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Comparison of morbidity between axillary lymph node dissection and sentinel node biopsy

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Aims: The use of axillary lymph node dissection (ALND) in women with breast cancer is associated with considerable morbidity. Sentinel node biopsy (SNB) removes the lymph node in the axillary basin indicative for receiving first lymphatic drainage from the breast. This study compares the nature and severity of physical morbidity among breast cancer patients who underwent primary surgery for breast cancer combined with either ALND or SNB. Also, it assesses influence of subsequent radiotherapy on morbidity.
Method: Two hundred and thirteen ALND patients were compared with 180 SNB patients retrospectively. Morbidity was measured using a disease-specific quality-of-life questionnaire.
Results: Patients' demographic characteristics were alike. The axillary procedure is the strongest and most consistent factor in explaining differences in a variety of self-reported complaints. Patients having had SNB have a 3.2-fold lower risk of experiencing pain, a 5-fold lower risk of lymph oedema, a 7.7-fold lower risk of numbness, a 3.7-fold lower risk of tingling sensations, a 7.1-fold lower risk of loss of strength in arm/hand, a 3.6-fold lower risk of loss of active motion range of the arm and a 2.9-fold lower risk of impaired use of the arm. Axillary radiation therapy adds to complaints next to the axillary surgical procedure by increasing the risk of lymph oedema 2.4-fold and enhancing the risk of impaired use of the arm by 2.6-fold. Axillary radiation therapy does not explain lymph oedema by itself.
Conclusion: SNB is associated with less morbidity compared to ALND in patients with primary breast cancer.

Key words: breast cancer; axillary lymph node dissection; sentinel node biopsy; lymph oedema; quality of life.

INTRODUCTION

For decades, axillary lymph node dissection (ALND) has been the standard procedure in surgical treatment of patients with breast cancer. In the past few years, screening mammography and increased public awareness has led to a decrease in detected tumour size. As a result, fewer women have axillary lymph node involvement. It is thought that over ninety per cent of woman having breast tumours smaller than 1 cm have no involvement of the axillary lymph nodes.[1–8] Next to tumour size, the extent of axillary involvement is considered to be the most important prognostic indicator for breast cancer survival.[8] Gold-standard in determining actual axillary lymph node involvement in breast cancer patients is by means of performing ALND. Of value in obtaining regional control of metastasized breast cancer in the axilla, the importance of ALND is shifting from being an integral part of breast cancer treatment towards being a critical element for staging purposes and adjuvant treatment determination. Routine performance of ALND, and its alleged impact on disease-free or overall survival is under discussion.[9–13] ALND comes at cost to the patient. It induces postoperative morbidity such as lymph oedema, pain, numbness, loss of strength and impaired range of motion of the involved arm.[11,14–17] Next to the extent of surgery in the axilla, the number of removed lymph nodes, the tumour burden of the nodes and

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postoperative axillary radiation therapy have been shown to be related to morbidity.[16] Limiting the extent of surgery to the axilla is likely to diminish morbidity. In this respect, sentinel node biopsy (SNB) has become the object of study in breast cancer patients. The technique has first been described by Cabanas in patients with penile carcinoma.[18] SNB has been extensively validated in patients with stage I melanoma by Morton *et al*., and the concept is currently extended to breast cancer populations.[19] Preliminary studies have shown that SNB in breast cancer populations, compared to standard ALND, has a sensitivity varying from 85% to 98%.[12,20–27]

In experienced hands, SNB may decrease axillary morbidity preserving optimal conditions for detecting axillary metastasis. ALND could then be reserved for those patients proven to have axillary lymph node metastasis by SNB.

Physical problems resulting from ALND are well documented.[1,2,17] Few studies have compared physical morbidity of ALDN with SNB reflecting the impact of both techniques on the patient's quality-of-life.[16] The present study focuses on frequency and severity of self-reported physical complaints and problems in daily life among breast cancer patients having had different surgical approaches to the axilla. The aim of this study is to assess the influence of the axillary procedure and subsequent adjuvant treatment on post-operative morbidity in breast cancer patients.

MATERIALS AND METHODS

Patients

From December 1998 until May 1999, specialists approached breast cancer patients having had ALDN within the last three years. Patients were considered eligible if they underwent ALND as part of surgical treatment for primary breast cancer, were at least three months post-treatment (including radiation and/or adjuvant hormonal or chemotherapy) and without signs of active disease. In order to prevent selection bias, specialists were requested to approach ALND patients consecutively during scheduled follow-up appointments irrespective of the presence of complaints after surgery. SNB patients were considered eligible for our study if they underwent SNB as part of surgical treatment for primary breast cancer within the last 3 years, were at least three months post-treatment and without signs of active disease. SNB patients were consecutively selected from hospital patient files.

Technique

Patients underwent either lumpectomy or mastectomy, combined with ALND or SNB. ALND was performed according to established guidelines. Mean number of lymph nodes removed was 10. The SNB procedure was facilitated by administration of 100 Megabec querel (Mbq) in 0.5 mL of ^{99m}Tc-colloidal-labelled albumin (Nanocoll), peri-tumoural, the day prior to surgery. Static imaging of the axilla using a gamma-camera was done at the Department of Nuclear Medicine immediately before surgery. Under general anaesthesia, the patient was injected around the areola with Patent Blue V dye for optimal visualization of lymphatics and lymph nodes (2.5% solution, Laboratoire Guerbet, Aulnay-sous-Bois, France, injected peri-areolar subdermally). The sentinel node was harvested through a small, 2–3 cm wide skin-crease incision guided by skin surface markings indicative for the visualized sentinel nodes on static films, and by combined visual/hand-held gamma probe localization.

ALND patients started physical therapy from day one post-operatively until optimal motion range was achieved. Most patients were given a drain during surgery in the axillary region. The drain was usually removed when production was below 40 cc/24 h. At discharge, patients were instructed by a trained nurse how to resume optimal use of the arm and how to exercise at home. Patients were seen on outpatient basis according to protocoled follow-up schedule, starting one week after discharge. SNB patients were not given routine wound drains. SNB patients were usually discharged one to two days post-operatively. No routine hospital physical therapy was started in the SNB group.

Radiation therapy to the axilla and/or supraclavicular region was recommended for patients with inadequate ALND, extra-capsular malignant growth at lymph node involvement or nodal involvement in the apex of the axilla. In the SNB group, ALND was performed in patients with a positive sentinel node on H&E staining, and radiation therapy recommended according to the pathological outcome of ALND. Irradiation of the axilla and the supraclavicular region was recommended for patients with inadequate ALND, extra-capsular extension of tumour growth or nodal involvement in the apex of the axilla. Patients received post-operative adjuvant hormone or chemotherapy depending on their individual characteristics combined with the results of pathology including breast tissue and axillary node histology, mitosis index of the tumour and its oestrogen/progesterone receptor status.

Questionnaire

Eligible patients received a treatment-specific quality-of-life questionnaire. This questionnaire was developed and validated by the department of Clinical Health Psychology of Tilburg University, The Netherlands. The questionnaire was pre-tested and construct- as well as content-validated in pilot study.[28] Additional data, such as *p*TNM classification and post-operative treatment regimen were retrieved from hospital patient files.

Statistics

Fisher's exact test, Student's *t*-test and the Kolmogorov–Smirnov test were used to analyse variables in frequency tables, depending on scale of measurement. Multivariate logistic regression analysis was applied to assess association between patient and treatment characteristics and risk on complaints. For this purpose, the original four-point Likert scale was dichotomized. Response categories 2 and 3 were recoded as 'complaint present', categories 0 and 1 as 'complaint absent'. Odds Ratios (OR) and 90% confidence intervals – as a direction of diminishment of the complaint in the SNB group was to be expected – were computed. Variables included in the regression model were: *axillary procedure* (SNB vs ALND); *cancer stage* (stage 2 vs stage 1); *time since axillary surgery* ($>$2 years ago vs $\leq$2 years ago); *age* groups 1 and 2 ($<$50 years vs 65+ and 50–64 years vs 65+); *treatment* (lumpectomy vs mastectomy); *radiation therapy* one and two (not irradiated vs irradiated on breast/chest wall, but not on axilla or supraclavivular; and irradiated on breast/chest wall, but not on axilla or supraclavicular); *chemotherapy* (yes vs no); *hormonal therapy* (yes vs no); *axillary surgery ipsilateral to handedness* (yes vs no). Only variables with *P*-values less or equal to 0.05 (alpha) were considered to be of statistical significance, and kept in regression analysis using the stepwise-backward selection principle, selecting variables with a significance level of $P < 0.10$ into the model.

This study was set up and coordinated by the Section of Clinical Health Psychology of Tilburg University and the Comprehensive Cancer Centre South in Eindhoven, The Netherlands. Eight departments of surgery, one department of radiotherapy and one department of internal medicine of eight community centre hospitals in the South-East Netherlands participated in the study. Approval was obtained from the Medical Ethical Committees of participating hospitals and of the Comprehensive Cancer Centre South. The departments of surgery of the Catharina Hospital Eindhoven and the St Joseph Hospital Veldhoven, being the first ones in the region performing sentinel node biopsy, were selected for inclusion of SNB patients. Both centres evaluated reliability of their clinical application of the SNB procedure.[29,30]

RESULTS

Of the 465 questionnaires sent to ALND patients, 400 (86%) were returned. In addition, of the 248 questionnaires sent to SNB patients, 198 (79%) were returned. Only patients with updated and comprehensive patient records, who filled in the questionnaire completely, were included. This resulted in a reduction of group size for the ALND patients to 213 patients and a group size for SNB patients of 180 patients.

Patient characteristics

Variables representing patients' demographics and treatment characteristics are presented in Table 1. Groups do not differ in age, level of education, civil status, number of children, professional activity and health care insurance. In contrast, primary surgery differs among groups; patients who underwent SNB received breast-conserving primary surgery more often. Considering the *p*TNM-classification, patient groups do not to differ significantly in tumour size, although there is skewness-to-the-side towards a more favourable tumour size in the SNB group. Table 2 illustrates relationships between tumour stage, primary procedure and axillary surgery. SNB patients having a mastectomy mostly did so because they were diagnosed with ductal carcinoma *in situ* (Tis), whereas ALND patients having a mastectomy did so because of larger tumour size. Both groups have a similar percentage of pT1 patients, in the mastectomy population (approx. 50%) as well as in the lumpectomy population (approx. 75%). Axillary nodal state and tumour size, reflected in the stage-classification of patients, are unequally divided between groups. This can partly be explained by the larger proportion of Tis patients in the SNB group, and partly by less involvement of the axillary nodes in the SNB group.

It is important to realize that the staging of the patient actually is a pathologically based figure, calculated after the surgical procedure has been performed. Therefore, staging as a parameter is invalid in its proposed influence on morbidity itself. However, it is indicative of the selection of individual–adjuvant therapy. Radiotherapy differs among groups. Radiotherapy is more frequently applied in the SNB group, but relatively more patients in the ALND group received radiotherapy to the axillary region. ALND patients received chemotherapy more often but hormonal therapy less often. The majority of patients in the SNB group underwent surgery (less than) one year from questioning; the majority of patients in the ALND group underwent surgery 2–3 years from participation in the present study.

Frequency and severity of arm problems and arm-related complaints: SNB group versus ALND group

The frequency and severity of arm-related complaints are presented in Tables 3 and 4. Table 3 represents the entire set of complaints patients where asked for in the Physical Domain section of the questionnaire. The four-point Likert scale has been dichotomized to complaint 'absent' or 'present'. Selection of complaints resulted according to authors' opinion on importance, as well as their results when tested for significance (Table 3). Frequently (i.e. $>$20%) reported physical complaints in the ALND group were: loss of strength in arm/hand

Table 1 Comparison of demographic-, treatment- and disease-specific characteristics between ALND patients and SNB patients

Patient and treatment characteristics	ALND (%) ($n = 213$)	SNB (%) ($n = 180$)	*P*-value
Age when having surgery (years)[3]			
< 50	27.7	20.5	
50–65	54.4	46.5	
≥ 65	17.8	33.0	0.17
Time since axillary surgery (years)[2]			
< 1	0.0	9.1	
1	38.0	50.0	
2	36.2	36.9	
3	25.8	4.0	0.00*
Primary surgery[1(see also Table 1a)]			
Lumpectomy	66.2	88.3	
Mastectomy	33.8	11.7	0.00*
Axillary surgery on ipsilateral side as primary surgery[2]			
No	44.6	48.0	
Yes	54.9	50.3	
Ambidextrous	0.5	1.7	0.75*
pTNM-classification[2]			
pTis	0.5	6.7	
pT1 (tumour size ≤ 2 cm)	67.1	71.1	
pT2 (tumour size > 2 cm and ≤ 5 cm)	27.2	21.1	
pT3 (tumour size > 5 cm)	1.9	0.6	
pT4 (tumour invading skin or thorax, regardless of size)	3.3	0.6	0.27
pN0 (no positive axillary lymph node/s)[1]	58.8	78.9	
pN1 or pN2 (metastasis in movable ipsilateral node/s; metastasis in fixed ipsilateral node/s)	41.2	21.1	0.00*
Stage[2]			
Stage 0 (is)	0.5	6.7	
Stage 1	46.9	58.3	
Stage 2	46.5	33.9	
Stage 3	6.1	1.1	
Stage 4	0	0	0.01*
Radiotherapy[2]			
No	28.4	17.2	
Yes, on axilla	13.9	8.3	
Yes, not on axilla	57.7	74.4	0.01*
Chemotherapy[1]			
No	81.2	89.4	
Yes	18.8	10.6	0.02*
Hormonal therapy[1]			
No	76.1	64.4	
Yes	23.9	35.6	0.01*
Civil status[1]			
Single/divorced/widow	25.9	27.0	
Married/living together	74.1	73.0	0.82
Children[1]			
No	8	15.2	
Yes	92	84.8	0.04*
Level of Education[2]			
Primary	27.5	27.3	
Secondary/Professional	58.3	55.2	
Higher (e.g. college or university)	14.2	17.4	1.0
Professionally active (other than full-time housewife)[1]			
No	59.1	62.2	
Yes	40.9	37.8	0.62

Table 1 *Continued*

Patient and treatment characteristics	ALND (%) ($n = 213$)	SNB (%) ($n = 180$)	*P*-value
Professional inactivity related to surgery[2]			
Inactive before surgery	47.7	48.3	
Inactive since surgery	8.7	9.2	
active	43.6	42.5	1.0
Health care insurance[1]			
Public	64.8	69.3	
Private	35.2	30.7	0.39

[1] Fishers exact test, 2-tailed.
[2] two-sample Kolmogorov–Smirnov test, 2-tailed.
[3] T-test for equality of means (mean ALND: 56.1 years, stdev 11.15, mean SNB: 59.8 years, stdev 11.83).
* Statistically significant at α: 0.05.

Table 2 Relationship between tumour stage, primary procedure and axillary surgery

Stage	Mastectomy		Mastectomy		Lumpectomy		Lumpectomy	
	SNB (%)	*n*	ALND (%)	*n*	SNB (%)	*n*	ALND (%)	*n*
Tis	23.8	5	1.4	1	4.4	7		
pT1	47.6	10	51.4	37	74.2	118	75.2	106
PT2	23.8	5	34.7	25	20.8	33	23.4	33
PT3	4.8	1	4.2	3			0.7	1
PT4			8.3	6	0.6	1	0.7	1

Table 3 Comparison of the proportion of patients with complaints after ALND/SNB

Morbidity after axillary surgery	ALND ($n = 213$) complaint present %	SNB ($n = 180$) complaint present %	*P*-value*
Painful arm/shoulder	23.0	7.8	0.00
Lymph edema	7.1	1.1	0.00
Numbness of arm/hand	24.4	3.9	0.00
Tingling sensations in arm/hand	14.6	3.9	0.00
Loss of strength in arm/hand	26.3	3.9	0.00
Cannot use arm to former extent	21.2	7.7	0.00
Treated by physiotherapist[1]	37.6	11.2	0.00
Currently being treated by physiotherapist[1]	18.8	10.3	0.02
Loss of full active motion range of arm	18.3	6.0	0.02
Use of other hand due to discomfort of hand on affected side	20.6	4.5	0.00
Experience of difficulties at domestic tasks	15	7.8	0.00

All tests, unless stated otherwise, performed trough: two-sample Kolmogorov–Smirnov test, 2-tailed.
[1] Fishers exact test, 2-tailed.
* Statistically significant at α: 0.05.

(26.3%); numbness of arm/hand (24.4%); painful arm/shoulder (23%); inability to use arm to former extent (21.1%); and use of other hand due to discomfort of hand on affected side (20.6%). In the SNB group, all complaints are reported less frequently. Most frequently reported complaints in the SNB group are a painful arm/shoulder (7.8%) and the experience of difficulties performing domestic tasks (7.8%). A variable often mentioned in literature to be debilitating after ALND is lymph oedema. Virtually non-existent in the SNB group (1.1%), in the ALND group, 1:15 patients is reporting severe oedema.

Table 4 Multivariate logistic regression analysis for seleted physical complaints

Item	OR[1]	1/OR[2]	90% CI	*P*-value
Painful arm/shoulder				
SNB vs ALND	0.31	3.23	(0.18–0.52)*	0.03
Lymph edema				
SNB vs ALND	0.2	5.0	(0.12–0.32)*	0.00
Axillary/supraclavicular irradiation vs irradiation on breast or chestwall, but not on axilla/supraclavicular region	2.44	0.41	(1.31–4.52)*	0.02
Time since axillary surgery >2 years ago vs ≤2 years ago	2.19	0.46	(1.41–3.40)*	0.00
No irradiation vs irradiation on breast or chestwall, but not on axilla/supraclavicular region	0.90	1.10	(0.54–1.48)	0.72
Numbness of arm/hand				
SNB vs ALND	0.13	7.69	(0.06–0.26)*	0.00
Age < 50 years vs age 65+	3.39	0.29	(1.55–7.45)*	0.01
Age 50–64 years vs age 65+	1.34	0.74	(0.70–2.59)	0.46
Chemotherapy vs no chemotherapy	0.47	2.12	(0.22–1.00)	0.10
Tingling sensations in arm/hand				
SNB vs ALND	0.27	3.70	(0.13–0.54)*	0.00
Loss of strength in arm/hand				
SNB vs ALND	0.14	7.14	(0.07–0.28)*	0.00
Lumpectomy vs mastectomy	0.55	1.82	(0.33–0.92)*	0.05
Loss of full active motion range of arm				
SNB vs ALND	0.28	3.57	(0.15–0.53)*	0.01
Stage 2 or 3 vs stage *in situ* or 1	2.03	0.49	(1.18–3.50)*	0.03
Cannot use arm to former extent				
SNB vs ALND	0.34	2.94	(0.20–0.58)*	0.00
Axillary/supraclavicular irradiation vs irradiation on breast or chestwall, but not on supraclavicular/supraclavicular region	2.64	0.37	(1.41–4.96)*	0.01
No irradiation vs irradiation on breast or chestwall, but not on axilla/supraclavicular region	0.76	1.32	(0.41–1.43)	0.48
Treated by physiotherapist				
SNB vs ALND	0.24	4.17	(0.15–0.39)*	0.00
Lumpectomy vs mastectomy	0.5	2.00	(0.28–0.88)*	0.04
No irradiation vs irradiation on breast or chestwall, but not on axilla/supraclavicular region	0.51	1.96	(0.27–0.95)*	0.07
Axillary/supraclavicular irradiation vs irradiation on breast or chestwall, but not on supraclavicular/supraclavicular region	1.69	0.59	(0.90–3.15)	0.17
Currently being treated by physiotherapist				
SNB vs ALND	0.45	2.22	(0.27–0.78)*	0.02
No irradiation vs irradiation on breast or chestwall, but not on axilla/supraclavicular region	0.54	1.85	(0.27–1.07)	0.14
Axillary/supraclavicular irradiation vs irradiation on breast or chestwall, but not on supraclavicular/supraclavicular region	2.02	0.49	(1.06–3.83)	0.07
Hormonal therapy vs no hormonal therapy	1.75	0.57	(1.04–2.95)	0.08
Use of other hand due to discomfort of hand on affected side				
SNB vs ALND	0.25	4.00	(0.13–0.49)*	0.00
Lumpectomy vs mastectomy	0.36	2.78	(0.18–0.70)*	0.01
No irradiation vs irradiation on breast or chestwall, but not on axilla/supraclavicular region	0.65	1.54	(0.30–1.39)	0.35
Axillary/supraclavicular irradiation vs irradiation on breast or chestwall, but not on supraclavicular/supraclavicular region	1.97	0.51	(0.94–4.13)	0.13

Table 4 *Continued*

Item	OR[1]	1/OR[2]	90% CI	*P*-value
Experience of difficulties at domestic tasks				
SNB vs ALND	0.58	1.72	(0.33–1.00)	0.10
Axillary surgery on contralateral side as primary surgery vs axillary surgery on ipsilateral side as primary surgery	0.58	1.72	(0.34–0.98)*	0.09

[1] Interpretation of results: e.g. patients who underwent Sentinel Node Biopsy showed a 0.31 *greater* risk of having a painful arm/shoulder after surgery than patients who underwent Axillary Lymph Node Dissection.
[2] Interpretation of results: e.g. patients who underwent Sentinel Node Biopsy showed a 3.22 *lower* risk of having a painful arm/shoulder after surgery than patients who underwent Axillary Lymph Node Dissection.
* statistically significant at CI 90%

Table 5 Relationship between axillary surgery, radiation therapy and lymph edema

Lymph Edema	No radiation therapy				Radiation therapy to axilla				Radiation therapy not to axilla			
	SNB	*n*	ALND (%)	*n*	SNB	*n*	ALND (%)	*n*	SNB	*n*	ALND (%)	*n*
Absent	100%	31	96.6	57	100%	15	82.8	24	98.5%	131	93.3	112
Present			3.3	3			17.2	5	1.5%	2	6.7%	8
Fisher exact test 1-sided *P*-value	0.427				0.109				0.036*			

Over one in three ALND patients have had physiotherapy, compared to 1 to 9 patients in the SNB group. Almost 19% of ALND patients are still being treated by the physiotherapist.

RISK FACTORS

Table 4 specifies the odds ratios (ORs), resulting from multivariable logistic regression analysis on the selected set of complaints. SNB patients have a 3.2-fold lower risk of experiencing a painful arm or shoulder after surgery than ALND patients. SNB patients are five times less likely to experience lymph oedema. Axillary radiation and elapsed time since surgery are also important variables in the model for estimating the risk on lymph oedema. Table 5 illustrates relation between radiation therapy, axillary surgical procedure and presence of lymph oedema. In the SNB group, lymph oedema is absent even when patients are irradiated on the axilla. In the ALND group, there is a difference of 14% in reported lymph oedema between patient without and patients with radiation therapy to the axilla. There is a difference of 10.5% between patients with radiation therapy to the breast or chest wall but not to the axilla and patients with radiation therapy to the axilla. Only two patients in the SNB group report often to have lymph oedema. These two patients have both had a lumpectomy, and were both node-negative, but have been irradiated on the breast. Radiation therapy seems not to explain the presence of lymph oedema in patients having had none (FET 0.43) and for patients having had radiation therapy to the axilla (FET 0.11). The axillary procedure contributes significantly to experiencing numbness of the affected arm/hand. In addition, the age of the patient is of importance, indicating that patients younger than 50 years have a 3.4-fold *higher* risk on reporting numbness compared to patients over 65 years of age. For the questions concerning tingling sensations (OR 3.7), loss of full active motion range (OR 3.6) and use of arm to former extent (OR 2.9), SNB patients have significant lower risk of complaints. The pathologic stage of the patients is, in retrospect, of importance for indicating loss of full active motion range (higher stage indicating a 2.1-fold *higher* risk). Patients who underwent radiation therapy to the axilla are 2.4 times *more* at risk for experiencing lymph oedema and 2.6 times *more* prone to experiencing impaired use of the arm. Axillary radiation therapy does not contribute significantly for being, ever, under treatment of a physiotherapist; neither is axillary radiation therapy explaining the use of the other hand due to discomfort. Considering loss of strength and use of the other hand due to discomfort on the affected side, primary procedure and axillary procedure are both of influence, favouring less invasive surgery. SNB patients have a 7.1-fold lower risk of loss of strength, and a 4-fold lower risk of use of the other hand due to discomfort.

SNB patients have a 4-fold, and in the lumpectomy patients have a 2-fold lower chance of ever being treated

by a physiotherapist compared to ALND patients and mastectomy patients, respectively. Having had no radiation therapy at all seems to be reducing the risk for needing a physiotherapist by 2-fold.

DISCUSSION

The purpose of this study was to compare nature and severity of morbidity among breast cancer patients having undergone traditional axillary lymph node dissection (ALND) vs breast cancer patients having undergone sentinel node biopsy (SNB). Our findings indicate that self-reported morbidity after SNB is significantly reduced in comparison to post-ALND morbidity.

Lymph oedema is a common and troublesome problem that can develop following breast cancer treatment. It is believed to cause a significant diminution in health-related quality of life for breast cancer patients.[31] Lymph oedema can cause limitations in range of motion, pain, weakness or stiffness in the affected extremity.[32] In literature, a broad range of incidence for post-operative lymph oedema, varying widely from 6% to 56% in ALND patients, depending on definition, method of measurement, extent of axillary surgery, number of different surgeons, choice of adjuvant therapy and time elapsed since operation.[17,33] Across treatment and time since treatment, approximately a quarter of patients are believed to develop arm oedema.[34] The addition of radiotherapy to the dissected axilla is thought to be a strong contributor to lymph oedema. In one study, radiation therapy to the breast and to the breast and axillary nodes is reported to increase lymph oedema over mastectomy alone by 4–15% and 30%, respectively.[35] Liljegren and Holmberg argue, according to their randomized controlled trial, that radiation therapy to the breast alone does not adversely affect the arm during the first three post-operative years. Only age and number of lymph nodes harvested predict oedema or subjective arm symptoms in their multivariate model.[36] Borup Christensen and Lundgren found incidence of arm oedema to be significantly higher in a group with ALND and axillary radiation therapy (44%) than in the group with axillary radiation therapy alone (10%) or in the groups with axillary sampling, with or without radiation therapy (0%).[37] Across a number of studies, lymph oedema has been reported to occur in approximately 41% (range 21–51%) of patients who undergo axillary radiation therapy in addition to surgery therapy as opposed to approximately 17% (range 6–39%) of patients treated with surgery but no radiation therapy.[17] Only one, non-randomized study has focused on the presence of lymph oedema in patients receiving ALND ($n = 35$) vs patients receiving SNB ($n = 35$). This resulted in a percentage of zero for lymph oedema among SNB patients. No patients in either ALND or SNB in this setting received axillary radiation therapy.[16] In our study, two SNB patients complain of lymph oedema. As their complaints cannot be explained by radiotherapy on the axilla, the question is: can their complaints be attributed to the SNB procedure? Only one patient is consistent in reporting having lymph oedema, localized in the axilla, upper arm, elbow, lower arm and hand. The other patient indicates having lymph oedema but, asked more precisely, no location is indicated. Thus, a report-error might be most likely. SNB patients in our study have a 5-fold *lower* chance of lymph oedema in comparison to ALND patients. Radiation therapy to the axilla increases the risk on oedema 2.4-fold. However, this association is not as strong as the surgical axillary procedure. In percentages, axillary radiation therapy in the ALND population increases the chance of lymph oedema by 13.9%. In the SNB population, there is no increase in lymph oedema between patients who were not irradiated and patients who received axillary radiation therapy. SNB is, therefore, most likely to be the strongest factor in explaining low figures on lymph oedema in SNB patients compared to ALND patients.

In the ALND group, patients received chemotherapy more often but hormonal therapy less often, indicative for a larger proportion of pre-menopausal woman with axillary metastasis. This is a finding congruent with the age distribution within both groups. Remarkable in our study is the fact that as many as 8.3% of the SNB group received radiotherapy on the axilla. This might reflect different pathological work-up of the sentinel node, including multiple cross-sections, use of the polymerase chain reaction in order to detect micro-metastasis next to conventional paraffin section histology with haematoxylin–eosin staining and anticytokeratin staining. Increased work-up of the sentinel node may indeed lead to stage migration, seemingly improving prognosis in the group of breast cancer patients with small lesions. A problem much discussed is what to do with patients exhibiting micro-metastasis. Should they receive axillary radiotherapy, additional full axillary dissection, or should micro-metastasis be regarded as indicative of systemic disease? The impact of micro-metastasis in the sentinel node and its influence on long-term survival is controversial, unknown and needs to be determined in larger series, before the above questions can be answered sensibly.[38] Nevertheless, it is believed that a selective policy for the management of the axilla is associated with no increase in axillary recurrence or mortality rate compared with routine axillary node clearance. Patients who are node-negative after axillary sampling can thus avoid axillary radiotherapy or axillary clearance.[11]

Pain, numbness, a tingling or a burning sensation in the (upper) arm region are likely to result from transsection of one or more branches of the intercostobrachial nerves during the axillary surgical procedure. Radiation therapy can contribute to these complaints by direct

damage to the nerve or by post-irradiative inflammatory response, leading to scar tissue formation and fibrosis.

Kuehn found 23% of patients to experience pain, 73% of patients to report sensitivity problems and 14.1% to report restriction of arm following ALND without radiotherapy to the axilla.[1] Others found self-assessed sensitivity problems in 58–81%, pain in 16–55%, impairment of strength in 17–26% and restriction of arm motion range in 17–32% of ALND patients. Variation resulted from various definitions and measurement techniques.[1] The study of Schrenk, comparing ALND to SNB, reports no pain in 94% of patients against 54% of ALND patients. In this study, there was no restriction to arm motion in the SNB group, against 17% of patients in the ALND group. Also, there was no reported loss of arm strength and no effect of operation on daily living in the SNB group.[16] In our study, about 23% of ALND patients reported pain to the arm/shoulder on the ipsilateral side of surgery, only 7.8% of SNB patients did. About 24% of ALND patients complained of numbness, only 3.9% of SNB patients did. Loss of the arm's full motion range was present in 18.3% of ALND patients, and only in 6% of SNB patients. There was loss of strength in 26.3% of ALND patients, and only in 3.9% of SNB patients. Fifteen per cent of ALND patients report experiencing difficulties performing household tasks due to their operation. Of patients who underwent SNB, only half this percentage (7.8%) indicate experiencing difficulties in performing household tasks. In multivariate analysis, the axillary procedure is the dominant variable explaining pain, numbness, tingling sensations, loss of strength and loss of full active motion range. No significant effect of radiation therapy as a co-factor could be established. As no standardized interval-scaled scoring system was used, results should be interpreted cautiously. In general, multivariate logistic regression on variables as mentioned in Table 3 show that, for most complaints, the axillary surgical procedure is the factor of strongest influence in experiencing a variety of physical complaints in breast cancer patients, favouring less invasive surgery. Radiation therapy is increasing odds ratios on having a variety of complaints, but does not always seem to contribute to the model significantly.

LIMITATIONS OF PRESENT STUDY

Although the questionnaire was extensive and carefully formatted, patients were not questioned about what problem is considered *most* important to them, or most of impact on their life after their surgery for breast cancer. Furthermore, arm-circumference measurements as an objective indication of lymph oedema were not routinely performed. Parameters such as numbness of skin, pain and arm strength and mobility were not objectified by clinical measurements. In our study, almost all SNB patients were questioned within one year from intervention. Time since axillary surgery is important in estimating morbidity, as reflected in our study by a twofold higher risk on lymph oedema for patients having had axillary surgery over 2 years ago, compared to patients having more recently undergone surgery. Then again, the greater proportion of patients having had surgery over 2 years ago are ALND patients. Less-invasive techniques for staging of the axilla are most likely to decrease morbidity in breast cancer patients. One could state that this remains to be proven by a randomized controlled trial comparing SNB to ALND. Our study used a historic cohort group of ALND patients to match a less historic cohort of SNB patients. Only patients with updated and comprehensive records were selected. This poses a threat to the internal validity of the study itself, as selection bias is thus introduced. However, it is considered to be introduced randomly, and a matched and comprehensive data set was preferred above numbers of groups. Futhermore, it is unlikely that patients with small, e.g. non-palpable, tumours are willing to participate in a randomized trial, as level-2 evidence is mounting up preferring SNB for small tumour sizes. Several authors have even questioned the need for axillary surgery in older patients or in patient having a small-sized tumour. In addition, less invasive procedures enable earlier discharge, contributing to positive psychosocial effects.[39]

CONCLUSION

Our study shows clear differences in various aspects related to postoperative morbidity between SNB and ALND patients. Bias that is inevitably invoked due to the retrospective character and the cohort setting of the study will undoubtedly be of influence but authors feel it is highly unlikely to explain such differences in itself. Postoperative sequelae after ALND are frequently reported and may have an adverse affect on patients' quality of life. Postoperative morbidity after sentinel node procedure seems to be virtually absent. A properly implemented sentinel node technique in experienced hands is not only a safe technique for staging the axilla, in the authors' view, mandatory at least to consider as technique-of-choice in patients having small-sized breast carcinoma. Patients with a positive sentinel node will, however, still need to undergo further axillary surgery either by ALND with or without radiotherapy or, under study, by radiotherapy alone. Hence, these patients will remain at risk for the physical side-effect. Nevertheless, a substantial part of the patients with small-sized breast tumours will profit from SNB, since chances on a positive sentinel node are low.

The results of the present study firmly support the need to offer SNB to eligible breast cancer patients.

Patients with small-sized tumours and a clinically negative axilla are most likely the ones to be optimal candidates for SNB.

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