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CLINICAL TRIAL

Comparison of upper extremity lymphedema after sentinel lymph node biopsy and axillary lymph node dissection: patient-reported outcomes in 3044 patients

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Abstract

Purpose A limited number of studies have examined the impact of type of axillary lymph node surgery on breast cancer-related lymphedema (BCRL) from the patient's perspective. The objective of this study was to assess the impact of sentinel lymph node dissection (SLND) and axillary lymph node dissection (ALND) on the health-related quality of life (HRQOL) in women diagnosed with BCRL using a condition specific patient-reported outcome measure (PROM), the LYMPH-Q upper extremity (UE) module.

Methods Adult women diagnosed with BCRL were identified from the Danish National Health Data Authority database for the period 2008 to 2020 and were sent an online REDCap survey with the LYMPH-Q UE module. Information pertaining to axillary surgery was obtained from an online pathology repository. Multivariable linear regression was used to examine differences in the SLND and ALND groups on the LYMPH-Q UE scale scores.

Results Three thousand and fourty four women with BCRL were included in the analysis. The mean follow-up duration was 8.6 ± 5.15 years (range, 0–36 years). The majority of participants underwent ALND ($n = 2805$, 92.1%) and only 7.9% ($n = 239$) received SLND. The mean number of lymph nodes removed in the SLND group was 2.2 ± 1.4. No statistically significant difference was found in the two groups on the LYMPH-Q UE scale scores.

Conclusion There is no difference in women with upper extremity lymphedema after SLND or ALND on the LYMPH-Q UE module scales measuring arm symptoms, function, distress, and appearance.

Keywords Lymphedema · Breast cancer · Patient-reported outcome · Patient-reported outcome measure · Sentinel lymph node dissection · Axillary lymph node dissection

Introduction

The disease status of the axillary lymph nodes has been recognized as the most significant prognostic factor for women diagnosed with breast cancer [1, 2]. Hence, the standard of care has been histologic examination of the lymph nodes removed at the time of breast surgery. A thorough assessment of the lymph nodes removed is important for staging breast cancer and consequently determining the prognosis. Further, an assessment of the lymph nodes is used to guide the selection and nature of adjuvant therapy. Axillary lymph node dissection (ALND) has been established as the most accurate method for assessing local spread of the disease. However, an undesirable outcome of the anatomic disruption caused by the ALND is the increased prevalence of breast cancer-related lymphedema (BCRL) [3].

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The clinical practice guidelines from the American Society of Clinical Oncology and the Society of Surgical Oncology concerning sentinel lymph node dissection (SLND) in early-stage breast cancer recommend that SLND is an appropriate alternative to routine staging ALND for women with early-stage breast cancer with clinically negative axillary nodes [2, 4, 5]. The Danish Breast Cancer Cooperative Group (DBCG) recommends that SLND should be the method of choice for women with clinically negative axillary nodes and with micro-metastasis to the sentinel nodes, reserving ALND for women with macro-metastasis [6–8]. Studies examining the impact of ALND and SLND on the health-related quality of life (HRQOL) impact of BCRL from the patient's perspective are limited. The majority of studies in the BCRL literature follow patients for less than three years, which is worrisome since BCRL is a progressive condition that often takes years to manifest. Additionally, very few studies have used rigorous, scientifically sound upper extremity or BCRL-specific patient-reported outcome measures (PROMs). This represents an important limitation as BCRL can result in a substantial negative impact on the HRQOL of women due to impairments related to physical function, such as reduced range of motion and arm weakness, as well as body image concerns due to feeling self-conscious about the size and appearance of the affected arm. These concerns, singularly or combined, can result in emotional distress and impact social and sexual well-being. The unique concerns of women with BCRL are not captured in generic PROMs, and the available BCRL-specific PROMs have limitations in terms of their content and psychometric properties [9].

Our team recently developed an upper extremity lymphedema-specific PROM, the LYMPH-Q upper extremity (UE) module, using established international guidelines for PROM development and validation [10]. The LYMPH-Q UE module consists of six independently functioning scales that measure arm symptoms, function, appearance, psychological, information, and arm sleeves. The content validity of the scales was demonstrated, and the reliability and construct validity were established in an international sample of 3222 women with BCRL in the USA and Denmark [10]. The objective of this study was to compare the impact of diagnosed BCRL on patients HRQOL after SLND versus ALND using the LYMPH-Q UE module.

Methods

Before commencement, the study was reported to The Region of Southern Denmark and included on the list of Health Research for data protection safety. In Denmark, questionnaire surveys do not require ethics approval and approval from the Regional Committee on Health Research Ethics was therefore not obtained.

Data collection

In December 2019, we applied to the Danish National Health Data Authority for a list of all women ≥ 18 years of age with both breast cancer and lymphedema diagnosis in the period from 2008 to January 2020. The received data were linked to mortality data and thus did not include anyone who had died. Invitations to fill out the LYMPH-Q UE were sent shortly after using a secure electronic mailbox (Eboks) and included a link to an online REDCap (Research Electronic Data Capture) survey [11, 12]. Before starting the actual survey, patients were asked to confirm the lymphedema diagnosis and that it was associated to breast cancer treatment. Women were also asked for permission for the study team to review their patient files for research purposes. Two reminder emails were sent to non-responders separated by a one-week interval.

Outcome parameters

Participants were asked to fill out demographics (age, height, weight, marital status, education, employment status), diagnosis (cancer stage at the time of diagnosis, current or previous additional cancer treatment(s)), surgery-related (type of breast procedure, type of axillary surgery, time since first breast cancer-related surgery, complications related to surgery, if they had breast reconstruction), and lymphedema-related (age at diagnosis of lymphedema, affected breast(s) and arm(s), lymphedema treatment(s) within the past 6 months) questions. Participants also completed four independently functioning scales from the LYMPH-Q UE module measuring arm symptoms, arm function, arm appearance, and psychological (Table 1).

In Denmark, pathology reports of all patients are stored in an online pathology repository. We extracted breast cancer surgery-relevant information for the study sample from this repository including type of primary axillary surgery (SNLD or ALND), type of primary breast procedure (lumpectomy, mastectomy, or none), and time of surgery. For the SNLD procedure, the number of lymph nodes extracted was also recorded. If participants had any recurrence(s) where surgery was performed, the same parameters were noted for the recurrence except the number of lymph nodes for SNLD. If the pathology report was incomplete or unclear, participants were excluded from the study.

Statistical analysis

Analyses were performed using IBM SPSS Statistics for Windows, Version 26.0. (Armonk, NY: IBM Corp.). Body

Table 1 Independently functioning scales included in the LYMPH-Q upper extremity module

Scale	Number of items	Response options	Example items
Arm symptoms	15	Severity—none, mild, moderate, severe	Arm feels heavy, tired, numb, pain, stiff, swelling, tingling, disturbs sleep
Arm function	12	Difficulty—not at all, a little, moderately, extremely	Dress, wash, button, reach, grip, hold, physical activities using arm
Arm appearance	10	Bothered—not at all, a little, moderately, extremely	Size, symmetry, noticeable, looks in photos, how clothes fit, people seeing arm
Psychological	12	Frequency—never, sometimes, often, always	Feel hopeless, depressed, anxious, fed-up, unattractive, irritated, frustrated

All scales have a recall period of one week and score range from 0 to 100, with higher scores representing a better outcome

mass index (BMI) was calculated from self-reported height and weight. Number of years since surgery was calculated from the review of pathology answers (requisition date) and the date of the REDCap survey. For participants who had a breast cancer recurrence-related surgery, the data were recoded such that the more extensive surgery was chosen as the surgical variable (i.e., mastectomy was selected as the final variable for participants who had lumpectomy followed by mastectomy, ALND was the final variable for participants who had SLND followed by ALND). Participant demographics were analyzed and compared for the two groups (SNLD versus ALND) using Chi-square test for categorical variables, and for continuous variables either Student's *t* test or Mann–Whitney *U* test depending on distribution of the data. The differences in LYMPH-Q UE scale scores by the type of axillary surgery (SNLD versus ALND) were assessed by multivariable linear regression and adjusted for significant confounding participant demographics. All participant demographics were investigated as potential confounders. Complications were recoded into total number of complications and for cancer and lymphedema treatments, only actual known treatments were included in the analysis. Cancer treatments included chemotherapy, radiation therapy, hormone therapy, and targeted treatment. Lymphedema treatments included compression sleeve, manual lymph drainage, and physical activity prescribed by physiotherapist, all within the past 6 months. Before analysis, normality of data was assessed with histograms, and we evaluated whether all assumptions for regression analysis were met for further analyses. P values < 0.05 were considered statistically significant, and 95% confidence intervals were computed.

Results

A total of 8139 persons with both upper extremity BCRL and breast cancer diagnosis were identified through the list provided by the Danish National Health Data Authority. Out of these, 6850 used electronic mailboxes and were invited to participate in the study. We received 3945 responses leading to an overall response rate of 57.6%. A total of 901 participants were excluded, and 3044 participants were included in the analysis. Figure 1 illustrates the study enrollment process.

Participant demographics

Out of the 3044 participants, 239 participants (7.9%) underwent SNLD only, while 2805 participants underwent ALND (92.1%). A total of 324 (10.6%) reported having had a cancer recurrence, and the patient electronic file review showed additional breast or axillary surgery for a total of 103 (3.4%) participants. Of these participants, 54 (1.8%) had additional axillary surgery (SNLD, $n = 7$; ALND, $n = 47$).

The demographic and clinical characteristics of the participants are provided in Table 2. We found a significant difference between the SLND versus ALND group for the following demographics and clinical factors: type of breast procedure, cancer stage, and years since the first surgery, with the ALND group more years after the first surgery. The prevalence of previous chemotherapy, radiation therapy hormone treatment, and complications was higher in the ALND group. In terms of lymphedema treatment, we found that more participants in the ALND group had used a compression sleeve within the past 6 months ($P < 0.05$). There were no significant differences for the remaining demographic and clinical characteristics.

Patient-reported outcome

Table 3 provides the results from the multivariable linear regression analysis of the impact of SLND versus ALND on the LYMPH-Q UE scale scores.

For the Arm symptoms scale, 2867 participants completed the scale, and the unadjusted mean scores were 66.39 for the SLND group and 66.13 for the ALND group. Our analysis showed no difference between the SLND and

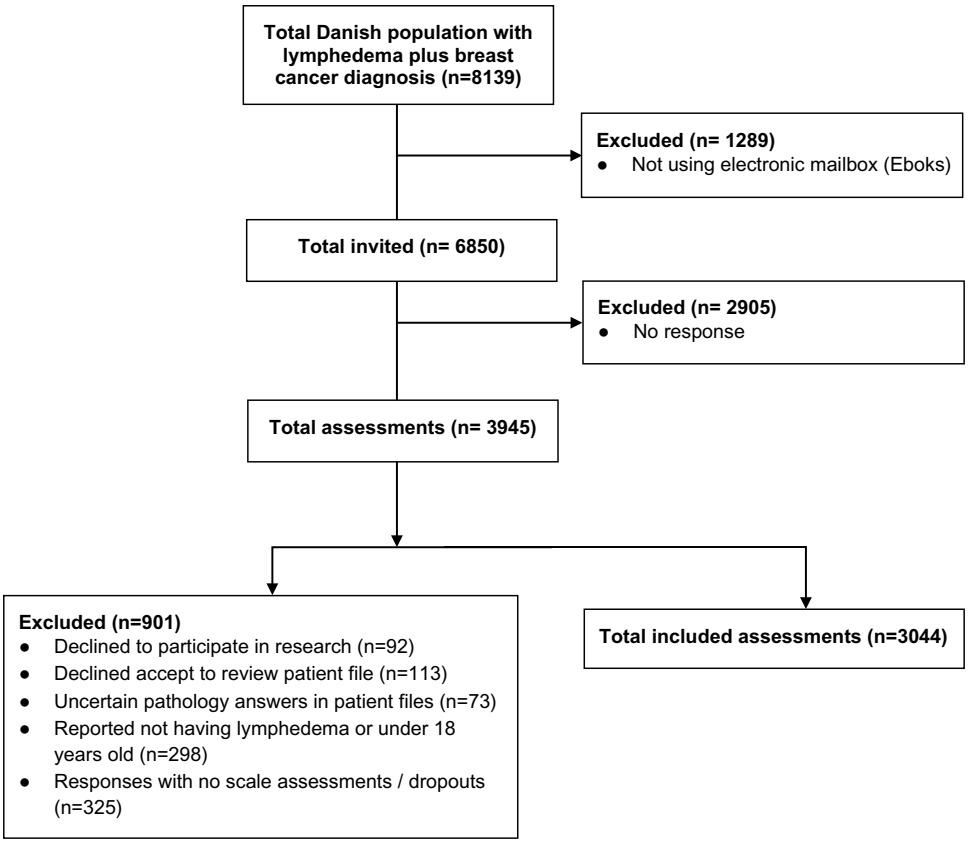

Fig. 1 Flow diagram illustrating study enrollment process

ALND groups (mean difference = 4.363, $P = 0.320$) when adjusted for significant confounders.

For the Arm function scale, 2715 participants completed the scale, and the unadjusted mean scores were 70.66 for the SLND group and 73.65 for the ALND group. There was no significant difference between SLND and ALND groups (mean difference = 7.957, $P = 0.131$) in the adjusted analysis.

For the Arm appearance scale, 2705 participants completed the scale, and the unadjusted mean scores were 70.79 for the SLND group and 60.58 for the ALND group. Our adjusted analysis showed no difference between the SLND and ALND groups (mean difference = − 7.148, $P = 0.269$).

For the Psychological scale, 2693 participants completed the scale, and the unadjusted mean scores were 77.13 for the SLND group and 78.67 for the ALND group. The adjusted analysis revealed no significant difference between the SLND versus ALND group (mean difference = 7.012, $P = 0.136$).

Number of sentinel nodes

The mean number of lymph nodes excised in the SLND only group was 2.21 (SD = 1.38). Our analysis revealed no significant correlation between the number of lymph nodes removed in the SLND group and any of the LYMPH-Q UE scale scores. Table 4 shows the detailed results from the correlation.

Discussion

This study found that in women with BCRL, after adjusting for comorbidities, oncological, and treatment differences, the type of axillary lymph node dissection (i.e., SLND or ALND) does not impact the HRQOL (measured using the 4 LYMPH-Q UE module scales) at a mean follow-up of 8.6 years. As expected, the rates of (neo) adjuvant chemotherapy, radiotherapy, and hormone and targeted therapy were higher in the ALND group, but there was no difference in the two groups with respect to current oncological treatments. A higher prevalence of postoperative complications, including infections and seroma, was noted in the ALND group. We also found no correlation between the number of lymph nodes removed in the SLND only group and the LYMPH-Q UE module scores.

In the BCRL literature, few previous studies have reported discordance between arm morbidity-related outcomes such as arm circumference, range of motion, strength, and neurological function and HRQOL assessments using validated PROMs. A recent observational study of 631 breast cancer patients used the Patient-Reported Outcomes

Table 2 Patient characteristics; comparison of patients having either sentinel node procedure or axillary lymph node dissection

	All			SLND				ALND				*P* value
	N	Mean (range)	SD	N	Valid %	Mean (range)	SD	N	Valid %	Mean (range)	SD	
Gender												
Female	3044	–	–	239	7.9	–	–	2805	92.1	–	–	–
Age	3044	63.68 (23–96)	10.50	239	–	61.08 (35–86)	10.66	2805	–	63.90 (23–96)	10.46	0.754
BMI	3042	27.34 (13.43–49.68)	5.20	239	–	28.19 (17.33–44.15)	5.44	2803	–	27.27 (13.43–49.68)	5.17	0.097
Age at diagnosis of lymphedema	3023	54.13 (20–90)	10.32	234	–	53.79 (26–84)	10.18	2789	–	54.16 (20–90)	10.34	0.371
Years since first surgery	3043	8.60 (0–36)	5.14	239	–	5.95 (1–29)	3.94	2804	–	8.83 (0–36)	5.17	0.000*
Number of affected breasts												
One	2773	–	–	217	7.8	–	–	2556	92.2	–	–	0.638
Two	257	–	–	18	7.0	–	–	239	93.0	–	–	
Number of affected arms												
One	2686	–	–	151	5.6	–	–	2535	94.4	–	–	0.062
Two	51	–	–	6	11.8	–	–	45	88.2	–	–	
Breast procedure												
Lumpectomy	1429	–	–	56	3.9	–	–	1373	96.1	–	–	0.000*
Mastectomy	1580	–	–	182	11.5	–	–	1398	88.5	–	–	
None	35	–	–	1	2.9	–	–	34	97.15	–	–	
Cancer stage at diagnosis												
Stage 0 (i.e., DCIS, LCIS	29			3	10.3			26	89.7			0.006*
Stage 1	206			29	14.1			177	85.9			
Stage 2	269			12	4.5			257	95.5			
Stage 3	273			24	8.8			249	91.2			
Stage 4	89			4	4.5			85	95.5			
Not confirmed	2			0	0			2	100			
Don't know	2161			162	7.5			1999	92.5			
Complications related to breast surgery												
None	574	–	–	37	6.4	–	–	537	93.6	–	–	0.165
Bleeding	49	–	–	3	6.1	–	–	46	93.9	–	–	0.650
Wound dehiscence	52	–	–	2	3.8	–	–	50	96.2	–	–	0.279
Infection	259	–	–	5	1.9	–	–	254	98.1	–	–	0.000*
Skin necrosis	78	–	–	3	3.8	–	–	75	96.2	–	–	0.183
Seroma	466	–	–	17	3.6	–	–	449	96.4	–	–	0.000*
Fat tissue necrosis	25	–	–	2	8.0	–	–	23	92.0	–	–	0.978
Other	214	–	–	7	3.3	–	–	207	96.7	–	–	0.010*
Total number of complications	1143	0.38 (0–7)	0.74	39	-	0.16 (0–3)	0.45	1104	–	0.39 (0–7)	0.76	0.000*

Table 2 (continued)

	All			SLND				ALND				*P* value
	N	Mean (range)	SD	N	Valid %	Mean (range)	SD	N	Valid %	Mean (range)	SD	
Previous additional cancer treatment												
None	76	–	–	6	7.9	–	–	70	92.1	–	–	0.989
Chemotherapy	2238	–	–	139	6.25	–	–	2099	93.8	–	–	0.000*
Radiation therapy	2754	–	–	192	7.0	–	–	2562	93.0	–	–	0.000*
Hormone therapy (e.g., Tamoxifen, Arimidex, Femara)	2040	–	–	137	6.7	–	–	1903	93.3	–	–	0.001*
Targeted treatment (e.g., Herceptin, Ibrance, Avastin)	498	–	–	30	6.0	–	–	468	94.0	–	–	0.097
Other	183	–	–	11	6.0	–	–	172	94.0	–	–	0.340
Don't know	39	–	–	2	5.1	–	–	37	94.9	–	–	0.525
Current additional cancer treatment												
None	1948	–	–	140	7.2	–	–	1808	92.8	–	–	0.069
Chemotherapy	75	–	–	7	9.3	–	–	68	90.7	–	–	0.629
Radiation therapy	40	–	–	2	5.0	–	–	38	95.0	–	–	0.500
Hormone therapy (e.g., Tamoxifen, Arimidex, Femara	860	–	–	72	8.4	–	–	788	91.6	–	–	0.503
Targeted treatment (e.g., Herceptin, Ibrance, Avastin)	70	–	–	3	4.3	–	–	67	95.7	–	–	0.262
Other	253	–	–	21	8.3	–	–	232	91.7	–	–	0.782
Don't know	23			4	17.4	–	–	19	82.6	–	–	0.088
Lymphedema treatment within past 6 months												
Compression sleeve	1808	–	–	80	4.4	–	–	1728	95.6	–	–	0.000*
Manual lymph drainage	621	–	–	40	6.4	–	–	581	93.6	–	–	0.143
Physical activity prescribed by physiotherapist	665	–	–	46	6.9	–	–	619	93.1	–	–	0.311
None of the above	732	–	–	46	6.3	–	–	686	93.7	–	–	0.070
Don't know	12	–	–	1	8.3	–	–	11	91.7	–	–	0.950
Breast reconstruction												
Yes	469	–	–	26	5.5	–	–	443	94.5	–	–	0.787
No	923	–	–	48	5.2	–	–	875	94.8	–	–	
Marital status												
Single	329	–	–	27	8.2	–	–	302	91.8	–	–	0.116
Living together	276	–	–	34	12.3	–	–	242	87.7	–	–	
Married	1944	–	–	145	7.5	–	–	1799	92.5	–	–	
Widow	290	–	–	15	5.2	–	–	275	94.8	–	–	
Divorced	169	–	–	14	8.3	–	–	155	91.7	–	–	
Separated	22	–	–	2	9.1	–	–	20	90.9	–	–	
Other	9	–	–	1	11.1	–	–	8	88.9	–	–	
Prefer to not answer	4	–	–	0	0	–	–	4	100	–	–	

Table 2 (continued)

	All			SLND				ALND				*P* value
	N	Mean (range)	SD	N	Valid %	Mean (range)	SD	N	Valid %	Mean (range)	SD	
Education												
Primary school	348	–	–	29	8.3	–	–	319	91.7	–	–	0.485
Youth, vocational, or secondary	375	–	–	25	6.7	–	–	350	93.3	–	–	
Short higher education	701	–	–	50	7.1	–	–	651	92.9	–	–	
Medium higher education	1186	–	–	106	8.9	–	–	1080	91.1	–	–	
Long higher education	295	–	–	21	7.1	–	–	274	92.9	–	–	
PhD or Doctorate	29	–	–	2	6.9	–	–	27	93.1	–	–	
Other	57	–	–	1	1.8	–	–	56	98.2	–	–	
Prefer to not answer	52	–	–	4	7.7	–	–	48	92.3	–	–	
Employment												
Full time	637	–	–	55	8.6	–	–	582	91.4	–	–	0.223
Part time	480	–	–	47	9.8	–	–	433	90.2	–	–	
Unemployed (not looking)	22	–	–	1	4.5	–	–	21	95.5	–	–	
Unemployed (looking)	52	–	–	6	11.5	–	–	46	88.5	–	–	
Retired	1584	–	–	103	6.5	–	–	1481	93.5	–	–	
Unable to work	82	–	–	8	9.8	–	–	74	90.2	–	–	
Student	15	–	–	1	6.7	–	–	14	93.3	–	–	
Other	159	–	–	15	9.4	–	–	144	90.6	–	–	
Prefer to not answer	12	–	–	2	16.7	–	–	10	83.3	–	–	

SLND sentinel node procedure, *ALND* full axillary lymph node dissection, *SD* standard deviation

*P value < 0.05

Table 3 Results from the multivariable linear regression analysis by axillary procedure and LYMPH-Q upper extremity scales

Outcome	Model	Mean difference (Regression coefficient B)	SE	95% confidence interval		*P* value
				Lower bound	Upper bound	
Arm symptoms	Unadjusted	−0.259	1.172	−2.556	2.038	0.825
	Adjusted[a]	4.363	4.381	−4.255	12.981	0.320
Arm function	Unadjusted	2.981	1.563	−0.83	6.045	0.057
	Adjusted[b]	7.957	5.262	−2.391	18.306	0.131
Arm appearance	Unadjusted	−10.211	2.146	−14.419	−6.004	0.000*
	Adjusted[c]	−7.148	6.464	−19.858	5.562	0.269
Psychological	Unadjusted	1.538	1.416	−1.238	4.314	0.277
	Adjusted[d]	7.012	4.690	−2.210	16.234	0.136

Regression coefficient B = mean ALND − mean SLND

SLND sentinel node procedure, *ALND* full axillary lymph node dissection, *SE* standard error

[a]Adjusted for compression sleeve treatment, number of affected arms, current age, number of complications, breast procedure, employment status, BMI, previous chemotherapy, age at diagnosis, cancer recurrence, previous radiation therapy, cancer stage, years since first breast cancer surgery, breast reconstruction, marital status, physiotherapy lymphedema treatment, hormone therapy, education, and manual lymph drainage treatment

[b]Adjusted for breast reconstruction, compression sleeve treatment, breast procedure, BMI, number of complications, cancer stage, years since first breast cancer surgery, physiotherapy lymphedema treatment, and employment status

[c]Adjusted for breast reconstruction, compression sleeve treatment, cancer stage, years since first breast cancer surgery, and breast procedure

[d]Adjusted for cancer stage, compression sleeve treatment, breast reconstruction, current age, breast procedure, number of complications, years since first breast cancer surgery, BMI, age at diagnosis, previous chemotherapy, physiotherapy lymphedema treatment, and manual lymph drainage treatment

*P value < 0.05

Table 4 Results from the correlation between the number of lymph nodes in the SLND group and the LYMPH-Q upper extremity scale scores

Outcome	N	Pearson correlation	*P* value
Arm symptoms	184	−0.020	0.791
Arm function	153	0.015	0.858
Arm appearance	153	−0.020	0.803
Psychological	154	−0.068	0.400

version of the Common Terminology Criteria for Adverse Events (PRO-CTCAE) to compare SLND and ALND groups and reported that arm circumference was a poor surrogate for HRQOL outcomes [13]. Similarly, Barranger et al. compared morbidity and HRQOL outcomes in women undergoing breast-conserving treatment with SNLD, ALND with or without SNLD, or SNLD followed by ALND using the European Organization for Research and Treatment of Cancer Quality of Life Questionnaires—Cancer-30 and breast reconstruction-23 and concluded that there was no significant difference in global quality of life of participants [14]. While one would postulate none to low correlations between the two procedures using a generic cancer PROM that is not sensitive to the unique concerns of women with BCRL, ours is the first study to demonstrate that the HRQOL outcomes of the two procedures are comparable when using a lymphedema-specific PROM in a long-term follow-up study of a large sample of patients.

Our results support the theory that the likelihood of developing BCRL increases when the main lymphatics are compromised, irrespective of the number of lymph nodes that are removed. This theory is partially confirmed by the finding that approximately 60% of women who underwent ALND and regional lymph node radiation, the top two risk factors associated with BCRL did not develop BCRL [15, 16]. Recent studies have proposed the presence of the Mascagni–Sappey Pathway and its anatomic course as one of the factors that account for BCRL [17]. This theory suggests that when the main lymphatic pathways are damaged intraoperatively or due to chemotherapy port placement or radiation, secondary lymphatic pathways provide an alternate route for lymph drainage, preventing the occurrence of lymphedema or reducing its severity. Recent studies that have used dyes such as fluorescein isothiocyanate and isosulfan blue for visualization in live surgery advocate for their use on a routine basis to establish the presence of the M–S pathway and prevent damaging it. In patients in whom the M–S pathway is not visualized or present, ongoing surveillance for clinical signs and symptoms of BCRL has been

recommended [18]. Other non-treatment-related risk factors for BCRL include high BMI at the time of cancer diagnosis, weight fluctuations postoperatively, subclinical edema, and cellulitis [19]. Further prospective long-term follow-up studies should investigate these factors in the context of SLND and ALND and its influence on HRQOL using validated PROMs, such as the LYMPH-Q UE module.

We found a significant difference for the two groups according to the type of breast procedure, cancer stage, and years since the first surgery. Patients in the ALND group reported being further out from the first surgery at the time of the survey. This was not surprising as changes in guidelines supporting less extensive surgery imply that SLND is now more commonly performed. We also noted a higher prevalence of infection and seroma in the ALND group, which is supported in the literature. Previous studies have shown that ALND is a significant predictor for axillary seromas, paresthesia, brachial plexus injury, and wound infection in the first 6 months, postoperatively [20–23]. Additionally, ALND has been associated with long-term morbidity in terms of decreased range of motion in the upper extremity, ongoing paresthesia, skin breakdown, and BCRL [22]. A higher proportion of women in the ALND group reported wearing a compression sleeve and receiving manual lymphatic drainage or exercises prescribed by a physiotherapist in the past 6 months. These findings may be related to preemptive management of BCRL, where the women with ALND may receive more educational support and resources concerning BCRL or it is likely that the women in the ALND group had more severe BCRL.

This study has some limitations. Due to our study's self-report nature, the accuracy of survey information, such as the cancer stage, time since first diagnosis, and type of lymphedema treatment in the past 6 months, could not be verified. Further, as the survey was completed online, population subgroups with no access to smartphones or computers and internet connections were excluded. This may have led to exclusion of digitally illiterate and other vulnerable subgroups of the population, such as low socioeconomic groups, other ethnicity than Danish, and patients who reside in remote and rural areas. All of these factors might have influenced the modest response rate. Women who do not participate in Eboks and receive paper mail were also excluded. Our study was also limited due to the lack of arm circumference measurements, BMI at the time of surgery, fluctuations in BMI post-surgery, and presence of axillary paresthesia. The lack of objective and clinician-reported data prevented us from drawing any conclusions on the relationship between the aforementioned factors and HRQOL in women with BCRL in the long term. However, a recent study by Jorgensen et al. showed only minor impact of clinical outcomes, such as lymphedema severity and dominant arm affection [24]. Another limitation is the sample size in the evaluation of association between number of removed sentinel nodes and LYMPH-Q UE scores, where a larger sample size had been preferable and thus this result should be interpreted with caution. Finally, our study only describes total LYMPH-Q UE scale scores. Future research is needed to further investigate the multidimensionality of the individual constructs.

Conclusion

We found no difference in women who had upper extremity lymphedema after SLND or ALND on the LYMPH-Q UE module scales measuring arm symptoms, function, distress, and appearance. Additionally, we found no correlation between the number of lymph nodes removed in the SLND only group and the LYMPH-Q UE module scores. Future longitudinal studies should continue to explore the role of SLND and ALND in HRQOL of women with breast cancer beyond the immediate recovery period using objective measures of lymphedema (e.g., arm circumference, range of motion) and valid and reliable PROMs, such as the LYMPH-Q UE module.

Declarations

Conflict of interest A. Klassen and A. Pusic are co-developers of the LYMPH-Q upper extremity module and, as such, could potentially receive a share of any license revenues as royalties based on the institution inventor sharing policy. The remaining authors declare no conflict of interest.

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