

Research Article

Correlation of Tumor Biology (ER/PR/HER2) With SLN Metastasis

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ABSTRACT

Background: Breast cancer is a complex disease, meaning it can have different biological characteristics and spread to other parts of the body. SLNB is a crucial procedure used in the axillary staging of early breast cancer, which is clinically node-negative. Estrogen receptor (ER), progesterone receptor (PR) and human epidermal growth factor receptor 2 (HER2) are tumor biology markers that could affect the risk of lymphatic spread.

Objective: To determine the correlation of ER, PR and HER2 status with sentinel lymph node metastasis among patients with Stage I-II invasive breast carcinoma.

Methods: In this descriptive analytical study, 85 women with histologically confirmed Stage I-II invasive breast carcinoma who had sentinel lymph node biopsy were included. The study was conducted at a Tertiary Care Hospital of Rawalpindi, over a period of six months, from January 2026 to June 2026. Patients who received neoadjuvant therapy, had locally advanced breast cancer, had distant metastasis or had recurrent disease were excluded. Data regarding demographic features, tumor stage, tumor grade, lymphovascular invasion, ER status, PR status, HER2 status and sentinel lymph node findings were recorded. Chi-square test or Fisher's exact test was used to determine the association of tumor biology markers with sentinel lymph node metastasis, and logistic regression was used to determine the value of tumor biology markers as predictors of SLN positivity. The p value < 0.05 was regarded as statistically significant.

Results: The mean age of patients was 48.7 ± 10.6 years. Stage II disease was present in 54 patients (63.5%), while Stage I disease was present in 31 patients (36.5%). Sentinel lymph node metastasis was identified in 28 patients (32.9%), whereas 57 patients (67.1%) were SLN-negative. ER-negative tumors showed a higher rate of SLN metastasis than ER-positive tumors (48.3% vs 25.0%, $p=0.041$). PR-negative tumors were also more frequently associated with SLN positivity than PR-positive tumors (44.4% vs 24.5%, $p=0.049$). HER2-positive tumors demonstrated the highest SLN positivity rate compared with HER2-negative tumors (52.0% vs 25.0%, $p=0.015$). SLN metastasis was also significantly associated with Stage II disease, T2 tumor size, Grade III tumors and lymphovascular invasion. On logistic regression, HER2-positive status, ER-negative status, Stage II disease, Grade III tumor and lymphovascular invasion were significant predictors of SLN metastasis.

Conclusion: Sentinel lymph node metastasis was observed in nearly one-third of patients with Stage I-II invasive breast carcinoma. ER-negative, PR-negative and HER2-positive tumors were more frequently associated with SLN involvement. HER2 positivity, ER negativity and lymphovascular invasion were important predictors of sentinel lymph node metastasis. Assessment of tumor biology markers along with clinicopathological features may improve nodal risk stratification in early-stage breast cancer.

Keywords: Breast Cancer, Sentinel Lymph Node, ER Status, PR Status, HER2 Status, Tumor Biology, Lymph Node Metastasis.

INTRODUCTION

Breast cancer is one of the most prevalent cancers among women worldwide and is still a leading cause of cancer-related morbidity and mortality. The clinical characteristics are very different between patients as breast cancer is

a wide range of tumors. Tumors that are of similar size and stage can have different molecular and receptor profiles which can mean that they will behave differently. So the evaluation of tumor biology has become an

integral component of the diagnosis, prognosis and treatment planning of breast cancer (1-3). One of the most significant factors of prognosis in breast cancer is axillary node status. Nodal metastasis is a sign of regional spread and is indicative of a higher risk of recurrence and worse clinical outcome. Axillary lymph node dissection was traditionally performed for staging of axilla, but it has a high risk of complications including lymphedema, arm swelling, pain and limited shoulder motion. The sentinel lymph node biopsy has thus emerged as an important and less invasive technique for the axillary staging in clinically node-negative early breast cancer. It aids to determine whether there is nodal metastasis or not, and to avoid unnecessary axillary dissection of patients with no nodal involvement (4-6).

Sentinel lymph node metastasis is a sign of the initial spread of the cancer via the lymphatic system. The detection of SLN involvement in early breast cancer has a direct clinical relevance since it can guide surgery, determine adjuvant therapy and follow up. Although tumor size, grade, lymphovascular invasion and stage are well-recognized predictors of nodal metastasis, increasing attention has been given to the role of biological markers in predicting lymph node involvement. These markers may be of more value than the traditional histopathological characteristics in determining the metastatic potential of the tumour (7-9).

Breast cancer patients routinely have their estrogen receptor, progesterone receptor and HER2 status evaluated. Tumors that are ER and PR positive tend to be better differentiated and have a stronger response to hormone therapy. Hormone receptor-negative tumors, on the other hand, tend to be more aggressive. The specific characteristics of HER2-positive tumors are higher proliferation, invasiveness and higher metastatic potential, but with targeted anti-HER2 therapy, clinical outcomes have improved. The link between these receptor markers and sentinel lymph node metastasis is clinically relevant as it may help to identify those at higher risk of SNDC (10, 11).

Understanding the correlation between ER, PR, HER2 status and sentinel lymph node metastasis is important for improving risk assessment in early breast cancer. Receptor patterns that correlate with increased SLN positivity could be used as useful clinical tools to inform clinical decision making and

personalize treatment. This is of particular value in stage I-II breast cancer, when the patients are clinically node-negative, but may have occult nodal disease on histopathology.

The present study was conducted to determine the correlation of tumor biology markers, including ER, PR and HER2 status, with sentinel lymph node metastasis among patients with Stage I–II invasive breast carcinoma. The study also assessed the association of sentinel lymph node metastasis with clinicopathological factors such as tumor stage, tumor size, grade and lymphovascular invasion.

METHODOLOGY

This study was designed as a descriptive analytical study to evaluate the correlation of tumor biology markers, including estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2), with sentinel lymph node metastasis among patients with early-stage breast carcinoma. The study was conducted at a Tertiary Care Hospital of Rawalpindi, over a period of six months, from January 2026 to June 2026. A total of 85 female patients diagnosed with invasive breast carcinoma were included in the study after applying the predefined selection criteria.

All female patients with invasive breast cancer (Stage I or Stage II) diagnosed by histopathology and scheduled for primary Sentinel lymph node biopsy were eligible for the study. Eligible patients were those who showed clinically node-negative disease at physical examination and/or imaging evaluation, and had complete immunohistochemistry reports for ER, PR, and HER2 status. Patients who were excluded were those with locally advanced breast cancer, distant metastasis, recurrent breast carcinoma, a previous breast surgery, a previous chemotherapy or radiotherapy, incomplete histopathological records, and non-invasive carcinoma. Here the following criteria were used to assure that patients included in the study were early-stage breast cancer patients for which sentinel lymph node biopsy is clinically relevant.

Demographic and clinical data were collected in a structured proforma with informed consent. Data collected included age, menopausal status, tumor side, clinical stage, tumor size, and clinical findings. Tumor staging was done following the breast cancer staging criteria and the patients were staged

as Stage I or Stage II. Preoperative evaluation was done by clinical examination and imaging studies available, including sentinel lymph node biopsy, to confirm that patients were clinically node-negative.

Biopsy or surgical specimens from tumors were subjected to histopathological examination. Histological type of breast carcinoma, tumour grade, tumour size, and the presence or absence of lymphovascular invasion were noted. The grading of tumors was based on the standard histopathological grading system (Grade I, Grade II, or Grade III). The size of the tumor was defined as T1 or T2. Lymphovascular invasion was assessed on the tumor sections and was classified as present or absent.

The immunohistochemistry method was used to determine the biology of tumors. The nuclear staining of tumor cells was used for reporting ER and PR status as positive or negative. Immunohistochemical staining was used to determine HER2 status and the positivity was defined using standard scoring criteria. Patients with equivocal HER2 results were managed per institutional protocol, and only patients whose final HER2 result was documented were included in the analysis. Patients were divided into groups based on their receptor status: ER positive, ER negative, PR positive, PR negative, HER2 positive and HER2 negative. These markers were deemed as the principal independent variables in the study.

Surgery with sentinel lymph node biopsy (SLNB) was used in the treatment of clinically node-negative early breast cancer patients. Sentinel nodes that were found during the procedure were taken out and examined with a microscope. The number of sentinel lymph nodes removed, and the number of positive sentinel lymph nodes was recorded. Sentinel lymph node metastasis was considered to be the presence of metastatic tumors in the Sentinel lymph nodes after histopathology examination. Patients were divided into two main outcome groups: SLN-positive and SLN-negative. When present, the patterns of metastasis were further characterized as either micrometastasis or macrometastasis in SLN-positive cases.

Sentinel lymph node metastasis (positive or negative) was the primary outcome measured. ER status, PR status and HER2 status were the key explanatory variables. Other clinicopathological parameters such as age, menopausal status, tumor size, clinical stage, tumor grade, tumor histological type, and lymphovascular invasion were also examined to assess their correlation with SLN involvement. This allowed the evaluation of the relationship of nodular metastasis with the occurrence of biologically aggressive tumor profiles.

The data were inputted and analyzed using SPSS version 26. The quantitative variables like age were represented as mean and SD. Categorical variables such as receptor status, tumour stage, tumour grade, the presence of lymphovascular invasion and sentinel lymph node status were reported as frequencies and percentages. The relationship between ER, PR, HER2 status and sentinel lymph node metastasis was determined by the chi-square test or Fisher's exact test, as appropriate. A p value < 0.05 was taken as statistically significant. Logistic regression analysis was used to determine independent predictors of sentinel lymph node metastasis. The clinical relevance or significant association of each variable on univariate analysis was included in the regression model. Results were presented as OR (95% CI) and P value. This assessment was used to establish if tumor biology markers (ER negativity, PR negativity or HER2 positivity) would independently be associated with sentinel lymph node metastasis after adjusting for other clinicopathological parameters.

RESULTS

The study included 85 female patients with early stage (Stage I–II) invasive breast carcinoma. The mean age of the patients was 48.7 ± 10.6 years, and the age group with the highest number of patients was the 41–50 age group. The most common stage of the disease was Stage II, with the most common histological type being invasive ductal carcinoma. Twenty-eight patients (32.9%) had sentinel lymph node metastases and fifty-seven patients (67.1%) did not have sentinel lymph nodes.

Table 1. Baseline demographic and clinical characteristics of patients

Variable	Frequency (n)	Percentage (%)
Age group		
≤40 years	19	22.4

41–50 years	34	40.0
51–60 years	21	24.7
>60 years	11	12.9
Mean age	48.7 ± 10.6 years	
Menopausal status		
Premenopausal	46	54.1
Postmenopausal	39	45.9
Tumor side		
Right breast	43	50.6
Left breast	42	49.4
Clinical stage		
Stage I	31	36.5
Stage II	54	63.5

In the cohort of included patients, there were more patients with Stage II than Stage I disease. A marginally larger proportion of premenopausal women was part of the study

participants. There was a nearly equal distribution of laterality of tumor between right breast and left breast lesions.

Table 2. Histopathological and tumor biology profile of patients

Variable	Frequency (n)	Percentage (%)
Histological type		
Invasive ductal carcinoma	72	84.7
Invasive lobular carcinoma	8	9.4
Other types	5	5.9
Tumor grade		
Grade I	13	15.3
Grade II	46	54.1
Grade III	26	30.6
Tumor size		
T1	32	37.6
T2	53	62.4
Lymphovascular invasion		
Present	30	35.3
Absent	55	64.7
ER status		
Positive	56	65.9
Negative	29	34.1
PR status		
Positive	49	57.6
Negative	36	42.4
HER2 status		
Positive	25	29.4
Negative	60	70.6

The most common histological type was invasive ductal carcinoma. The majority of the tumors were Grade II and T2. Patients had high levels of hormone receptor positivity, with

65.9% of patients expressing estrogen receptors and 57.6% expressing progesterone receptors. The 29.4% of cases that were positive for HER2 were identified.

Table 3. Frequency and pattern of sentinel lymph node metastasis

SLN finding	Frequency (n)	Percentage (%)
SLN negative	57	67.1
SLN positive	28	32.9
Type of SLN metastasis among positive cases, n=28		

Micrometastasis	9	32.1
Macrometastasis	19	67.9
Number of positive SLNs among positive cases, n=28		
1 positive node	17	60.7
2 positive nodes	8	28.6
≥3 positive nodes	3	10.7

Almost one-third of patients had sentinel lymph node involvement. Macrometastasis was more common than micrometastasis among the patients with a positive SLN.

Limited nodal disease was seen in most of the patients with involvement of sentinel lymph nodes, as the majority of them had only a single positive node.

Table 4. Association of ER, PR and HER2 status with sentinel lymph node metastasis

Tumor biology marker	SLN positive n (%)	SLN negative n (%)	p-value
ER status			
ER positive, n=56	14 (25.0)	42 (75.0)	0.041
ER negative, n=29	14 (48.3)	15 (51.7)	
PR status			
PR positive, n=49	12 (24.5)	37 (75.5)	0.049
PR negative, n=36	16 (44.4)	20 (55.6)	
HER2 status			
HER2 positive, n=25	13 (52.0)	12 (48.0)	0.015
HER2 negative, n=60	15 (25.0)	45 (75.0)	

There was a strong correlation between the tumor receptor profile and sentinel lymph node metastasis. The percentage of SLN metastasis was higher in ER-negative tumors than in ER-positive tumors. Likewise, SLN was

more common among PR-negative than PR-positive tumors. The highest number of SLNs with metastasis was seen in HER2+ tumors and this was statistically significantly associated.

Table 5. Association of tumor stage, grade and lymphovascular invasion with SLN metastasis

Variable	SLN positive n (%)	SLN negative n (%)	p-value
Clinical stage			
Stage I, n=31	5 (16.1)	26 (83.9)	0.018
Stage II, n=54	23 (42.6)	31 (57.4)	
Tumor size			
T1, n=32	6 (18.8)	26 (81.2)	0.029
T2, n=53	22 (41.5)	31 (58.5)	
Tumor grade			
Grade I, n=13	2 (15.4)	11 (84.6)	0.036
Grade II, n=46	13 (28.3)	33 (71.7)	
Grade III, n=26	13 (50.0)	13 (50.0)	
Lymphovascular invasion			
Present, n=30	18 (60.0)	12 (40.0)	<0.001
Absent, n=55	10 (18.2)	45 (81.8)	

Sentinel lymph node metastasis was significantly higher in patients with Stage II, T2, Grade III and in those with lymphovascular invasion. The greatest

association was seen with lymphovascular invasion (60.0% vs. 18.2% for SLN positive vs. negative, respectively).

Table 6. Logistic regression analysis for predictors of sentinel lymph node metastasis

Predictor	Odds ratio	95% CI	p-value
ER-negative status	2.18	1.01–5.62	0.047

PR-negative status	1.94	0.91–4.78	0.068
HER2-positive status	2.76	1.15–6.63	0.023
Stage II disease	2.92	1.04–8.21	0.042
Grade III tumor	2.41	1.02–5.91	0.046
Lymphovascular invasion	4.85	1.91–12.30	0.001

Logistic regression analysis revealed that HER2 positivity, ER negativity, Stage II disease and Grade III tumor and lymphovascular invasion were significant factors associated with sentinel lymph node metastasis. There were significant differences in the odds of SLN positivity, with the highest odds for tumors with vascular or lymphatic invasion. However,

the relationship between PR-negative status and SLN metastasis was not significant. Overall, the results indicated that the presence of sentinel lymph node metastasis was more common in biologically aggressive breast cancers, specifically ER-negative, HER2-positive, high grade, larger, stage II, and with lymphovascular invasion.

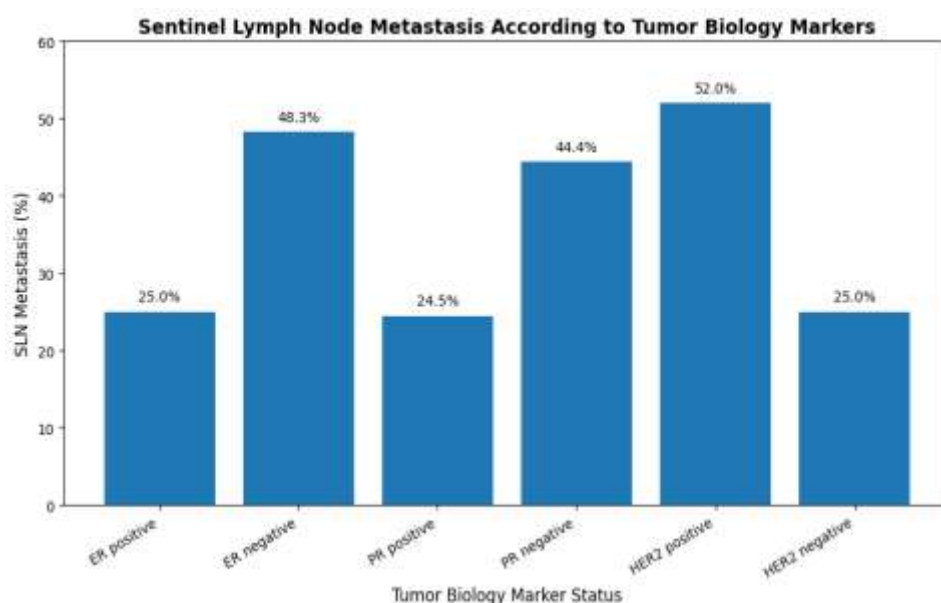


Figure 1. Sentinel lymph node metastasis according to ER, PR and HER2 status. The graph shows that SLN metastasis was more frequent in ER-negative, PR-negative, and HER2-positive tumors, with the highest rate observed among HER2-positive cases.

DISCUSSION

The present study evaluated the correlation of tumor biology markers, including ER, PR and HER2 status, with sentinel lymph node metastasis in patients with early-stage breast carcinoma. Sentinel lymph node metastasis was identified in 28 out of 85 patients, giving an overall positivity rate of 32.9%. This finding indicates that nearly one-third of clinically early-stage breast cancer patients had microscopic or macroscopic nodal involvement on histopathological assessment. The presence of SLN metastasis is clinically important because it reflects early lymphatic spread and may influence further axillary management, adjuvant treatment planning and risk stratification (12-14).

The rate of metastasis to Sentinel Lymph Node was higher for ER-negative tumors than for

ER-positive tumors in this study. Likewise, the SLN positivity was more common in PR-negative than PR-positive tumors. The results indicate a possible correlation between loss of hormone receptor expression and the more aggressive tumor phenotype and metastatic potential. Endocrine therapy is more likely to be effective on hormone receptor-positive tumors, which are typically less aggressive and grow slower, while hormone receptor-negative tumors tend to grow faster and have a higher grade and/or regional spread. Therefore, the observed link between ER/PR negativity and SLN metastasis, reinforces the value of receptor status as a biological parameter in the assessment of breast cancer (15, 16).

The current study showed that the most common sentinel lymph node metastasis group was HER2-positive. SLN involvement

was more common in the HER2-positive tumors (more than 50%) compared to the HER2-negative tumors. Cancer cells that overexpress HER2 tend to multiply rapidly, invade tissues and behave more aggressively than those that do not overexpress the protein. In the current study, the strong correlation of HER2 positivity with SLN metastases implies that, even in the absence of clinically palpable nodes, HER2 positive tumors may be more likely to be involved in the SLN. This discovery underscores the need for careful evaluation of the axilla in patients with early breast cancer that is HER2-positive (17).

The other clinicopathological factors, apart from receptor status, were also significantly associated with SLN metastasis. SLN positivity was significantly statistically associated with more frequent staging of II and III, more frequent Grade III tumors and more frequent lymphovascular invasion. Microscopic tumor invasion into the lymphatic or vascular spaces (lymphovascular invasion) was the strongest association with SLN involvement, highlighting that it is a strong marker of nodal spread. Higher tumor size and tumor grade also indicate more tumor burden and biological aggressiveness, which could account for the correlation between these tumors and sentinel lymph node positivity. It is important to recognise that these findings must not be seen in isolation, and must be considered in conjunction with stage, grade, tumour size and lymphovascular invasion (18-20).

Logistic regression revealed that HER2 positivity, ER negativity, stage II disease, grade III tumor and LVI were significant predictors of SLN metastasis. Of these, SLN positivity was associated with highest odds followed by Stage II disease and HER2 positivity. PR negative status was associated with higher odds, although this was not statistically significant, which implies that PR status may also be a risk factor for nodal disease, but may not be as strong when other tumor factors are taken into account. In summary, this study indicates that biologically aggressive breast cancer (ER negative and HER2 positive) may be more likely to be linked to sentinel lymph node metastasis especially when the tumor is of high grade and with lymphovascular invasion. The findings could aid clinicians in identifying patients that need a more detailed examination of the nodes, or in tailoring treatment for each person.

CONCLUSION

This study concluded that sentinel lymph node metastasis was present in a considerable proportion of patients with early-stage breast carcinoma. Tumor biology showed a meaningful association with SLN involvement, as ER-negative, PR-negative and HER2-positive tumors had higher rates of nodal metastasis compared with their respective counterparts. HER2 positivity and ER negativity were significant predictors of sentinel lymph node metastasis.

Clinicopathological factors including Stage II disease, larger tumor size, higher tumor grade and lymphovascular invasion were also significantly associated with SLN positivity. Lymphovascular invasion emerged as the strongest predictor of nodal metastasis. These findings suggest that assessment of ER, PR and HER2 status, together with conventional histopathological features, can improve prediction of sentinel lymph node involvement in early-stage breast cancer patients. Tumor biology should therefore be considered an important component of risk assessment and treatment planning in patients undergoing sentinel lymph node biopsy.

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