

Incidence of Arm Lymphoedema Following Sentinel Node Biopsy, Axillary Sampling and Axillary Dissection in Patients with Breast Cancer*

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Abstract. *The aim of this study was to compare the incidence of lymphoedema after different treatments of the axilla in patients with breast cancer (BC). Medical records of 205 women (median age 61 years, range 26-72 years) who underwent curative surgery for primary BC were reviewed. According to the treatment of the axilla, the study population was divided into four age- and stage-matched groups of patients: Group A (N=54 patients), sentinel node biopsy (SLNB) alone; Group B (N=48 patients), SLNB followed by axillary node (AN) sampling using ultrasound scissors (harmonic scalpel); Group C (N=53 patients), AN dissection using ultrasound scissors; Group D (N=50 patients), traditional AN dissection. The median follow-up was 22 months (range 18-28 months). The intraoperative frozen section of SLNB (Groups A and B) showed 32 out of 102 (31.4%) patients with metastasis to AN, while final pathology showed AN metastases in 20, 17, 16 and 17 patients of groups A, B, C and D, respectively (p=NS). The sensitivity of SLNB alone was 80% and that of SLNB followed by AN sampling was 95% (p=NS). At follow-up patients with lymphoedema were 2 (3.7%), 2 (4.2%), 3 (5.6%) and 8 (16%) in groups A, B, C and D, respectively (p=NS). In conclusion, AN sampling is a sensitive and low-morbidity procedure which, in conjunction with the use of harmonic scalpel, may reduce the onset of arm lymphoedema.*

*Presented at the 6th European Breast Cancer Conference (EBCC-6), Berlin (Germany) 15-19 April, 2008. Eur J Cancer Suppl 6: 151-152, 2008. Elsevier, Oxford (UK).

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Key Words: Breast cancer, sentinel node, axillary sampling, axillary lymphadenectomy, lymphoedema, harmonic scalpel.

Axillary lymph node (AN) status is the most important prognostic factor in breast cancer (BC) (1, 2). Axillary lymph node dissection (ALND) was for decades the standard surgical approach for staging the axilla, but unfortunately this procedure is associated with high morbidity and increases risk of lymphoedema (3). Recently, sentinel lymph node biopsy (SLNB) was introduced as a less invasive technique for evaluation of axillary involvement (4). Intraoperative examination of the SLNB may correctly detect AN metastases in more than 90% of patients with BC. The aim of this study was to compare the incidence of lymphoedema after different treatments of the axilla in patients with BC.

Patients and Methods

Medical records of 205 women (median age 61 years, range 26-72 years) who underwent curative surgery for primary BC were reviewed. Patients with bilateral, multicentric or multifocal BC were previously excluded from the study, as well as those who had undergone preoperative neoadjuvant chemotherapy. The diagnosis of BC was obtained by fine-needle aspiration biopsy (N=156, 76.1%), core-biopsy (N=28, 13.7%) or open biopsy (N=21, 10.2%). Patients requiring breast-conserving surgery with SLNB or axillary cleaning (N=118, 57.6%) or a modified radical mastectomy (N=87, 42.4%) were eligible to enter the study, whilst those who underwent immediate reconstruction following mastectomy were excluded. The median follow-up was 22 months (range 18-28 months). Written informed consent was obtained from all the participants and the study had full ethical approval by the Institutional Review Boards. A combined method using radioisotope and blue dye was used for SLNB. The removed ANs were bisected and two frozen sections (FS) were obtained (hematoxylin-eosin stain, 40 µm between levels). In patients with positive SLNB or axillary sampling, a standard level I and II ALND was performed. In all patients, electrocautery was used only for skin flap dissection and two closed suction drains were placed in the axilla and on the chest, respectively, as previously reported (5). A standard non-compressive dressing was used at the end of operation. Each drain was removed when their output was

less than 10-20 mL per day. The diagnosis of lymphoedema was made when a difference of 2 cm or more was observed in the arm circumference between affected and non-affected arms. Tumour staging was obtained according to the TNM staging system at final pathological examination (pTNM). The ANs were examined by serial sections (150-200 µm) and immunostained with an anti-cytokeratin antibody (AE1/AE2) to detect micrometastases. The main characteristics of the tumour are reported in Table I. No pT1a BC was observed. According to the treatment of the axilla, the study population was divided into four age- and stage-matched groups of patients: Group A (N=54 patients): SLNB alone; Group B (N=48 patients): SLNB followed by AN sampling using ultrasound scissors (harmonic scalpel); Group C (N=53 patients): ALND using ultrasound scissors; Group D (N=50 patients): traditional ALND. The reported data are expressed as mean±standard deviation (SD). Comparisons between groups were performed using Student's *t*-test and the chi-squared (χ^2) test, when required. A *p*-value <0.05 was considered statistically significant.

Results

No significant differences (*p*=NS) between groups were found (Table II). The intraoperative frozen section of SLNB (groups A and B) showed 32 out of 102 (31.4%) patients with metastasis to AN, while final pathology showed AN metastases in 20, 17, 16 and 17 patients of groups A, B, C and D, respectively (*p*=NS). There were 70 (34.1%) N1 patients and 135 (65.9%) N0 patients. In groups C and D the average number of removed AN was 17.0±4.6, while the number of involved nodes was 9±4. The sensitivity of SLNB alone was 80% and that of SLNB followed by AN sampling was 95% (*p*=NS). At follow-up patients with lymphoedema were 2 (3.7%), 2 (4.2%), 3 (5.6%) and 8 (16%) in groups A, B, C and D, respectively (*p*=NS).

Discussion

AN involvement is a strong predictor of recurrence and a major prognostic factor in patients with early BC (6). Unfortunately, neither preoperative techniques nor SLNB may at present exclude the presence of AN metastases and the long-term survival of women with negative AN still remains less than 80-85% (7). Increased public awareness of BC has led to an earlier diagnosis of small BC, which can benefit of more conservative surgical approach (8). The management of the axilla should guarantee high accuracy and low morbidity, but is highly dependent on the real number of involved AN at final pathology, because in frozen sections the findings of micro-metastases could be missed (9). ALND still represent the most accurate means of determining AN status and it has been routinely performed for decades in all patients with BC (10). The incidence of axillary recurrence after ALND is low (2-5%), but the procedure is associated with high morbidity, including

Table I. Main characteristics of the tumours (mean±SD).

Parameter	No. of cases	Percentage
Left sided	111	54.1%
Right sided	94	45.9%
pT1b	29	14.1%
pT1c	75	36.6%
pT2	101	49.3%
Infiltrating ductal	166	81.0%
Other types	39	19.0%
ER>10%	155	72.6%
PgR>10%	149	72.7%

ER, estrogen receptor rate; PgR, progesterone receptor rate.

neuropathy, pain and lymphoedema (11). Such a complication, which appears in 6% to 50% of patients, is known to be related to several risk factors: enclosed extensive surgery, number of the removed ANs, post-surgical radiotherapy of the axilla, and it seems to be likely multifactorial (3, 12, 13). In a previous report, it was found that in patients with BC who underwent ALND, the volume of drainage significantly correlates with body mass index (BMI), AN status, number of both total and positive ANs and size of the tumour (5). It has been suggested that less invasive procedures (*i.e.* SLNB) might reduce the incidence of lymphoedema at short- and medium-term follow-up (14). SLNB has been introduced as an invasive procedure in patients with clinically node-negative BC and it was considered an appropriate alternative to routine staging ALND by The American Society of Clinical Oncology (ASCO) Expert Panel in their guidelines (15). Assuming that the sentinel node receives a direct drainage from the primary cancer, a negative SLNB makes further AN dissection unnecessary and this technique has already become a standard of care for BC patients (1, 16). Both patients who underwent SLNB and those who underwent ALND show comparable axillary recurrence rates (17, 18). However, most patients with a positive sentinel node who undergo ALND do not have further AN metastases (19). Many authors have suggested strategies to predict AN negativity in patients with positive SLNB. The Edinburgh group developed a four-node sampling procedure (20) and more recently, in a group of patients with stage 1-2 BC who underwent AN sampling followed by ALND, the accuracy of AN sampling was 98% (21). In a recent meta-analysis it is reported that the characteristics related with the highest likelihood of non-SN metastasis are tumour size (>2 cm), lymphovascular invasion in the primary tumour, number of positive SN (>1), size of SN metastasis (>2 mm) and extranodal extension in the sentinel node (22). However, data are conflicting and other studies found that there are

Table II. Differences between groups (mean±SD).

Group	No. of patients	Age (years)	G1/G2/G3	No. of N1 patients on FS	No. of N1 patients on FP	N1/N0	Percentage of N1	BMI>24
A	54	59.2±12.3	11/33/6	20	20	20/54	37%	19%
B	48	58.7±13.6	10/30/5	17	17	17/48	35%	21%
C	53	60.7±13.2	8/37/11	16	16	16/53	30%	21%
D	50	61.3±13.4	8/36/10	17	17	17/50	34%	18%

G, tumour grading; N1, metastasis to axillary lymph nodes; N0, no axillary lymph node metastasis; FS, frozen section; FP, final pathology; BMI, body mass index.

only a few independent predictors of non-sentinel node metastases (23, 24). Several clinical trials evaluated long-term survival and morbidity after SLNB alone and in conjunction with ALND (1). The Milan Study, found that the accuracy of SLNB was 89%, with less pain and arm swelling in the group treated with SLNB alone, but no differences in the overall survival (25). However, the relationship between AN positivity and development of lymphoedema is unclear (26). The reported incidence of lymphoedema in patients who underwent SLNB and ALND may reach 7% and 70%, respectively and the AN negative patients operated with SLNB have less arm morbidity (26, 27). In a previous study, it was found that the use of a harmonic scalpel reduces the total drained volume in patients requiring axillary dissection (28). In conclusion, AN sampling is a sensitive and low-morbidity procedure useful in reducing the false-negative results of SLNB alone. The use of harmonic scalpel may reduce the onset of arm lymphoedema, especially when ALND is required, although its real usefulness is still under discussion (28-30).

Acknowledgements

Special thanks are expressed to Miss Francesca Bissolotti for help in preparing the manuscript and for reviewing the English.

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Received December 15, 2008

Revised February 17, 2009

Accepted March 16, 2009