



## A STUDY OF CLINICOPATHOLOGICAL CHARACTERISTICS FOR SENTINEL LYMPH NODE METASTASIS IN EARLY BREAST CANCER

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### ABSTRACT

**Aims and objectives:** Our study aimed to identify the predictors for sentinel lymph node (SLN) metastasis in early breast cancer patients and provide evidence for rational decision-making in specified clinical situations..

**Methodology:** Medical records of 417 breast cancer patients who were treated with a breast surgical procedure and SLNB in our tertiary hospital in western India were retrospectively reviewed from jan 2015 to december 2016.

**Results:** In the cohort of 417 cases, the ratio of SLNM was 23.0%. Univariate analysis found that age, tumor size, histological grade, and Ki67 index were associated with SLN metastasis. However, age, tumor size, and histological grade were the only three independent predictors

**KEYWORDS :** breast neoplasm

### Introduction:

As we all know that Axillary lymph node status is the most important prognostic factor for predicting survival in cases of invasive breast cancer [1–5]. However, sentinel lymph node biopsy (SLNB), as a minimally invasive surgical procedure, has emerged as the preferred technique for axilla staging especially in patients who are free of clinically detected lymph node metastasis [6–9]. Moreover, compared with the standard AxLND, there are two advantages to SLNB. First, it has better cosmetic results [10] and is associated with less arm and shoulder complications, including upper limb pain, sensory loss, lymphedema, and lymphangiosarcoma [11–13]. Second, it can provide a rapid intraoperative diagnosis and help surgeons to decide whether AxLND should be performed.

However, the reported incidence of SLN metastasis varies from 33.2–39% [14–16] and approximately 60–70% of patients suffered from unnecessary invasive axilla surgery. Therefore, we reviewed consecutive patients with early breast cancer who underwent breast and SLN surgical procedure in our hospital to determine the predictors for SLN metastasis.

### Materials and methods:

A total of 561 breast cancer patients who had breast surgery and SLNB at a teaching Hospital in western India between Jan 2015 and december 2016 were considered for the study. Of these, 144 cases were excluded from the study for the following reasons: in situ carcinoma (123 cases), bilateral breast cancer (six cases), male breast cancer (two cases), SLNB failure (eight cases), and only one SLN detected (five cases). Thereafter, 417 eligible cases were enrolled in the study. All patients were female with median age of 51 years old (range 23–80 years).

### Results:

In all, 2,005 SLNs were detected, with the average of  $4.81 \pm 2.15$  (median: 5, range: 2–9). The majority of patients (95.2%) had more than two SLNs, and 4.8% of patients had only two SLNs. (table 1)

Our study found that patient age, tumor size, histological grade, and Ki67 index were associated with the presence of SLN metastasis, while other factors had no relationship with SLN metastasis (Table 2). Four predictive factors which were confirmed to be associated with SLN metastasis by univariate analysis were brought into the multivariate logistic regression analysis model, which found that

patient age, tumor size, and histological grade were independent predictive factors (Table 3).

### Discussion:

Dual tracer technique with isotopic tracer and blue dye tracer has a higher detection rate compared to either of these tracers alone [17,18]. Three blue dye tracers used in clinical research and practice are isosulfan blue, patent blue dye, and methylene blue dye, but none of these are considered the gold standard for SLNB according to the current literatures [17,19–21]. In the present study, we used a single tracer technique with methylene blue dye and identified an average of 4.81 SLNs per patient, and three or more SLNs were detected in 95.2% of patients, which together demonstrated that SLNB with methylene blue tracer technique was a reasonable and feasible surgical procedure, supported further by the fact that when three and more SLNs were identified, the false negative rate decreased to the acceptable 5% level recommended by the American Society of Clinical Oncology (ASCO) guideline [22].

In our series of 417 early breast cancer patients, the presence of SLN metastasis was 23.0%, which was lower than in previous reports, with an incidence range reported in the literature of 33.2–39% [14–16]. This difference may be due to the higher percentage of T1 tumor in our study (73.9%) compared to about 50% in other studies, which might account for the lower metastasis incidence in our study.

Young breast cancer or breast cancer in young women refers to patients with breast cancer who are younger than 35–40 years old, and presented with more aggressive biological behavior and unfavorable prognosis when compared to their counterparts. In the present study, we used 40 years of age as the cutoff point, and found that patient age at the time of diagnosis was significantly associated with a high risk of SLN metastasis. This predictive effect of age on nodal involvement was consistent with earlier evidence that indicated that breast tumors can be more aggressive in younger women [23–25]. Inconsistent results have been reported in recent literature [26], and there are obvious differences in the cutoff point chosen for age, which was younger in our study (40 years old) than has been reported in some other studies (50 years old).

Tumor size was the second predictor for SLN metastasis in our study, which was found to be predictive of axillary lymph node metastasis.

Other studies have found that even in patients with tumor size less than 5–10 mm, there was a significant nodal metastasis in 5–15% of cases. Similar results were also found in our study: 18.8% of patients with tumors no larger than 20 mm and 34.9% of patients with tumor larger than 20 mm had SLN involved.

Previous studies have shown that histological grade has important prognostic value, which is equivalent to that of lymph node status [22] and greater than that of tumor size. A retrospective study demonstrated that patients with grade I, stage II disease had the same survival as those with grade III, stage I disease. However, in a recent report, tumor histological grade was related with SLN metastasis by univariate analysis either in overall sample or in luminal subgroup, but lost predictive value by multivariate logistic regression analysis [26].

The limitations of the study should be acknowledged. First, this was a retrospective, single-institution study with small sample size, which may decrease the reliability of the present study findings. Second, in our study a single tracer technique with methylene blue dye was applied, which was not the preferred technique recommended by the National Comprehensive Cancer Network (NCCN).

**TABLE 1: Clinicopathological characteristic**

	Numbers (n)	Percentage (%)
<b>Age (years)</b>		
<40	68	16.3
40–60	282	67.6
>60	67	16.1
<b>Menstrual status</b>		
Premenopausal	253	60.7
Postmenopausal	164	39.3
<b>BMI</b>		
≤25	273	65.5
>25	144	34.5
<b>Family history</b>		
Yes	27	6.5
No	390	93.5
<b>Laterality of tumor</b>		
Left	210	50.4
Right	207	49.6
<b>Tumor size (cm)</b>		
<1 cm	78	18.7
1–2 cm	230	55.2
>2 cm	109	26.1
<b>Histological grade</b>		
I	62	14.9
II	270	64.7
III	85	20.4
<b>Histological type</b>		
IDC	388	93.0
ILC	4	1.0
Mucinous	20	4.8
Medullary	5	1.2

**Table 2 Relationship of clinicopathologic factors for SLN metastasis.**

Variable	SLNM (n)	SLN-NM (n)	p Value	Hazard ratio	95%CI
<b>Age</b>					
<40 years	24	44			
≥40 years	72	277	0.009	2.098	1.198–3.677
<b>Menstrual status</b>					
Premenopausal	32	132			
Postmenopausal	64	189	0.171	0.716	0.443–1.156
<b>BMI</b>					
≤25	58	215			
>25	38	106	0.235	0.753	0.470–1.205
<b>Family history</b>					
Yes	9	18			
No	87	203	0.188	1.741	0.756–4.013
<b>Laterality of the tumor</b>					
Left	52	158			
Right	44	163	0.392	1.219	0.772–1.926
<b>Tumor size</b>					
≤2 cm	58	250			
>2 cm	38	71	0.001	0.433	0.266–0.705
<b>Histological grade</b>					
I–II	62	270			
III	34	51	0.000	0.344	0.206–0.576
<b>ER</b>					
Positive	76	232			
Negative	20	89	0.178	1.458	0.841–2.526
<b>PR</b>					
Positive	68	222			
Negative	28	99	0.754	1.083	0.657–1.785
<b>HER2</b>					
Positive	16	60			
Negative	80	261	0.652	0.870	0.475–1.594

**Table 3: Multivariate analysis for SLN metastasis predictive parameters.**

Variable	SLNM (n)	SLN-NM (n)	p Value	Hazard ratio	95%CI
<b>Age</b>					
<40 years	24	44			
≥40 years	72	277	0.011	2.188	1.198–4.001
<b>Tumor size</b>					
≤2 cm	58	250			
>2 cm	38	71	0.028	0.616	0.401–0.949
<b>Histological grade</b>					
I–II	62	270			
III	34	51	0.003	0.408	0.224–0.743
<b>Ki67</b>					
Low index	54	224			
High index	42	97	0.574	0.851	0.485–1.494

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