



Features, Predictors, and Treatment of Breast Cancer–Related Lymphedema

Xiaochen Zhang¹ · Jill M. Oliveri¹ · Electra D. Paskett¹

Accepted: 28 August 2020 / Published online: 9 September 2020
© Springer Science+Business Media, LLC, part of Springer Nature 2020

Abstract

Purpose of Review Breast cancer–related lymphedema (BCRL) is a common sequelae among breast cancer survivors. This review provides updated information on recent studies to prevent, diagnose, and actively treat women with BCRL.

Recent Findings In total, 63 articles were identified from 2015 and 2020 that assessed incidence, risk factors, surveillance, measurement and definition, treatment, and awareness of BCRL. Depending on the approach and timing of assessment, BCRL incidence rates ranged from 9.1 to 39%. Modified radical mastectomy, number of positive lymph nodes, and postoperative complications were linked to BCRL risk, in addition to chemotherapy, radiation, axillary lymph node dissection, advanced cancer stage, and higher body mass index. Early detection showed favorable BCRL outcomes (e.g., severity, symptoms). Exercise, self-management, complete decongestive therapy, bandaging, and surgery had positive effects on BCRL outcomes.

Summary Numerous gaps exist within BCRL literature, such as the value of self-reported surveillance options to identify BCRL early, measurement strategies, and definitions of BCRL. In terms of policies, efforts are needed to educate providers, patients, payers, and legislators about the need for consensus to reduce the burden of BCRL in women being treated for breast cancer.

Keywords Breast cancer–related lymphedema · Survivorship · Surveillance · Symptoms · Quality of life

Introduction

Breast cancer is the second most common cancer among women in the United States (U.S.), with one in 8 women developing breast cancer during their lifetime [1]. Due to early detection from screening and advances in treatment, more than 3.8 million breast cancer survivors were living in the U.S. in 2019 [2]. As women with breast cancer are living longer, cancer treatment–related sequelae are important issues.

Women who receive breast cancer treatment, such as radiation and lymph node removal (both complete dissection and sentinel), have a lifetime risk of developing breast cancer–related lymphedema (BCRL) [3, 4]. Depending on

the method of measurement, threshold of diagnosis, length of follow-up, and study population, the incidence of BCRL ranges from 9.1 to 39% [5–14]. BCRL results from disruption of the lymphatic system which prevents adequate drainage from lymphatic vessels. The accumulation of excess protein-rich lymph fluid can cause abnormal swelling in the upper extremity near and distal to the treatment site [15, 16]. In the early stages of BCRL, soft tissue swelling is observed due to lymphatic edema. As BCRL progresses, the tissue consistency becomes more firm and is characterized by fibrosclerosis and fat deposition [17]. Women with BCRL may experience pain, arm tightness, fullness, heaviness, impaired upper extremity mobility and function, psychological distress, and poorer quality of life (QOL) [15, 18–20]. BCRL may also negatively affect breast cancer survivors' ability to engage in activities of daily living and maintain employment, as well as increasing financial burden due to incremental out-of-pocket costs of BCRL management [18, 21–23].

The recent National Comprehensive Cancer Network (NCCN) guidelines for BCRL focus on prospective screening, education, and intervention [24]. Among women at risk of developing BCRL, the goal of secondary

This article is part of the Topical Collection on *Lymphedema Incidence, Prevention and Treatment*

✉ Electra D. Paskett
electra.paskett@osumc.edu

¹ Division of Population Sciences, Comprehensive Cancer Center, The Ohio State University, 1590 N High Street, Suite 525, Columbus, OH, USA

prevention is to control arm swelling and manage BCRL symptoms. In order to do so, the NCCN guidelines recommend pretreatment limb measurement of both arms at baseline. When a woman treated for breast cancer notices swelling or other BCRL symptoms on the treated side, her healthcare provider should be notified. Healthcare providers should be notified immediately if a woman with or at risk for BCRL experiences signs of infection in the affected area. The NCCN guidelines also suggest that survivors should be educated about strategies for self-care management, such as infection prevention measures, risk reduction strategies, and maintenance of skin integrity on the affected side. As BCRL negatively affects survivorship quality among women with breast cancer, it is necessary to consider current guidelines for clinical practice and review recent studies to prevent, diagnose, and actively treat women with BCRL.

Review of Recent Studies in BCRL

A narrative review of the literature was conducted in the PubMed database using the search term “breast cancer–

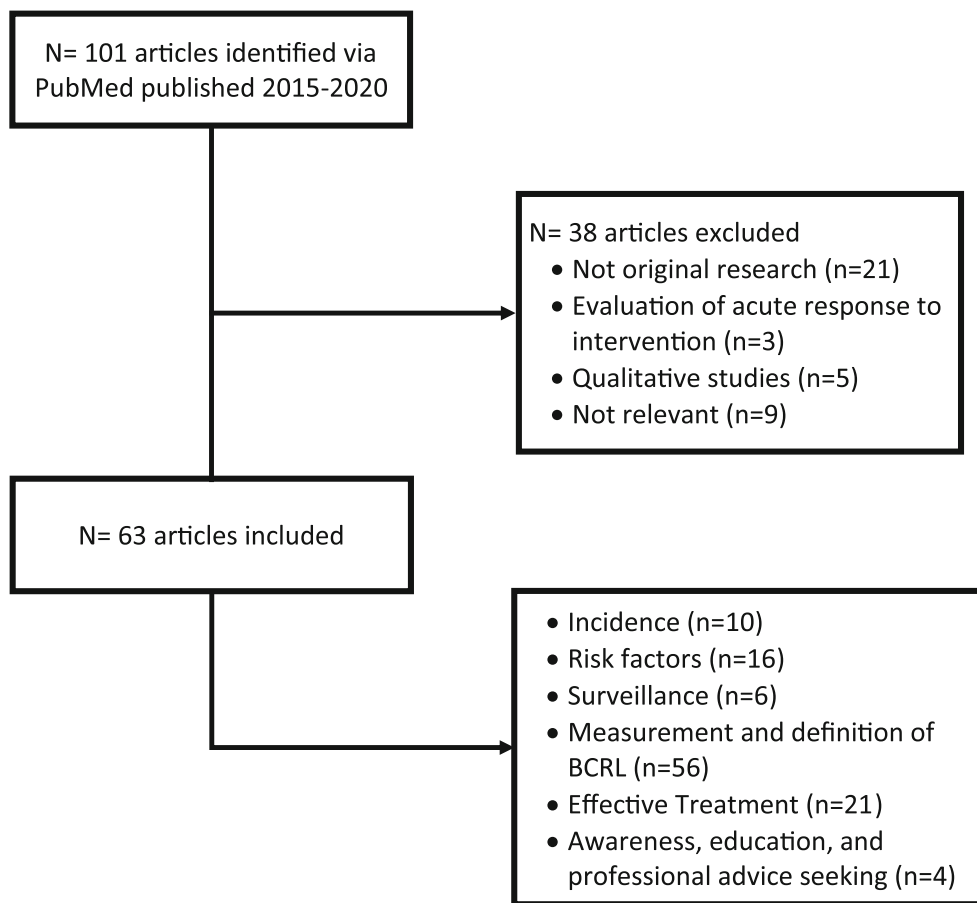
related lymphedema” and restricted to articles published between 2015 and 2020. We initially identified 101 relevant articles (Fig. 1), with 38 articles excluded due to not reporting original research ($n = 21$), acute response to intervention ($n = 3$), qualitative studies ($n = 5$), and lack of relevance ($n = 9$). The 63 articles included in this paper focused on BCRL incidence ($n = 10$), risk factors ($n = 16$), surveillance ($n = 6$), measurement and definition of BCRL ($n = 56$), effective treatment ($n = 21$), and awareness, education, and professional advice-seeking ($n = 4$).

Incidence

Incidence rates for BCRL vary depending on several factors, including surgery type (axillary lymph node dissection (ALND) vs. sentinel lymph node dissection (SND)), surveillance method (self-report, bioimpedance spectroscopy [BIS], arm circumference, perometry), and timing. Cumulatively, within the past 6 years, published incidence rates ranged from 9.1 to 39% [5–14].

Several investigators still assessed BCRL incidence using self-report [11–13], while others relied on BIS or arm circumference for diagnosis [7, 8, 14]. Koelmeyer et al. ($N = 753$)

Fig. 1 Articles included in the current breast cancer reports



*some articles are located at ≥ 1 categories

demonstrated that the timing of surveillance initiation may play a role in BCRL diagnosis [8]. When surveillance via BIS began more than 90 days post-surgery, 39% of those screened met the criteria for BCRL; however, if surveillance began pre-surgery or within 90 days of surgery, only 14% were diagnosed with BCRL. Others noted a similar increasing trend over time [14], with most patients with BCRL reporting mild (68%) or moderate (24%) severity.

Risk Factors

Consistent with previous literature, recent studies demonstrated that receipt of chemotherapy (type not specified) [5, 10, 13], radiation [5, 10, 14], and axillary lymph node dissection (ALND vs. SND) [5, 10, 14], as well as advanced cancer stage [5, 10] and higher body mass index [10, 14, 25] were associated with higher risk of BCRL. Other factors, such as modified radical mastectomy [14], number of positive lymph nodes [14], and post-operative complications [13], were also linked to increased risk of BCRL.

When using BIS measurement to indicate clinical lymphedema (lymphedema index [L-Dex] score ≥ 10), women with ALND or regional nodal irradiation had a higher L-Dex score [6, 26]. Those with more severe BCRL as measured by higher inter-limb volume difference were associated with lower education, increasing time since cancer treatment, receipt of ALND, and receipt of BCRL care ($N=331$) [27]. Among women with BCRL who underwent complete decongestive therapy (a treatment strategy for BCRL), older age and longer duration of tamoxifen use were associated with greater pre-treatment arm volume, while lower activity level, shorter post-operative duration, and greater post-operative weight gain were associated with greater post-treatment arm volume [28]. Additionally, older age (≥ 50 years), receipt of ALND, radiation, and/or chemotherapy, advanced cancer stage disease, and abdominal obesity were associated with greater severity of lymphedema [29, 30]. In another study ($N=342$), lymph node metastasis, weight gain since surgery, and greater inter-limb circumferential difference were associated with increased risk of persistent BCRL [31].

Among women at risk for BCRL ($N=462$), those who had greater self-efficacy regarding the ability to manage BCRL and experienced BCRL-related emotional distress were more likely to seek professional healthcare advice if symptoms arose [32]. Alcorso et al. ($N=166$) found that medical history and psychosocial factors were associated with adherence to BCRL self-management strategies [33]. For example, greater time since lymphedema diagnosis and higher levels of BCRL distress were associated with lower levels of adherence to self-management strategies, while those who underwent hormone replacement therapy, had higher knowledge about BCRL, and had positive beliefs about personal control of BCRL were associated with higher levels of adherence to these strategies [33].

Regarding physical function, BCRL chronicity and severity were not associated with arm weakness. However, depressive mood, fear of using the affected arm, receipt of advice to restrict use of the affected arm, activity limitation in the affected arm, and less upper extremity physical activity were associated with higher risk of arm weakness ($N=80$) [34]. Consequently, women who had arm weakness also self-reported poorer upper extremity physical function [34, 35]. Women with greater fear of lymphedema, more pain, BMI ≥ 25 kg/m², receipt of mastectomy, and receipt of ALND reported lower function, whereas women with higher emotional well-being and who had chemotherapy reported higher function. Interestingly, low-level changes in arm volume (relative volume change 5–10%) and clinical BCRL (relative volume change $\geq 10\%$) did not impact women's ability to use the affected arm for activities of daily living among those with BCRL ($N=324$) [35].

Surveillance

Routine surveillance beginning prior to surgery or the start of neoadjuvant therapy offers the best opportunity for early detection of BCRL. Early detection allows for early treatment which can reduce the severity of BCRL. An increasing focus in BCRL research is the use of BIS as a feasible and useful surveillance tool to assess limb volume and identify subclinical swelling. Kaufman et al. assessed breast cancer patients for BCRL pre-surgery via BIS ($N=206$) [6]. Those who were diagnosed with subclinical BCRL and subsequently treated with over-the-counter compression garments for 4 weeks did not progress to chronic BCRL, even when they were high-risk (i.e., ALND, radiation, and/or neoadjuvant chemotherapy). Similar results have been published by others [7, 9, 36, 37]. Kilgore et al. ($N=146$) noted that the mean time to BCRL onset was less than 1 year post-surgery [7], and Ridner et al. ($N=508$) reported that significantly more patients assessed via arm circumference measurement required compression garment use ($p<0.001$) and began using the garments sooner compared with patients assessed with BIS ($p<0.002$) [36]. One Australian study ($N=753$) examined surveillance timing and found that fewer breast cancer patients who began surveillance via BIS pre-surgery or within 90 days of surgery were diagnosed with BCRL (14%) compared with patients who began BIS surveillance more than 90 days post-surgery (39%; $p<0.001$). Those who began surveillance later also reported more severe disease [8].

Measurement and Definition of BCRL

Arm Circumference and Volume

The definition and cut points of BCRL using arm circumference differed by study, which led to variations of BCRL prevalence across studies. For example, Zou et al. ($N=387$) used

an absolute circumference change of 2 cm in the affected arm at any point after breast cancer surgery [14]. Between 1 and 24 months post-surgery, 2.5–29.4% women experienced BCRL onset. Among women who developed BCRL, severity also changed over time. Between 1 and 24 months post-surgery, 53.8–68.4% women had mild (circumference change \leq 4 cm), 23.7–46.2% had moderate (circumference change 4–6 cm), and 0–7.9% had severe BCRL (circumference $>$ 6 cm) [14]. Yoon et al. ($N=33$) used the maximal circumference difference to classify BCRL severity from mild ($<$ 2 cm) to moderate or above (\geq 2 cm). According to this criteria, 42% had mild and 58% had above moderate BCRL [29].

Penn et al. defined BCRL as having a circumference difference \geq 1 cm between arms or having a circumference difference $<$ 1 cm, but having evident pitting edema or subcutaneous tissue hardening [31], whereas Buchan et al. ($N=41$) used an inter-limb circumference difference \geq 5% indicating clinical lymphedema [38]. Moreover, the inter-limb circumference difference among women with BCRL varied across studies by measurement methods. The average inter-limb circumference difference calculated using the sum of arm circumferences ranged from 2 to 7% [38–42], while using truncated cone formula to calculate the inter-limb circumferential difference ($N=128$), the average difference was 15% [39].

Similarly, the inter-limb volume difference varied across studies by measurement methods. BIS is routinely used to measure arm volume [7–9, 29, 36, 38, 39, 43]. Reported inter-limb BIS ratios ranged from 1.0 to 3.7%, with a ratio \geq 3 indicating lymphedema [38, 39, 43]. L-Dex is another commonly used ratio, comparing the extracellular fluid of the affected and non-affected limbs by BIS [44]. Among women with BCRL, the L-Dex scores ranged from 16.1 to 23.5, varied by garment use status [8, 40], and progressed over time with an average increase of 1.6–2.3 L-Dex units per year [8].

The International Society of Lymphology recommended calculating arm volume from circumferences using the truncated cone formula [28, 36, 45–52]. The average inter-limb volume difference (percentage of excess volume) ranged from 20 to 34% among women with BCRL [28, 48–50]. Using this method among 32 women with BCRL, 14–22% had mild lymphedema (inter-limb volume difference \leq 250 mL), 22–29% had moderate (inter-limb volume difference 250–500 mL), and 56–57% had severe lymphedema (inter-limb volume difference $>$ 500 mL) [45]. The Upper Extremity Lymphedema Index (UEL index) was developed to assess arm volume calculated from circumferences and adjusted for BMI [53]. The average UEL index was 103.6 ($N=50$, range 73.4–143.3) [30], and the inter-limb difference in UEL index was 16.2 before BCRL treatment ($N=25$) [54]. Among women with BCRL ($N=50$), those $>$ 50 years and cancer stage $>$ 3 were more likely to have a higher UEL index [30].

When using displaced water to quantify BCRL severity, the inter-limb volume differences ranged from 16 to 25%

(sample size ranged from 41 to 141) [39, 55, 56]. Among women with BCRL (sample size ranged from 23 to 141), 20–61% had grade 1, 39–42% had grade 2, and 0–31% had grade 3 lymphedema according to the NCI Common Terminology Criteria for Adverse Events (CTCAE) v3.0 [39, 56, 57]. When using an optoelectronic perometer to quantify inter-limb volume, the average inter-limb volume difference among women with BCRL ranged from 2 to 13% (sample size range from 26 to 296) [27, 34, 43, 51]. Among women with BCRL ($N=129$), 49–59% had inter-limb volume difference $<$ 5%, 14–16% had inter-limb volume difference 5–9.99%, 8–20% had inter-limb volume difference 10–19.99%, and 14–17% had inter-limb volume difference \geq 20% [51].

Other measures of BCRL have been investigated to potentially allow measurement in non-clinical settings. Self-report and self-measurement of BCRL symptoms, arm circumference, and risk assessment have been studied in the recent past. Self-reported lymphedema symptoms successfully identified women at risk for BCRL and those with BCRL ($N=250$), focusing on the number of symptoms reported rather than the symptoms themselves [58]. Other researchers developed a clinical evaluation tool that could standardize BCRL assessment (Breast Cancer-related Lymphedema of the Upper Extremity [CLUE]), which incorporated multiple constructs with results compared with findings from perometry, clinician assessment, and self-report ($N=71$). The developers are currently examining the tool's response to change over time [59]. Rafn et al. studied the reliability and validity of arm circumference self-measurement by patients with and without BCRL ($N=41$), with comparisons with physical therapists' arm circumference measurements, as well as perometry to assess volume [60]. Agreement was strong and self-efficacy was high without increasing patient anxiety. The Risk Assessment Tool Evaluating Lymphedema (RATE-L) developed by Basta et al. estimated BCRL risk accurately and was easy to use ($N=3136$) [5].

Arm Function and Strength

According to objective dynamometer measured strength (lbs), women with BCRL ($N=20$) had lower arm strength in the affected arm compared with the unaffected arm in shoulder abduction (26.65 vs. 28.31 lbs), but similar in elbow flexion (40.41 vs. 41.34 lbs), wrist flexion (24.28 vs. 24.21 lbs), and grip strength (64.68 vs. 64.47 lbs) [46]. While among 80 women with BCRL, 61–97% self-reported arm weakness, only 36% women were classified as having impaired arm strength according to an objective measure using grip strength [34].

Range of motion (ROM) is another objective function assessment measured by goniometer for women with BCRL [61]. The ROM for the affected shoulder ranged from 126 to

166° in flexion, 24–37° in extension, 107–156° in abduction, 25–39° in adduction, 48–90° in external rotation, and 25–68° in internal rotation (sample size ranged from 20 to 69) [11, 46, 48, 62]. Mazor et al. ($N=20$) found that compared with the unaffected arm, ROM in the affected arm was lower in shoulder flexion, abduction, external rotation, and wrist extension, but not in elbow flexion, extension, and wrist flexion [46]. When assessed by self-reported questionnaire, 11% of women with BCRL experienced ROM deficits ($N=32$) [45].

Additionally, clinical features of the affected arm can be evaluated by ultrasound. Jang et al. ($N=47$) found that 87% of women with BCRL had detectable abnormalities in the affected shoulder. Specifically, 28% had a supraspinatus tendon tear, 55% had subdeltoid bursal thickening, 30% had distension of the biceps brachii tendon sheath, and 23% had adhesive capsulitis [63].

The Disability of Arm, Shoulder, and Hand Questionnaire (DASH) is a valid, commonly used assessment for women with BCRL to evaluate upper extremity limitations and the ability to perform functional activities, with a higher score indicating a higher level of functional ability [34, 35, 38, 48, 51, 63–66]. The average DASH score among women with BCRL ranged from 27 to 60 (sample size ranged from 47 to 129) [34, 48, 51, 63, 65], and among women who underwent breast cancer treatment ($N=61$), it was 15–34 [64]. Findings are consistent when using the shorter version of DASH questionnaires, the Quick-Disabilities of Arm, Shoulder, and Hand ($N=160$) [67].

BCRL Symptoms and Severity

The Norman Lymphedema Questionnaire is commonly used for self-reported BCRL symptoms and severity [68]. A score of 1–3 indicates mild edema, 4–6 moderate edema, and 7–9 severe edema. Among women with BCRL (sample size ranged from 41 to 387), the average score ranged from 0.7 to 2.0, and 44–63% were classified as mild edema, 25–48% were moderate edema, and 0–15.1% were severe edema [14, 25, 38, 39, 56]. The average number of symptoms ranged from 5 to 6 (sample size ranged from 41 to 141) [38, 51, 56]. Although the number of symptoms did not change, symptom severity decreased over time without statistical significance ($N=41$) [40].

The International Society of Lymphology staging is another approach to define BCRL severity. Specifically, stage 1 was defined as mild edema which was reversible with appropriate limb position (with/ without pitting), stage 2 was moderate edema that was not reversible with limb elevation (pitting was present except in late stage 2 when more fibrosis occurs), and stage 3 was lymphostatic elephantiasis with trophic skin changes [69]. Using this definition, 8–54% women with BCRL were classified as stage 1, 38–64% were stage 2, and 1–31% were stage 3 (sample size ranged from 41 to 180) [38, 50, 70]. Schmitz et al. recently developed a valid and reliable

clinical assessment (CLUE) to assess upper extremity symptoms including obscuration and contour, tissues texture, and edema among breast cancer survivors ($N=351$) [59, 71].

Penn et al. focused on persistent lymphedema among 342 women with BCRL [31]. They found that 67% breast cancer survivors with unilateral arm swelling had persistent lymphedema, and 47.6% had mild (circumference difference ≤ 2 cm), 27.9% had moderate (circumference difference 2.1–3 cm), and 24.4% had severe (circumference difference > 3 cm) [31] swelling. Using BIS, Kilgore et al. found that 6% of women at risk for BCRL ($N=146$) may have persistent lymphedema. In addition, women with more positive nodes were more likely to have persistent BCRL, but time to onset of BCRL, clinical tumor size, and number of lymph nodes were not associated with the risk of persistent BCRL [7].

Most women who had BCRL experienced shoulder/arm pain (sample size ranged from 41 to 324) [11, 13, 34, 35, 48, 55, 63, 65, 72]. A self-reported visual analog scale (0–10 or 0–100) is commonly used to assess pain. On average, women with BCRL (sample size ranged from 41 to 169) reported experiencing a moderate level of shoulder/arm pain [11, 48, 55, 65, 72].

Various BCRL-related symptoms were evaluated across studies. Visual analog scales were self-reported in terms of arm heaviness [48, 72], tightness [48, 62, 65], sensation of weight, tension, sense of numbness, and limitation of daily living activities [62, 65]. Among women with BCRL ($N=134$), 37% experienced at least one cellulitis episode since diagnosis [49] and had an average of 2.2–2.8 episodes of cellulitis per year ($N=180$) [41]. Other BCRL-related symptoms, such as stiffness [47], chronic skin damage [13], fibrosis [13], peripheral neurologic symptoms [13], and BCRL recurrence [38], were also examined across individual studies. Ochalek et al. ($N=45$) used stiffness index to compare active-resting pressures under the sleeve between affected and unaffected arms and found the average stiffness index was 10 mmHg [47]. In a study conducted by Rupp et al., among women who underwent breast-conserving cancer treatment who had BCRL ($N=284$), 59% reported chronic skin damage, 51% reported fibrosis, and 67% reported peripheral neurologic symptoms [13]. Buchan et al. ($N=41$) examined BCRL presentation and found 36.6% of women had recurrent BCRL [38].

Quality of Life

Various questionnaires have been developed and used among women with BCRL to evaluate QOL, including the Lymphedema Quality of Life (LYMQoL) [41], EORTC QLC-C30 [12, 73] and EORTC QLQ-BR23 [12], Functional Assessment of Cancer Therapy-Breast +4 (FACT-B+4) [38], Lymphedema Symptom Intensity and Distress Scale-Arm (LSIDS-A) [67], Profile of Mood States-Short (POMS) [67], Coping Orientation to Problems Experienced (COPE) [67], Medical Outcome Study (MOS) Social Support Survey [67], Lymphedema Evaluation Following Treatment of Breast

Cancer (LEFT-BC) [35], and the Lymphedema International Classification of Functioning (LYMPH-ICF) questionnaires [54]. A new 14-item QOL scale developed by Williams et al. for those with upper limb lymphedema was both feasible and valid for use in multiple settings, as well as being responsive to change [74]. A newer QOL questionnaire developed by De Vrieze was also shown to be responsive to change [75].

Although QOL questionnaires differed across studies, women with BCRL reported consistent physical and psychological burden, including fear of lymphedema, difficulty with activities of daily living, minimization of arm use due to BCRL, impairment of shoulder/arm movement, poorer physical and emotional well-being, and lower scores in the domains of role, cognitive, social, behavioral, sexuality, neurological symptoms, general health, future perspective, mood, fatigue, coping, appearance, breast symptoms, arm symptoms, and overall QOL [12, 13, 34, 35, 38, 41, 49, 54, 67, 73].

Healthcare Utilization, Financial Toxicities, and Occupational Impact

Recent studies examined healthcare utilization among women with BCRL. Women with BCRL ($N = 753$) who had completed at least 6 months of BCRL surveillance had 4 healthcare visits per year on average [8]. Within 2 years after breast cancer surgery ($N = 56,075$), 2.3% women with BCRL had at least 1 hospitalization for complicated lymphedema [76]. Compared with women without BCRL, women with complicated BCRL had higher rates of all-cause admissions (IRR = 5.02, 95%CI 4.76–5.29) and higher rates of lymphedema-related admissions (IRR = 2.09, 95% CI 1.93–2.26) [76]. In terms of long-term healthcare in breast cancer survivorship, Cheville et al. ($N = 1800$) evaluated various aspects of healthcare utilization, including (1) evaluation and management, (2) procedures, (3) imaging, (4) tests, (5) durable medical equipment, (6) physical/occupational therapy, (7) other, and (8) exceptions/unclassified categories [77]. Women with BCRL used > 30% more overall services annually compared with breast cancer survivors without BCRL, and the increasing utilization of each aspect ranged from 24.6 to 97.4%. Although the increased utilization attenuated over time, it persisted for at least 10 years after diagnosis [77].

Compared with women without BCRL ($n = 54,796$), women with BCRL ($n = 1279$) had higher total healthcare costs (\$58,088 vs. \$31,819 per patient) [76]. In a study ($N = 129$) where 98% of breast cancer survivors had insurance, the annual health-related out-of-pocket costs excluding productivity losses was higher among those with BCRL compared with those without BCRL (\$2306 vs. \$1090), corresponding to a 112% higher cost [51]. About half of the out-of-pocket costs were attributed to lymphedema-related needs. Higher out-of-pocket cost was linked to delayed retirement, reduced employment, and increased inability to access lymphedema care [51].

Additionally, women with BCRL faced higher overall monthly direct costs, higher office visit co-pays, higher costs of medication, and higher other out-of-pocket costs [51].

Among women with BCRL ($N = 134$), more than half reported that lymphedema affected their careers (e.g., work disturbance, changed relationship with colleagues and superior, workplace adaptations), especially among those with severely impaired arm use [49]. Those who had higher global and lymphedema-related impairments (e.g., dominant arm lymphedema) were more likely to have arm-use limitations for professional activities. In addition, 7.5% women with BCRL had job changes related to BCRL or treatment [49].

Effective Treatment

Exercise

Exercise continues to be a widely studied treatment modality for BCRL, with many studies reporting positive outcomes. Zhang et al. found that among BCRL patients ($N = 141$) who participated in slowly progressive weight-lifting for 12 months, arm composition (e.g., lean mass, bone mineral density and arm fat) improved, and improvements in lean muscle mass were associated with lower BCRL severity [56]. Another study ($N = 69$) combined aerobic activity with strength-training, and after 4 weeks, patients reported better shoulder ROM and pain when compared with patients receiving decongestive therapy ($p < 0.05$) [11]. When aerobic activity and resistance training were evaluated separately, Buchan et al. ($N = 41$) observed no change in BCRL status for either group after 12 weeks; however, clinically meaningful improvements in endurance, aerobic fitness, and QOL were noted for both groups, although they were not significant [38]. Considering alternatives to aerobic and resistance-training activities, BCRL patients ($N = 40$) who participated in an 8-week yoga intervention reported no significant change in limb volume, although significant improvement in QOL was noted ($p < 0.05$) [73]. Schmitz et al. ($N = 351$) found that overweight BCRL patients who participated in a home-based exercise and weight loss program for 1 year (included walking plus resistance training, meal replacements, and lifestyle modification counseling) experienced no significant improvement in limb volume, suggesting that a facility-based program may produce better results [71].

Two studies examined the effect of compression garment use when engaged in physical activity as treatment for BCRL. In an 8-week intervention involving low-intensity resistance training with and without compression garment use, Omar et al. ($N = 60$) observed no between-group differences, but significant improvements in limb volume, pain severity, limb heaviness and tightness, shoulder ROM, and QOL for both groups were reported [48]. Singh et al. ($N = 41$) noted similar

results, questioning whether compression garment use during exercise was necessary for women with BCRL [40].

Two studies examined exercise as a prevention strategy for breast cancer patients who were at higher risk for lymphedema. After 6 months of resistance training ($N=27$), no differences in arm circumference from pre- to post-intervention were observed, although no adverse events were reported, suggesting that resistance training may be safe for those at higher risk for lymphedema [42]. Mazor et al. ($N=20$) reported significant improvement in both ROM and strength among high-risk BCRL patients who completed an 8-week yoga program [46].

Self-management

Effective lymphedema self-management includes behaviors such as compression garment use, lymph flow exercises, good hygiene, self-lymphatic drainage, and avoiding injury and infection. One study found that BCRL patients ($N=166$) were adherent to an average of 5 out of 7 behaviors, with few (19.5%) adherent to all 7. Most (98.2%) were adherent to skin care, with far fewer (65%) adherent to self-lymphatic drainage. Higher knowledge of self-management recommendations was associated with greater adherence [33]. Mestre et al. conducted a pilot study ($N=40$) to evaluate a novel auto-adjustable nighttime arm sleeve for use by BCRL patients undergoing decongestive therapy [78]. Patients were adherent most (85%) nights over the 3-month study period with no adverse events reported. The sleeve was easy to use, comfortable and well-tolerated by patients, and while not significant, limb volume increase was lower among patients using the nighttime arm sleeve compared with those not wearing the sleeve.

Self-management was also studied for BCRL prevention ($N=61$). The Self-management of Lymphedema Program included prevention education (e.g., injury prevention, signs and symptom), arm circumference measurement, QOL assessment, and lymphatic drainage. After 6 months, significant positive outcomes were observed between intervention and control patients in BCRL development; 61.2% of those in the control group developed BCRL, while none of the intervention patients developed it ($p=0.000$). Better QOL ($p<0.05$) and fewer symptoms ($p\leq 0.05$) were also reported for the intervention group [64].

Complete Decongestive Therapy

Complete decongestive therapy (CDT) is a common treatment method that incorporates multiple components (e.g., manual lymphatic drainage, compression, bandaging), and ongoing research seeks to improve methods used. One recent trial ($N=169$) determined that at least 7 sessions (CDT sessions 5 days per week for 3–4 weeks) were needed to improve symptom severity in at least 83% of the patients, with positive changes noted for both pain and heaviness [72]. Cakit et al. ($N=58$) also noted that obesity negatively impacted long-

term CDT efficacy [50]. Examining a new approach, Ligabue et al. enrolled BCRL patients ($N=41$) in a 1-month training program to learn self-administered CDT [55]. After 6 months, women participating in self-administered CDT reported less pain ($p=0.01$) and less asymmetry ($p<0.01$). In addition, excess limb volume decreased by 8% in the intervention group.

Bandaging

Bandaging is an important element of CDT, and a few studies have investigated bandaging techniques and adherence to improve outcomes. Oh et al. ($N=46$) found that the spica bandaging method (i.e., wrapped in a figure 8 style) produced greater limb volume reduction ($p<0.05$) and limb function ($p<0.05$) compared with the spiral method [79], while Ergin et al. ($N=32$) reported that Kinesio Taping did not improve limb volume [45]. In a separate study ($N=39$), Ergin and colleagues also noted that the length of time a bandage was left in place (7–12 h vs. the preferred 13–24 h) had no effect on limb volume [80].

Surgery

Surgical treatment for BCRL (i.e., vascular lymph node transfer [VLNT] or lymphovenous anastomosis [LVA]) is still not widely published, although Ngo et al. conducted a long-term follow-up of 10 patients who underwent VLNT 28–66 months prior (mean follow-up = 46 months) [81]. Half had lower or stable excess volume compared with volume at the time of surgery, and most of those had reduced or discontinued compression garment use. Non-adherence to compression garment use was reported by more than half of the patients who experienced increased excess limb volume at follow-up, which may have contributed to poorer outcomes. In a study of BCRL patients 12 months post-LVA ($N=25$), 76% maintained patency and reported significantly improved QOL ($p<0.000$); although not significant, researchers noted clinically meaningful improvements in arm circumference, compression garment use, and infection [54]. Chang and colleagues evaluated breast reconstruction surgery with VLNT ± LVA ($N=33$) and observed significant limb volume reductions at 3 and 6 months post-surgery ($p=0.037$ and $p=0.043$, respectively), but those improvements disappeared by 12 months ($p=0.43$) [82]. All patients who had the addition of LVA surgery reported symptom improvement.

Awareness, Education, and Professional Advice-Seeking

Unfortunately, few breast cancer patients receive information about lymphedema prior to diagnosis [70]. Those who are encouraged to seek advice from a healthcare professional

may benefit from a better understanding of BCRL risk management, improved adherence to risk management strategies, and better QOL [41]. Sherman et al. reported that women at risk for BCRL ($N = 462$) are more likely to seek lymphedema advice from healthcare professionals if they had some lymphedema knowledge, believed that seeking advice was useful, and experienced distress concerning their lymphedema risk [32]. In a study among BCRL patients ($N = 160$), Ridner et al. evaluated a Web-based Multimedia Intervention (WBMI) focused on symptom burden, function, psychological well-being, arm volume, and cost vs. an informational pamphlet [67]. While more patients read the pamphlet than completed the WBMI ($p = 0.011$), the WBMI was reported to offer better self-care education ($p = 0.001$).

Conclusion

BCRL is a side effect of treatment for breast cancer, although less acknowledged over time. There has been an abundance of research on the incidence, prevalence, morbidity, and treatment/prevention of BCRL, as well as surveillance techniques. This review has identified, however, many areas that need more attention to fully understand BCRL and its sequelae.

First, there are many opportunities to explore self-reported surveillance options to identify BCRL early in order to reduce the burden on healthcare system (e.g., self-measured arm circumference); however, replication and reproducibility studies of this method are needed [60]. Moreover, pre-surgery surveillance with BIS could identify patients with subclinical BCRL who could benefit from compression garment use for 4–6 weeks after surgery, as consistent evidence has shown a positive response to this approach in terms of BCRL resolution [6–9, 36, 37].

Secondly, in the area of BCRL-related outcomes, several areas need further investigation. In terms of arm circumference/volume, not all of the studies reported the average percent of inter-limb difference. The absolute value of arm circumference/volume is not interpretable without controlling for the unaffected arm and body weight. Unfortunately, different methods were used to assess circumference/volume in the reported studies. Some studies used direct measurement, while some used arm volume that was calculated from indirect measures, e.g., volume was calculated from measured circumference. Additionally, the cut points for BCRL and BCRL severity have persistently varied across studies, making standardized guidelines necessary for effective diagnosis and treatment extremely difficult to establish.

Arm function and strength is also not well-studied. Objective measures of ROM were used in several studies; however, all focused on absolute values. The extent to which BCRL affects ROM of the affected shoulder/arm is not clearly known. Multiple questionnaires have been developed and

used to assess BCRL-related symptoms across the studies. Without consistency, however, it is impossible to compare results across studies. For example, a visual analog scale was used for some of the questionnaires where pain was scored 0–10 [34, 48, 65], 0–100 [11, 72], or 0–5 scale [35], making it difficult to summarize and compare pain severity across studies.

While QOL is an important and common outcome in treatment and survivorship studies, many different QOL questionnaires have been used to acquire assessments to cover various domains, resulting in the lack of consistency across studies. Financial toxicity is a commonly ignored long-term effect of cancer/cancer-related treatment. Besides comparing healthcare visits/costs between patients with and without BCRL, other valid and reliable measures on financial burdens should be considered, such as loss of productivity, use of and the ability to use sick days, and inability to perform activities of daily living. Thus, much more work needs to be done to assess, quantify, and address the effects of BCRL. Once identified, these aspects can be studied to move implementations into clinical care.

The last area that has received even less attention is policy. This area is broad and involves standards of care, as well as national policies. At the clinical care level, standards of care should include the use of routine processes for identifying patients at increased risk for BCRL; education of at risk women regarding the risk factors, signs/symptoms, and strategies to avoid serious swelling; measurement before surgery/treatment and at regular intervals as part of surveillance/routine care; referral to physical therapy to assist with return to full ROM as soon as possible after surgery and easy exercises to improve arm strengthen; and training and certification of appropriate staff to provide lymphedema services. To achieve this ideal situation, concerted effort will need to be made to educate providers, patients, payers, and legislators to all come to a common agreement about how to reduce the burden of BCRL in women being treated for breast cancer.

Funding This study is funded by an award from The Breast Cancer Research Foundation.

Compliance with Ethical Standards

Conflict of Interest Electra Paskett reports grants from Breast Cancer Research Foundation, grants from NIH, during the conduct of the study; grants from Merck Foundation, grants from Pfizer, grants from Komen Columbus Foundation, grants from Ohio Department of Health, other from FoxConn, grants from Social Impact Fund, grants from Komen Foundation, and grants from PICORI, outside the submitted work.

Jill Oliveri and Xiaochen Zhang declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

References

- Siegel RL, Miller KD, Jemal A. Cancer statistics, 2020. *CA Cancer J Clin.* 2020;70(1):7–30.
- Miller KD, Nogueira L, Mariotto AB, Rowland JH, Yabroff KR, Alfano CM, et al. Cancer treatment and survivorship statistics, 2019. *CA Cancer J Clin.* 2019;69(5):363–85.
- Lawenda BD, Mondry TE, Johnstone PA. Lymphedema: a primer on the identification and management of a chronic condition in oncologic treatment. *CA Cancer J Clin.* 2009;59(1):8–24.
- McLaughlin SA, Bagaria S, Gibson T, Arnold M, Diehl N, Crook J, et al. Trends in risk reduction practices for the prevention of lymphedema in the first 12 months after breast cancer surgery. *J Am Coll Surg.* 2013;216(3):380–9.
- Basta MN, Wu LC, Kanchwala SK, Serletti JM, Tchou JC, Kovach SJ, et al. Reliable prediction of postmastectomy lymphedema: the Risk Assessment Tool Evaluating Lymphedema. *Am J Surg.* 2017;213(6):1125–33 e1.
- Kaufman DI, Shah C, Vicini FA, Rizzi M. Utilization of bioimpedance spectroscopy in the prevention of chronic breast cancer-related lymphedema. *Breast Cancer Res Treat.* 2017;166(3):809–15.
- Kilgore LJ, Korentager SS, Hangge AN, Amin AL, Balanoff CR, Larson KE, et al. Reducing breast cancer-related lymphedema (BCRL) through prospective surveillance monitoring using bioimpedance spectroscopy (BIS) and patient directed self-interventions. *Ann Surg Oncol.* 2018;25(10):2948–52.
- Koelmeyer LA, Borotkanics RJ, Alcorso J, Prah P, Winch CJ, Nakhel K, et al. Early surveillance is associated with less incidence and severity of breast cancer-related lymphedema compared with a traditional referral model of care. *Cancer.* 2019;125(6):854–62.
- Laidley A, Anglin B. The impact of L-Dex((R)) measurements in assessing breast cancer-related lymphedema as part of routine clinical practice. *Front Oncol.* 2016;6:192.
- Nguyen TT, Hoskin TL, Habermann EB, Cheville AL, Boughey JC. Breast cancer-related lymphedema risk is related to multidisciplinary treatment and not surgery alone: results from a large cohort study. *Ann Surg Oncol.* 2017;24(10):2972–80.
- Park JH. The effects of complex exercise on shoulder range of motion and pain for women with breast cancer-related lymphedema: a single-blind, randomized controlled trial. *Breast Cancer.* 2017;24(4):608–14.
- Penha TR, Botter B, Heuts EM, Voogd AC, von Meyenfeldt MF, van der Hulst RR. Quality of life in patients with breast cancer-related lymphedema and reconstructive breast surgery. *J Reconstr Microsurg.* 2016;32(6):484–90.
- Rupp J, Hadamitzky C, Henkenberens C, Christiansen H, Steinmann D, Bruns F. Frequency and risk factors for arm lymphedema after multimodal breast-conserving treatment of nodal positive breast cancer - a long-term observation. *Radiat Oncol.* 2019;14(1):39.
- Zou L, Liu FH, Shen PP, Hu Y, Liu XQ, Xu YY, et al. The incidence and risk factors of related lymphedema for breast cancer survivors post-operation: a 2-year follow-up prospective cohort study. *Breast Cancer.* 2018;25(3):309–14.
- Chowdhry M, Rozen WM, Griffiths M. Lymphatic mapping and preoperative imaging in the management of post-mastectomy lymphoedema. *Gland surgery.* 2016;5(2):187–96.
- Hespe GE, Nitti MD, Mehrara BJ. Pathophysiology of lymphedema. *Lymphedema:* Springer; 2015. p. 9–18.
- Rusznayk I, Földi M, Szabó G. Lymphatics and lymph circulation: physiology and pathology: Elsevier; 2013.
- Shih Y-CT XY, Cormier JN, Giordano S, Ridner SH, Buchholz TA, et al. Incidence, treatment costs, and complications of lymphedema after breast cancer among women of working age: a 2-year follow-up study. *J Clin Oncol.* 2009;27(12):2007–14.
- Paskett ED, Dean JA, Oliveri JM, Harrop JP. Cancer-related lymphedema risk factors, diagnosis, treatment, and impact: a review. *J Clin Oncol.* 2012;30(30):3726–33.
- 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.
- Albright HW, Moreno M, Feeley TW, Walters R, Samuels M, Pereira A, et al. The implications of the 2010 patient protection and affordable care act and the health care and education reconciliation act on cancer care delivery. *Cancer.* 2011;117(8):1564–74.
- Mehnert A. Employment and work-related issues in cancer survivors. *Crit Rev Oncol Hematol.* 2011;77(2):109–30.
- Lam R, Wallace A, Burbidge B, Franks P, Moffatt C. Experiences of patients with lymphoedema. *J Lymphoedema.* 2006;1(1):16–21.
- Paskett E BS, Khakpour N, O'Connor T, Silverman P. . Lymphedema. In: NCCN clinical practice guidelines in oncology (NCCN guidelines): Survivorship. Version 2.2019 ed: National Comprehensive Cancer Network; 2019.
- Park S, Lee JE, Yu J, Paik HJ, Ryu JM, Kim I, et al. Risk factors affecting breast cancer-related lymphedema: serial body weight change during neoadjuvant anthracycline plus cyclophosphamide followed by taxane. *Clin Breast Cancer.* 2018;18(1):e49–54.
- Vicini F, Shah C, Whitworth P, Walker M, Shi J. Correlation of bioimpedance spectroscopy with risk factors for the development of breast cancer-related lymphedema. *Lymphat Res Biol.* 2018.
- Dean LT, Kumar A, Kim T, Herling M, Brown JC, Zhang Z, et al. Race or resource? BMI, race, and other social factors as risk factors for interlimb differences among overweight breast cancer survivors with lymphedema. *J Obes.* 2016;2016:8241710.
- Eyigor S, Cinar E, Caramat I, Unlu BK. Factors influencing response to lymphedema treatment in patients with breast cancer-related lymphedema. *Support Care Cancer.* 2015;23(9):2705–10.
- Yoon JA, Shin YB, Shin MJ, Yun RY, Kim KY, Song YS, et al. An assessment of the relationship between abdominal obesity and the severity of upper extremity lymphedema. *Lymphat Res Biol.* 2018;16(5):458–63.
- Coriddi M, Khansa I, Stephens J, Miller M, Boehmler J, Tiwari P. Analysis of factors contributing to severity of breast cancer-related lymphedema. *Ann Plast Surg.* 2015;74(1):22–5.
- Penn IW, Chang YC, Chuang E, Chen CM, Chung CF, Kuo CY, et al. Risk factors and prediction model for persistent breast-cancer-related lymphedema: a 5-year cohort study. *Support Care Cancer.* 2019;27(3):991–1000.
- Sherman KA, Kilby CJ, Elder E, Ridner SH. Factors associated with professional healthcare advice seeking in women at risk for developing breast cancer-related lymphedema. *Patient Educ Couns.* 2018;101(3):445–51.
- Alcorso J, Sherman KA, Koelmeyer L, Mackie H, Boyages J. Psychosocial factors associated with adherence for self-management behaviors in women with breast cancer-related lymphedema. *Support Care Cancer.* 2016;24(1):139–46.
- Lee D, Hwang JH, Chu I, Chang HJ, Shim YH, Kim JH. Analysis of factors related to arm weakness in patients with breast cancer-related lymphedema. *Support Care Cancer.* 2015;23(8):2297–304.
- O'Toole JA, Ferguson CM, Swaroop MN, Horick N, Skolny MN, Brunelle CL, et al. The impact of breast cancer-related lymphedema on the ability to perform upper extremity activities of daily living. *Breast Cancer Res Treat.* 2015;150(2):381–8.
- Ridner SH, Dietrich MS, Cowher MS, Taback B, McLaughlin S, Ajkay N, et al. A randomized trial evaluating bioimpedance spectroscopy versus tape measurement for the prevention of lymphedema following treatment for breast cancer: interim analysis. *Ann Surg Oncol.* 2019;26(10):3250–9.

37. Whitworth PW, Shah C, Vicini F, Cooper A. Preventing breast cancer-related lymphedema in high-risk patients: the impact of a structured surveillance protocol using bioimpedance spectroscopy. *Front Oncol.* 2018;8:197.
38. Buchan J, Janda M, Box R, Schmitz K, Hayes S. A randomized trial on the effect of exercise mode on breast cancer-related lymphedema. *Med Sci Sports Exerc.* 2016;48(10):1866–74.
39. Brown JC, Kumar A, Chevillat AL, Tchou JC, Troxel AB, Harris SR, et al. Association between lymphedema self-care adherence and lymphedema outcomes among women with breast cancer-related lymphedema. *Am J Phys Med Rehabil.* 2015;94(4):288–96.
40. Singh B, Buchan J, Box R, Janda M, Peake J, Purcell A, et al. Compression use during an exercise intervention and associated changes in breast cancer-related lymphedema. *Asia Pac J Clin Oncol.* 2016;12(3):216–24.
41. Lin CY, Liu HE, Cheng MH. Factors associated with professional healthcare advice seeking in breast cancer-related lymphedema. *J Surg Oncol.* 2020;121(1):67–74.
42. Simonavice E, Kim JS, Panton L. Effects of resistance exercise in women with or at risk for breast cancer-related lymphedema. *Support Care Cancer.* 2017;25(1):9–15.
43. Czerniec SA, Ward LC, Kilbreath SL. Breast cancer-related arm lymphedema: fluctuation over six months and the effect of the weather. *Lymphat Res Biol.* 2016;14(3):148–55.
44. Cornish B, Chapman M, Hirst C, Mirolo B, Bunce I, Ward L, et al. Early diagnosis of lymphedema using multiple frequency bioimpedance. *Lymphology.* 2001;34(1):2–11.
45. Ergin G, Sahinoglu E, Karadibak D, Yavuzsen T. Effectiveness of Kinesio Taping on anastomotic regions in patients with breast cancer-related lymphedema: a randomized controlled pilot study. *Lymphat Res Biol.* 2019;17(6):655–60.
46. Mazor M, Lee JQ, Peled A, Zerzan S, Irwin C, Chesney MA, et al. The effect of yoga on arm volume, strength, and range of motion in women at risk for breast cancer-related lymphedema. *J Altern Complement Med.* 2018;24(2):154–60.
47. Ochalek K, Gradalski T, Partsch H. Preventing early postoperative arm swelling and lymphedema manifestation by compression sleeves after axillary lymph node interventions in breast cancer patients: a randomized controlled trial. *J Pain Symptom Manag.* 2017;54(3):346–54.
48. Omar MTA, Gwada RFM, Omar GSM, El-Sabagh RM, Mersal AAE. Low-intensity resistance training and compression garment in the management of breast cancer-related lymphedema: single-blinded randomized controlled trial. *J Cancer Educ.* 2019.
49. Vignes S, Fau-Prudhomot P, Simon L, Sanchez-Brechot ML, Arrault M, Locher F. Impact of breast cancer-related lymphedema on working women. *Support Care Cancer.* 2020;28(1):79–85.
50. Duyur Cakit B, Pervane Vural S, Ayhan FF. Complex decongestive therapy in breast cancer-related lymphedema: does obesity affect the outcome negatively? *Lymphat Res Biol.* 2019;17(1):45–50.
51. Dean LT, Moss SL, Ransome Y, Frasso-Jaramillo L, Zhang Y, Visvanathan K, et al. “It still affects our economic situation”: long-term economic burden of breast cancer and lymphedema. *Support Care Cancer.* 2019;27(5):1697–708.
52. Sitzia J. Volume measurement in lymphoedema treatment: examination of formulae. *Eur J Cancer Care.* 1995;4(1):11–6.
53. Yamamoto T, Yamamoto N, Hara H, Mihara M, Narushima M, Koshima I. Upper extremity lymphedema index: a simple method for severity evaluation of upper extremity lymphedema. *Ann Plast Surg.* 2013;70(1):47–9.
54. Wolfs J, de Joode L, van der Hulst R, Qiu SS. Correlation between patency and clinical improvement after lymphaticovenous anastomosis (LVA) in breast cancer-related lymphedema: 12-month follow-up. *Breast Cancer Res Treat.* 2020;179(1):131–8.
55. Ligabue MB, Campanini I, Veroni P, Cepelli A, Lusuardi M, Merlo A. Efficacy of self-administered complex decongestive therapy on breast cancer-related lymphedema: a single-blind randomized controlled trial. *Breast Cancer Res Treat.* 2019;175(1):191–201.
56. Zhang X, Brown JC, Paskett ED, Zemel BS, Chevillat AL, Schmitz KH. Changes in arm tissue composition with slowly progressive weight-lifting among women with breast cancer-related lymphedema. *Breast Cancer Res Treat.* 2017;164(1):79–88.
57. Arinaga Y, Sato F, Pillar N, Kakamu T, Kikuchi K, Ohtake T, et al. A 10 minute self-care program may reduce breast cancer-related lymphedema: a six-month prospective longitudinal comparative study. *Lymphology.* 2016;49(2):93–106.
58. Fu MR, Axelrod D, Cleland CM, Qiu Z, Guth AA, Kleinman R, et al. Symptom report in detecting breast cancer-related lymphedema. *Breast Cancer (Dove Med Press).* 2015;7:345–52.
59. Spinelli B, Kallan MJ, Zhang X, Chevillat A, Troxel A, Cohn J, et al. Intra-and interrater reliability and concurrent validity of a new tool for assessment of breast cancer-related lymphedema of the upper extremity. *Arch Phys Med Rehabil.* 2019;100(2):315–26.
60. Rafn BS, McNeely ML, Camp PG, Midtgaard J, Campbell KL. Self-measured arm circumference in women with breast cancer is reliable and valid. *Phys Ther.* 2019;99(2):240–53.
61. Norkin CC, White DJ. Measurement of joint motion: a guide to goniometry: FA Davis; 2016.
62. Sanal-Toprak C, Ozsoy-Unubol T, Bahar-Ozdemir Y, Akyuz G. The efficacy of intermittent pneumatic compression as a substitute for manual lymphatic drainage in complete decongestive therapy in the treatment of breast cancer related lymphedema. *Lymphology.* 2019;52(2):82–91.
63. Jang DH, Kim MW, Oh SJ, Kim JM. The influence of arm swelling duration on shoulder pathology in breast cancer patients with lymphedema. *PLoS One.* 2015;10(11):e0142950.
64. Temur K, Kapucu S. The effectiveness of lymphedema self-management in the prevention of breast cancer-related lymphedema and quality of life: a randomized controlled trial. *Eur J Oncol Nurs.* 2019;40:22–35.
65. Donmez AA, Kapucu S. The effectiveness of a clinical and home-based physical activity program and simple lymphatic drainage in the prevention of breast cancer-related lymphedema: a prospective randomized controlled study. *Eur J Oncol Nurs.* 2017;31:12–21.
66. Beaton DE, Katz JN, Fossel AH, Wright JG, Tarasuk V, Bombardier C. Measuring the whole or the parts?: validity, reliability, and responsiveness of the Disabilities of the Arm, Shoulder and Hand outcome measure in different regions of the upper extremity. *J Hand Ther.* 2001;14(2):128–42.
67. Ridner SH, Dietrich MS, Davis AJ, Sinclair V. A randomized clinical trial comparing the impact of a web-based multimedia intervention versus an educational pamphlet on patient outcomes in breast cancer survivors with chronic secondary lymphedema. *J Women's Health (Larchmt).* 2020;29(5):734–44.
68. Norman SA, Localio AR, Kallan MJ, Weber AL, Torpey HAS, Potashnik SL, et al. Risk factors for lymphedema after breast cancer treatment. *Cancer Epidemiol Prev Biomarkers.* 2010;19(11):2734–46.
69. Isl I. The diagnosis and treatment of peripheral lymphedema 2009 consensus document of the International Society of Lymphology. *Lymphology.* 2009;42(2):51–60.
70. Borman P, Yaman A, Yasrebi S, Ozdemir O. The importance of awareness and education in patients with breast cancer-related lymphedema. *J Cancer Educ.* 2017;32(3):629–33.
71. Schmitz KH, Troxel AB, Dean LT, DeMichele A, Brown JC, Sturgeon K, et al. Effect of home-based exercise and weight loss programs on breast cancer-related lymphedema outcomes among overweight breast cancer survivors: the WISER Survivor Randomized Clinical Trial. *JAMA Oncol.* 2019;5:1605.
72. Mobarakeh ZS, Mokhtari-Hesari P, Lotfi-Tokaldany M, Montazeri A, Heidari M, Zekri F. Combined decongestive therapy and

- reduction of pain and heaviness in patients with breast cancer-related lymphedema. *Support Care Cancer*. 2019;27(10):3805–11.
73. Pasyar N, Barshan Tashnizi N, Mansouri P, Tahmasebi S. Effect of yoga exercise on the quality of life and upper extremity volume among women with breast cancer related lymphedema: a pilot study. *Eur J Oncol Nurs*. 2019;42:103–9.
 74. Williams AE, Rapport F, Russell IT, Hutchings HA. Psychometric development of the Upper Limb Lymphedema Quality of Life Questionnaire demonstrated the patient-reported outcome measure to be a robust measure for breast cancer-related lymphedema. *J Clin Epidemiol*. 2018;100:61–70.
 75. De Vrieze T, Gebruers N, Nevelsteen I, Tjalma WAA, Thomis S, De Groef A, et al. Responsiveness of the Lymphedema Functioning, Disability, and Health Questionnaire for upper limb lymphedema in patients with breast cancer-related lymphedema. *Lymphat Res Biol*. 2020.
 76. Basta MN, Fox JP, Kanchwala SK, Wu LC, Serletti JM, Kovach SJ, et al. Complicated breast cancer-related lymphedema: evaluating health care resource utilization and associated costs of management. *Am J Surg*. 2016;211(1):133–41.
 77. Cheville A, Lee M, Moynihan T, Schmitz KH, Lynch M, De Choudens FR, et al. The impact of arm lymphedema on healthcare utilization during long-term breast cancer survivorship: a population-based cohort study. *J Cancer Surviv*. 2020:1–9.
 78. Mestre S, Calais C, Gaillard G, Nou M, Pasqualini M, Ben Amor C, et al. Interest of an auto-adjustable nighttime compression sleeve (MOBIDERM(R) Autofit) in maintenance phase of upper limb lymphedema: the MARILYN pilot RCT. *Support Care Cancer*. 2017;25(8):2455–62.
 79. Oh SH, Ryu SH, Jeong HJ, Lee JH, Sim YJ. Effects of different bandaging methods for treating patients with breast cancer-related lymphedema. *Ann Rehabil Med*. 2019;43(6):677–85.
 80. Ergin G, Sahinoglu E, Karadibak D, Yavuzsen T. Effect of bandage compliance on upper extremity volume in patients with breast cancer-related lymphedema. *Lymphat Res Biol*. 2018;16(6):553–8.
 81. Ngo QD, Munot S, Mackie H, Czerniec S, Koelmeyer LA, Lam T, et al. Vascularized lymph node transfer for patients with breast cancer-related lymphedema can potentially reduce the burden of ongoing conservative management. *Lymphat Res Biol*. 2020.
 82. Chang EI, Ibrahim A, Liu J, Robe C, Suami H, Hanasono MM, et al. Optimizing quality of life for patients with breast cancer related lymphedema: a prospective study combining DIEP flap breast reconstruction and lymphedema surgery. *Plast Reconstr Surg*. 2020;145:676e–85e.

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.