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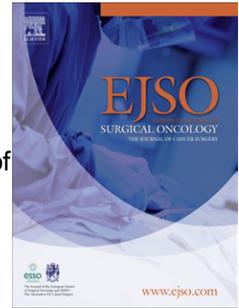
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**The relationship between morbidity after axillary surgery and long-term quality of life  
in breast cancer patients: the role of anxiety**

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**Abstract***Aims*

Although arm/shoulder morbidity after sentinel lymph node biopsy (SLNB) and/or axillary lymph node dissection (ALND) has been studied before, information is lacking concerning self-imposed restrictions in activities and long-term consequences of both surgical procedures in relationship to quality of life (QoL) and anxiety.

*Methods*

Eighty-nine disease-free breast cancer survivors completed a set of questionnaires assessing arm/shoulder symptoms, limitations in daily life, anxiety and QoL. Also, the ipsi- and contra lateral arm circumference and the range of shoulder motion were measured.

*Results*

Fifty-one women had SLNB, 25 had SLNB followed by ALND and 13 had ALND. Although ALND patients experienced more shoulder symptoms, limitations in daily life and imposed more restrictions on themselves than SLNB patients, no significant differences during physical examination were found. A decreased range of motion and a higher score on trait anxiety resulted in a lower QoL. Trait anxiety and perceived limitations in daily life predicted long-term quality of life.

*Conclusions*

There is a discrepancy between experienced and measured limitations in range of shoulder motion. Anxiety and self-imposed restrictions play an important role in predicting long-term QoL and should get the necessary attention when addressing shoulder symptoms in breast cancer patients.

Keywords: shoulder morbidity, breast cancer, anxiety, quality of life

## Introduction

SLNB, with or without completing ALND, is used to stage the axilla in early breast cancer [1-3]. Existing studies indicate that patients who underwent an ALND, experience more pain [1,4-6], numbness [1,3-4,6-7], restricted range of shoulder motion [2-6], surgical complications [8], and have more lymph oedema [1-3], compared with patients who received a SLNB. Regarding health status, women reported more limitations in daily life after ALND [1-2,4], and they have less improvement of arm/shoulder mobility than the patients who only had SLNB [6]. However, no differences were found comparing depression and anxiety in SLNB and ALND patients during 1 year follow-up [2-3]. Recently, a randomized multicenter trial indicated that SLNB is preferred over ALND in women with early-stage breast cancer, because SLNB patients reported less arm morbidity and a better health status after 12 months follow-up compared with ALND patients [3].

Despite our familiarity with arm morbidity in SLNB and ALND patients, self-imposed restrictions in performing activities after axillary surgery have not been studied so far. In addition, most studies report short-term follow-up, and only consider physical symptoms. Furthermore, information is lacking about the influence of type of surgery and anxiety on self-imposed restrictions in activities, long-term (> 2 years) shoulder, and arm morbidity and QoL.

Therefore, the consequences of ALND and SLNB in women > 2 years after breast cancer surgery were investigated, with special attention to shoulder impairments, self-imposed restrictions, QoL, and anxiety.

## Methods

### *Patients*

All women diagnosed with early-stage breast cancer who had ALND, SLNB or both, between January 2002 and December 2005 at the St. Elisabeth Hospital, Tilburg (The Netherlands) were asked to participate. The study protocol was approved by the Institutional Ethical Review Board of the hospital and all patients gave written informed consent. Exclusion criteria were recurrent breast cancer or development of distant metastases, dementia, insufficient knowledge of the Dutch language, bi-lateral surgery, and pre-existing pathology of the arm or the glenohumeral joint on either the operated or contra lateral arm. To screen for dementia, patients who visited the outpatient clinic performed the Mini-Cog test [9]. Patients who had both SLNB and ALND, were included in the ALND group.

### *Questionnaires*

Participants completed the following questionnaires:

The *World Health Organization Quality of Life assessment instrument-Bref (WHOQOL-Bref)* [10-11] is a generic QoL questionnaire consisting of 26 items. The questionnaire measures overall QoL and four domains: physical health, psychological health, social relationships, and environment. The scores on these domains vary between 4 to 20. A high score indicates a better QoL. The WHOQOL-Bref has good psychometric properties [12].

The *State Trait Anxiety Inventory (STAI)* measures trait and state anxiety, each with 20 items [13]. Trait anxiety concerns differences in individuals in the disposition to respond to stressful situations with varying amounts of stress. State anxiety is a momentary emotional condition characterized by subjective feelings of apprehension and tension, and heightened autonomic nervous system activity. The questionnaire has a good reliability and validity [13-14]. In this

study we only used the 10-item short form of the STAI-trait, because this reflects personality (i.e. the disposition to respond in a certain way to stressful situations) [14]. The rating scale for each item ranges from 1 to 4, with a cut-off score of  $\geq 22$  meaning the patient has a disposition to respond with an increased amount of stress in stressful situations [13-14].

Patients also completed questions regarding demographic characteristics (age, marital status/partner, education/work/income, children) and specific questions regarding pain, lymph oedema (therapy), numbness, loss of strength, and loss of motor function (response scale 0 = 'no symptoms' to 10 = 'worst symptoms imaginable'). We also posed questions concerning perceived/not self-imposed limitations in daily life (response scale 1 = 'no perceived limitations' to 4 = 'severe limitations in daily life') and consequently self-imposed restrictions in activities (i.e. sauna visits, sport, lifting heavy objects, housekeeping, flying, sun-bathing).

### *Procedure*

Women were contacted by phone and asked to participate in our study. When they agreed to participate, they visited the outpatient clinic once to complete the questionnaires and undergo a physical exam, consisting of arm circumference measurements at five different sites on both arms (see also Sakorafas et al [15]), and range of motion measurements of both shoulders in five directions (i.e. abduction, endorotation, exorotation, ventral elevation, and dorsal elevation) using a 12-inch universal goniometer. More than 2 cm difference between the ipsi- and contra lateral lower or upper arm was considered to be lymph oedema [15]. Differences of  $\geq 10$  degrees in range of motion between the ipsi- and contra lateral shoulder in any direction, indicated impairment of shoulder movement [16]. A difference of  $\geq 10$  degrees was chosen as cut-off point, because previous research [17] showed that most patients did not experience a difference of  $< 10$  degrees as a limitation in range of motion. The investigator

who performed the measurements had no knowledge of the type of surgery the women had received.

### *Statistical analyses*

To examine differences in patient characteristics, shoulder symptoms and impairments between both groups (SLNB versus ALND), Chi-square tests and Student's t-tests were employed. Mann-Whitney U tests were used in case of non-parametric variables.

Multiple analysis of variance (MANOVA) was performed to investigate decreased range of shoulder motion in association with QoL. Spearman and Pearson correlations were used to investigate the relationship between trait anxiety, shoulder symptoms/imposed restrictions, anxiety and QoL.

Regression analyses (method stepwise) were carried out with QoL as dependent variable, and shoulder symptoms/imposed restrictions, type of surgery and trait anxiety as independent variables. Results were considered significant if p-values were  $< 0.05$ . All analyses were performed with the Statistical Package for Social Sciences (SPSS version 16.0).

## Results

### *Patient characteristics*

Two hundred and sixty women underwent SLNB and/or ALND, and eventually 89 women were included in our study. Reasons for exclusion and refusal to participate are shown in Figure 1. Comparing participants with non-participants, study participants had more operations of the breast and axilla than women who declined participation ( $p = 0.038$ ). Concerning patient characteristics, the tumour was smaller ( $p=0.002$ ) in the SLNB group ( $n=51$ ) compared to the ALND group ( $n=38$ ). ALND patients more often received chemotherapy ( $p < 0.001$ ) and hormone therapy ( $p < 0.001$ ). Also, ALND patients indicated more shoulder symptoms, daily life limitations and self-imposed restrictions compared with SLNB patients. There were no significant differences between range of motion, the presence of lymph oedema, and radiotherapy between these groups.

[Insert table 1 about here]

### *Range of motion and QoL*

Thirty-four SLNB patients and 25 ALND patients had impaired shoulder movements. Decreased range of motion resulted in lower scores on the QoL domains 'social functioning' (SLNB patients,  $p = 0.030$ ), 'physical health' (ALND patients,  $p = 0.011$ ), and 'physical health' and 'psychological health' (in the whole patient group,  $p = 0.003$  and  $p = 0.047$ , respectively; see Table 2).

[Insert table 2 about here]

*Anxiety and shoulder symptoms*

A higher score on trait anxiety was correlated with more shoulder symptoms, self-imposed restrictions and limitations in daily life (see table 3). Also, patients with a higher score on trait anxiety imposed more restrictions on themselves, and subsequently had lower QoL scores in the 'physical health' and 'psychological health' domains ( $r = -0.32$  to  $-0.52$ ;  $p < 0.05$ ).

[Insert table 3 about here]

*Predictors of QoL*

Using multivariate linear regression analysis to identify a *cause and effect* relation between anxiety, shoulder symptoms and QoL, more than 40% of the variance ( $R^2$ ) in quality of life can be explained by trait anxiety ( $R^2 = 0.340$ ,  $p < 0.001$ ) and perceived limitations in daily life ( $R^2 = 0.074$ ,  $p 0.002$ ). Shoulder symptoms, restricted range of motion, self-imposed restrictions, and type of surgery had no significant relation with QoL.

[Insert table 4 about here]

## Discussion

### *Self imposed restrictions and daily life limitations*

This study examined the long-term influences of ALND and SLNB on shoulder symptoms and QoL in early-stage breast cancer patients. Although women experienced more shoulder symptoms after ALND, physical examination revealed no differences. It appeared that women's experiences and the doctor's observations not always matched. These findings contradict a recently conducted study by Kootstra et al. [18], describing better range of motion for SLNB patients during 2 year follow-up. Although their study was performed with a greater number of patients, they indicate that the clinical relevance of statistically significant results appeared to be negligible. So, despite the absence of *objective* range of motion limitations in patients with shoulder symptoms, we believe that *perceived* shoulder symptoms need special attention during patient follow up.

### *Coping*

As expected, ALND patients imposed more restrictions on themselves and had lower QoL scores. Surprisingly, this did not result in more objective range of motion limitations. Instead, ALND patients adjusted their lives according to their restrictions (e.g., heavy lifting with the arm at the contra lateral side). The question remains whether this coping mechanism can explain these findings, or whether a psychological factor (e.g. personality) also plays a role.

### *Quality of life and anxiety*

Although there was a medium to high correlation between range of shoulder motion versus QoL, and between trait anxiety versus shoulder symptoms, limitations/restrictions, and QoL, we realise that a rather small group of ALND patients was analysed in this study. Anxiety resulted in lower QoL scores, but perhaps the restrictions women impose on themselves as a

consequence of their anxiety may have an even greater negative effect on QoL. Therefore, further research with a larger group of patients (i.e. separate groups for SLNB, SLNB + ALND, and ALND) is necessary to investigate this issue.

#### *Predictors of QoL*

We found an *association* between anxiety, shoulder symptoms and QoL, meaning a higher score on anxiety was correlated with more shoulder symptoms and a lower QoL score.

Because our study is a prospective follow-up study, we have also examined the cause and effect relation between anxiety, symptoms and QoL by means of a multivariate regression analysis. This showed that trait anxiety is an important predictor of QoL, meaning a high score on trait anxiety results in a lower QoL.

Van der Steeg et al. [19] already showed that trait anxiety predicts QoL six months after surgical treatment. In this study, we showed that trait anxiety, together with perceived limitations in daily life, also predicts long-term QoL in breast cancer patients.

#### *Study limitations*

No baseline measurements of QoL were present. Also, a considerable amount of patients with pre-existing shoulder symptoms had to be excluded. However, we believed this was necessary to eliminate the bias of pre-existing decreased shoulder mobility.

For investigating shoulder impairments, we did not use a validated assessment tool like the DASH-questionnaire [20], because this questionnaire is not designed to investigate shoulder symptoms after breast cancer surgery. Furthermore, we had no baseline DASH-score, which is necessary to correctly calculate and interpret the DASH outcome measure.

#### *Conclusions*

After ALND surgery, patients *experience* more shoulder symptoms and limitations in daily life. Also, patients impose more restrictions on themselves in undertaking activities.

Decreased range of motion of the shoulder results in a lower QoL and in addition, a high score on trait anxiety correlates with more shoulder symptoms, self-imposed limitations and a lower QoL. Therefore, the role of anxiety on long-term QoL and shoulder function should not be underestimated and warrants explicit attention by health care professionals.

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**Conflicts of interest statement**

No conflicts of interest were reported.

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**Table 1. Demographic and medical characteristics and upper arm morbidity in participants**

	SLNB (n=51)	ALND <sup>a</sup> (n=38)	p
Age (median, range)	61 (35-86)	57 (43-76)	0.296
Education: Primary school / Secondary school / College	4 / 38 / 9	3 / 28 / 7	0.995
Employment	22	17	0.880
Partner			
at time of diagnosis	39	34	0.114
at the moment	40	31	0.715
Children	40	30	0.953
Surgical treatment: BCT / MTC	31 / 20	24 / 14	0.820
Tumour side: left / right	29 / 22 (43.1)	21 / 17	0.880
<b>Tumour size: &lt; 1 / 1 – 3 / &gt; 3 cm</b>	<b>13 / 35 / 3</b>	<b>3 / 24 / 9<sup>b</sup></b>	<b>0.009</b>
Lymph oedema	4	6	0.240
Complications	7	5	0.938
Radiotherapy <sup>c</sup>			
Chest wall	35	25	0.778
Axillary	0	2	0.089
<b>Chemotherapy</b>	<b>10</b>	<b>25</b>	<b>&lt;0.001</b>
<b>Hormone therapy</b>	<b>12</b>	<b>24</b>	<b>&lt;0.001</b>
Medication use <sup>c</sup>	26	20	0.953
Pain	23	23	0.150
<b>Loss of strength</b>	<b>16</b>	<b>23</b>	<b>0.006</b>
<b>Numbness</b>	<b>23</b>	<b>33</b>	<b>&lt;0.001</b>

<b>Loss of motor function</b>	<b>11</b>	<b>19</b>	<b>0.005</b>
<b>Perceived limitations in daily life</b>	<b>11</b>	<b>20</b>	<b>0.002</b>
Restricted range of motion			
Abduction	17	11	0.659
Endorotation	20	15	0.980
Exorotation	5	5	0.620
Ventral elevation	13	9	0.845
Dorsal elevation	6	8	0.234
Lymph oedema	4	6	0.240
<b>Self-imposed restrictions<sup>d</sup></b>	<b>20</b>	<b>24</b>	<b>0.025</b>

Significant differences are indicated in bold. SLNB = sentinel lymph node biopsy; ALND = axillary lymph node

dissection; BCT = breast conserving therapy; MTC = mastectomy; <sup>a</sup> ALND = SLNB + ALND and ALND only.

<sup>b</sup> 2 cases missing. <sup>c</sup> 1 case missing. <sup>d</sup> i.e. sauna visits, sport, lifting heavy objects, housekeeping, flying, sun-bathing.

**Table 2. Range of motion versus quality of life**

	Measured restricted range of motion		p
SLNB	No (n=17)	Yes (n=34)	
Quality of life (SD)			
Physical domain	17.3 (1.7)	16.1 (2.4)	0.066
Psychological domain	15.9 (1.9)	15.1 (1.9)	0.150
<b>Social domain</b>	<b>16.9 (2.1)</b>	<b>15.5 (2.2)</b>	<b>0.030</b>
Environment	16.6 (1.8)	16.8 (1.8)	0.658
General health	4.1 (0.5)	4.1 (0.5)	0.777
ALND	No (n=13)	Yes (n=25)	p
Quality of life (SD)			
<b>Physical domain</b>	<b>16.6 (2.1)</b>	<b>14.4 (2.5)</b>	<b>0.011</b>
Psychological domain	15.3 (1.6)	14.5 (1.9)	0.167
Social domain	16.0 (2.6)	15.6 (2.7)	0.647
Environment	16.8 (1.7)	16.2 (2.2)	0.409
General health	4.3 (0.6)	3.9 (0.8)	0.152
SLNB + ALND	No (n=30)	Yes (n=59)	p
Quality of life (SD)			
<b>Physical domain</b>	<b>17.0 (1.9)</b>	<b>15.3 (2.5)</b>	<b>0.003</b>
<b>Psychological domain</b>	<b>15.6 (1.8)</b>	<b>14.8 (1.9)</b>	<b>0.047</b>
Social domain	16.5 (2.4)	15.5 (2.4)	0.065
Environment	16.7 (1.7)	16.6 (2.0)	0.787
General health	4.2 (0.5)	4.0 (0.7)	0.191

*Significant differences are indicated in bold. SLNB = sentinel lymph node biopsy; ALND = axillary lymph node dissection*

**Table 3. Correlations between anxiety and shoulder symptoms and quality of life**

	<i>STAI-trait</i>	
<i>Spearman correlations (<math>\rho</math>)</i>	<i>SLNB</i>	<i>ALND</i>
Pain	—	<b>0.41<sup>f</sup></b>
Loss of strength	<b>0.47<sup>f</sup></b>	<b>0.46<sup>f</sup></b>
Numbness	0.31 <sup>e</sup>	—
Loss of motor function	0.32 <sup>e</sup>	0.34 <sup>f</sup>
Perceived limitations in daily life	—	0.37 <sup>e</sup>
Self-imposed restrictions in activities	—	0.33 <sup>e</sup>
<i>Pearson correlations (<math>r</math>)</i>	<i>SLNB</i>	<i>ALND</i>
Physical domain	-0.32 <sup>e</sup>	<b>-0.45<sup>f</sup></b>
Psychological domain	-0.32 <sup>e</sup>	<b>-0.52<sup>f</sup></b>
Social domain	—	—
Environment	—	—
General health	—	—

Only significant correlations are shown, the highest correlations are indicated in bold.

$\rho/r$ : absolute correlations between 0.30 to 0.49 are considered medium, and  $\geq 0.50$  as large. [21] Positive correlation coefficients indicate that a higher score on trait anxiety results in more physical symptoms and limitations. Negative correlation coefficients indicate that a higher score on trait anxiety results in lower QoL scores. <sup>e</sup> significant at the 0.05 level (2-tailed); <sup>f</sup> significant at the 0.01 level (2-tailed).

**Captions**

Figure 1. Participants and non-participants

*SLNB = sentinel lymph node biopsy; ALND = axillary lymph node dissection.*

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