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The Accuracy of Sentinel Lymph Node Biopsy Compared with Axillary Lymph Node Dissection in Breast Cancer

Sedigheh Tahmasebi♦, Ali Azimi, Abdolrasoul Talei, Zeinab Zakeri

Department of Surgery, Shiraz University of Medical Sciences, Shiraz, Iran

Abstract

Background: Sentinel lymph node biopsy is used as an accurate staging procedure to detect early breast cancer. Several studies have documented that sentinel lymph node biopsy can accurately determine the status of axillary nodes. Sentinel node biopsy offers the advantage of accurately staging the axilla and eliminating the need for a full axillary dissection for patients who have a negative sentinel node. The aim of this study is to determine the predictors of non-sentinel lymph node metastasis by sentinel node biopsy.

Methods: In this study, all patients (n=88) who underwent sentinel node biopsy for invasive breast cancer from June 2005 to June 2010 in Shahid Faghihi Hospital, Shiraz, Iran were enrolled. We reviewed the medical files of patients and their tumor characteristics. Statistical analysis was performed to determine whether any of these characteristics alone could accurately predict the remaining non-sentinel node status. SPSS statistical package was used.

Results: The mean age of the patients was 46.1 years. Tumor size was 2.73 cm. Of the 88 patients who underwent complete axillary node dissection, 34 had metastases in the non-sentinel nodes, with a mean of 4 positive non-sentinel nodes in each patient. Statistically, neither the patient's age nor the clinicopathological features of the tumor were significantly associated with non-sentinel node metastases (all: $P>0.05$).

Conclusion: Our study shows that neither the primary tumor characteristics nor the size of metastasis in the sentinel lymph node can predict the status of non-sentinel nodes. However, further investigation is necessary. Complete axillary node dissection should remain the most appropriate management for patients with positive sentinel lymph nodes.

Keywords: Sentinel lymph node, Axilla, Metastasis, Breast cancer

♦Corresponding Author:
Sedigheh Tahmasebi, MD
Department of Surgery, Shiraz University of Medical Sciences, Shiraz, Iran
Tel: +98-917-703-4508
Email: Tahmasebis@sums.ac.ir

Introduction

Sentinel lymph node (SLN) biopsy is used as an accurate staging procedure to detect early breast cancer. Several studies have documented that SLN biopsy can accurately determine the status of axillary nodes.[1] When the results of

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histopathological examination of SLN are negative; the remaining non-SLNs in the axilla are unlikely to contain tumor cells, even with more intensive pathological analysis of the non-SLNs.

Therefore, SLN biopsy offers the advantage of accurately staging the axilla and eliminating the need for a full axillary dissection in patients with negative SLN. If the SLN is positive, the non-SLNs are much more likely to harbor metastases.[2] Complete axillary lymph node dissection (CALND) is recommended for patients who have SLN metastases. However, the need for routine complete dissection in these patients is questionable.[3-5]

A means for identifying patients at low risk for residual axillary metastases after positive SLN would be helpful in counseling patients regarding the need for CALND. On the other hand, predictive factors for positive non-SLNs are controversial according to different studies. This study evaluates different factors to determine if they can predict the presence of axillary lymph node metastases in patients with positive SLNs.

Patients and Methods

In this study, all patients who underwent SLN biopsy for invasive breast cancer from June 2005 to June 2010 in Shahid Faghihi Hospital, a major academic center for breast cancer in Shiraz, were enrolled. Patients with negative SLN were excluded from analysis. In total, 88 patients participated. In this study, we reviewed the medical files of patients who underwent SLN biopsy by the same technique during the study period.

Based on medical files, we reviewed different patients and tumor characteristics such as age; tumor size; histological type; pathological grade; presence of vascular and lymphatic invasion; tumor necrosis and calcification status; size of metastasis in the SLN; estrogen, progesterone, and HER-2 neu receptor status; and type of surgery performed for each patient. According to the surgical pathology reports, we calculated the ratio of the involved sentinel nodes to total sentinel nodes (Ratio l) and the involved non-sentinel nodes to total non- sentinel nodes (Ratio 2), which were new entities.

Table 1: Patient and primary tumor characteristics.

Characteristics	Number
Mean patient age in years (range)	46.1 (26-78)
Mean tumor size in cm (range)	2.73 (0.8-7)
Mean number SLNs involved (range)	1.6 (1-7)
Mean number non-SLN involved (range)	4 (0-14)
Invasive ducal carcinoma	73 (83%)
Invasive lobular carcinoma	2 (2.2%)
Medullary carcinoma	6 (6.8%)
Other tumor types	7 (7.9%)
Grade 1	27 (30%)
Grade 2	44 (50%)
Grade 3	8 (9.1%)
Grade not reported	9 (10.2%)

Statistical comparisons were performed with Pearson correlation to determine if any association between Ratio 1 and Ratio 2 existed. Then, t-test for quantitative variables, in addition to chi-square and Fisher's exact tests for qualitative variables were performed to determine whether any of these characteristics alone could accurately predict the remaining non-SLN status. SPSS statistical package was used.

Results

Table 1 shows the patients and primary tumor characteristics. The mean age of the patients was 46.1 years. Tumor size was 2.73 cm. Of the 88 patients who underwent complete axillary node dissection, 34 had metastases in the non-SLNs, with a mean of 4 (range: 0 to14) positive non-SLNs.

Invasive ductal carcinoma was noted in 73

Table 2. Distribution of involved SLN to resected SLN (Ratio 1).

Ratio 1	Number of patients
0.1	1
0.13	1
0.2	1
0.25	7
0.33	9
0.4	1
0.5	21
0.6	2
0.66	2
0.67	3
1	40

Table 3. Clinicopathological features evaluated in terms of presence or absence of non-SLN metastasis (quantitative variables).

Patient	Non-SLN positive (mean)	Non-SLN negative (mean)	T	*P* value
Age	46.11	46.15	0.16	0.987
Tumor size	2.82	2.66	0.691	0.491
Ratio 1	0.73	0.66	1.086	0.28

Non-SLN: Non-sentinel lymph node.

(83%) patients, 6 (6.8%) had medullary carcinoma, and 2 (2.2%) had invasive lobular carcinoma. The remaining 7 (7.9%) had other tumor types. Tumor grade was variable. Grade 1 was noted in 27 (31%) patients, 44 (50%) had grade 2, and 8 (9.1%) had grade 3. In 9 (10%) patients, tumor grade was not reported.

Table 2 outlines the distribution of the ratio of the involved SLN to resected SLN. Ratio 1 ranged from 0.1 to 1. Non-SLN metastasis was found in 34 (38%) patients. Ratio 2 ranged from 0 to 0.87.

The results of the Pearson correlation test showed no association between Ratio 1 and Ratio 2 ($P = 0.16$). These entities were not significantly associated, thus we cannot predict Ratio 2 according to Ratio 1.

Tables 3 and 4 show the different clinicopathological features of tumors according to surgical pathological reports. Statistical analysis showed that neither the patient's age nor clinicopathological features of the tumor were significantly associated with non-SLN metastases (all: $P>0.05$).

There were micrometastases (0.2–2 mm) in the SLNs of 5 patients. In one, metastasis was detected in the non-SLN but according to statistical analysis the size of the SLN metastasis did not have a significant association with the non-SLN metastasis ($P>0.05$).

Discussion

In this study, 38% of the patients with positive SLN had non-SLN metastases. None of the tumor characteristics predicted the status of non-SLNs. These results differed from most previous studies.

Chu et al.[4] reported that the number of SLNs with metastases was a significant predictor of residual axillary involvement on a univariate analysis, but it was not a significant independent factor in multivariate analysis because of the confounding covariate of the primary tumor size.[2,5] In another study with the same investigators,[6] the number of positive SLNs was an independent predictor of non-SLN metastases. In the same studies, the size of SLN metastases predicted the risk of metastases in non-SLNs.[2,7] However according to our study, neither the number nor the size of SLNs (micrometastasis vs. macrometastasis) have predicted non-SLN status. In order to reach a better conclusion, more investigations are required.

In other studies, some tumor characteristics have been considered as the critical factors that contributed to non-SLN metastases. Weiser et al.[7] had a large scale study on 1000 patients who underwent successful SLN dissection. Of these, 231 (23%) had positive SLN findings. In their study, it was shown that tumor size, lymphovascular invasion (LVI) and micrometastases were critical factors for non-SLN metastases. Another study was conducted by Abdessalam et al.[8] which showed that extranodal extension of the tumor has a correlation with non-SLN metastases as well as LVI and micrometastases.

Similar results regarding size and extranodal extension have been reported in a study conducted by Joseph et al.[9] In another study by Sachdev et al.,[10] LVI along with macroinvasion and tumor size were predictors of non-SLN metastasis. In our study, tumor size and LVI did not reveal a statistically significant difference in non-SLN metastases, which was similar to a study by Fleming et al.[1] In their study, tumor size and LVI were not predictors of additional positive nodes.

In our study, tumor characteristics such as tumor type, grade, necrosis and calcification, the presence of estrogen receptor (ER) and progesterone receptor (PR), HER-2 neu receptor, and the type of surgery were evaluated in all

Table 4. Clinicopathological features evaluated in terms of presence or absence of non-SLN metastasis (qualitative variables).

Feature	Positive SLN (N)	Positive non-SLN N (%)	*P* value
Tumor type			0.864
Invasive ductal	73	28 (38.3)	
Invasive lobular	2	1 (50)	
Medullary	6	3 (50)	
Other	7	2 (28.5)	
Tumor grade			0.301
1	27	13 (48.1)	
2	44	13 (29.5)	
3	8	3 (37.5)	
Not reported	9	5 (55.5)	
Vascular invasion			0.501
Present	11	6 (54.5)	
Absent	68	25 (36.7)	
Not reported	9	3 (33.3)	
Lymphatic invasion			0.181
Present	31	16 (51.6)	
Absent	48	15 (31.2)	
Not reported	9	3 (33.3)	
Tumor necrosis			0.792
Seen	40	17 (42.5)	
Not seen	37	13 (35.1)	
Not reported	11	4 (36.3)	
Tumor calcification			0.809
Seen	14	6 (42.8)	
Not seen	64	25 (39)	
Not reported	10	3 (30)	
Size of metastasis			0.645
Micrometastasis (0.2-2 mm)	5	1 (20)	
Macrometastasis (>2mm)	83	33 (39.7)	
Estrogen receptor (ER) status			0938
Positive	54	21 (38.88)	
Negative	17	6 (85.3)	
Not reported	17	7 (41.1)	
Progesterone (PR) receptor status			0.660
Positive	40	17 (42.5)	
Negative	31	10 (32.2)	
Not reported	17	7 (41.1)	
HER-2 neu receptor status			0.697
Positive	28	10 (35.71)	
Negative	24	11 (45.83)	
Not reported	36	13 (36.1)	
Type of surgery			0.918
Lumpectomy	72	28 (38.88)	
MRM*	16	6 (37.5)	

*MRM: Modified radical mastectomy.

patients, but none were significantly associated with the presence of non-SLN metastases. These results were in line with those studies.

We also reported two new entities: Ratio 1 and Ratio 2. Our study has shown no significant association with these entities. It should be emphasized that SLN biopsy is the most sensitive technique for sampling the axilla for metastatic disease. Clinicians want to predict the presence of non-SLN metastases from both primary tumor

characteristics and SLN biopsy results. Because SLN biopsy is considered less invasive, if one could predict which patients have non- SLN metastases it would not be necessary for these patients to undergo complete axillary node dissection. According to our study, it seems that CALND should remain the most appropriate management for patients with SLN metastases.

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