



Published in final edited form as:

J Cancer Surviv. 2013 March ; 7(1): 83–92. doi:10.1007/s11764-012-0247-5.

Quality of life among breast cancer patients with lymphedema: a systematic review of patient-reported outcome instruments and outcomes

Andrea L. Pusic,

Memorial Sloan Kettering Cancer Center, 1275 York Ave, New York, NY 10065, USA

Yeliz Cemal,

Memorial Sloan Kettering Cancer Center, 1275 York Ave, New York, NY 10065, USA

Claudia Albornoz,

Memorial Sloan Kettering Cancer Center, 1275 York Ave, New York, NY 10065, USA

Anne Klassen,

McMaster University, Hamilton, ON, Canada

Stefan Cano,

Clinical Neurology Research Group, Peninsula College of Medicine and Dentistry, Plymouth University, Plymouth, UK

Isabel Sulimanoff,

Memorial Sloan Kettering Cancer Center, 1275 York Ave, New York, NY 10065, USA

Marisol Hernandez,

Memorial Sloan Kettering Cancer Center, 1275 York Ave, New York, NY 10065, USA

Marga Massey,

The Dr. M Massey Practice Group, Roper Office Medical Building Suite #550, Charleston, SC, USA

Peter Cordeiro,

Memorial Sloan Kettering Cancer Center, 1275 York Ave, New York, NY 10065, USA

Monica Morrow, and

Memorial Sloan Kettering Cancer Center, 1275 York Ave, New York, NY 10065, USA

Babak Mehrara

Memorial Sloan Kettering Cancer Center, 1275 York Ave, New York, NY 10065, USA

Andrea L. Pusic: pusica@mskcc.org

Abstract

Purpose—Lymphedema following breast cancer surgery remains a common and feared treatment complication. Accurate information on health-related quality of life (HRQOL) outcomes among patients with lymphedema is critically needed to inform shared medical decision making and evidence-based practice in oncologic breast surgery. Our systematic review aimed to (1) identify studies describing HRQOL outcomes in breast cancer-related lymphedema (BCRL)

patients, (2) assess the quality of these studies, and (3) assess the quality and appropriateness of the patient-reported outcome (PRO) instruments used.

Methods—Using the PRISMA statement, we performed a systematic review including studies describing HRQOL outcomes among BCRL patients. Studies were classified by levels of evidence and fulfillment of the Efficace criteria. PRO instruments were assessed using the COSMIN criteria.

Results—Thirty-nine studies met inclusion criteria, including 8 level I and 14 level II studies. Sixteen of 39 studies were compliant with the Efficace criteria. Seventeen HRQOL instruments were used, two specific to lymphedema patients. Exercise and complex decongestive therapy treatment interventions were associated with improved HRQOL.

Conclusions—High-quality data on HRQOL outcomes is required to inform surgical decisions for breast cancer management and survivors. Of the lymphedema-specific PRO instruments, the Upper Limb Lymphedema 27 (ULL-27) was found to have strong psychometric properties. Future studies should strive to use high-quality condition-specific PRO instruments, follow existing guidelines for HRQOL measurement and to consider economic burdens of BCRL.

Implications for Cancer Survivors—As lymphedema may develop many years after breast cancer surgery, the ULL-27 may offer greater content validity for use in survivorship research.

Keywords

Lymphedema; Breast cancer; Quality of life

Introduction

Breast cancer is the most common cancer in women with an estimated 230,480 new cases in 2011 [1]. While treatment of breast cancer has improved, arm lymphedema following axillary lymph node dissection (ALND) remains a common complication occurring in as many as 30–50 % of patients who undergo this treatment. Affected patients develop chronic accumulation of interstitial fluid resulting in fibro-adipose deposition and swelling. This swelling can lead to pain, decreased function, body image disturbance, and anxiety [2]. Treatment for lymphedema is limited and primarily palliative in nature, aiming to prevent disease progression. Accurate information on health-related quality of life (HRQOL) outcomes among patients with breast cancer-related lymphedema (BCRL) is important since lymphedema is known to have a significant impact on the physical, psychological, and social health of patients [2, 3]. In fact, recent studies have shown that some patients develop symptoms of lymphedema without objective changes in arm circumference, indicating that clinical measurements may underestimate the incidence and impact of lymphedema [4].

Assessments of patient symptoms and HRQOL outcomes are made using patient-reported outcome (PRO) instruments, or questionnaires, that quantify significant outcome variables from the patient's perspective [5, 6]. When developed and validated according to international guidelines, PRO instruments can facilitate reliable and valid patient assessment. While generic PRO instruments are designed to measure outcomes across diverse patient populations, condition- or disease-specific measures may provide more sensitive assessment for specific populations, such as patients with lymphedema. International standards have also now been established to evaluate HRQOL study methodology (Efficace criteria, Table 1) with a goal of improving study design and minimizing the risk of bias [7]. As researchers seek to better understand the impact of BCRL on HRQOL, high-quality studies that incorporate the best available PRO instruments and use the most rigorous study methodology are needed in order to provide the highest level of evidence to guide treatment decisions.

To better understand the level of scientific evidence afforded by existing studies, the aims of our systematic review were threefold: (1) To identify and summarize results from studies that describe HRQOL outcomes in BCRL patients, (2) to assess the quality of these studies using established criteria for HRQOL study methodology; and (3) to assess the quality and appropriateness of the PRO instruments used in these studies.

Methods

Search Strategy

Our review was guided by the PRISMA statement and included a search strategy focused on three components (1) breast cancer; (2) lymphedema; and (3) quality of life (Fig. 1) [8]. Limitations were placed to exclude non-BCRL studies, conference abstracts, and breast cancer in men. Potentially relevant papers were examined by two reviewers (YC and CA) who worked independently, with discrepancies of opinion resolved by a third (AP). Inclusion criteria were as follows: (1) the study cohort was composed of BCRL patients and (2) the study described HRQOL outcomes among BCRL patients using a formally developed and validated PRO instruments. Studies were excluded if they were not in English, used a non-validated PRO instrument, or a modified version of standardized instrument that was itself not validated. Citations for relevant articles were examined to identify additional articles.

Indicators of the methodological quality of each publication included study design and Efficacy compliancy. Studies were classified by levels of evidence (Table 2) [9]. PRO instruments used to evaluate HRQOL in each study were assessed using the Consensus-based Standards for the Selection of Health Measurement Instruments (COSMIN) criteria [10].

Results

Search results

The literature search identified 1,792 articles and of these 85 studies met some or all inclusion criteria. An additional seven articles were identified through review of citations. A total of 39 manuscripts met inclusion criteria (Table 3).

Study quality: levels of evidence and Efficacy criteria

Studies were categorized by level of evidence as follows: 8 studies were level I [4, 11–17], 14 studies level II [18–31], 8 level III [2, 32–38], and 9 studies level IV [39–47]. Sixteen [4, 11–13, 15, 16, 18, 20–22, 26, 27, 31, 34, 38, 46] of 39 studies were compliant with the Efficacy criteria (Table 1). Of the 16 compliant studies, six were level I studies, seven level II, two level III, and one level IV.

HRQOL instrument quality: COSMIN criteria

Seventeen HRQOL instruments were identified in the 39 articles. Most studies used a generic instrument with or without oncology-specific instruments. Four different generic HRQOL instruments were used including the SF-36 (used in 15 studies). Nine HRQOL instruments were oncology-specific including the EORTC-QLQ-30 (11 studies), EORTC-QLQ-BR23 (2 studies), WHOQOL-BREF (1 study), FACT-B (5 studies), and FACT-B +4 (4 studies). Table 3 also provides a summary of the HRQOL instrument and the HRQOL domains evaluated. While all these instruments have been extensively validated, they are relatively generic (with the notable exception of the FACT-B +4 which has five lymphedema-specific questions).

We identified two HRQOL instruments developed specifically for BCRL patients. These instruments were the Wesley Clinic Lymphedema Scale (WCLS) [31] and the Upper Limb Lymphedema—27 questionnaire (ULL-27) [48].

The WCLS was used in two studies and the ULL-27 in three. The WCLS was developed by adapting the Functional Living Index-Cancer (FLIC) instrument [49]. The term “lymphedema” was substituted for the words “illness” or “cancer” in the FLIC. Qualitative work to confirm the validity of the scale in patients with lymphedema was not published nor was formal psychometric analysis. The ULL-27 was developed specifically to address the need for a condition-specific instrument in assessing the unique HRQOL issues of importance to BCRL patients. Its conceptual framework and content were developed from patient interviews. The ULL-27 has a total of 27 items and measures the following domains: functional (15 items); psychological (7 items); and social (5 items) [48]. Psychometric evaluation was performed in a sample of 304 patients. Convergent and discriminant validity were evaluated against the Patient’s Arm Comfort Scale, Global Symptom Index, and the SF-36. The ULL-27 has good reliability (the extent to which scores for patients whose HRQOL has not changed are the same for repeated measurements; Cronbach’s alpha >0.9 and intra-class correlation coefficients of >0.8), validity (as measured by the degree of interrelatedness among the items in a scale; internal consistency 0.42–0.77) and responsiveness (ability to detect change over time; effect size of >0.4) [48]. Despite its careful qualitative development and strong psychometric properties, the ULL-27 has been used in only three published studies to date.

HRQOL Outcomes in BCRL patients

The focus of most studies (15 of 39 studies) was to compare HRQOL in BCRL patients to that of breast cancer patients without lymphedema. The majority of studies reported significantly poorer HRQOL outcomes in patients with BCRL resulting in decreased physical functioning, as well as psychological and social well-being. Patient age, body weight, and race were all noted to influence or confound HRQOL outcomes among patients with BCRL. Changes in social well-being were most marked among younger patients, with women under the age of 40 experiencing decreased social well-being compared to older patients [42]. Body weight also emerged as an important covariate. Interestingly, one level II study found that BCRL patients who were either under or overweight were more likely to report decreased HRQOL compared to women of normal weight with lymphedema [18]. Obese women with lymphedema reported the most significant diminution in HRQOL [18]. Racial differences were also noted; in one level III study, 99 Caucasian women with lymphedema reported significantly higher FACT-B scores and hence better HRQOL compared with a small sample of ten non-Caucasian women with lymphedema [32].

Of the 39 studies included in this review, 18 evaluated the impact of different treatment interventions on HRQOL. Exercise and its effects on HRQOL in BCRL patients were assessed in six studies (three level I and three level II). One level I study found that older women (>50 years) had significantly improved strength and health scores after twice weekly exercise regardless of lymphedema status [11]. Among lymphedema patients participating in an exercise physiotherapy program (level II study), physical function was not reported to improve over 5 years; however, global health was found to significantly improve from baseline [19]. Similar findings were reported in another exercise study, where general health, vitality, and physical functioning all improved in patients undergoing exercise compared to control groups [16].

The treatment modality of complex decongestive therapy (CDT) was evaluated in six studies (five level II and one level IV). Significant improvements in physical and psychological function were reported when CDT was combined with exercise regimens [12]. Several novel

therapies were also assessed such as aqua lymphatic therapy, flexi-touch, and liposuction in combination with CDT. Psychological and social function improved significantly in patients having aqua lymphatic therapy (level I study) [13].

Discussion

The objective of this review was to identify and examine published studies on HRQOL outcomes among patients with BCRL. Of the 39 publications that fulfilled our inclusion criteria, 8 provided level I evidence and 14 were level II. While these level I and II studies had generally smaller sample sizes, they utilized robust study methodology and were more likely to meet guidelines for HRQOL measurement as established by the Efficace criteria. Notably, six high level studies were performed in 2010, highlighting the growing interest in HRQOL outcomes among BCRL patients and awareness of the importance of good study design. Somewhat disappointingly, only 16 studies were compliant with the Efficace criteria.

The majority of studies reported diminished HRQOL in patients with BCRL patients. Specific HRQOL domains most affected were body image, physical, psychological, and social function. Patient age, body weight, and race were all noted to be important covariates. This has important implications for clinical decision making and patient education. For women with early-stage breast cancer who are struggling with the decision whether or not to undergo axillary lymph node dissection, it is important that they understand not only their estimated risk of developing lymphedema, but also the anticipated impact on QOL should the condition develop. As an example, obese women are not only more likely to develop BCRL, but when they do the diminution in HRQOL is greater.

In terms of targeted treatments for BCRL, exercise and CDT treatment were associated with the most profound improvements in HRQOL. For years, patients at risk of lymphedema have been admonished to avoid vigorous exercise [50]. Five level I and II trials refute this contention [11, 12, 19, 22, 28]. With respect to CDT therapy, the published body of evidence clearly shows that this form of treatment is of benefit; nevertheless, in an era of cost restriction, insurance payment for this therapy may still be denied. In order to optimally allocate healthcare resources, it is important that the results of such trials be acknowledged and that payers recognize the HRQOL burden of BCRL when left untreated. Importantly, no studies evaluated new therapies such as micro-lymphatic bypass and lymph node transfer despite the growing application of these procedures.

Only one study evaluated cost or provided health utility analyses [25]. As lymphedema is a chronic disease, this topic is of vital importance. Additionally, as patients and payers consider the therapeutic benefits of ALND, the economic burden of BCRL should be further evaluated. Patients with BCRL may not be able to return to work and this may further diminish their HRQOL as well as economic productivity.

We also evaluated the quality and appropriateness of the PRO instruments used in published studies of BCRL. Seventeen PRO instruments were used overall. Most studies incorporated well-established generic or cancer-specific PRO instruments. Such generic instruments are not developed to evaluate the specific issues of importance to lymphedema patients. As an example, the SF-36 does not capture the specific symptoms suffered by BCRL patients such as heavy and swollen arms or difficulty grasping or holding objects. While it is appropriate to use generic PRO instruments to compare and contrast values across studies, trials that rely on generic PRO instruments alone cannot be expected to detect subtle but perhaps clinically important changes before and after an intervention or changes over time. For this reason, use of a condition-specific instrument alongside a generic instrument is recommended. In this

review, two lymphedema-specific PRO instruments were identified [31, 48]. Based on assessment using the COSMIN criteria, only the ULL-27 can be recommended without hesitation.

An important additional consideration is the extent to which PRO instruments developed for use among patients in active cancer treatment are valid for cancer survivors. As lymphedema is a chronic condition that may develop many years after breast cancer surgery, this is a relevant concern and should be considered when researchers are selecting outcome measures for a new study or interpreting study results. As noted above, the ULL-27 was developed with qualitative input from cancer survivors with lymphedema. As such, this instrument may offer greater content validity for use in survivorship research.

In conclusion, BCRL has a significant impact on the HRQOL of breast cancer survivors and is an important consideration when contemplating elective ALND in patients with early-stage breast cancer. Although lymphedema research has gained momentum recently, additional levels I and II studies are required. These studies will help promote therapeutic innovation, provide support for newly developed treatment options such as microsurgical bypass or lymph node transfer, and shape health care policy.

References

1. Cancer Facts & Figures 2011. American Cancer Society; Atlanta: 2011.
2. Ahmed RL, Prizment A, Lazovich D, Schmitz KH, Folsom AR. Lymphedema and quality of life in breast cancer survivors: the Iowa Women's Health Study. *J Clin Oncol*. 2008; 26(35):5689–96. [PubMed: 19001331]
3. Rockson SG. Lymphedema. *Am J Med*. 2001; 110(4):288–95. [PubMed: 11239847]
4. Hormes JM, Bryan C, Lytle LA, et al. Impact of lymphedema and arm symptoms on quality of life in breast cancer survivors. *Lymphology*. 2010; 43(1):1–13. [PubMed: 20552814]
5. Winters ZE, Benson JR, Pusic AL. A systematic review of the clinical evidence to guide treatment recommendations in breast reconstruction based on patient-reported outcome measures and health-related quality of life. *Ann Surg*. 2010; 252(6):929–42. [PubMed: 20729711]
6. Pusic A, Liu JC, Chen CM, et al. A systematic review of patient-reported outcome measures in head and neck cancer surgery. *Otolaryngol Head Neck Surg*. 2007; 136(4):525–35. [PubMed: 17418246]
7. Efficace F, Bottomley A, Osoba D, et al. Beyond the development of health-related quality-of-life (HRQOL) measures: a checklist for evaluating HRQOL outcomes in cancer clinical trials—does HRQOL evaluation in prostate cancer research inform clinical decision making? *J Clin Oncol*. 2003; 21(18):3502–11. [PubMed: 12972527]
8. Liberati A, Altman DG, Tetzlaff J, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. *J Clin Epidemiol*. 2009; 62(10):e1–e34. [PubMed: 19631507]
9. Making health care safer: a critical analysis of patient safety practices. Evidence-based review methodology. Chap 3 <http://www.ahrq.gov/clinic/ptsafety/chap3.htm>.
10. Mokkink LB, Terwee CB, Patrick DL, et al. The COSMIN checklist for assessing the methodological quality of studies on measurement properties of health status measurement instruments: an international Delphi study. *Qual Life Res*. 2010; 19(4):539–49. [PubMed: 20169472]
11. Speck RM, Gross CR, Hormes JM, et al. Changes in the Body Image and Relationship Scale following a one-year strength training trial for breast cancer survivors with or at risk for lymphedema. *Breast Cancer Res Treat*. 2010; 2:421–30. [PubMed: 19771507]
12. Kim do S, Sim YJ, Jeong HJ, Kim GC. Effect of active resistive exercise on breast cancer-related lymphedema: a randomized controlled trial. *Arch Phys Med Rehabil*. 2010; 91(12):1844–8. [PubMed: 21112424]

13. Tidhar D, Katz-Leurer M. Aqua lymphatic therapy in women who suffer from breast cancer treatment-related lymphedema: a randomized controlled study. *Supportive Care in Cancer*. 2010; 18(3):383–92. [PubMed: 19495810]
14. McClure MK, McClure RJ, Day R, Brufsky AM. Randomized controlled trial of the breast cancer recovery program for women with breast cancer-related lymphedema. *Am J Occup Ther*. 2010; 64(1):59–72. [PubMed: 20131565]
15. Tsai HJ, Hung HC, Yang JL, Huang CS, Tsao JY. Could Kinesio tape replace the bandage in decongestive lymphatic therapy for breast-cancer-related lymphedema? A pilot study. *Support Care Cancer*. 2009; 11:1353–60. [PubMed: 19199105]
16. McKenzie DC, Kalda AL. Effect of upper extremity exercise on secondary lymphedema in breast cancer patients: a pilot study. *J Clin Oncol*. 2003; 21(3):463–6. [PubMed: 12560436]
17. Williams AF, Vadgama A, Franks PJ, Mortimer PS. A randomized controlled crossover study of manual lymphatic drainage therapy in women with breast cancer-related lymphoedema. *Eur J Cancer Care (Engl)*. 2002; 11(4):254–61. [PubMed: 12492462]
18. Vassard D, Olsen MH, Zinckernagel L, Vibe-Petersen J, Dalton SO, Johansen C. Psychological consequences of lymphoedema associated with breast cancer: a prospective cohort study. *Eur J Cancer*. 2010; 46(18):3211–8. [PubMed: 20797846]
19. Sagen A, Karesen R, Sandvik L, Risberg M. Changes in arm morbidities and health-related quality of life after breast cancer surgery: a five-year follow-up study. *J Clin Oncol*. 2009; 27(15):e20602.
20. Paskett ED, Naughton MJ, McCoy TP, Case LD, Abbott JM. The epidemiology of arm and hand swelling in premenopausal breast cancer survivors. *Cancer Epidemiol Biomarkers Prev*. 2007; 16(4):775–82. [PubMed: 17416770]
21. Kim SJ, Yi CH, Kwon OY. Effect of complex decongestive therapy on edema and the quality of life in breast cancer patients with unilateral lymphedema. *Lymphology*. 2007; 40(3):143–51. [PubMed: 18062617]
22. Cheema BS, Gaul CA. Full-body exercise training improves fitness and quality of life in survivors of breast cancer. *J Strength Cond Res*. 2006; 20(1):14–21. [PubMed: 16506861]
23. O'Neill J, Beatus J. The effects of complete decongestive physical therapy treatment on edema reduction, quality of life, and functional ability of persons with upper extremity lymphedema. *J Women's Health Phys Therapy*. 2006; 30(1):5–10.
24. Brorson H, Ohlin K, Olsson G, Langstrom G, Wiklund I, Svensson H. Quality of life following liposuction and conservative treatment of arm lymphedema. *Lymphology*. 2006; 39(1):8–25. [PubMed: 16724506]
25. Wilburn O, Wilburn P, Rockson SG. A pilot, prospective evaluation of a novel alternative for maintenance therapy of breast cancer-associated lymphedema. *BMC Cancer*. 2006; 6:84. [PubMed: 16571129]
26. Strauss-Blasche G, Gnad E, Ekmekcioglu C, Hladschik B, Marktl W. Combined inpatient rehabilitation and spa therapy for breast cancer patients: effects on quality of life and CA 15–3. *Cancer Nurs*. 2005; 28(5):390–8. [PubMed: 16192831]
27. Mondry TE, Riffenburgh RH, Johnstone PA. Prospective trial of complete decongestive therapy for upper extremity lymphedema after breast cancer therapy. *Cancer J*. 2004; 10(1):42–8. [PubMed: 15000494]
28. Turner J, Hayes S, Reul-Hirche H. Improving the physical status and quality of life of women treated for breast cancer: a pilot study of a structured exercise intervention. *J Surg Oncol*. 2004; 86(3):141–6. [PubMed: 15170652]
29. Coster S, Poole K, Fallowfield LJ. The validation of a quality of life scale to assess the impact of arm morbidity in breast cancer patients post-operatively. *Breast Cancer Res Treat*. 2001; 68(3):273–82. [PubMed: 11727963]
30. Velanovich V, Szymanski W. Quality of life of breast cancer patients with lymphedema. *Am J Surg*. 1999; 177(3):184–7. [PubMed: 10219851]
31. Mirolo BR, Bunce IH, Chapman M, et al. Psychosocial benefits of postmastectomy lymphedema therapy. *Cancer Nurs*. 1995; 18(3):197–205. [PubMed: 7600551]
32. Beaulac SM, McNair LA, Scott TE, LaMorte WW, Kavanah MT. Lymphedema and quality of life in survivors of early-stage breast cancer. *Arch Surg*. 2002; 137(11):1253–7. [PubMed: 12413312]

33. Nesvold IL, Foss SD, Holm I, Naume B, Dahl AA. Arm/shoulder problems in breast cancer survivors are associated with reduced health and poorer physical quality of life. *Acta Oncol.* 2010; 49 (3):347–53. [PubMed: 19842790]
34. Nesvold IL, Reinertsen KV, Fossa SD, Dahl AA. The relation between arm/shoulder problems and quality of life in breast cancer survivors: a cross-sectional and longitudinal study. *J Cancer Surviv.* 2010; 5(1):62–72. [PubMed: 20972640]
35. Chachaj A, Malyszczak K, Pyszel K, et al. Physical and psychological impairments of women with upper limb lymphedema following breast cancer treatment. *Psychooncology.* 2010; 19(3):299–305. [PubMed: 19399782]
36. Mak SS, Mo KF, Suen JJ, Chan SL, Ma WL, Yeo W. Lymphedema and quality of life in Chinese women after treatment for breast cancer. *Eur J Oncol Nurs.* 2009; 13(2):110–5. [PubMed: 19246241]
37. Paim CR, de Paula Lima ED, Fu MR, de Paula Lima A, Cassali GD. Post lymphadenectomy complications and quality of life among breast cancer patients in Brazil. *Cancer Nurs.* 2008; 31 (4):302–9. [PubMed: 18600117]
38. Pyszel A, Malyszczak K, Pyszel K, Andrzejak R, Szuba A. Disability, psychological distress and quality of life in breast cancer survivors with arm lymphedema. *Lymphology.* 2006; 39(4):185–92. [PubMed: 17319631]
39. Ridner SH, Dietrich MS, Kidd N. Breast cancer treatment-related lymphedema self-care: education, practices, symptoms, and quality of life. *Support Care Cancer.* 2011; 19(5):631–7. [PubMed: 20393753]
40. Karadibak D, Yavuzsen T, Saydam S. Prospective trial of intensive decongestive physiotherapy for upper extremity lymphedema. *J Surg Oncol.* 2008; 97(7):572–7. [PubMed: 18459131]
41. Dawes DJ, Meterissian S, Goldberg M, Mayo NE. Impact of lymphoedema on arm function and health-related quality of life in women following breast cancer surgery. *J Rehabil Med.* 2008; 40 (8):651–8. [PubMed: 19020699]
42. Heiney SP, McWayne J, Cunningham JE, et al. Quality of life and lymphedema following breast cancer. *Lymphology.* 2007; 40 (4):177–84. [PubMed: 18365532]
43. Ridner SH. Quality of life and a symptom cluster associated with breast cancer treatment-related lymphedema. *Support Care Cancer.* 2005; 13(11):904–11. [PubMed: 15812652]
44. Wilson RW, Hutson LM, Vanstry D. Comparison of 2 quality-of-life questionnaires in women treated for breast cancer: the RAND 36-Item Health Survey and the Functional Living Index-Cancer. *Phys Ther.* 2005; 85(9):851–60. [PubMed: 16117596]
45. Pain SJ, Vowler SL, Purushotham AD. Is physical function a more appropriate measure than volume excess in the assessment of breast cancer-related lymphoedema (BCRL)? *Eur J Cancer.* 2003; 39(15):2168–72. [PubMed: 14522374]
46. Kwan W, Jackson J, Weir LM, Dingee C, McGregor G, Olivotto IA. Chronic arm morbidity after curative breast cancer treatment: prevalence and impact on quality of life. *J Clin Oncol.* 2002; 20 (20):4242–8. [PubMed: 12377968]
47. Kirshbaum M. The development, implementation and evaluation of guidelines for the management of breast cancer related lymphoedema. *Eur J Cancer Care (Engl).* 1996; 5(4):246–51. [PubMed: 9117070]
48. Launois R, Megnigbeto AC, Pocquet K, Alliot F. A specific quality of life scale in upper limb lymphoedema: the ULL-27 questionnaire. *Lymphology.* 2002; 35(1–760):181–7.
49. Schipper H, Clinch J, McMurray A, Levitt M. Measuring the quality of life of cancer patients: the Functional Living Index-Cancer: development and validation. *J Clin Oncol.* 1984; 2 (5):472–83. [PubMed: 6374052]
50. Cemal Y, Pusic A, Mehrara BJ. Preventative measures for lymphedema: separating fact from fiction. *J Am Coll Surg.* 2011; 213 (4):543–51. [PubMed: 21802319]

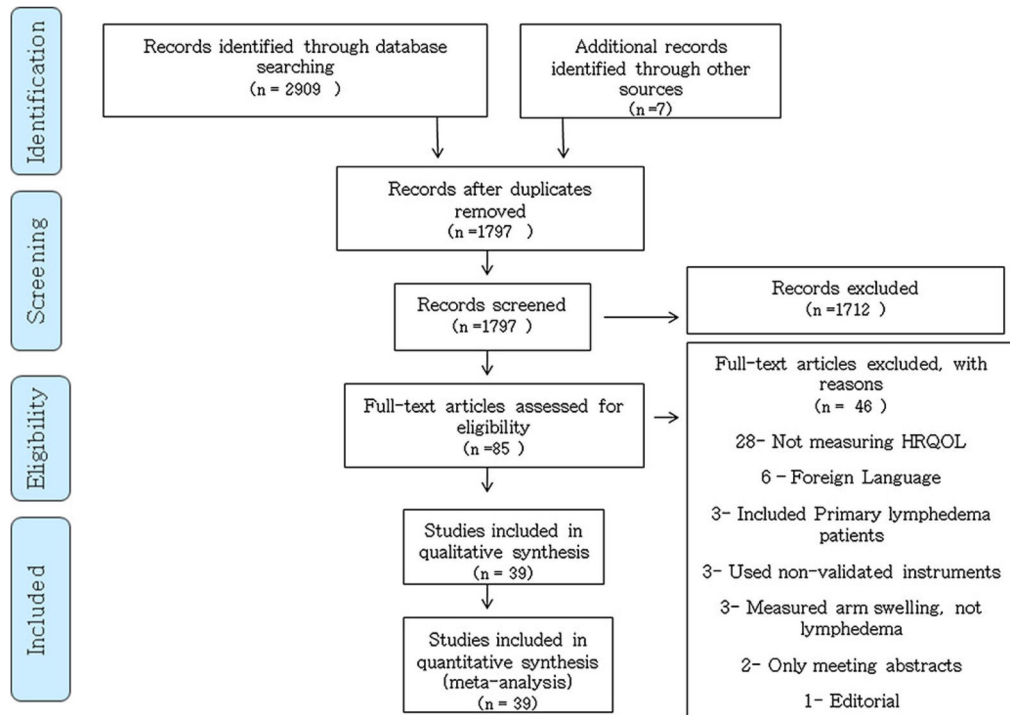


Fig. 1. Flow diagram for systematic review methodology in line with PRISMA guidelines [8]

Table 1

The Efficace criteria [7]

Efficace criteria checklist for evaluating HRQOL			
HRQOL	Answer		
Conceptual			
A priori hypothesis stated	Yes	No	N/A ^a
Rational for instrument reported	Yes	No	
Measurement			
Psychometric properties reported	Yes	No	N/A ^b
Cultural validity verified	Yes	No	
Adequacy of domains covered	Yes	No	
Methodology			
Instrument administration reported	Yes	No	
Baseline compliance reported	Yes	No	
Timing of assessments documented	Yes	No	
Missing data documented	Yes	No	
Interpretation			
Clinical significance addressed	Yes	No	
Presentation of results in general	Yes	No	

^aIf a study explicitly states an exploratory HRQOL evaluation

^bIf the HRQOL instrument is validated in the same population as the one of the trials

Table 2

Description of scientific levels of evidence and corresponding studies as outlined by the AHRQ [9]

Level of evidence	Description
Level I	Randomized controlled trials with adequate follow-up Meta analysis of multiple randomized control trials
Level II	Non-randomized, controlled prospective trial Prospective cohort studies
Level III	Well designed observational studies (e.g., comparative studies, correlation study, case control study)
Level IV	Retrospective observational studies without controls Case series
Level V	Expert opinions or committee recommendations

Table 3

Studies assessing HRQOL in breast cancer-related lymphedema patients

Author	Year	Population	Timings of assessment (after breast cancer treatment/diagnosis) mean/range	Sample size	HRQOL instrument	Efficacy Criteria compliant	Study design and evidence levels	QOL domains assessed	Findings
Speck et al. [11]	2010	Breast cancer patients	78 months Range not stated	234	BIRS SF-36	Yes	RCT (I)	Social, appearance, sexuality, psychosocial, physical, body image	BIRS scores improved significantly with twice weekly strength training exercise regardless of lymphedema status
Kim et al. [12]	2010	Breast cancer patients with lymphedema	4.3 months 0.5–68 months	40	SF-36	Yes	RCT (I)	Social, physical, energy/fatigue, psychological	Both exercise and non-exercise group had improved HRQOL but exercise group had significantly greater improvements in the role physical and general health sections of the SF-36
Homes et al. [4]	2010	Breast cancer patients (141 with lymphedema, 154 without)	Mean not stated 1–15 years	295	SF-36, BIRS	Yes	RCT (I)	Social, appearance, sexuality, psychosocial, physical, energy/fatigue, psychological	Number of arm symptoms correlated significantly with decreased HRQOL on all scales; pain most commonly associated with decreased HRQOL in patients with/without lymphedema
Tidhar& Katz-Laurer [13]	2010	BCRL patients	Study group 5 years Control group 6 years Range not stated	48	ULL-27	Yes	RCT (I)	Social, psychosocial, physical, psychological	HRQOL improved in Aqua lymphatic therapy group compared to control group who reported worsening of HRQOL with a statistically significant

Author	Year	Population	Timings of assessment (after breast cancer treatment/diagnosis) mean/range	Sample size	HRQOL instrument	Efficace Criteria compliant	Study design and evidence levels	QOL domains assessed	Findings
McClure et al. [14]	2010	BCRL patients	Treatment group 5 months Control group—14 months 5–228 months	32	SF-36	No	RCT (I)	Physical, energy/fatigue	difference between the two groups HRQOL improved significantly in patients doing breast cancer recovery program compared to the control group
Tsai et al. [15]	2008	BCRL patients	64 months 7–241 months	42	EORTC- QLQ-C30	Yes	RCT (I)	Social, physical, energy/fatigue, psychological, cognitive, body image, sexual, pain, symptoms	Emotional functional aspect of HRQOL improved in group using bandage for decongestive physical therapy but significantly decreased in group using kinesio tape with no other aspects of HRQOL changed
McKenzie & Kalda [16]	2003	Breast cancer patients with unilateral lymphedema	Mean not stated Range not stated	14	SF-36	Yes	RCT (I)	Social, physical, energy/fatigue, psychological	HRQOL improved in exercise group (not statistically significant change)
Williams et al. [17]	2002	BCRL patients	125.9 months Range not stated	31	EORTC- QLQ-C30	No	RCT (I)	Psychological, pain, symptoms, sleep	Manual lymphatic drainage improved emotional function and decreased sleep disturbance significantly
Vassard et al. [18]	2010	Breast cancer patients (125 with lymphedema, 508 without)	Mean not stated 1 month–5 years	633	EORTC- QLQ-C30	Yes	Prospective cohort (II)	Social, physical, psychological, emotional	Patients with lymphedema had significantly reduced emotional well-being and adjustments to life compared to women without it
Sagen et al. [19]	2009	Breast cancer patients	Mean not stated Baseline–5 years	204	EORTC- QLQ-C30	No	Prospective cohort (II)	Physical, energy/fatigue, symptoms	HRQOL improved significantly from 6 months – 5 years in patients following an exercise

Author	Year	Population	Timings of assessment (after breast cancer treatment/diagnosis) mean/range	Sample size	HRQOL instrument	Efficace Criteria compliant	Study design and evidence levels	QOL domains assessed	Findings
Paskett et al. [20]	2007	Stage I/II breast cancer within previous 8 months	Mean not stated Baseline–3 years	627	FACT-B SF-12	Yes	Prospective cohort (II)	Unable to determine	physiotherapy regime Patients reporting arm swelling had significantly decreased HRQOL
Kim, Yi & Kwon [21]	2007	BCRL patients	2.5 years 3 months–5 years	53	SF-36	Yes	Prospective cohort (II)	Social, physical, energy/fatigue, psychological,	HRQOL significantly improved at 1–6 months after CDT
Cheema et al. [22]	2006	Breast cancer survivors (Dragon boat team members)	5.8 years 1–22 years	34	WHOQOL- BREF	Yes	Prospective cohort (II)	Social, physical, psychological	Upper body resistance training significantly improved HRQOL in breast cancer patients with lymphedema without exacerbating lymphedema
O'Neill & Beatus [23]	2006	BCRL patients	Mean not stated 3 months–28 years	17	COOP	No	Prospective cohort (II)	Physical, psychological, pain	CDT significantly improved HRQOL in BCRL patients
Bronson et al. [24]	2006	BCRL patients	10 years 1–43 years	49	NHP, PGWB HAD	No	Prospective cohort (II)	Social, physical, energy/fatigue, psychological, pain, sleep	Liposuction and conservative compression therapy (CCT) reduced pain and improved emotional well-being significantly compared to CCT alone
Wilburn et al. [25]	2006	BCRL patients	103 months 36–288 months	10	SF-36	No	Prospective cohort Cross-over design (II)	Psychosocial, physical	No change found in HRQOL with either flexitouch or compression therapy compared to baseline
Strauss-Blasche et al. [26]	2005	Breast cancer patients (105 with lymphedema, 44 without)	Median 18 months 3–72 months	149	EORTC-QLQ-C30	Yes	Prospective cohort (II)	Social, physical, energy/fatigue, cognitive, pain, symptoms, emotional	HRQOL improved significantly 2 weeks before rehabilitation-to end of

Author	Year	Population	Timings of assessment (after breast cancer treatment/diagnosis) mean/range	Sample size	HRQOL instrument	Efficace Criteria compliant	Study design and evidence levels	QOL domains assessed	Findings
Mondry et al. [27]	2004	BCRL patients	Mean not stated Range not stated	20	FACT-B	Yes	Prospective cohort (II)	Unable to determine	rehabilitation (no distinction of BCRL patients) HRQOL improved significantly with CDT
Tumer et al. [28]	2004	Breast cancer patients (2 patients with lymphedema)	17 months 4–60 months	10	FACT-B	No	Prospective cohort (II)	QOL	HRQOL improved significantly with exercise program and did not precipitate onset of lymphedema
Coster Pole, Fallowfield [29]	2001	279 breast cancer patients pre-ALND with WLE/mastectomy versus 29 with lymphedema after ALND	Mean not stated Range not stated	308	FACT-B +4	No	Prospective cohort (II)	Social, physical, symptoms, emotional	HRQOL is significantly lower in lymphedema patients compared to patients pre-ALND
Velanovitch & Szymanski [30]	1999	Breast cancer patients without ALND, with ALND but no lymphedema and with ALND and lymphedema	Mean not stated 6 months–4 years	101	SF-36	No	Prospective cohort (II)	Social, physical, energy/fatigue, psychological,	HRQOL significantly reduced in patients with BCRL
Mitrolo et al. [31]	1995	Post-mastectomy patients with lymphedema	8.3 years 6 months–37.6 years	25	FLJC WCLS	Yes	Prospective cohort (II)	Social, physical, psychological, symptoms	HRQOL decreased during intensive phase of CDT but improved in self-management phase with gentle massage and compression bandaging at home
Beaulac et al. [32]	2002	Breast cancer patients with ALND	Mean not stated 1–4.8 years	151	FACT-B	No	Retrospective cohort (III)	Physical, symptoms, emotional	HRQOL significantly lower in patients with BCRL
Nesvold et al. [33]	2010	Breast cancer patients with lymph node metastases	4.1 years Range not stated	256	SF-36	No	Case control (III)	Social, physical, energy/fatigue, psychological,	BCRL patients had no significant change in HRQOL as assessed by the SF-36 compared to patients with arm/shoulder problems

Author	Year	Population	Timings of assessment (after breast cancer treatment/diagnosis) mean/range	Sample size	HRQOL instrument	Efficace Criteria compliant	Study design and evidence levels	QOL domains assessed	Findings
Nesvold & Reinertsen [34]	2010	Breast cancer survivors with ALND and radiotherapy (17 % with lymphedema)	4.1 in 2004 and 7 years in 2007 Range not stated	255 (2004) 187 (2007)	SF-36 IOC EORTC-QLQ-C30	Yes	Cross-sectional survey (III)	Social, sexuality, psychological, body image	after surgical treatment and local radiation for breast cancer. Patients with self-rated lymphedema reported lower HRQOL on most SF-36 domains
Chachaj et al. [35]	2010	Breast cancer patients	6.3 years Range not stated	328	EORTC-QLQ-C30 EORTC-QLQ- BR23	No	Cross-sectional survey (III)	Physical, psychological, pain	BCRL patients had significantly decreased HRQOL compared to patients without lymphedema
Mak et al. [36]	2009	Breast cancer patients with ALND (101 with lymphedema and 101 without)	3.5 years 4 months-13 years	202	FACT-B +4	No	Case control (III)	Social, physical, symptoms, emotional	BCRL patients had significantly decreased HRQOL compared to patients without lymphedema
Rodrigues-Paim et al. [37]	2008	Breast cancer patients with either ALND or SLNB	23 months 6-60 months	60	FACT-B	No	Cross-sectional (III)	Social, sexuality, physical, body image, pain, emotional	No statistically significant correlation with lymphedema and HRQOL and no significant difference between ALND and SLNB with HRQOL
Ahmed et al. [2]	2008	Breast cancer patients with and without lymphedema, and arm symptoms without lymphedema	8.1 years Range not stated	1,287	SF-36	No	Cross-sectional survey (III)	Social, physical, energy/fatigue, psychological,	BCRL patients had significantly decreased HRQOL compared to patients without lymphedema
Pyszczel et al. [38]	2006	Breast cancer patients (181 with lymphedema and 84 without)	Mean not stated Range not stated	283	EORTC-QLQ- C30 EORTC- QLQ- BR23	Yes	Cross-sectional survey (III)	Social, physical, energy/fatigue, psychological, cognitive, body image, sexual, pain, symptoms, sleep	Patients with lymphedema have significantly reduced HRQOL and increased psychological distress compared to those without lymphedema.

Author	Year	Population	Timings of assessment (after breast cancer treatment/diagnosis) mean/range	Sample size	HRQOL instrument	Efficace Criteria compliant	Study design and evidence levels	QOL domains assessed	Findings
Ridner et al. [39]	2010	BCRL patients	Mean not stated Range not stated	58	ULL-27	No	Cross-sectional survey (IV)	Unable to determine	Patients with more lymphedema symptoms have poorer HRQOL (not statistically significant)
Karadibak et al. [40]	2008	ALND and SLNB patients with breast cancer and lymphedema	Mean not stated Range not stated	62	FACT-B +4	No	Cross-sectional (IV)	Social, physical, psychological	HRQOL increases significantly after decongestive physiotherapy
Dawes et al. [41]	2008	Stage I/II breast cancer patients	3.6 years Range not stated	204	SF-36 EORTC- QLQ-C30	No	Cross-sectional survey (IV)	Social, physical, energy/fatigue, psychological, cognitive, body image, sexual, pain, symptoms, sleep, emotional	Patients with self-reported lymphedema have significantly reduced HRQOL
Heiney et al. [42]	2007	Breast cancer survivors	Median 37.8 months 1 month–15 years	557	HRQOL-BCV	No	Cross-sectional survey (IV)	Social, physical, psychological, emotional	HRQOL significantly lower in lymphedema patients, younger, and less educated patients
Ridner [43]	2005	Breast cancer patients (64 with lymphedema, 64 without)	73 months Range not stated	128	FACT-B +4 ULL-27 WCLS	No	Retrospective observational study (IV)	Social, physical, psychological	HRQOL significantly reduced in BCRL patients
Wilson et al. [44]	2005	Breast cancer patients (32 with lymphedema, 78 without)	Mean not stated Range not stated	110	SF-36 FLIC	No	Cross-sectional survey (IV)	Social, physical, energy/fatigue, psychological, symptoms	HRQOL significantly worse in BCRL patients compared to patients without lymphedema
Pain et al. [45]	2003	BCRL patients	8 years 1–37 years	48	SF-36	No	Cross-sectional (IV)	Social, physical, energy/fatigue, psychological	Impairment of manual dexterity in BCRL patients has greater (not statistically significant) impact on reducing psychological well-being compared to symptoms of excess arm volume in these patients

Author	Year	Population	Timings of assessment (after breast cancer treatment/diagnosis) mean/range	Sample size	HRQOL instrument	Efficace Criteria compliant	Study design and evidence levels	QOL domains assessed	Findings
Kwan et al. [46]	2002	Invasive/in situ breast cancer patients (14 with lymphedema, 98 without)	Mean not stated 2–7 years	112	EORTC-QLQ-C30	Yes	Cross-sectional survey (IV)	Social, physical, energy/fatigue, psychological, cognitive, body image, sexual, pain, symptoms, sleep, emotional	Patients with lymphedema and arm symptoms have substantial impairment of HRQOL compared to asymptomatic patients (not statistically significant)
Kirshbaum et al. [47]	1996	Breast cancer patients	1 week–15 years	16	SF-36 EORTC-QLQ-C30	No	Retrospective observational study (IV)	Social, physical, energy/fatigue, psychological, cognitive, body image, sexual, pain, symptoms, sleep, emotional	Using guidelines for management of BCRL patients resulted in slight improvement (not statistically significant) in HRQOL in 75 % of patients

RCT randomized controlled trial. *NA* not available, *BCRL* breast cancer-related lymphedema, *CDT* complex decongestive therapy, *SF-36/SF-12* Medical Outcome Study-Short Form, *FACT-B* functional assessment of cancer therapy—breast, *FACT-B +4* functional assessment of cancer therapy—breast cancer subscale with five lymphedema-specific questions, *WHOQOL-BREF* World Health Organization Quality of Life assessment—abbreviated version, *EORTC-QLQ C-30* European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core questionnaire version 3.0, *EORTC-QLQ BR23* European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Breast cancer module 23, *ULL-27* upper limb lymphedema 27, *WCLS* Wesley Clinic Lymphedema Scale, *FLIC* Functional Living Index-Cancer, *COOP/Dartmouth* Primary Care Cooperative Information Project healthcare questionnaire, *BIRS* body image and relationships scale, *NHP* Nottingham Health Profile, *PGWB* Psychological General Well-Being Index, *HAD* hospital anxiety depression scale, *QLQ-BCV* quality of life—breast cancer patient version, *IOC* impact of cancer scale, *ALND* axillary lymph node dissection, *SLNB* sentinel lymph node biopsy