

ROLE OF SENTINEL LYMPH NODE BIOPSY IN HIGH GRADE DUCTAL CARCINOMA IN SITU

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Abstract

This prospective observational study explored the clinical relevance of sentinel lymph node biopsy (SLNB) in patients diagnosed with high-grade ductal carcinoma in situ (DCIS) at Tertiary care hospital Karachi over a six-month period. Sixty female patients undergoing mastectomy or breast-conserving surgery were enrolled, all of whom received SLNB as part of their surgical management. Final histopathological analysis revealed that 33.3% of these patients had invasive carcinoma, with 16.7% showing microinvasion and another 16.7% exhibiting more extensive invasion. Notably, SLNB detected lymph node metastases in 48.3% of the cohort. SLN positivity was significantly associated with the presence of invasive disease (70% in invasive cases vs. 37.5% in non-invasive, $p = 0.001$), and was also closely linked with high-risk histopathological features such as comedonecrosis, calcifications, and microinvasion. Among patients who exhibited two or more of these features, the incidence of invasive carcinoma exceeded 60%, suggesting their strong predictive value for occult invasion and potential nodal spread. These findings indicate that SLNB may provide critical staging information even in patients preoperatively diagnosed with non-invasive DCIS, particularly those undergoing mastectomy or displaying aggressive pathological features. While this study did not find a statistically significant relationship between SLNB status and recurrence during the follow-up period, the high incidence of nodal involvement supports a selective approach to SLNB in high-grade DCIS. Implementing such a strategy could help refine treatment plans, avoid under-staging, and potentially improve outcomes, while still minimizing unnecessary procedures in low-risk patients. Future studies with longer follow-up and larger sample sizes should further assess the prognostic implications of SLNB findings and explore the integration of molecular and imaging biomarkers to enhance patient selection criteria.

High-grade ductal carcinoma in situ (DCIS), Sentinel lymph node biopsy (SLNB), Occult invasion, Microinvasion, Comedonecrosis, Calcifications, Breast cancer staging.

INTRODUCTION

Ductal carcinoma in situ (DCIS) is a recognized non-invasive precursor to breast cancer, often discovered through routine mammography. This condition includes various lesions characterized by malignant cells restricted to the ductal epithelium, with no invasion into surrounding tissues. One subtype, high-grade DCIS, warrants particular focus due to its aggressive nature, higher chances of recurrence, and greater risk of advancing to invasive ductal carcinoma (IDC) ^{1, 2}. Notable features include significant nuclear pleomorphism, necrotic areas, and elevated Ki-67 proliferation indices, all of which highlight the importance of careful diagnostic and therapeutic approaches in managing high-grade DCIS ³.

In treating high-grade DCIS, clinicians must accurately evaluate the extent of the disease and the risk of progression or the presence of invasive cancer. Typical management strategies include breast-conserving surgery or mastectomy, often accompanied by radiation therapy. However, treatment decisions can become complex due to the potential presence of hidden invasive components, which significantly impact axillary staging and further treatment planning ⁴.

Sentinel lymph node biopsy (SLNB) has become integral in invasive breast cancer management, yet its role in high-grade DCIS is still debated ⁵. Although SLNB is not routinely prescribed for DCIS, given the low likelihood of nodal metastasis, certain clinical scenarios like mastectomy, larger tumor size, or imaging suggestive of invasive disease may justify its use ^{6,8}. This topic is important as it weighs the advantages of accurate nodal staging against the risks of unnecessary treatments in cases without invasive traits.

Recent developments in sentinel node mapping and findings from studies conducted between 2022 and 2024 have added depth to this discussion, providing valuable insights into patient selection for SLNB in high-grade DCIS ^{9, 10}. This study aims to critically assess the changing role of SLNB in high-grade DCIS by integrating current evidence and clinical guidelines. By examining the intricate relationship between the characteristics of DCIS, clinical challenges, and

the ongoing debate surrounding SLNB, we can better understand situations where SLNB may be beneficial. Our analysis is based on the latest diagnostic methods and treatment advances, to refine personalized management strategies for patients with high-grade DCIS while minimizing unnecessary interventions. This review plays a significant role in efforts to enhance outcomes for this distinct group of breast cancer patients.

METHODOLOGY

This study investigates the significance of sentinel lymph node biopsy (SLNB) for patients diagnosed with high-grade ductal carcinoma in situ (DCIS) at a Tertiary care hospital in Karachi from ~~September 2024- February 2025~~. Given the considerable risk that high-grade DCIS may progress to invasive cancer, assessing the role of SLNB in informing treatment strategies is crucial. The study employs a prospective observational design, with the sample size calculated based on a 95% confidence interval and a 5% margin of error, indicating that around 60 patients will be necessary to achieve statistically meaningful results.

Inclusion Criteria: Eligible participants included female patients aged 18 to 70 years diagnosed with high-grade ductal carcinoma in situ (DCIS) on biopsy and scheduled for mastectomy or breast-conserving surgery.

Exclusion Criteria: Patients were excluded if they had a history of invasive breast carcinoma, metastatic disease, or previous diagnosis or treatment for breast cancer. Additionally, those with contraindications to sentinel lymph node biopsy (SLNB), such as active infections or allergies to biopsy materials, were excluded.

Data were thoroughly gathered for each participant, including demographic information (such as age, gender, and medical history), details about the tumor (including size, grade, type, and presence of microinvasion or calcifications), treatment strategies, and evaluations of lymph nodes. The study's methodology included recruiting patients from the surgical oncology

clinic, with informed consent secured before their involvement.

In the SLNB procedure, a standard protocol was adhered to that involved the injection of blue dye /or a radioactive tracer. The sentinel lymph nodes were then surgically removed and sent for histopathological evaluation (e.g, micro invasion, necrosis, and calcifications). Statistical analyses were conducted using SPSS version 25.0, which provided descriptive statistics to summarize patient demographics, tumor features, and lymph node status. Continuous variables were expressed as mean $\pm$ standard deviation (SD) and compared using t-tests. In contrast, categorical variables were evaluated through chi-square tests or Fisher's exact tests to determine significant associations, with a p-value of less than 0.05 considered statistically significant. Additionally, the study assessed the diagnostic accuracy, sensitivity, specificity, and predictive values of SLNB for high-grade DCIS using standard formulas.¹¹ The goal of this research is to shed light on the role of SLNB in managing patients with high-grade DCIS, ultimately aiming to enhance management strategies and improve patient outcomes.

Results

This study included 60 female patients diagnosed preoperatively with high-grade ductal carcinoma in situ (DCIS). The average age of the participants was 53.97 years ($\pm$ 4.91), ranging from 44 to 63 years. Imaging indicated an average tumor size of 2.80 cm ($\pm$ 0.55), with sizes ranging from 2 cm to 4 cm.

Post-surgery, the final histopathological results showed that 20 patients (33.3%) had invasive disease. Among these, 10 patients (16.7%) exhibited microinvasion ($\leq$ 1 mm), while the other 10 had more significant invasive characteristics ($>$ 1 mm). The remaining 40 patients (66.7%) were confirmed to have noninvasive DCIS.

Sentinel lymph node biopsy (SLNB) was conducted for all participants. Lymph node metastases were found in 29 patients (48.3%), with the highest incidence in those diagnosed with invasive disease. Specifically, 70% (14 out of 20) of patients with invasive carcinoma had positive SLNB results, compared to only 37.5% (15 out of 40) in the noninvasive group. This difference was statistically significant ($p = 0.001$).

The study also explored the histopathological subtypes relative to the invasion status. Pure DCIS was more commonly seen in the noninvasive cohort (62.5%). On the other hand, invasive cases often featured necrosis and microinvasion, with comedonecrosis occurring in 70% (14 out of 20) of invasive cases, while just 27.5% (11 out of 40) in the noninvasive category exhibited this characteristic. A similar pattern was found with microinvasion, which appeared only in patients later identified with invasive disease.

The preoperative diagnostic methods were not evenly represented. A larger proportion of patients diagnosed with invasive cancer were identified through core needle biopsy rather than excisional biopsy, reflecting findings from previous studies; however, a statistical analysis of this association was not performed due to a small sample size.

In terms of surgical intervention, 35 patients (58.3%) underwent mastectomy and 25 patients (41.7%) had breast-conserving surgery. There was no statistically significant correlation between the type of surgery and recurrence ($p = 0.267$). Disease recurrence was observed in 17 patients (28.3%) during the follow-up period.

When evaluating multiple risk factors such as necrosis, microinvasion, and calcifications, it was found that the chance of invasive disease increased progressively. Patients with two or more risk factors (necrosis, microinvasion, calcifications) had $>$ 60% probability of invasion, consistent with stratification models like DCIS-Met¹².

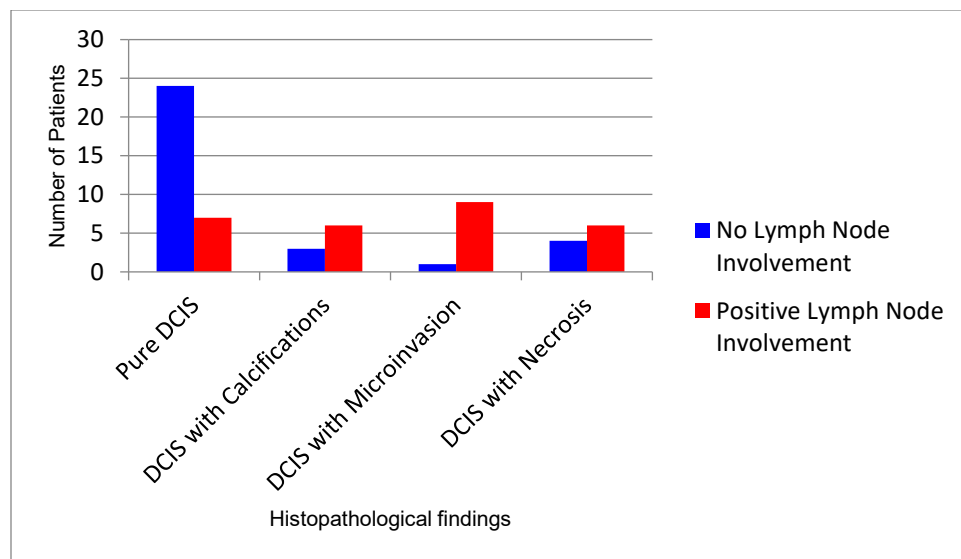
Table 1: Histopathological findings (n=60)

Histopathological Finding	Frequency (n)	Percentage (%)
Pure DCIS (Noninvasive)	40	66.7
DCIS with Microinvasion ($\leq$ 1 mm)	10	16.7
DCIS with Invasion ($>$ 1 mm)	10	16.7

Comedonecrosis (Any group)	25	41.7
Calcifications (Any group)	9	15.0

Table 2: Sentinel lymph node biopsy (SLNB) results

SLNB Result	Frequency (n)	Percentage (%)
Negative	31	51.7
Positive	29	48.3

**Figure 1: Lymph node involvement by histopathology**

Discussion

While DCIS is defined by non-invasiveness, occult invasion is not uncommon in high-grade subtypes, especially those diagnosed via core biopsy [13]. Our 48.3% SLN positivity rate exceeds that in many studies, but aligns with those examining high-grade, larger lesions, or microinvasion [14]. Predictive markers like comedonecrosis and calcifications have shown consistent association with upstaging and SLN metastasis [15].

Some researchers advocate limiting SLNB to cases involving mastectomy or biopsy features suggestive of invasion [16]. Others oppose routine use of SLNB in DCIS, citing overtreatment risks and minimal survival benefit [17,18]. Our findings support a selective approach—reserving SLNB for patients with histological indicators of invasion or those undergoing mastectomy.

Interestingly, we found no significant correlation between SLNB status and recurrence ($p = 0.267$), possibly due to limited follow-up. Long-term outcome studies will be essential to determine

whether SLN involvement predicts poorer prognosis [19]

The clinical application of sentinel lymph node biopsy (SLNB) in cases of high-grade ductal carcinoma in situ (DCIS) remains a topic of ongoing discussion. While DCIS is generally considered a non-invasive condition, our research indicates a noteworthy occurrence of invasive carcinoma at 33.3% and sentinel lymph node positivity at 48.3%.

The detection of SLN metastasis in nearly half of our cohort suggests that a substantial portion of patients diagnosed with high-grade DCIS may harbor occult invasion. This observation echoes previous findings where SLNB identified nodal metastases in up to 12–18% of high-risk DCIS patients (Rutstein et al.)¹³. In particular, the strong association between SLN positivity and microinvasion (32.1%) underscores the role of SLNB in surgical planning, especially when high-risk histologic features are present¹⁴.

This study identified statistically significant associations between SLN positivity and microinvasion, comedonecrosis, and calcifications. These findings are consistent with prior literature suggesting that high nuclear grade, lesion size >2 cm, and comedonecrosis are predictive of upstaging or nodal spread (Villegas-Carlos et al.)¹⁵. Such histopathological markers can aid in triaging which patients may benefit from SLNB, rather than basing the decision solely on the planned surgical approach¹⁶.

Despite our findings and those from similar studies, some authors argue against routine SLNB in DCIS. Farkas et al. and Kelly et al. reported no or minimal nodal involvement among DCIS patients undergoing SLNB or ALND, especially in the absence of microinvasion (González-Vidal et al.)^{16, 17, 18}. These studies emphasize the risk of overtreatment and recommend SLNB only in clearly high-risk or surgically constrained contexts. Given that 58.3% of our patients underwent mastectomy and SLNB detected metastatic disease in a subset lacking invasive features, this study data supports the growing consensus that SLNB should be performed concurrently with mastectomy in high-grade DCIS. This study analysis found no significant link between SLN status and recurrence ($p = 0.267$), the follow-up duration was limited. Longitudinal data will be essential to determine if SLN positivity predicts poorer long-term outcomes¹⁹.

Our findings, consistent with those of several other high-risk DCIS studies, advocate for the selective use of SLNB based on histopathological features. In patients undergoing mastectomy or those diagnosed via core biopsy with necrosis or microinvasion, SLNB appears justified. More studies should be conducted with special focus with integrating molecular profiling and imaging tools to refine risk stratification further.

Conclusion

Our study highlights the **high rate of SLN positivity in high-grade DCIS**, particularly in cases with **microinvasion, necrosis, and calcifications**. These findings suggest that **SLNB should be considered in selected high-risk patients**, regardless of surgical approach. While our results

do not establish a direct link between SLN involvement and recurrence, they emphasize the need for further investigation into the prognostic significance of SLN metastases in DCIS. Future studies should focus on **refining patient selection criteria** to ensure optimal management while minimizing unnecessary procedures.

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