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ORIGINAL ARTICLE

Prediction of nonsentinel lymph node metastasis in breast cancer patients with one or two positive sentinel lymph nodes

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Received 25 February 2016; received in revised form 26 May 2016; accepted 24 June 2016

KEYWORDS

breast cancer;
non sentinel lymph
node;
Ki-67;
extracapsular
invasion;
Her-2 status;
clinically node
negative

Objective: The aim of the present study was to investigate the association between non sentinel lymph node metastasis (NSLNM) and clinicopathological factors, particularly in the case of sentinel lymph node (SLN) metastasis in one or two, in clinically node negative patients with breast cancer.

Methods: Between 10/2010 and 10/2014, 350 sentinel lymph node biopsy (SLNB) were performed in patients with histologically proven primary breast cancer in our clinic. The data collection includes the following characteristics: age, pathological tumor size, histological type, histological grade, lymphovascular invasion (LVI), number of positive SLN, size of the SLN metastasis (macrometastasis, micrometastasis, isolated tumor cells), multifocality (MF), extracapsular invasion (ECI) of the SLN, the estrogen receptor (ER) status, the progesterone receptor (PR) status and the Her 2 receptor status, Ki 67 reseptor status. Data were collected retrospectively and then analyzed.

Results: A successful SLN biopsy were performed in 345 (98.5%) cases. SLN metastases were detected in 110 (31.8%) cases. These patients then underwent axillary dissection; among these patients, 101 (91.8%) had only one to two positive SLNs. Of the 101 patients with positive SLN biopsies, 32 (31.6%) had metastases in the NSLNs. Univariate and multivariate analysis showed that lymphovascular invasion, extracapsular invasion (ECI), Her-2 receptor positive, and Ki-67 > 14% were related to NSLNM ($p < .05$).

Conflicts of interest: The authors declare that they have no conflicts of interest.

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<http://dx.doi.org/10.1016/j.asjsur.2016.06.001>

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Please cite this article in press as: Öz B, et al., Prediction of nonsentinel lymph node metastasis in breast cancer patients with one or two positive sentinel lymph nodes, Asian Journal of Surgery (2016), <http://dx.doi.org/10.1016/j.asjsur.2016.06.001>

Conclusion: The predicting factors of NSLNM were LVI, ECI, Ki-67 level, Her-2 reseptor positive and but should be further validated in our institutions, different institutions and different patient groups prospectively.

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1. Introduction

The status of the axillary lymph node (LN) is one of the most important prognostic markers for invasive breast cancer. Sentinel LN biopsy (SLNB) is an accepted method for identification of pathologic axillary status in early cancer cases with clinically negative axilla, which allows for correct and reliable staging of the axillary nodal status with significantly decreased shoulder arm morbidity.^{1–4} When positive LN metastasis is detected by SLNB, the patient undergoes complete axillary LN dissection (ALND). However, previous reports suggest that additional LN metastasis is not found on axillary dissection in approximately 40–60% of clinically node-negative patients.^{5–7} Furthermore, in a recent prospective randomized study, omitting ALND did not affect local control or prognosis for SLN-positive patients. The Z0011 trial found that omitting ALND did not result in poor survival or local control in SLN-positive patients with low T stage, no more than two SLNs, and no gross extracapsular extension in the involved nodes. The trial also indicated that ALND should be avoided if SLN metastases (SLNMs) are detected in only one or two nodes.⁸ Several authors have suggested using nomograms and scoring systems to predict the risk of non-SLMs (NSLNM) to omit ALND and increase the quality of life in the optimal management of patients with early breast cancer.^{9–17} Although numerous studies have been performed in this regard, it is not yet clear in which subgroup of patients with a positive SLN ALND can be safely omitted.

The aim of this study was to investigate the association between NSLNM and clinicopathologic factors, particularly in the case of SLNM in one or two nodes of clinically node-negative patients with breast cancer.

2. Methods

Between October 2010 and October 2014, 350 SLNBs were performed in patients with histologically proven primary breast cancer in our clinic. Histological diagnosis was confirmed by core-needle biopsy preoperatively ($n = 330$) or by frozen section ($n = 20$) during the surgical procedure. SLNBs were performed using blue dye and radiocolloid injections. All patients received a lymphoscintigraphy either on the day prior to or on the day of surgery. The dose of the injected radioisotope was 20–30 MBq (on the day before surgery) or 10–12 MBq (on the day of surgery). Patients were surgically treated by either total mastectomy or breast-conserving surgery. ALND was performed for Level I and II LNs if any macrometastases or micrometastases in SLN were detected in the frozen section analysis. In the

case of false negativity, ALND was performed in a second operation. However, if SLNB failed, ALND was considered ineludible. ALND was avoided in patients with isolated tumor cells in SLN.

In this work, we aimed to evaluate the clinicopathologic features to predict NSLNM in breast cancer patients with one to two positive SLNs.

The following data were collected from all patients: age (<50 years or ≥ 50 years), pathological tumor size (≤ 2 cm, 2–5 cm, or > 5 cm), histological type (invasive ductal, invasive lobular, or mixed), histological grade (I, II, or III), lymphovascular invasion (LVI; yes or no), number of positive SLNs, size of the SLNM (macrometastasis, micrometastasis, or isolated tumor cells), multifocality (yes or no), extracapsular invasion (ECI) of the SLN (yes or no), estrogen receptor (ER) status (negative or positive), progesterone receptor (PR) status (negative or positive), HER2 receptor status (negative or positive), and Ki-67 receptor status (<14% or $> 14\%$). Data were collected retrospectively and then analyzed.

Informed consent was obtained from all patients. Data were collected retrospectively. Exclusion criteria were as follows: ductal carcinoma *in situ*, palpable regional LNs, neoadjuvant chemotherapy, known allergic reactions to blue dye or isotope, previous surgery in the ipsilateral breast, pregnancy, and distant metastasis at diagnosis. Informed consent was obtained from all patients.

Multiple breast cancer included both multifocal and multicentric breast cancers. Multifocal breast cancer is defined as a case in which multiple invasive foci existed in the same quadrant, and multicentric cancer was defined as one in which the multiple invasive lesions were interspersed in the pleural quadrants.

Breast cancer was considered multifocal if two or more lesions were located in the same quadrant and the distance between each lesion was < 5 cm. If nodules arise in different quadrants of the breast and/or if the distance between each lesion was > 5 cm, the cancer was considered multicentric. Treatment decision making was made in a multidisciplinary tumor board setting attended by surgeons, medical oncologists, and radiation oncologists specializing in breast cancer. Based on size, metastasis was divided into macrometastases, micrometastases, or isolated tumor cells, according to the American Joint Committee on Cancer Staging Classification (AJCC) of Breast Cancer.¹⁸ Macrometastasis was defined as a cancer focus measuring over 2 mm in the greatest diameter within SNs. Micrometastasis was defined as a cancer focus measuring between 0.2 mm and 2 mm in the greatest diameter within SLN, and isolated tumor cells were defined as cancer foci smaller than 0.2 mm across their greatest diameter within SLN.

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