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Original Research Article

The influence of the extended indications for sentinel node biopsy on the identification of metastasis-free and metastatic sentinel nodes

Linas Martinaitis [a,*], *Žilvinas Dambrauskas* [a,b], *Algirdas Boguševičius* [a]

[a] *Department of Surgery, Medical Academy, Lithuanian University of Health Sciences, Kaunas, Lithuania*
[b] *Laboratory of Surgical Gastroenterology, Institute for Digestive Research, Medical Academy, Lithuanian University of Health Sciences, Kaunas, Lithuania*

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ABSTRACT

Background and objective: Rates of sentinel node (SN) identification and metastasis-positive SNs were compared between the group with highly selective indications for sentinel node biopsy (SNB) and the group with merely no contraindications for SNB (Groups A and B, respectively).

Materials and methods: We performed a single-center retrospective data analysis of 471 breast cancer patients treated during 2004–2010. Data on clinical and pathologic staging, frozen section results, radiological measurements and pathologic examination results were obtained from patient records. Patients were analyzed in two groups. Group A ($n = 143$) had SNB performed only when the patients fulfilled to the following criteria: breast tumor no greater than 3 cm in diameter, unifocal disease, no pure ductal carcinoma in situ, no history of previous breast or lymph node surgery, and no neoadjuvant chemotherapy. Indications for SNB were extended in Group B ($n = 328$) so that inflammatory breast cancer and positive lymph nodes became the only exclusion criteria.

Results: The rate of SN identification was 97.9% in Group A vs. 99.09% in Group B ($P = 0.29$). SNs were metastasis positive and frozen sections false negative at comparable proportions in both groups.

Conclusions: The extension of indications for SNB did not reduce the rates of SN identification or did not create any impact on the rate of metastatic SNs.

* *Corresponding author at*: Department of Surgery, Medical Academy, Lithuanian University of Health Sciences, Eivenių 2, 50161 Kaunas, Lithuania.
E-mail address: lmartinaitis@gmail.com (L. Martinaitis).

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1. Introduction

Sentinel node biopsy (SNB) has become a standard method to determine the metastatic involvement of regional lymph node basin in breast cancer. At the onset of SNB adoption, the indications for the procedure were strict. The American Society of Clinical Oncology (ASCO) published the recommendations for SNB in 2005 [1] where it was stated that SNB should not be employed in case of T_3 or T_4 tumors, inflammatory breast cancer, ductal carcinoma in situ (DCIS) without mastectomy, nodes suspicious for metastasis, pregnancy, prior axillary surgery, previous nononcologic breast surgery, and after preoperative systemic therapy. The ASCO guidelines supported the use of SNB for multicentric tumors, DCIS when mastectomy or immediate reconstruction is planned, for older or obese patients, in male breast cancer, previous excisional or diagnostic biopsy, and before preoperative systemic therapy [1].

Currently, indications for SNB are widely discussed in the literature. The overall fraction of patients who cannot benefit from SNB is very small. Cheng et al. [2] have suggested that this proportion should be limited to patients with histologically confirmed positive axillary or extra-axillary lymph nodes and patients with inflammatory breast cancer. Similarly, SNB can be omitted if information on SNs does not affect treatment decisions, e.g. patients with low-grade DCIS [2] in whom resection is surely curable.

The aim of the study was to evaluate the influence of the extended indications for SNB on the rates of SN identification and metastasis-positive SNs.

2. Materials and methods

Data on 471 patients treated for breast cancer in 2004–2010 in a single institution (Clinic of Surgery, Hospital of Lithuanian University of Health Sciences Kauno Klinikos) were analyzed retrospectively. Patient records were reviewed to obtain information on clinical and pathologic staging, frozen section results, radiological measurements and histopathologic examination results. The patients were divided in two groups:

- The first cohort of patients ($N = 143$) had SNB performed only when they fulfilled to the following criteria: breast tumor no greater than 3 cm in diameter, unifocal disease, no pure DCIS, no history of previous breast or lymph node surgery, and no neoadjuvant chemotherapy (Group A, highly selective indications).
- Indications for SNB were extended in the second cohort of patients ($N = 328$) so that inflammatory breast cancer and positive lymph nodes (verified by ultrasound or biopsy) became the only exclusion criteria (Group B, extended indications).

SNs were marked with 99 m technetium-labeled colloid and identified employing the lymphoscintigraphy technique. Radioisotope injection was applied 24 h before surgery.

The study was approved by the Local Bioethics Committee (no. of approval 125/2004).

Data analysis was performed with Statistica 8.0, using the Student t and Pearson chi-square tests. Confidence level of $P < 0.05$ was considered statistically significant.

3. Results

The groups were matched for age or clinical tumor staging. The mean age of the patients in Group A and Group B was 58.66 years (SD 11.04; range 34–83), and 57.1 years (11.6; 28–88), respectively ($P = 0.17$). In Group A, 67.83% of the patients had no clinically detectable lymph nodes compared with 68.6% of the patients in Group B ($P = 0.87$). No patients had distant metastases in either group.

Tumor size was smaller in Group A in comparison to Group B based on mammography (16.8 mm vs. 20.25 mm; $P = 0.005$) and ultrasound (12.98 mm vs. 16 mm; $P = 0.048$). Pathologic tumor size was 14.42 mm (SD 6.13; 1–37) and 15.86 (8.34; 1–60) in Group A and Group B, respectively ($P = 0.08$).

Among the patients of Group B, 1 patient was male, 4 patients with locally advanced tumor ($T_{3–4}$), and 2 patients after previous breast surgery. There were also 4 patients after neoadjuvant chemotherapy in Group B: 2 were downstaged after neoadjuvant treatment (one case $T_4 \rightarrow T_2$, another $T_2 \rightarrow T_1$). No such cases were included in Group A.

Carcinoma in situ (pT_{is}) was found in 4.31% of the cases in Group B; invasive tumors less than 2 cm in size (pT_1) occurred in 83.69% cases in Group A vs. 73.23% cases in Group B. Tumors measuring 2 to 5 cm in size (pT_2) were diagnosed in 16.31% of the cases in Group A vs. 21.85% of the cases in Group B; gross tumors exceeding 5 cm ($pT_{3–4}$) were observed in 2 patients (0.62%) in Group B ($P = 0.02$).

The two groups were comparable by most tumor pathologic characteristics (Table 1). The patients did not differ by the histological type of carcinoma, lymph vessel invasion, and vascular invasion. However, the prevalence of better differentiated tumors (G_1 and G_2) was significantly greater in Group A than Group B ($P = 0.007$).

The density of progesterone receptors and the degree of expression of Her2/neu gene was similar in both groups, but the density of estrogen receptors differed between the groups. ER-negative tumor accounted for 50.37% of all cases in Group A and only 27.8% of cases in Group B ($P < 0.00001$).

The rate of SN identification was 97.9% in Group A compared to 99.09% in Group B ($P = 0.29$) (Table 2). The mean number of harvested SNs was greater in Group A than Group B (2.21 vs. 1.95, $P = 0.02$).

The rates of metastatic SNs and accuracy of frozen section did not differ. SNs were found to be metastasis-free in 76.43% and 76.31% of the cases in Groups A and B, respectively. Occurrence of macrometastases in SNs was observed in 20.71% of the cases in Group A and in 21.85% of the cases in Group B. Occurrence of micrometastases was observed in 2.14% and 1.54% of the cases in Groups A and B, respectively. There was one case in both groups (0.71% in Group A and 0.31% in Group B, respectively), when SNs were macroscopically metastatic and frozen sections were omitted ($P = 0.89$).

Intraoperative diagnoses from frozen sections were correct in 94.2% of the cases in Group A and in 92.88% of the cases in Group B; intraoperative false negative results were obtained in