Efficacy of Sentinel Lymph Node Biopsy in Detecting Axillary Metastasis in Breast Cancer Using Methylene Blue

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Abstract Breast cancer is the leading malignancy and the second leading cause of cancer-related deaths. Axillary lymph node status is a very important prognostic factor in breast cancer patients; nodal evaluation is therefore a critical part of breast cancer management. Axillary lymph node dissection results in significant morbidity. Sentinel lymph node biopsy (SLNB) is being used in many centers to stage the axilla in planning axillary dissection management of patients and hence plays an important part in reducing morbidity among patients with carcinoma breast. The objectives of this paper is to study the (1) efficacy of sentinel lymph node biopsy in detecting axillary metastasis, (2) location of sentinel lymph node in the axilla, (3) rate of involvement of sentinel lymph nodes, and (4) incidence of skip metastasis. Thirty-five patients with breast cancer with clinically node-negative axilla were selected for the study. Methylene blue dye was injected intralesional and perilesional 20 min prior to surgery. All patients underwent modified radical mastectomy with sentinel lymph node biopsy and axillary dissection and after pathological examination diagnostic statics, namely sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy were computed. Sentinel lymph node was identified in all of these patients. Sixty percent patients had pathologically positive lymph nodes in the axilla. 90.48% patients of these had sentinel lymph nodes positive for malignant cells. Incidence of skip metastasis is 9.52%. 88.57% patients had sentinel lymph node mapped to level I lymph nodes. Sensitivity of SLNB is 90.48%, specificity is 85.71%, PPV of

is 90.48%, NPV is 85.71%, and accuracy is 88.57%. Sentinel lymph node biopsy is an effective method of staging the axilla and deciding on axillary clearance in patients of carcinoma breast. Unnecessary axillary dissection and associated complications can be prevented in most of patients due to sentinel lymph node biopsy.

Keywords Breast cancer · Sentinel lymph node biopsy · Efficacy · Axillary lymph node dissection

Introduction

Breast cancer is the leading malignancy and the second leading cause of cancer-related deaths [1]. It is well established that axillary lymph node status is a very important prognostic factor in breast cancer patients; nodal evaluation is therefore a critical part of breast cancer management. For this reason, axillary lymph node dissection has been an integral component in the surgical treatment of invasive breast cancer. Furthermore, axillary nodal metastasis is an important aspect in staging breast cancer. Effective adjuvant therapy is currently available and widely accepted [1]. Axillary lymph node dissection also helps with locoregional control of breast cancer [2].

Axillary lymph node dissection has been part of the standard treatment of breast carcinoma since it was proposed by William Halsted (America 1852–1922) [3]. In 1991, Giuliano and coworkers [4] (USA) came with a new concept of axillary lymph node assessment, sentinel lymph node biopsy.

A sentinel lymph node is defined as the first lymph node to which a primary tumor drains. Therefore, the sentinel lymph node is the first lymph node in which metastasis can be found when dissemination has occurred. In analogy to melanoma, lymphatic dissemination of breast carcinoma has been shown to occur in a stepwise fashion [5].

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In 40% of patients with breast cancer, lymph node metastases were found. For the remaining 60% without lymph node metastases, axillary dissection is not beneficial and they are unnecessarily at risk of complications. However, axillary lymph node dissection results in significant morbidity. In 15–30% of patients, permanent lymphedema has been reported. Other complications such as wound infection, seroma, arm weakness, decreased shoulder range of motion, and neurological changes can occur. [6] Skip metastases represent false-negative value for sentinel lymph node biopsy (SLNB). False negativity = (false negative/true positive + false negative) $\times$ 100.

There is a need for a less invasive procedure with lesser morbidity and good prognostic value comparable to axillary lymph node dissection. With this view in mind, there is need to develop technique to identify the spread of cancer in the axillary nodes before the nodes became palpable. Some of the methods of nodal evaluation are axillary sampling, SLNB, ultrasound assessment of axillary nodes followed by aspiration cytology of suspicious lymph node, and PET scan.

Material and Methods

Thirty-five patients of carcinoma breast with clinically negative axilla were subjected to sentinel lymph node biopsy during a period of 2 years from September 2013 to September 2015. These patients were subjected to the required preoperative investigations. Patients suffering from early breast carcinoma (confirmed using FNAC) with clinically node-negative axilla were included in the study. Patients with advanced breast carcinoma, clinically palpable axillary nodes, patients with previous scar on the breast due to any cause, or patients on SSRI therapy were excluded from the study. After ensuring fitness for surgery, these patients were taken for modified radical mastectomy. For sentinel lymph node biopsy, methylene blue dye 10 mg/ml was injected intralesional (1 ml undiluted) and perilesional (2–5 ml undiluted) 20 min prior to surgery for all tumor patients. Primary procedure performed was modified radical mastectomy (Auchincloss) with clearance of the axilla and was done up to level III lymph nodes. The incision was taken over the breast which included the nipple-areola complex and the skin over the tumor, and it was through this incision that the breast tissue and the axilla were cleared to give the best clearance of disease.

Intraoperatively, sentinel lymph node was searched after raising the upper flap. Dissection of axillary tissue to identify stained lymph node was done. After excising the stained lymph nodes, complete axillary clearance and removal of breast tissue were done. Lymph nodes were divided into two groups: the dye-stained lymph node as sentinel node and the rest of the lymph nodes removed by axillary clearance. These

Table 1 Descriptive statistics for size of sentinel node, number of sentinel node, and number of axillary nodes level of axillary lymph node involvement

	Present study (%)	S.P. Somashekhar et al. (2007) [7] (%)	Parmar et al. (2003) [8] (%)
Only level 1	88.57	86	94.8
Only level 2	5.71	6	
Levels 1 and 2	2.86	6	5.2
Intramammary node	2.86	1	
Internal mammary		1	
Total	100.0	100	100

along with the breast specimen were sent for histopathology examination.

Diagnostic statistics, namely sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy were computed to find the relationship and diagnostic value of various tests.

Results and Discussion

Thirty-five patients of carcinoma breast with clinically negative axilla were subjected to sentinel lymph node biopsy. Most of the patients were in the 51–60-year age group. Sixty percent patients had left-side breast cancer. Seventy percent patients had tumor located in the upper outer quadrant, 11% in the inner quadrant, and 17% in the central quadrant. 85.71% patients had T2 tumor with 8.76% patients with invasive ductal carcinoma on cytological examination.

Sentinel lymph node was identified in all 35 cases.

In 88.57% patients, sentinel lymph node was identified in level I axillary lymph node (Table 1: descriptive statistics for level of axillary lymph node involvement.).

The largest sentinel lymph node found is 1.5 cm, and the smallest was 0.5 cm with an average of 0.8 cm. Average number of sentinel lymph nodes identified is 1.8

Table 2 Average size and number of sentinel lymph nodes

Parameters	Present study	S.P. Somashekhar et al. (2007) [7]	Roderick R. Turner (1997) [9]
Size of sentinel node (cm) (mean)	0.80	0.7	
Number of sentinel node	1.80	2	2 (1–8)
Number of axillary nodes	17.34	16	18.9 (range, 7–37)

Table 3 Efficacy of sentinel lymph node biopsy

	Axillary clearance positive	Axillary clearance negative	Total
SLN+	19	2	21
SLN–	2	12	14
Total	21	14	35
	Present study (%)	S.P. Somashekhar et al. (2007) [7] (%)	95% confidence interval
Sensitivity	90.48	96.2	69.62–98.83
Specificity	85.71	100	57.19–98.22
Positive predictive value	90.48	100	69.62–98.83
Negative predictive value	85.71	98.6	57.19–98.22
Accuracy	88.57	99	

(minimum of one node to maximum of three nodes identified in all patients) (Table 2: average size and number of sentinel lymph nodes).

Sensitivity, specificity, positive predictive value, and negative predictive value of sentinel lymph node biopsy is 90.48, 85.71, 90.48, and 85.71%, respectively, accuracy of sentinel lymph node biopsy being 88.57%. False-positive rate of sentinel lymph node biopsy was 14.29% (Table 3: efficacy of sentinel lymph node biopsy).

Thirty-five patients underwent SLNB, out of which 21 patients had pathologically positive axillary clearance. Among 21 patients with positive axillary clearance, 19 patients had pathologically involved sentinel node. So, rate of involvement of SLNB in patient with positive axillary dissection was 90.48% (Table 4: rate of involvement of sentinel lymph nodes in patients with pathologically positive axilla).

Patients in whom sentinel lymph node (node stained with methylene blue) was negative for malignant cell but had positive axillary lymph nodes on axillary clearance were said to have skip metastasis. Out of 21 patients that were axillary clearance lymph node positive, sentinel lymph node was

Table 4 Rate of involvement of sentinel lymph nodes in patients with pathologically positive axilla

	SLN+	SLN–	Total
No of patient	19	2	21
Percentage (%)	90.48	9.52	100.0

Table 5 Incidence of skip metastases

	Present study	S.P. Somashekhar et al. (2007) [7]	Deo et al. (2004) [10]
Incidence of skip metastasis	9.52%	3.7%	8%

positive for metastasis in 19 (90.48%) patients and negative for metastasis in 2 (9.52%). Incidence of skip metastasis is 9.52% in our study (Table 5: incidence of skip metastases).

No adverse effects were noted due to methylene blue injection. Green staining of urine was noted in all the patients for 1 to 2 days. None of the patients had any hypersensitivity reactions.

Conclusion

Sentinel lymph node biopsy is an effective method of staging the axilla in patients with clinically negative axilla. Sensitivity of SLNB in the present study is 90.48%, specificity of SLNB is 85.71%, positive predictive value is 90.48%, negative predictive value is 85.71%, and overall accuracy of SLNB is 88.57%. Thus, patients with SLNB with lymph nodes negative for tumor cell need not be subjected to morbidity associated with axillary clearance and hence better patient outcome in cancer-affected patients.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

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