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Breast Lymphedema after Breast Conserving Treatment

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The authors aimed to evaluate breast lymphedema after breast conserving therapy (BCT) and sentinel node biopsy (SNB) or axillary clearance (AC). Fifty-seven breast cancer patients with BCT underwent SNB only and 103 underwent AC (57 with tumor negative and 46 with positive axillary nodes). Clinical examination and breast ultrasonography (US) were performed one year after surgery. Clinical examination revealed breast edema in 48% of patients in the AC node positive group, in 35% in the AC node negative group, and in 23% in the SNB group ($p < 0.05$ between SNB and AC node positive). US revealed subcutaneous edema in the operated breast in 69–70% of the patients in the AC groups and in 28% in the SNB group ($p = 0.001–0.0001$ between the SNB and the AC groups). Breast lymphedema was less common one year after BCT in patients with SNB only than in those with more extensive axillary treatment.

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Numerous studies have reported arm morbidity after breast cancer treatment, with a focus especially on the extent of axillary surgery. Breast morbidity after breast cancer treatment has been investigated in only a few studies (1–3). Breast lymphedema may be considered as a minor problem compared with other side effects encountered after breast cancer treatment. However, delayed breast cellulitis, the most severe form of breast lymphedema, may pose problematic diagnostic and management dilemmas (4). Breast lymphedema seems to be increased after more extensive axillary surgery (1, 5) and postoperative radiotherapy (1, 3). Also the location of the tumour in the breast may influence the prevalence of breast lymphedema (6), especially delayed cellulitis (4).

A decreased risk of early and long-term morbidity after the introduction of sentinel node biopsy without further axillary treatment has been expected. The first studies have reported significantly less arm morbidity after SNB compared with axillary clearance (AC) (5, 7–10). However, to our knowledge, the prevalence of breast lymphedema after SNB has not been widely reported.

For these reasons our aim was to evaluate the risk of breast morbidity, especially breast lymphedema, after breast conserving treatment (BCT) and SNB.

MATERIAL AND METHODS

Altogether 160 consecutive patients with unilateral breast cancer and axillary surgery visited the outpatient clinic one year after BCT at the Breast Surgery Unit of Helsinki University Hospital, Helsinki, Finland. These patients were included in a prospective cross-sectional study. The project plan was approved by the Ethical Committee of Helsinki University Hospital.

The patients were operated on between 4 April 2000 and 28 December 2001. Fifty-seven patients underwent SNB without further axillary treatment and the remaining 103 (46 with and 57 without axillary lymph node metastases) underwent level I–II AC with or without SNB. The indications for AC in the node negative patients were unidentified sentinel nodes, a suspicion of multifocal tumor, a clinical or radiological suspicion of axillary lymph node metastases and a wide local tumor excision prior to axillary surgery. Altogether 87 (59 axillary node negative) patients underwent SNB with or without AC. The median number of removed lymph nodes was 3 (1–13) in the SNB group and 15 (2–20) in the AC group (Table I).

Almost all of the 160 patients, 157, received postoperative radiotherapy (RT). All these 157 patients received external RT to the entire breast area using tangential fields to 50–50.2 Gy at the isocenter in standard fractionation

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Table I

Characteristics of the 160 patients who underwent breast-conserving therapy and axillary surgery

	Patients with SNB only n = 57	Patients with AC and tumor negative nodes n = 57	Patients with AC and tumor positive nodes n = 46
Patients:			
Age (years)[1]	59 (39–77)	58 (37–80)	58 (39–81)
Tumor histology			
DCIS[2]	4	2	0
Invasive ductal	20	32	27
Invasive lobular	24	18	11
Invasive other	9	5	8
Tumor grade:			
I	21	35	16
II	29	12	21
III	6	7	9
Not determined	1	3	0
Tumor classification:			
T1	48	48	30
T2	5	7	16
T0	4	2	0
Tumor location:			
Central	4	1	1
Upper medial	9	10	8
Lower medial	4	3	3
Upper lateral	37	36	24
Lower lateral	3	7	9
Histological tumor size, mm:[1]	14 (3–31)	13.5 (4–30)	17.7 (8–35)
SNB:	57	2	28
Number of harvested nodes[1]	3 (1–13)	15 (2–27)	15 (8–30)

[1]Median, range.
[2]DCIS = ductal carcinoma in situ.
AC = Axillary clearance.
SNB = Sentinel node biopsy.

(1.8–2 Gy daily, 5 days a week). Patients with axillary metastases received RT also to the axillary and supraclavicular fields at the same doses and fractionation. Radiation was delivered using a linear accelerator with 6 MeV photons. None of the patients received a boost. Postoperative adjuvant chemotherapy was included in the treatment in 26% of the patients (Table II).

Surgery

A wide local excision of the tumor aiming at 1–2 cm free tissue margins was performed. The underlying pectoral fascia and most often a slice of overlying skin were included in the resected specimen (11). The sentinel nodes were harvested using preoperative lymphatic mapping, a hand-held gamma probe, and vital blue dye. All the operations,

Table II

Adjuvant treatment in the 160 patients with breast-conserving treatment and axillary surgery

	SNB n = 57	Patients with AC and tumor negative nodes n = 57	Patients with AC and tumor positive nodes n = 46
Radiotherapy	55 (96%)	56 (98%)	46 (100%)
Chemotherapy	8 (14%)	7 (12%)	20 (57%)
Period between the end of the radiotherapy and the clinical examination (months)[1]	9.4 (4.6–16.7)	9.6 (6.6–14.4)	6.5 (3.7–11.6)

[1]Median (range).
AC = Axillary clearance.
SNB = Sentinel node biopsy.

breast surgery, SNB, and /or level I–II AC were performed or directly supervised by experienced surgeons specialized in breast surgery. Axillary surgery was performed in most cases using one oblique incision covering both the breast and the axilla.

The follow-up visit

Clinical examination of the operated and the contralateral breast was performed a median of 12.6 (11.3–18.8) months after the operation by specialist surgeons or surgical residents. The data were collected using case report forms (CRFs). The size, tenderness, pigmentation of the breast, and the condition of the skin in the scar area and in the whole breast were recorded.

Radiological methods

Before the clinical follow-up visits a routine mammography and breast US were performed. In addition an extra US of the breasts was performed by an experienced breast radiologist (MP) after the clinical examination, without knowing the exact surgical procedure performed, in order to evaluate the breast edema. Patients from remote residential areas were excluded from the extra US examination. The ultrasound examinations were performed using a real-time US unit with a linear probe of 5–13 MHz focused on the area of interest. The total skin thickness of the four quadrants of the breasts was recorded for both the operated breast and the contralateral breast, as well as the presence of interstitial edema and fluid collections. The presence of axillary lymph nodes with normal or pathological structure was recorded.

The thickness of normal breast skin varies between 1 and 2 mm with a mean thickness of 1.7 mm (12). The skin complex comprises two thin echogenic lines with a hypoechoic dermis between them (13).

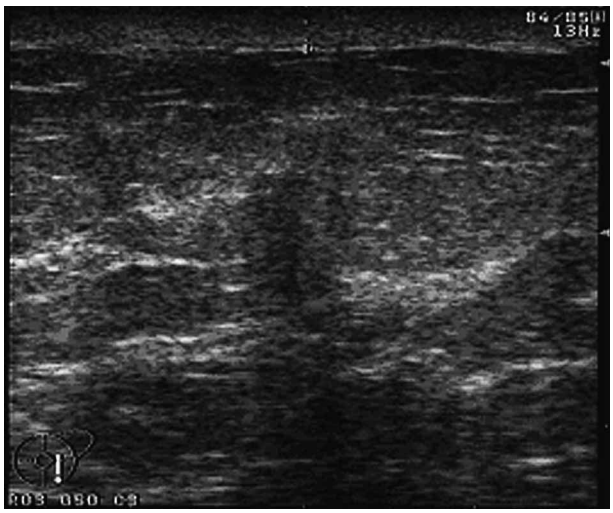

Fig. 2. Thickening of the skin with increased echogenicity of the dermis (between asterisks). The echogenic line at the dermis/subcutaneous fat interface is well seen.

In this study skin complex was classified in the US examination in the following way:

1) normal skin thickness and structure (Fig. 1);
2) skin thickening – thickness of the dermis >2 mm with increased echogenicity (Fig. 2);
3) skin thickening and disturbance/poor visibility of the deeper echogenic line (dermis/subcutaneous fat interface) (Fig. 3);
4) in addition to the above-mentioned, interstitial fluid accumulations were also recorded (Fig. 4);
5) postoperative fluid collections were recorded (Fig. 5).

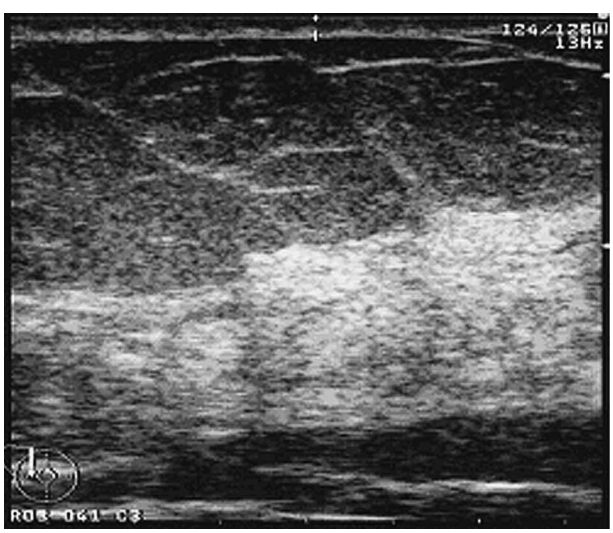

Fig. 1. Normal skin (between asterisks). The dermis/subcutaneous fat interface is seen as a bright echogenic line. Scale left side of the image 5 mm intervals.

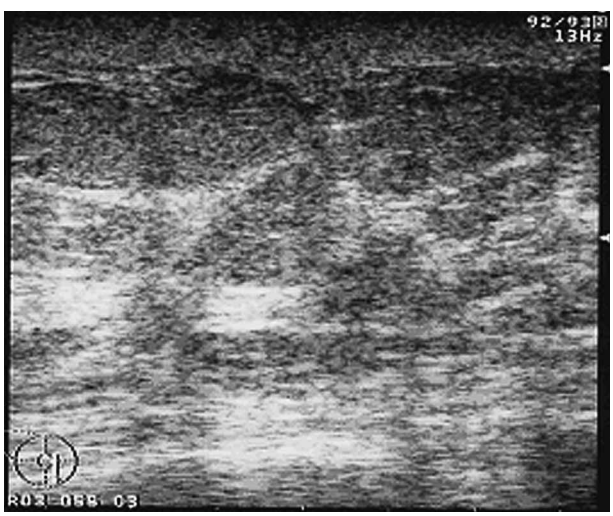

Fig. 3. Thickening of the skin with poor visibility of the dermis/subcutaneous fat interface representing subcutaneous edema.

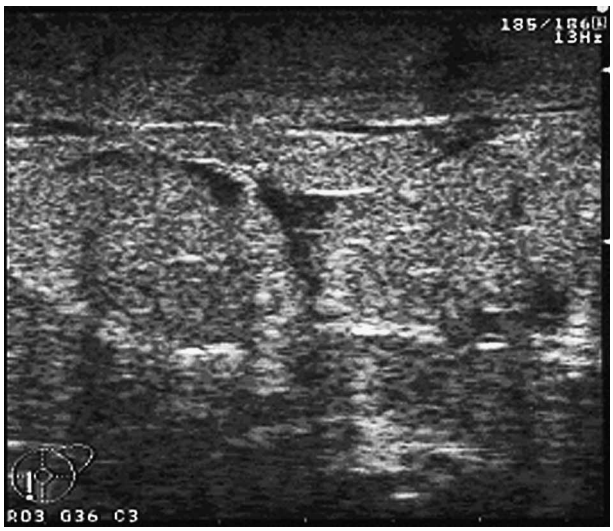

Fig. 4. Thickening of the skin with subcutaneous edema and interstitial fluid between the fat lobules.

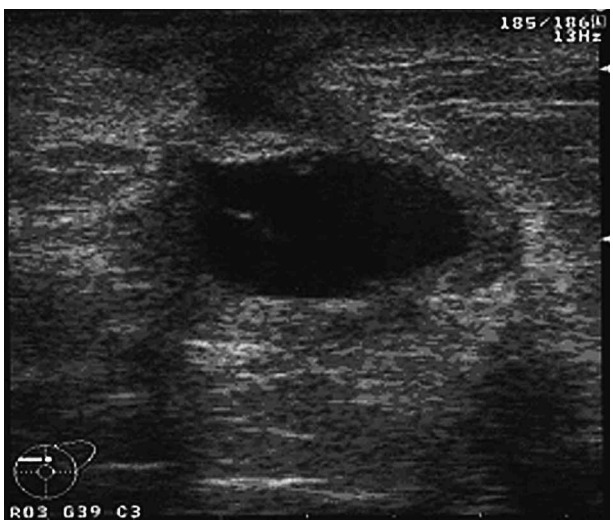

Fig. 5. Postoperative fluid collection below the scar with skin thickening and subcutaneous edema.

In this study thickening of skin over 2 mm with increased echogenicity, disturbance, or poor visibility of the deeper echogenic line and interstitial fluid accumulation were considered as an edema. Both interstitial fluid and fluid accumulation were considered as the extent of lymphedema.

Statistical methods

The statistical analysis was performed using a computer system (SPSS, Inc., Chicago IL). The medians were compared using the non-parametric, Mann–Whitney U-test. In cross-tabulations the $\chi^2$and Fisher's exact tests were used. P-values of less than 0.05 in two-sided tests were considered statistically significant.

RESULTS

Clinical examination

The operated breast was more tumid than the contralateral one on clinical examination in 34% (55/160) of the patients. The postoperative edema of the breast varied significantly between the treatment groups ($p = 0.0290$). Clinical breast edema was most common, in 48% (22/46) of the patients with AC and involved axillary nodes, and least common, in 23% (13/57) of the patients, with SNB only ($p = 0.0188$). The operated breast was as large as the non-operated one in 42% (67/160) and smaller than the non-operated one in 46% (74/160) of the patients without significant differences between the groups (Table III).

Some abnormal clinical signs, such as lymphedema, pigmentation, or tenderness, were observed in the operated breast in 78% (124/160) of the patients in the whole study population. Thirty-seven percent of the patients had edematous or thickened skin (orange peel), erythema, significant pigmentation and/or other skin damage after RT. In general, pigmentation of the skin in the operated breast was a common clinical finding with a prevalence of 59% (94/160), including also the slightest pigmentation. Abnormal tenderness during breast palpation was experienced by 46% (73/160) of the patients. The prevalence of these signs did not differ statistically between the patient groups (see Table III).

Ultrasonography

The skin thickness of the non-operated breast did not differ between the patient groups. A thicker skin on the operated side was observed more often in patients in the AC groups compared with patients with SNB only ($p = 0.004–0.0001$) (Table IV).

Subcutaneous edema in the operated breast was encountered in 70% of the patients after AC and in 28% after SNB alone ($p = 0.001$ between the SNB and AC groups). Fluid collection in the operated breast was more common in the AC groups, in 56% of patients, than after SNB only, 17% of patients ($p = 0.0001$ between SNB and AC groups) (Table V).

The location of the tumor of the breast had no influence on the prevalence of clinically or ultrasonographically detected lymphedema (Table VI).

DISCUSSION

The etiology of breast lymphedema is less well known than its symptoms and signs (1, 14). Postoperative edema can be divided into early and late onset types. Early onset edema develops within the first 2 months while late breast edema occurs about 20 months after operation and/or RT (1). Breast surgery as well as RT to the breast and/or to the axilla can disturb the lymphatic circulation of the breast (1). The risk of post-operative breast lymphedema seems to be

Table III

Findings in the clinical examination one year after breast-conserving treatment and axillary surgery

Breast finding	SNB n = 57	Patients with AC and tumor negative nodes n = 57	Patients with AC and tumor positive nodes n = 46	p-value
Edema	13 (23%)	20 (35%)	22 (48%)	0.029
Breast size:				ns
Equal	23 (40%)	21 (37%)	23 (50%)	
Smaller	26 (46%)	28 (49%)	20 (44%)	
Larger	7 (12%)	8 (14%)	3 (6%)	
Not applicable	1 (2%)			
Pigmentation:				ns
None	28 (49%)	21 (37%)	16 (35%)	
Slight	24 (42%)	24 (42%)	18 (39%)	
Clear	5 (9%)	12 (21%)	11 (24%)	
Not evaluated			1 (2%)	
"Orange peel" skin	0 (0%)	4 (7,4%)	2 (4,8%)	ns
Erythema	1 (1.8%)	2 (3.7%)	5 (11.9%)	ns
Breast firm/compact	7 (12%)	10 (18%)	8 (17%)	ns
Tenderness	21 (37%)	30 (53%)	22 (48%)	ns
Scar area normal	47 (82%)	39 (68%)	38 (83%)	ns

AC = Axillary clearance.
SNB = Sentinel node biopsy.

increased in obese patients with surgery to an upper outer quadrant tumor (6).

According to the findings in the present and previous studies, approximately every third patient suffers from breast edema one year after operation (1, 2). Breast edema seems to be indisputably related to the extent of axillary surgery. Clarke and co-workers observed breast lymph edema in 25% of patients after axillary sampling (1). This finding is in close agreement with our 23% prevalence of breast edema after SNB without further axillary treatment. Breast edema was observed clearly more often, in 35–79% of the patients, after AC in the present and the previous study by Clarke and co workers (1). The risk of breast edema without any axillary surgery is about 6% (1).

Adjuvant breast RT is another risk factor for breast lymphedema. Senofsky and co-workers (3) observed a 21% incidence of breast edema after breast resection and RT while the incidence of breast edema was only 5% among non-irradiated patients (3). The influence of breast RT on the risk of breast edema was not assessed in the present study, because practically all our patients received adjuvant breast RT.

It is not known whether the risk of breast edema is further increased by adding RT to the axillary and supraclavicular fields to AC. In the present study, the risk of breast edema was pronounced after AC in patients with tumor-positive axillary nodes who all received RT also to the axillary and the supraclavicular fields. Whether the

Table IV

Median breast skin thickness on ultrasonography one year after breast-conserving treatment

	SNB n = 36	Patients with AC and tumor negative nodes n = 37	Patients with AC and tumor positive nodes n = 29	p-value
Breast segment, non-operated breast:				
Upper lateral	1.1 (0.7–2.5)	1.1 (0.6–1.6)	1.0 (0.6–1.6)	ns
Upper medial	1.2 (0.9–2.9)	1.2 (0.7–1.6)	1.3 (0.9–1.7)	ns
Lower lateral	1.3 (0.7–2.1)	1.3 (0.8–1.9)	1.3 (0.8–1.9)	ns
Lower medial	1.1 (0.7–2.2)	1.1 (0.7–1.7)	1.1 (0.7–1.6)	ns
Breast segment, operated breast:				
Upper lateral	1.5 (1–4.4)	1.9 (0.7–5.5)	1.8 (1.1–6.6)	0.004
Upper medial	1.7 (0.9–4.6)	2.5 (1.2–6.5)	2.7 (0.9–6.1)	0.0001
Lower lateral	1.9 (0.9–5.5)	2.9 (1.4–6.4)	3.4 (1.1–7.5)	0.0001
Lower medial	2.1 (1.1–4.6)	3.1 (1.4–6.4)	3.6 (1.1–7.5)	0.0001

mm (range).
AC = axillary clearance.
SNB = sentinel node biopsy.

Table V

Findings on breast ultrasonography one year after breast-conserving treatment and axillary surgery

Finding	SNB n = 36	Patients with AC and tumor negative nodes n = 37	Patients with AC and tumor positive nodes n = 29
Subcutaneous edema[1]	10 (28%)	26 (70%)	20 (69%)
Interstitial fluid[2]	6 (17%)	20 (54%)	17 (59%)

AC = axillary clearance.
SNB = sentinel node biopsy.
[1]p = 0.0003, p = 0.0001 between SNB and AC groups.
[2]p = 0.0006, p = 0.0001 between SNB and AC groups.

Table VI

Influence of the location of surgery on clinically or ultrasonographically (US) detected breast lymphedema one year after BCT

Tumor location	Clinical lymphedema	Interstitial fluid collection in US	Subcutaneous edema in US
Central	1/6 (17%)	2/5 (40%)	2/5 (40%)
Upper medial	13/27 (48%)	8/17 (47%)	9/17 (53%)
Lower medial	3/10 (30%)	2/4 (50%)	2/4 (50%)
Upper lateral	30/97 (31%)	24/64 (38%)	34/64 (53%)
Lower lateral	8/19 (42%)	8/13 (62%)	10/13 (77%)
p-value	ns	ns	ns

reason for increased breast morbidity in this patient group was the more extensive RT or the axillary node involvement itself or both could not be concluded on the basis of our findings. Another possible explanation for the more prevalent breast edema in patients with AC and involved axillary nodes is a three-month shorter period between finishing RT and clinical and US examinations. This because RT was started and accordingly finished later in these patients because it was often preceded by adjuvant chemotherapy. The timing of radiotherapy in relation to the US examination may also have influenced the findings regarding the skin thickness of the operated breast.

The location of the tumor in the breast may also influence the prevalence of breast lymphedema (4, 6). In particular, delayed breast cellulitis, the most severe form of breast lymphedema, seems to be most common in patients with breast conserving treatment because of breast cancer in the upper lateral breast segment (4). However, in the present study, the location of the tumor in the breast had no influence on the prevalence of breast lymphedema. This may be because none of the patients in the present study had delayed breast cellulitis but only milder forms of breast lymphedema. In addition, all of our patients underwent axillary surgery, SNB, or AC. Although SNB is less extensive than AC, it is also an invasive procedure disrupting lymphatic drainage from the breast to the axilla. To evaluate the role of the location of the resection in the breast precisely, a patient group with breast surgery without any axillary procedure should be studied.

In addition to varying the extent and timing of radiotherapy, our results may be biased because of the small study population and the non-randomized study setting as regards AC and SNB. Also other confounding factors like systemic adjuvant therapy, the age, and the body mass index of the patients have possibly influenced our results. Despite the limitations of our study, our results, as well as those of the previous study by Clarke and co-workers (1), indicate that the extent of the axillary procedure increases the risk of breast lymphedema.

There are few simple objective methods for evaluation of post-treatment symptoms in the upper extremity and especially those in the breast. In addition to the clinical examination we evaluated the breasts using US and compared the operated breast with the non-operated one. The radiologist made the US evaluations not knowing the type of axillary procedure; in fact the axillary scars of the different groups looked almost the same. The US findings were concordant with those of the clinical examination. Furthermore the thickness of the skin and the amount of interstitial fluid was similar on the non-operated side in all three treatment groups. For these reasons breast US is a feasible method for evaluation of breast edema.

In conclusion, breast symptoms, especially lymphedema, are significantly less common after BCT and SNB than after BCT and more extensive axillary treatment. Furthermore, breast US provides a feasible method for evaluation of breast lymphedema.

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