2020;20(1):106.
- Moreth M, Herröder N, Hödl P, Bufe A, Bretschneider C, Möbus V, et al. Clinical axillary staging in breast cancer patients using ultrasound imaging. *Breast Care.* 2024;19(3):149-54.

- Zaheer S, Yasmeen F. Historical trends in breast cancer presentation among women in Pakistan from join-point regression analysis. *Pak J Med Sci.* 2024;40(1Part-I):134-9.
- Fu M, Peng Z, Wu M, Lv D, Li Y, Lyu S. Current and future burden of breast cancer in Asia: a GLOBOCAN data analysis for 2022 and 2050. *Breast.* 2024;79:103835.
- Munawwar A, Sajjad A, Faisal S, Rasul A, Zarbab A, Bibi A, et al. Basic findings of incidence of breast cancer in allied hospital Faisalabad, Pakistan: a retrospective study. *Iran J Public Health.* 2023;52(6):1199-206.
- Bhushan A, Gonsalves A, Menon JU. Current state of breast cancer diagnosis, treatment, and theranostics. *Pharmaceutics.* 2021;13(5):723.
- Rezapour M, Wesolowski R, Gurcan MN. Identifying key genes involved in axillary lymph node metastasis in breast cancer using advanced RNA-Seq analysis: a methodological approach with GLMQL and MAS. *Int J Mol Sci.* 2024;25(13):7306.
- Zhou J, Zhang Q, Zhang Q, Yan L, Gao Q. Evaluation of the property of axillary lymph nodes and analysis of lymph node metastasis factors in breast cancer by ultrasound elastography. *Comput Math Methods Med* 2022; 2022(1):8066289.
- Mu WN, Li JH, Liu Y, Wen Y, Liu X. Clinical application of ultrasound-guided core needle biopsy histology and fine needle aspiration cytology in cervical lymph nodes. *Pak J Med Sci.* 2023;39(3):752-6.
- Lőrincz KZ, Pap Z, Mocan SL, Lőrincz CE, Baróti B. Ultrasound-guided core-needle biopsy of suspicious breast lesions. *J Interdiscip Med.* 2020;5(2):48-55.
- Jain R, Khanna R, Verma A, Mishra SP, Meena RN, Khanna S, et al. Evaluation of axillary lymph nodes in breast cancer patients with clinically negative axilla using contrast enhanced ultrasonography. *World J Surg Oncol.* 2024;22(1):211.
- Szaro P, Wong A, Blain E, Gataa KG, Geijer M. The diagnostic value of ultrasound-guided percutaneous core needle biopsy of musculoskeletal soft tissue lesions. *J Ultrason* 2021;21(84):22-33.
- Mansoor I, Afzal S, Vohra LM, Khan N, Nadeem A. To determine diagnostic accuracy of axillary ultrasound in the assessment of axillary lymph nodes for metastasis in breast cancer. *Pak J Radiol.* 2022;32(2):70-5.
- Sidhwani SK, Khan MW, Suhag AH, Najeeb S, Humayun L, Syed S. Accuracy of Ultrasound-Guided Core Biopsy for Staging Axilla in Clinically Node-Negative Patients with Invasive Breast Cancer Taking Histopathology as Gold Standard. *J Dow Uni Health Sci.* 2024;18(3):137-43.
- Afzal S, Masroor I, Munir A, Idress R, Khan P, Khan S. Preoperative ultrasound-guided core biopsy of axillary nodes for staging of clinically negative axilla in breast cancer patients-a pilot study. *Cureus.* 2020;12(1):1-9.
- Stachs A, Göde K, Hartmann S, Stengel B, Nierling U, Dieterich M, et al. Accuracy of axillary ultrasound in preoperative nodal staging of breast cancer-size of metastases as limiting factor. *Springerplus.* 2013;2(1):350-8.