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Long term treatment related upper limb morbidity and quality of life after sentinel lymph node biopsy for stage I or II breast cancer

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Abstract

Background: In a prospective study, long term upper-limb morbidity, perceived disabilities in activities of daily life (ADL) and quality of life (QOL) were assessed before and 2 years after sentinel lymph node biopsy (SLNB) or axillary lymph node dissections (ALND) for breast cancer.

Methods: Two hundred and four patients with stage I/II breast cancer, mean age 55.6 years (SD: 11.6) entered the study and 181 patients (89%) could be evaluated after 2 years. Fifty-seven patients underwent SLNB (31%) and 124 patients underwent an ALND (69%). Assessments included pain, shoulder range of motion, muscle strength, arm volume, perceived shoulder disability in ADL and QOL.

Results: Significant ($P < 0.05$) changes between before and 2 years after surgery were found in almost all assessments of shoulder function, ADL and several QOL subscales. Patients in the ALND group showed significant more changes in range of motion (ROM), grip strength, arm volume, ADL and QOL physical- and role functioning, pain and sleeplessness and arm symptoms compared to the SLNB group. Multivariate linear regression analysis showed that ALND could predict decrease of ROM, grip strength, ADL and physical functioning (QOL) and increase of arm volume, pain and arm symptoms score (QOL). Radiation on the axilla predicts an additional decrease in shoulder ROM and increase of arm volume.

Conclusion: Two years after surgery for breast cancer, patients show significantly less treatment related upper limb morbidity, perceived disability in ADL and worsening of QOL after SLNB compared with ALND.

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Keywords: Breast cancer; Sentinel lymph node; Radiation; Morbidity; Quality of life

Introduction

The aim of modern breast cancer treatment is to obtain local tumour control, optimal lymph node staging with minimal treatment related morbidity and when possible preservation of the breast. Due to breast cancer screening programs and multimodality breast cancer treatment the

number of patients cured after breast cancer is still increasing as do the 5 and 10 year survival.^{1,2}

Axillary lymph node status is an important prognostic factor in patients with breast cancer.^{3–5} Axillary lymph node dissection (ALND) still is associated with upper limb morbidity.⁶ The impact of upper limb morbidity on disabilities in ADL and QOL in breast cancer patients has rarely been studied with modern assessment instruments.^{6–8} Sentinel lymph node biopsy (SLNB) was introduced for staging of the axilla to reduce the number of unnecessary ALND's.⁹ SLNB is an accurate and safe procedure to predict metastatic disease in clinically negative axillary lymph nodes.^{9–11} An increasing number of studies reported

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less treatment related morbidity for SLNB in comparison to ALND.^{12–20} Generally disability in ADL of the SLNB group was less than that of the ALND group.^{13,16,19} A shortcoming in most studies is the absence of pre-treatment assessment and the absence of reliable and validated assessment instruments. Although association between upper limb morbidity and poorer QOL was described, QOL is seldom considered in the debate on axillary surgery.^{6,8,20–22}

The aim of the current prospective study was to analyse long-term upper limb morbidity, perceived disability in ADL and QOL 2 years after SLNB or ALND. The second aim was to analyse to which extent ALND and other treatment variables could predict upper limb morbidity, perceived disability and decreased QOL.

Patients and methods

From June 1999 to June 2001, patients with breast carcinoma stage I or stage II entered the study.²³ Patients were retrieved from the Groningen University Medical Centre and the Martini Hospital Groningen. Informed consent was obtained from the participating patients. The protocol was approved by the Institutional Review Board of both hospitals. Two groups of breast cancer patients participated in the prospective study, patients who underwent conventional breast cancer treatment with an ALND and patients who were treated according to the SLNB concept. Sentinel lymph nodes were identified by pre-operative lymphoscintigraphy followed by intraoperative tracing using a gamma probe and Patent blue dye[®] (Blue Patenté; Labatoire Guerbet, Aulnay-sous-Bois, France). The procedure has been previously described in detail.²⁴ If pathological examination revealed metastases in the sentinel lymph node, ALND was performed within two weeks after SLNB.

Pain (VAS²⁵), upper limb function (range of motion, muscle strength, arm volume),^{26–31} numbness, ADL^{32–34} and QOL^{35,36} were assessed 1 day before surgery (t0) and 2 years after surgery (t1) (Table 1). The shoulder disability questionnaire (SDQ) was designed to evaluate the ability to perform daily activities in patients with shoulder disorders.^{32,37,38} The Groningen activity restriction scale (GARS) assesses the perceived restrictions (disability) in performing 18 ADLs.^{33,34} A higher score represents more functional status limitation.

Quality of life was assessed with help of the EORTC QLQ-C30 questionnaire supplemented with the EORTC breast module (EORTC QLQ-BR23).^{35,36}

Statistical analyses included descriptive statistics and *t*-tests for independent samples for between-group comparisons and *t*-tests for dependent samples for within-group comparisons. Pearson's chi-squared test was used for dichotomous variables. To answer the question in which extent treatment variables could predict upper limb morbidity, perceived disability and poorer QOL,

Table 1

Upper limb morbidity and disability 2 years after breast cancer treatment (*n* = 181)

	Before surgery (mean ± SD)	Change (mean ± SD)	<i>P</i> value
Pain (VAS: 0–10)	0.4 ± 1.1	0.3 ± 1.7	0.01
Numbness (<i>n</i>) ^a	0 (0%)	114	<0.001
Forward flexion (°)	172.4 ± 11.9	−4.4 ± 12.6	<0.001
Abduction (°)	168.0 ± 22.6	−16.2 ± 31.0	<0.001
Abduction/external rotation (°)	87.1 ± 6.6	−6.0 ± 12.3	<0.001
External rotation (°)	67.7 ± 13.0	−5.9 ± 13.6	<0.001
Strength shoulder abductors (Nm)	151.0 ± 36.8	−10.0 ± 29.9	<0.001
Strength elbow flexors (Nm)	180.0 ± 40.7	5.8 ± 40.5	0.057
Grip strength (Nm)	297.8 ± 64.0	−33.6 ± 51.7	<0.001
Volume arm (ml)	2162 ± 414	124 ± 241	<0.001
SDQ (0–100)	8.2 ± 19.7	10.5 ± 29.9	<0.001
GARS (18–72)	19.6 ± 3.7	1.8 ± 5.7	<0.001

(°), grades; Nm, Newton meter; ml, millilitre; SD, standard deviation; SDQ, the shoulder disability questionnaire³²; GARS, the Groningen activity restriction scale.^{33,34}

^a No standard deviations were given because it concerns a dichotomous variable.

multivariate linear regression analyses were performed. Differences were accepted as significant if *P* values were < 0.05. SPSS[®] Base 11.5 software for Windows[®], SPSS Inc., was used for statistical analysis.

Results

In the period 1999–2001, 204 consecutive patients with invasive breast carcinoma were included in the study. Two years after surgery 23 of the 204 patients (11%) could not be assessed. Fourteen patients belonged to the ALND group; six patients died of metastatic disease; one patient had a breast reconstruction and was excluded from assessment, seven patients withdrew from the study because of other reasons. Nine patients belonged to the SLNB group; one patient had distant metastasis, one patient refused further treatment and seven of them found the assessment protocol bothersome and chose to withdraw from the study.

One hundred and eighty-one patients could be evaluated after 2 years; 57 patients (32%) in the SLNB group and 124 patients (68%) in the ALND group. TNM classification, receptor status and treatment characteristics of these patients are presented in an earlier study.³⁸

Substantial long-term treatment-related upper-limb morbidity and increasing of disability was observed for the whole study group (Table 1). Also significant changes were found for QOL assessed with the EORTC QLQ-C30/QLQ-BR23 (Table 2).

Several changes in upper-limb function (upper-limb morbidity), ADL (perceived disability) and QOL between before surgery and 2 years after treatment were significantly

Table 2

QOL (EORTC QLQ C-30 and QLQ-BR23) 2 years after breast cancer treatment ($n=181$)

	Before surgery (mean $\pm$ SD)	Change (mean $\pm$ SD)	<i>P</i> value
Functional scales			
Physical functioning	91.3 $\pm$ 11.1	−5.2 $\pm$ 13.3	<0.001
Role functioning	92.4 $\pm$ 16.2	−5.4 $\pm$ 23.8	0.003
Emotional functioning	71.2 $\pm$ 19.9	15.8 $\pm$ 20.7	<0.001
Cognitive functioning	87.4 $\pm$ 15.5	−1.1 $\pm$ 30.5	0.624
Social functioning	92.3 $\pm$ 14.9	0 $\pm$ 18.8	1.000
General health score QOL	80.4 $\pm$ 18.0	−1.2 $\pm$ 19.8	0.411
Symptom scales/items			
Fatigue scale	16.4 $\pm$ 20.2	4.2 $\pm$ 17.5	0.002
Nausea and vomiting scale	3.0 $\pm$ 11.1	1.7 $\pm$ 16.1	0.166
Pain scale	8.8 $\pm$ 17.5	6.1 $\pm$ 21.4	<0.001
Dyspnoea	5.8 $\pm$ 15.4	3.7 $\pm$ 18.4	0.007
Insomnia (sleeplessness)	23.7 $\pm$ 27.3	−4.1 $\pm$ 29.4	0.063
Appetite loss	7.5 $\pm$ 16.4	−2.1 $\pm$ 20.1	0.173
Constipation	2.6 $\pm$ 11.9	2.4 $\pm$ 15.4	0.037
Diarrhea	4.1 $\pm$ 12.1	−1.5 $\pm$ 12.6	0.117
Financial difficulties	1.7 $\pm$ 7.3	4.2 $\pm$ 20.5	0.006
QLQ-BR23 (breast cancer module)			
Side-effects	8.0 $\pm$ 8.4	4.8 $\pm$ 13.2	<0.001
Hair loss (only three patients)	22.2 $\pm$ 38.5	22.2 $\pm$ 38.5	0.423
Body image	94.7 $\pm$ 10.6	−3.2 $\pm$ 17.1	0.014
Future perspective	59.7 $\pm$ 25.1	12.7 $\pm$ 28.2	<0.001
Sexual functioning ($n=137$)	22.6 $\pm$ 20.1	1.2 $\pm$ 19.3	0.496
Sexual satisfaction ($n=57$)	56.8 $\pm$ 22.1	−4.9 $\pm$ 27.0	0.185
Arm symptoms	4.9 $\pm$ 10.2	8.8 $\pm$ 19.4	<0.001
Breast symptoms	10.9 $\pm$ 14.2	1.3 $\pm$ 18.1	0.334

EORTC QLQ, European organization on research and treatment of cancer quality of life questionnaire.³⁵

different between the SLNB group and the ALND group in favour of the first (Table 3).

Multivariate linear regression analysis to predict the mean change in upper-limb function, ADL and QOL between before treatment and 2 years after treatment for independent variables: age, axillary surgery, breast surgery, radiation breast, radiation axilla and chemotherapy was performed. ALND was a significant factor in the prediction in the majority of mean changes in the performed assessments of upper-limb function (abduction, grip strength, arm volume), ADL (SDQ, GARS) and QOL (physical functioning, pain, sleeplessness, diarrhea, arm symptoms). Radiation of the axilla was significant in four analyses: forward flexion, abduction, abduction/external rotation and arm volume. Mastectomy was significant associated with a lower body image (details not shown).

Discussion

Significant treatment related upper limb morbidity, associated ADL disabilities and decreased QOL exist 2 years after SLNB or ALND. Treatment related upper limb morbidity, perceived disabilities in ADL and worsening of QOL 2 years after surgery is significantly less after SLNB compared to ALND. In the assessment of changes in upper

Table 3

Change of upper limb function, disability and QOL in the SLNB group and the ALND group between before surgery and 2 years after surgery

Variable	SLNB ($n=57$) (t1–t0) Mean change $\pm$ SD	ALND ($n=124$) (t1–t0) Mean change $\pm$ SD	Differences in mean change ALND–SLNB	
			Mean difference	<i>P</i> value
Numbness (n^a)	10 (18%)	104 (84%)*	94	<0.001
Abduction (°)	−5.5 $\pm$ 21.0	−21.0 $\pm$ 33.5*	15.5	<0.001
Abduction/external rotation (°)	−3.5 $\pm$ 8.0*	−7.2 $\pm$ 13.7*	3.7	0.025
Grip strength (Nm)	−17.2 $\pm$ 48.2*	−41.3 $\pm$ 51.7*	24.1	0.004
Volume arm (ml)	−2 $\pm$ 142.5	182 $\pm$ 255.6*	184	<0.0001
GARS (18–72)	0.2 $\pm$ 3.5	2.5 $\pm$ 6.3*	2.3	0.002
EORTC QLQ C30				
Physical functioning	−0.9 $\pm$ 10.6	−7.3 $\pm$ 13.9*	6.4	0.001
Role functioning	−0.3 $\pm$ 21.7	−7.8 $\pm$ 24.4*	7.5	0.041
Pain	0.6 $\pm$ 18.4	8.7 $\pm$ 22.4*	8.1	0.012
Insomnia (sleeplessness)	−11.3 $\pm$ 27.9*	−0.8 $\pm$ 29.6	10.5	0.027
QLQ-BR23 (breast cancer module)				
Arm symptoms	3.0 $\pm$ 11.5	11.5 $\pm$ 21.7*	8.5	0.001

Results of *t*-test for independent samples. Nm, Newton meter; cm, centimetre; (°), degree; *, significant changes between before and after surgery ($P<.05$). GARS, the Groningen activity restriction scale.^{33,34} EORTC QLQ, European organization on research and treatment of cancer quality of life questionnaire.³⁵

^a No standard deviations were given because it concerns a dichotomous variable.

limb function, ADL and QOL, ALND is the most frequent found predictor of deterioration. Additional radiation on the axilla predicts a further decrease in shoulder ROM and arm oedema.

This outcome confirms results of previous studies suggesting that SLNB is associated with less treatment related upper-limb morbidity although these are no long-term comparative studies.^{12–19,21,37,38} This is the first prospective study comparing SLNB and ALND with pre- and long-term post-surgical assessments of upper limb function, ADL and QOL. In a recent systematic review and two previous studies we emphasized the importance of the baseline assessment and the use of reliable and validated assessment instruments.^{6,37,38}

The perceived disabilities in ADL assessed in this study with the SDQ and GARS were significant but relatively mild. Concerning QOL for the whole study group a significant decrease was found over the 2 years for physical and role functioning and body image whereas emotional functioning and future perspective showed significant increase over this period (Table 2). The improvement of emotional functioning and future perspective can be explained by the fact that the first assessment took place 1 day before surgery. Obviously at this time patients were nervous and stressed and also uncertain about their future perspective.²¹ Two years later these aspects were highly improved.

Some scores on symptom scales increased significantly such as fatigue, pain, dyspnoea, constipation, side-effects of

systemic therapies and arm problems (Table 2). These outcomes correspond with results found in earlier studies done on breast cancer treatment and QOL.^{6–8,21} Comparing SLNB and ALNB significantly differences in mean change over the 2 years were found for physical and role functioning and also for symptom items such as pain, insomnia (sleeplessness) and arm symptoms in favour for the SLNB group (Table 3).

The interpretation of the scores on the EORTC QLQ-C30 and QLQ-BR23 in relation to clinical relevance needs some discussion. King did a review on the interpretation of scores from the EORTC QLQ-C30 and stated that the smallest clinically important difference may vary with clinical context.⁴¹ All the statistically significant differences found in our study within and between the groups could be interpreted as relatively small clinically important differences except the improvement of emotional functioning which could be interpreted as a very large clinically important difference.⁴¹

Multivariate linear regression analysis to predict mean change in upper-limb function, ADL and QOL between before and 2 years after surgery showed that radiation on the axilla is a significant factor in the prediction of impaired ROM and increase of arm volume. This finding is a conformation of results of some other studies and may be explained by radiation induced subcutaneous fibrosis affecting the ROM and lymph drainage.^{6,8,42,43} ALND as predictor of upper limb morbidity was observed for abduction, grip strength, arm volume, ADL and some scales of the QLQ-C30 and QLQ-BR23. This result confirms results of other studies in which the extent of axillary treatment was found to be related to late morbidity.^{6,19,20,42} Although the comparison between mastectomy and breast conserving surgery was not subject of this study we found that mastectomy predicts a part of the decrease in body image. A lower body image in mastectomy patients was earlier described.⁴⁴

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