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Original article

Clinical application of sentinel lymph node biopsy based on axillary anatomy in breast cancer: A single institution experience

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ABSTRACT

Background: Sentinel lymph node biopsy (SLNB), mostly with the use of vital dye or radioisotope, is a method for predicting axillary status in patients with breast cancer. Conventional axillary lymph node dissection (ALND) is used in cases where sentinel lymph node (SLN) is not detected by existing methods, but a series of studies have found that most of SLNs are present in specific anatomical spaces. We attempted to determine the feasibility of SLNB based on axillary anatomy in cases where SLN was not detected by conventional lymphatic mapping methods.

Methods: A retrospective analysis involving 208 patients who received anatomical SLNB between January 2003 and December 2010 was performed. Lateral border of the pectoralis major muscle and lateral thoracic vein were defined as the anatomical landmarks, and ALND was performed to at least level II, regardless of the results of frozen section analysis. Pathologic results were used to measure false negative rate and accuracy. Chi-square test and Fisher's exact test were performed to find factors affecting results.

Results: False negative rate and accuracy of anatomical SLNB were 21.7% (13/60) and 93.3% (182/195), respectively. T stage, clinical node status, number of dissected SLNs and body mass index were analyzed as factors affecting results, but none of them was found as having a statistically significant influence.

Conclusion: These results suggest that anatomical SLNB may not replace ALND in cases where SLN is not detected by conventional lymphatic mapping method, but may be considered as a method for predicting axillary status before conducting a node dissection.

Introduction

Since Krag et al. used Tc99m sulfur colloid and Guiliano et al. used isosulfan blue dye for sentinel lymph node biopsy in patients with breast cancer, a series of studies have established the feasibility and accuracy of sentinel lymph node biopsy, which is now commonly used with vital blue dye and/or radioisotope [1–4]. In a review of researches on the detection rate and accuracy depending on the method of lymphatic mapping, Gipponi et al. reported that sentinel lymph node detection rate was 65.4–93% when vital blue dye was used and 82–98.7% when radioisotope was used [5]. Axillary lymph node dissection generally involves level I and level II when sentinel lymph node is not detected by these two methods of lymphatic mapping. However, studies on axillary lymphatic drainage pathway found that most sentinel lymph nodes are concentrated in a specific range of anatomical space [6–9]. We performed feasibility and accuracy study to determine whether sentinel lymph node biopsy based on axillary anatomical structure could replace axillary lymph node dissection in cases where sentinel lymph node could not be detected by conventional lymphatic mapping methods.

Methods

A retrospective analysis was performed for the medical records of 208 patients who received anatomical sentinel lymph node biopsy among the patients who received surgery for primary breast cancer of clinical stage I–III between January 2003 and December 2010. Patients ($n = 13$) were excluded from the analysis if they had distant metastasis at the time of the surgery or had received neoadjuvant chemotherapy before the surgery. For the anatomical sentinel lymph node biopsy, lateral border of the pectoralis major muscle and lateral thoracic vein were defined as landmarks, and visibly or palpably enlarged lymph nodes and nearby lymph nodes

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in the axillary space between these two landmarks were classified as sentinel lymph nodes and removed by meticulous dissection, without using electrocautery. As for the skin incision for axillar approach, conventional mastectomy incision, radial incision toward the axilla, or curvilinear incision at the border of axillary hairline was performed depending on the surgical technique (total mastectomy or breast conservation surgery) and the location of tumor. Frozen section analysis was performed for the lymph nodes obtained by the anatomical method. Sentinel lymph nodes were sectioned in 4-μm thickness (one level) and were evaluated with hematoxylin & eosin staining. And lymph nodes were dissected at least to the level II, regardless of the result. False negative rate of the anatomical sentinel lymph node biopsy was defined as the proportion of the patients with negative sentinel lymph node biopsy among those confirmed as having axillary lymph node metastasis, including the sentinel lymph node, after axillary lymph node dissection. Accuracy was defined as the proportion of the patients whose anatomical sentinel lymph node biopsy was true negative or true positive. Chi-square test and Fisher's exact test were performed to find factors affecting false negative rate. SPSS version 20.0 for Windows (SPSS Inc., Chicago) was used for statistical analyses. A *p*-value of less than 0.05 was considered as statistically significant.

Results

The clinicopathologic characteristics of the 195 patients who were included in the analyses are presented in Table 1. Their mean age was 48 years old, ranging from 26 to 84. Postoperative T stage was T1 or T2 and N stage ranged between N0 and N3. Pathologic stage N3 was found in three patients: lymph node metastasis was not suspected on preoperative palpation or ultrasonography in one of them, while single node involvement was suspected in the others, although there was no evidence of multiple node metastases. Clinical nodal status was identified by preoperative physical examination and ultrasonography: 167 were clinically N0 and 28 showed suspicious node metastasis. Breast conserving treatment was used in 71 patients and total mastectomy was performed in 124 patients. Mean number of dissected sentinel lymph nodes was 5.3 and 14 lymph nodes were dissected by axillary lymph node dissection. In the axillary lymph node dissection, which was performed regardless of the result of frozen section analysis of anatomical sentinel lymph node biopsy, true positive result was observed in 47 cases and false negative result in 13 cases. False negative rate, which was estimated based on the proportion of the patients with false negative result among overall patients with node metastasis, was 21.7% (13/60) and accuracy was 93.3% (182/195). On the contrary, clinical nodal status showed a false negative rate of 26.3%, which was higher than that of anatomical method, and low accuracy (71.3%) (Table 2). T stage, clinical node status, number of dissected sentinel lymph node and body mass index were selected and analyzed as factors affecting the false negative rate, but none of them showed a statistical significance (all of them with *p*-value $\geq$0.05) (Table 3).

Table 1
Clinicopathologic characteristics of patients undergoing anatomical sentinel lymph node biopsy.

Characteristics	Value
Age	
Mean	48
Range	26–84
Tumor stage	
T1	137 (70.3%)
T2	58 (29.7%)
Node stage	
N0	135 (%)
N1	46 (23.6%)
N2	11 (5.6%)
N3	3 (%)
Clinical nodal status	
Negative	167 (85.6%)
Suspicious	28 (14.4%)
Surgery	
Breast conserving treatment	71 (36.4%)
Mastectomy	124 (63.6%)
SLNs removed	
Mean *N* (SD)	5.3 (±3.384)
ALNs removed	
Mean N	14 (±7.217)

SLNs, sentinel lymph nodes; ALNs, axillary lymph nodes.

Discussion

Axillary lymph node metastasis, one of the most important predictors of breast cancer, plays an important role in disease staging and establishing treatment strategy. Axillary lymph node dissection has been the mainstay of breast cancer surgery, but sentinel lymph node biopsy is recently established as an alternative method for axillary evaluation and treatment on the basis of its high diagnostic accuracy and lower risk of complications, such as lymphedema and nerve injury. The fact that the detection rate of early breast cancer is growing due to increased awareness of breast cancer and screening tests also highlights the importance of sentinel lymph node biopsy. Since the first introduction of sentinel lymph node in 1977 by Cabanas et al. in penile carcinoma, this concept was applied to malignant melanoma by Morton et al. and to breast cancer, with the use of isosulfan blue, by Guiliano et al. [2,10,11]. Sentinel lymph node biopsy generally uses vital dyes, such as isosulfan blue and methylene blue, or radioisotopes, such as technetium sulfur colloid. Vital dyes cause no radiation exposure and allow macroscopic identification of sentinel lymph nodes, but often blur the vision of injection site and carry the risk of anaphylaxis or dermal necrosis. Radioisotopes, on the other hand, cause radiation exposure but are capable of roughly locating sentinel lymph nodes through preoperative lymphoscintigraphy and portable gamma probe, which require a smaller skin incision and less extensive dissection. Gipponi et al. reported in a review that vital dyes have lower detection rate than radioisotopes and that both can be used simultaneously to achieve the highest detection rate [5].

Breast lymphatics was first reported by Cruishank in 1787, and Sappey described in 1874 that breast lymphatics meet at the subareolar plexus and then are drained to the axilla through the lymph collecting vessel [12]. Turner-Warwick et al. reported that breast lymphatics could be drained to the internal mammary node or posterior intercostal node as well, rather than through a fixed route toward the axilla [13]. In a three dimensional, cadaver study, Suami et al. reported that lymph collecting vessels partly pass through or

Table 2
Results of anatomical sentinel lymph node biopsy and comparison with clinical nodal status.

Characteristics	Value	Characteristics	Value
SLN+/ALN+	47	CNS+/PNS+	16
SLN-/ALN+	13	CNS-/PNS+	44
SLN-/ALN-	135	CNS+/PNS-	12
		CNS-/PNS-	123
False negative rate	21.7% (13/60)	False negative rate	26.3% (44/167)
Accuracy	93.3% (182/195)	Accuracy	71.3% (139/195)

CNS, clinical nodal status; PNS, pathologic nodal status.