

# Morbidity following Sentinel Lymph Node Biopsy versus Axillary Lymph Node Dissection for Patients with Breast Carcinoma

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**BACKGROUND.** Axillary lymph node dissection for staging the axilla in breast carcinoma patients is associated with considerable morbidity, such as edema of the arm, pain, sensory disturbances, impairment of arm mobility, and shoulder stiffness. Sentinel lymph node biopsy electively removes the first lymph node, which gets the drainage from the tumor and should therefore be associated with nearly zero morbidity.

**METHODS.** Postoperative morbidity (increase in arm circumference, subjective lymphedema, pain, numbness, effect on arm strength and mobility, and stiffness) of the operated arm was prospectively compared in 35 breast carcinoma patients after axillary lymph node dissection (ALND) of Level I and II and 35 patients following sentinel lymph node (SN) biopsy.

**RESULTS.** Patient characteristics were comparable between the two groups. Postoperative follow-up was 15.4 months (range, 4–28 months) in the SN group and 17.0 months (range, 4–28 months) in the ALND group. Following axillary dissection, patients showed a significant increase in upper and forearm circumference of the operated arm compared with the SN patients, as well as a significantly higher rate of subjective lymphedema, pain, numbness, and motion restriction. No difference between the two groups was found regarding arm stiffness or arm strength, nor did the type of surgery affect daily living.

**CONCLUSIONS.** SN biopsy is associated with negligible morbidity compared with complete axillary lymph node dissection. *Cancer* 2000;88:608–14.

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**KEYWORDS:** axillary lymph node dissection, sentinel lymph node biopsy, breast carcinoma, postoperative morbidity, complications.

**A**xillary lymph node dissection (ALND) in patients with breast carcinoma is performed mainly for staging purposes and to determine the need for adjuvant treatment.<sup>1–3</sup> Furthermore, it plays a role in local tumor control in the axilla,<sup>4,5</sup> whereas its impact on disease free survival or overall survival has yet to be determined.<sup>6</sup> The routine performance of axillary dissection in patients with breast carcinoma has been questioned due to the relatively high postoperative morbidity rate resulting from the procedure<sup>7–10</sup> and because most patients are treated with adjuvant therapy irrespective of their lymph node status.<sup>11</sup> The morbidity associated with ALND has led to a search for new methods that can stage the axilla accurately but are associated with minor postoperative sequelae. Preliminary studies have shown that sentinel lymph node (SLN) biopsy may stage the axilla accurately.<sup>12–18</sup> SLN biopsy is cost effective, is associated with a shorter postoperative time, and should decrease morbidity compared

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Received April 19, 1999; revision received October  
 12, 1999; accepted October 12, 1999.

with axillary dissection.<sup>19,20</sup> In a prospective study, the morbidity after SLN biopsy and ALND was compared among patients with lymph node negative breast carcinoma.

## MATERIALS AND METHODS

### Patients

After evaluation of the validity of SLN mapping in our breast carcinoma patients, we started with the clinical application of SLN biopsy in December 1996.<sup>21</sup> From December 1996 to December 1998, 35 patients with unilateral invasive breast carcinoma underwent breast surgery and SLN mapping. If the sentinel lymph node (SN) showed no metastatic disease in intraoperative frozen sections (6–8 sections) or in paraffin section histology with hematoxylin and eosin staining and anticytokeratin staining, then no further axillary dissection was done (Group A; the SN group). These patients were compared prospectively with 35 patients who underwent surgery for breast carcinoma during the same period and who underwent complete axillary dissection but in whom pathologic examination of the axillary specimen found that lymph nodes were free from tumor metastases (Group B; the ALND group). Group B patients were lymph node negative patients who underwent axillary dissection of Levels I and II. They did not undergo SLN biopsy, because 1) no SN was found intraoperatively in these patients, and a standard axillary dissection had to be performed (n = 4 patients); 2) palpable (but tumor free) lymph nodes were found clinically prior to surgery (n = 5 patients); 3) patients gave no consent for the SLN biopsy procedure after it was explained to them that SLN mapping was not standard procedure yet and carried the risk of falsely staging the axilla (n = 6 patients); 4) patients underwent complete axillary clearance for training reasons to control accuracy of the mapping technique (n = 11 patients); 5) a surgeon who did not perform SLN biopsies performed the axillary dissection, because, at that time, SLN biopsy was not our standard treatment of the axilla (n = 8 patients); or 6) preoperative lymphoscintigraphy showed a drainage exclusively to the parasternal lymph nodes (n = 1 patient).

Postoperative morbidity between both groups was compared in a prospective but not randomized study. The study was approved by the Institutional Review Board at the Allgemein Offentliches Krankenhaus Linz. Written informed consent to participate in the study was obtained from all patients.

### Surgery

Breast carcinoma surgery was either tumor resection (quadrantectomy) or mastectomy. Mastectomy was performed without dissecting the major or minor pec-

toralis muscle. Patients in Group A underwent SLN biopsy only. Sentinel lymph node(s) were identified by use of a vital blue dye (patent blue V; 2.5%; Guerbet<sup>®</sup>) only (n = 17 patients) or vital dye and Tc99m-labeled radiocolloids (40 MBq Tc99m; Nanocoll) (n = 18 patients). Our technique of SLN mapping and first clinical application have been described previously in detail.<sup>21</sup>

Patients in Group B underwent axillary dissection of Levels I and II. The dissection was carried out below the axillary vein without skeletonizing the vein. The long thoracic nerve and the thoracodorsal nerve and vessels were preserved, and the intercostobrachial nerve was preserved whenever possible. After axillary dissection, the axilla was drained, and the drain was removed when the amount of daily drainage was <30 cc. For patients who underwent SLN biopsy, the axilla was not drained.

### Postoperative Adjuvant Treatment

After undergoing quadrantectomy, 24 of 35 patients in Group A and 25 of 35 patients in Group B received postoperative radiation therapy to the breast with 45 grays (Gy) over 5 weeks with a boost to the tumor site. The axilla was excluded from the radiation field. All patients received postoperative adjuvant treatment, which was either chemotherapy or hormonal treatment.

### Postoperative Follow-Up

None of the patients had preexisting problems in the arm, such as edema, decreased range of motion, or pain. Postoperatively, the patients were not given any restrictions in their everyday habits, and they were allowed to start with arm exercises as soon as possible, which usually was the third day after surgery. Follow-up examinations were done in the outpatient clinic every 3 months after surgery, and the following measurements were taken:

For measurement of *arm swelling*, the circumference (in cm) of the arm (upper arm and forearm) was noted 15 cm above and 10 cm below the lateral epicondyle, and the mean of 3 measurements was recorded. Measurements were taken prior to surgery and during postoperative follow-up on both arms (operated and nonoperated arm) using the untreated arm as a control. The absolute numbers for both arms are shown in Table 2. To preclude the influence of the dominant arm circumference and to evaluate only the arm changes due to surgery, comparisons of both arms were done as follows: the upper arm difference (UADIF) 1 = postoperative circumference of the upper arm minus preoperative circumference of the upper arm for the operated side; UADIF 2 = postoperative

circumference of the upper arm minus preoperative circumference of the upper arm for the nonoperated side;  $UA = UADIF\ 1 - UADIF\ 2$ . The variable UA was examined statistically and represents the circumferential change in the operated arm compared with the nonoperated arm. Evaluation of the forearms were done in the same manner.

For the subjective assessment of arm *edema*, patients were asked to determine arm swelling of the operated arm compared with the nonoperated arm as none, mild, moderate, or severe (none, no arm swelling, tightness, or heaviness; mild, periods of arm swelling but no constant increase in greatest dimension and clothes fit the same; moderate, constant arm swelling and arm heaviness, clothes do not fit the same, and physical discomfort but no decrease in functional activity; and severe, constant arm heaviness, disability, decreased functional activity, huge arm swelling).

*Numbness* was assessed comparing sensitivities of inner and outer skin areas of the upper arm, axilla, and chest wall of the operated side with the nonoperated side. Sensitivity was recorded as either numbness or no numbness. *Pain* in the operated arm was evaluated using a Visual Analog Scale (VAS) ranging from 0 (no pain) to 10 (worst pain imaginable).

The effect on shoulder joint and *arm mobility* was assessed asking the woman to elevate the operated arm over her head to the other shoulder, to move the arm back and forth, to move the arm behind the back to reach the other scapula, and to perform internal and external arm rotation. Motion restriction was noted using a scale from 0 to 3 (0, no motion restriction; 1, minor restriction; 2, moderate restriction; and 3, severe restriction). Arm strength was measured when both arms were elevated to 90° and then asking the woman to elevate it farther against the strength of the surgeon.

*Arm strength* was rated as follows: 0, the same strength in both arms; 1, slightly decreased strength in the operated arm; 2, largely decreased strength in the operated arm; and 3, operated arm feeble. The scales for subjective assessment of arm edema, the effect on arm mobility, and the effect on arm strength are neither validated nor referenced.

*Stiffness* of the operated arm was assessed as either stiffness or no stiffness. All women were asked whether surgery negatively affected their day-to-day living (either yes or no).

### Statistical Analysis

The Fisher exact test or the chi-square test was used to analyze nominal variables in the form of frequency tables. The analysis of variables measured on an ordi-

nal scale was made using Mann–Whitney U tests. Normally distributed (Kolmogorov–Smirnov test with Lilliefors correction) quantitative variables were tested with a *t* test for independent samples with correction for heteroscedasticity. All tests were two-tailed with a significance of 95% ( $P < 0.05$ ). No alpha adjustment was made. Therefore, all test statistics are to be considered as descriptive only. Analyses were done on a computer system (SPSS, Inc., Chicago, IL) at the Institute for Statistics, University of Linz, Austria.

### RESULTS

Patient characteristics were comparable between both groups and are shown in Table 1. The mean follow-up was  $15.4 \pm 6.2$  months (range, 4–28 months) in Group A and  $17.0 \pm 5.6$  months (range, 4–28 months) in Group B ( $P = 0.236$ ).

The mean number of lymph nodes dissected was 1–4 lymph nodes (mean,  $1.9 \pm 1.1$  lymph nodes) in the SN group and were removed from Level I ( $n = 28$  patients), Level II ( $n = 4$  patients), or Levels I and II ( $n = 3$  patients). After axillary dissection, a mean number of  $16.2 \pm 3.6$  lymph nodes (range, 10–26 lymph nodes) were removed.

### Postoperative Sequelae

The intraoperative and postoperative courses were uneventful except for blue staining of the urine and the skin in Group A patients. There was no seroma in the axilla in Group A, and no patient required aspiration of fluid collection. Conversely, 15 of 35 patients in Group B required aspiration of axillary fluid collection (usually 1 aspiration of 10 cc) after the removal of drains. Two of 35 patients in Group B developed axillary seromas. However, they were only of small amounts and resolved after two or three aspirations; therefore, they did not seem to have an impact on postoperative sequelae. There have been no local (axillary or breast) disease recurrences or systemic spread in either of the two groups.

In both groups, 18 of 35 patients underwent surgery on the side of the woman's dominant arm. In both groups, the dominant arm circumference was increased slightly in the nondominant arm, but this was not statistically significant (SN group: dominant to nondominant upper arm,  $30.4 \pm 3.7$  cm to  $30.1 \pm 3.6$  cm;  $P = 0.70$ ; dominant to nondominant forearm,  $24.1 \pm 2.8$  cm to  $24.0 \pm 2.7$  cm;  $P = 0.82$ ; ALND group: dominant to nondominant upper arm,  $31.0 \pm 3.5$  cm to  $30.7 \pm 3.4$  cm;  $P = 0.63$ ; dominant to nondominant forearm,  $24.6 \pm 2.6$  cm to  $23.9 \pm 2.6$  cm;  $P = 0.76$ ).

**TABLE 1**  
Patient Characteristics

Characteristic	SN (n = 35)	ALND (n = 35)	P value
Mean $\pm$ SD age in yrs (range)	62.7 $\pm$ 10.4 (39–76)	58.9 $\pm$ 12.7 (33–77)	NS
Side of breast carcinoma (right:left)	22:13	21:14	NS
Type of surgery (quadrantectomy:mastectomy)	27:8	26:9	NS
Tumor size			
T1a	1	0	—
T1b	8	6	NS
T1c	19	20	—
T2	7	9	—
Premenopausal:postmenopausal	5:30	7:28	NS
Postoperative radiation therapy	24 of 35	25 of 35	NS
Postoperative chemotherapy	7 of 35	7 of 35	NS
Postoperative tamoxifen	28 of 35	28 of 35	NS
Mean $\pm$ SD postoperative follow-up in months (range)	15.4 $\pm$ 6.2 (4–28)	17.0 $\pm$ 5.6 (4–28)	NS

SN: sentinel lymph node biopsy; ALND: axillary lymph node dissection; SD: standard deviation; NS: not significant.

**TABLE 2**  
Preoperative and Postoperative Circumference of the Operated and Nonoperated Arm after Sentinel Lymph Node Biopsy and Axillary Lymph Node Dissection

Arm	SN (n = 35)		ALND (n = 35)	
	Preoperative	Postoperative	Preoperative	Postoperative
Mean $\pm$ SD upper arm circumference in cm				
Operated arm	30.3 $\pm$ 3.6	30.3 $\pm$ 3.6	30.9 $\pm$ 3.5	32.4 $\pm$ 3.8
Nonoperated arm	30.3 $\pm$ 3.7	30.3 $\pm$ 3.7	30.8 $\pm$ 3.5	30.8 $\pm$ 3.5
Mean $\pm$ SD forearm circumference in cm				
Operated arm	24.0 $\pm$ 2.8	24.0 $\pm$ 2.8	24.0 $\pm$ 2.6	24.9 $\pm$ 2.8
Nonoperated arm	24.1 $\pm$ 2.8	24.0 $\pm$ 2.8	23.8 $\pm$ 2.6	23.8 $\pm$ 2.6

SN: sentinel lymph node biopsy; ALND: axillary lymph node dissection; SD: standard deviation.

### Postoperative Circumference of the Arm

The preoperative circumferences of the upper arm and the forearm were comparable between the operated and nonoperated arm in both groups and also between both groups ( $P = \text{NS}$ ) (Table 2). There was no significant difference in preoperative measurements compared with postoperative measurements of the upper arm and the forearm in the SN group, whereas a significant increase was found in the greatest dimension of the arm (upper arm as well as forearm) in patients after axillary dissection (Table 3).

### Postoperative Subjective Arm Lymphedema

More patients complained about mild or moderate lymphedema after axillary dissection than after SN biopsy ( $P = 0.0001$ ). However, no severe lymphedema was seen (Table 4).

### Postoperative Numbness

Twenty-four of 35 patients reported numbness of the operated upper arm (inner side, 16 patients; outer side, 2 patients; both sides, 6 patients) after axillary dissection, which was significant compared with the SN group ( $P = 0.0001$ ) (Table 4).

### Postoperative Pain

There was significantly more pain in the operated arm after axillary dissection ( $P = 0.0001$ ), but no patient experienced more pain than a score of 5 on the VAS scale of 0–10 (Table 4). There also were two patients who complained of minor pain in the SN group. This may have been due to scar formation, because both patients underwent (simple) mastectomy.

**TABLE 3**  
Differences of Operated and Nonoperated Arm Circumferences after Sentinel Lymph Node Biopsy and Axillary Lymph Node Dissection<sup>a</sup>

Mean $\pm$ SD arm difference in cm	SN (n = 35)	ALND (n = 35)	P value
Upper arm	1.14 $\pm$ 0.15	1.50 $\pm$ 0.75	0.0001
Forearm	0.16 $\pm$ 0.86	0.95 $\pm$ 0.80	0.0001

SD: standard deviation; SN: sentinel lymph node biopsy; ALND: axillary lymph node dissection.  
<sup>a</sup> Differences in circumferences were evaluated as follows: UADIF 1, postoperative circumference of upper arm minus preoperative circumference of upper arm for the operated side; UADIF 2, postoperative circumference of upper arm minus preoperative circumference of upper arm for the nonoperated side; UA = UADIF 1 - UADIF 2. The variable upper arm (UA) was examined statistically and represents the circumferential changes of the operated arm compared with the nonoperated arm. Evaluation of the forearms was done the same way.

### POSTOPERATIVE MOTION RESTRICTION

After undergoing SLN biopsy, patients did not complain about any restriction in arm motion. However, there were six patients in the ALND group who reported minor but significantly decreased arm mobility (Table 4).

### POSTOPERATIVE ARM STIFFNESS

Two patients reported minor arm stiffness after axillary dissection, but this was not significant compared with the SN group (Table 4).

### Postoperative Arm Strength

Postoperative arm strength was not affected by the type of axillary surgery (Table 4).

### Daily Living

The type of axillary surgery had no impact on daily living (Table 4).

### DISCUSSION

ALND is associated with a relatively high morbidity that has a negative affect on quality of life for breast carcinoma patients. Arm problems include lymphedema, pain, numbness, and restricted arm mobility<sup>7-10</sup> and are influenced by the extent of surgery in the axilla,<sup>10,22-26</sup> the number of removed lymph nodes,<sup>23,25</sup> the tumor burden to the lymph nodes,<sup>25</sup> and whether postoperative radiotherapy is given.<sup>22,24-27</sup> Furthermore, the postoperative sequelae after breast carcinoma treatment increase in number with a more thorough evaluation of the patients in the postoperative follow-up and, although they usually are mild, they may have an impact on daily living.<sup>7-10</sup>

Morbidity from axillary dissection may be decreased by limiting the extent of axillary lymph node dissection.<sup>28</sup> Several authors have even questioned the

**TABLE 4**  
Postoperative Sequelae after Sentinel Lymph Node Biopsy and Axillary Lymph Node Dissection

Sequelae	SN (n = 35)	ALND (n = 35)	P value
Numbness			
Yes	0	24	0.0001
No	35	11	—
Pain (VAS 0-10)			
0	33	19	0.0001
1	2	8	—
2	0	5	—
3	0	1	—
4	0	1	—
5	0	1	—
Arm mobility (0-3)			
0	35	29	0.011
1	0	4	—
2	0	2	—
3	0	0	—
Arm stiffness			
Yes	0	2	0.493
No	35	33	—
Subjective lymphedema			
None	35	16	0.0001
Mild	0	14	—
Moderate	0	5	—
Severe	0	0	—
Arm strength			
0	35	32	0.239
1	0	3	—
2	0	0	—
3	0	0	—
Affects daily living			
Yes	0	4	0.114
No	35	31	—

SN: sentinel lymph node biopsy; ALND: axillary lymph node dissection; VAS: Visual Analog Scale.

need for axillary dissection in selected patients, such as older patients or those with small tumors.<sup>29-32</sup> Abandoning any axillary dissection may result in an increased number of patients with falsely staged axilla, because clinical staging of the axilla may not be accurate enough,<sup>3,33</sup> and the number of positive lymph nodes is greater than expected when the lymph nodes are examined more accurately.

Limiting the ALND to lymph node sampling or to Level I dissection may decrease surgical morbidity<sup>23,28</sup> but also may decrease the chance to identify lymph node metastases; therefore, it may not be accurate enough. The SLN biopsy electively removes the first lymph node that gets the drainage from the breast carcinoma, therefore providing the pathologist with the lymph node that carries the highest probability of containing potential metastases.<sup>12,13,15-18</sup> The SLN can be examined more accurately and through multiple sections, which may increase the detection of metas-



tases compared with other staging techniques.<sup>14</sup> Nevertheless, the impact of micrometastases on survival is controversial and has yet to be determined.<sup>34</sup> The validity of the SLN biopsy has been confirmed,<sup>14</sup> and the first reports of clinical application in breast carcinoma patients have been published.<sup>21</sup> Due to the limited dissection, it may be suggested that SLN biopsy is associated with nearly zero morbidity, because one lymph node or a few lymph nodes are identified in the axilla and are excised electively without major dissection.

Although no randomization was done (SLN biopsy was not the standard treatment when the study began), data from the current study show that morbidity resulting from SLN biopsy is largely reduced compared with axillary dissection of Levels I and II. After SLN biopsy, no increase in the circumference of the operated arm was found compared with the nonoperated arm. Patients after axillary dissection, however, showed a significant increase in upper and forearm circumference of the operated arm. Although this increase was only minor, subjectively, it was bothering the patients. Patients after SLN biopsy also revealed less paraesthesia, pain, and motion restriction of the operated arm, and the clinical benefit seen in these patients due to limited axillary dissection was striking.

Cosmetic results, such as the length of incisions or postoperative scars, were not compared between the two groups, because, usually, we use only a slightly shorter incision for SLN biopsy (2–3 cm) than for axillary dissection to gain sufficient access to the axilla so that Levels I and II are examined completely for the presence of an SLN. Although the length of the incision may be the same compared with that from axillary dissection, dissection in the axilla is limited to the SLN and avoids any dissection of nerve or vascular structures, which should be responsible for the absence of any morbidity.

In conclusion, postoperative sequelae after axillary dissection frequently are seen and may affect patient quality of life adversely. The SLN biopsy technique, however, has been shown to stage the axilla accurately and spares the patient the morbidity resulting from axillary dissection. Therefore, the SLN biopsy technique may become an alternative to routine axillary lymph node dissection in patients with lymph node negative breast carcinoma.

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