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REVIEW ARTICLE

Cancer-Related Lymphedema Risk Factors, Diagnosis, Treatment, and Impact: A Review

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ABSTRACT

Purpose
Cancer-related lymphedema (LE) is an incurable condition associated with lymph-involved cancer treatments and is an increasing health, quality of life (QOL), and cost burden on a growing cancer survivor population. This review examines the evidence for causes, risk, prevention, diagnosis, treatment, and impact of this largely unexamined survivorship concern.

Methods
PubMed and Medline were searched for cancer-related LE literature published since 1990 in English. The resulting references (N = 726) were evaluated for strength of design, methods, sample size, and recent publication and sorted into categories (ie, causes/prevention, diagnosis, treatment, and QOL). Sixty studies were included.

Results
Exercise and physical activity and sentinel lymph node biopsy reduce risk, and overweight and obesity increase risk. Evidence that physiotherapy reduces risk and that lymph node status and number of malignant nodes increase risk is less strong. Perometry and bioimpedence emerged as attractive diagnostic technologies, replacing the use of water displacement in clinical practice. Swelling can also be assessed by measuring arm circumference and relying on self-report. Symptoms can be managed, not cured, with complex physical therapy, low-level laser therapy, pharmacotherapy, and surgery. Sequelae of LE negatively affect physical and mental QOL and range in severity. However, the majority of reviewed studies involved patients with breast cancer; therefore, results may not be applicable to all cancers.

Conclusion
Research into causes, prevention, and effect on QOL of LE and information on LE in cancers other than breast is needed. Consensus on definitions and measurement, increased patient and provider awareness of signs and symptoms, and proper and prompt treatment/access, including psychosocial support, are needed to better understand, prevent, and treat LE.

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INTRODUCTION

Lymphedema (LE) is an incurable medical condition characterized by lymphatic fluid retention, resulting in tissue swelling. Cancer treatments involving lymph nodes can damage lymph drainage routes, causing accumulation of lymph fluid in the interstitial tissue of related limbs and body areas and secondary LE.[1] Subsequent swelling can cause pain, discomfort, heaviness, distortion, and reduced mobility and function,[2] thereby affecting quality of life (QOL) physically and psychologically.[3] Although there is no cure, symptoms of LE can be controlled if the disease is detected and treated before it has significantly progressed. The prevalence of secondary LE is increasing as improvements in cancer detection and treatment have led to a growing survivorship population.

Estimates of the incidence of secondary LE resulting from cancer treatment vary greatly because of the absence of uniform measurement, definition, and reporting. Most incidence estimates are available for the breast cancer survivor population, with rates ranging from 13% to 65%, depending on the criteria used and means of assessment.[4-6] Cancer-related LE can affect a survivor of any type of cancer in which the lymph nodes are involved in treatment, including skin, gynecologic, urologic, colorectal, and head and neck cancers; however, few estimates of LE in survivors from other cancers have been published.

This article offers a concise, critical, and current review of the LE literature, including recommendations on current best management practices for prevention and treatment. Limitations of previous studies and future directions are also discussed.

METHODS

PubMed and Medline were searched for studies published since 1990, addressing cancer-related LE, written in English. When cancer-related literature was sparse, general LE literature was explored (eg, surgical treatment for LE). Search terms included lymphedema, cancer, causes, prevention, diagnosis, definition, treatment, and QOL. Case studies, anecdotal reports, obsolete diagnostic criteria, and treatments rarely used in clinical practice were excluded. The 726 references that met these criteria were categorized (ie, causes/prevention, diagnosis, treatment, QOL) by two independent researchers (J.A.D., J.M.O.). Evidence within each category was ordered by study design in the following order: randomized controlled trials (RCTs), cohort studies, case-control studies, and cross-sectional studies.[7] When multiple RCTs and/or cohort studies supported the same finding, any other studies were excluded from evaluation. When few or no RCTs and/or cohort studies were available, lower-level evidence[7] was evaluated (case-control and cross-sectional studies) for that finding. Older studies of less rigorous study design, statistical methods, and smaller sample sizes were excluded (n = 669). A total of 60 studies were chosen to provide an overall depiction of the breadth of the LE literature.

RESULTS

Causes, Risk, and Prevention

Little is known about the causes of LE, and most preventive measures thus far have resulted from clinical observation rather than research. Knowledge of the causes of LE is limited to an assumed connection to the risk reduction strategies that have developed from clinical observations and the few RCTs and observational studies (mostly prospective cohort studies) that have been designed to examine etiology. The following are areas in which the literature provides the strongest evidence for risk factors and risk reduction behaviors studied. Results of studies summarized here are provided in the Data Supplement.

Evidence from six RCTs shows exercise and physical activity do not increase LE risk.[17-21] Although removal of lymph nodes as part of surgical treatment for breast cancer impairs the body's ability to respond to infection, trauma, injury, and inflammation, exercise can improve function in those areas.[17] In several RCTs,[17,19,22] resistance exercise did not increase the risk of LE or worsen LE symptoms in those already diagnosed with it. Courneya et al[18] reported both aerobic and resistance exercise significantly improved self-esteem, physical fitness, body composition, and chemotherapy completion rate; however, they had no effect on cancer-specific QOL.

Evidence for type of therapy regimen as a risk factor is mixed. One study found chemotherapy was a risk factor, but not radiation therapy (RT).[23] Two RCTs reported no associated risk of LE in patients with vulvar and breast cancers receiving RT.[24,25] An increased risk was associated with RT in four cohort studies in women with breast, uterine, and cervical cancers.[23,26-28]

Evidence demonstrates sentinel lymph node biopsy (SLNB) reduces LE risk in patients with breast and vulvar cancers compared with axillary lymph node dissection (ALND). Five RCTs involving patients with breast cancer found SLNB decreased the risk of LE,[29-33] and similar results were reported in a cohort of patients with vulvar cancer.[34] A cohort study examining SLNB versus ALND in patients with melanoma found no significant difference between groups in LE diagnosis.[35]

Two RCTs involving patients with breast cancer showed physiotherapy, including manual lymph drainage (MLD), massage of scar tissue, and progressive active and action-assisted shoulder exercise, reduces LE incidence.[36,37] In a third study, patients receiving a directed physiotherapy intervention had improved shoulder mobility, although no statistically different LE incidence.[38] Lymph node status (ie, positive or negative for malignancy) and number of positive nodes are positively related to LE risk; sparse evidence suggests that as the number of nodes resected increases, so does risk of LE. One RCT found an inverse relationship between number of positive nodes and arm volume[39] in patients with breast cancer, and a cohort study found an increased risk of lower extremity LE associated with resection of > 31 lymph nodes[26] in patients with endometrial cancer. A higher number of resected nodes was not found to be a risk factor for developing LE in another cohort study involving patients with breast cancer.[28] In addition, positive node status was associated with increased risk of breast cancer–related LE in two additional cohort studies.[40,41]

Early detection using lymphoscintigraphy and increased awareness of risk are two ways to reduce LE risk and severity, although evidence associating these strategies with reduction of LE incidence is scarce.[42,43] Lymphoscintigraphy allowed for early detection and treatment (ie, before clinical appearance of LE) in an RCT involving patients with breast cancer who had undergone radiation and surgery.[42] A study designed to assess the value of preoperative lymphoscintigraphy and education among women who had breast-conserving surgery or mastectomy detected a slight reduction in the incidence of LE compared with a control group.[43]

Overweight or obesity at cancer diagnosis is a well-supported risk factor for breast cancer–related LE.[23,28,41,44-47] In one cohort study, LE was positively correlated with patient size factors like body mass index,[44] whereas another cohort study found no such association.[23] A case-control study found a positive relationship between weight-related factors like diabetes, hypertension, hypothyroidism, chronic obstructive pulmonary disease, and body mass index with increased severity of LE.[45] A collection of case-control studies also concluded that obesity and weight at time of mastectomy or diagnosis were related to LE risk.[41,46,47]

Several other factors have been examined with conflicting or little evidence of association with LE. There is conflicting evidence that age is a risk factor for LE[23,28,47,48] and minimal evidence that air travel is a risk factor.[40] Needle sticks,[41] surgery on the dominant arm,[47,49] mastectomy (*v* wide local excision or lumpectomy),[41] and occupation and hobby (ie, hand use)[45] have been sparsely linked with increased risk of LE, whereas administration and use of sodium selenite[50] and use of fibrin sealant in wound closure during surgery[24] are sparsely associated with decreased LE risk.

Diagnosis of LE

Although many studies focused on estimates of the incidence, prevalence, and causes of LE, there is no widely agreed on standardized definition of LE. Measurement of affected limbs is the most common method to determine the presence of swelling, although this is not relevant for nonlimb swelling or LE that only causes pain and/or heaviness. Ultimately, the extent of size increase associated with an LE diagnosis depends on the method used to assess limb volume changes. The diagnostic process begins with a patient history and physical examination followed by any one or a combination of approaches to provide a measure of limb volume. Central to this assessment is the need for preoperative measurement to ascertain a true baseline.[11,51] This measurement, however, rarely occurs as part of clinical practice.

Table 1. Diagnostic Methods for Cancer-Related LE

Method	Study	Site	Design	Participants	Outcome Measures	Findings
Water displacement	Sagen et al[8]	Breast	Cross-sectional study of patients with breast cancer examined 6 years after ALND	23 women who had ALND 6 years before (Norway)	LVC in arm	Water displacement was simple and valid method for assessing LVC compared with MRI ($P < .001$)
Lymphoscintigraphy	Ter et al[9]	Upper and lower limbs (not limited to oncology patients; primary and secondary LE)	Cross-sectional study of patients with primary LE, secondary LE, and edema from other causes	17 patients (20 extremities) with edema	LE diagnosis *v* edema resulting from other causes by qualitative interpretation of image patterns from lymphoscintigraphy	Sensitivity reported at 73%; specificity reported at 100%; lymphoscintigraphy was reliable, objective, and noninvasive method of diagnosing LE
High-frequency ultrasound	Mellor et al[10]	Breast	Cross-sectional study of women with breast cancer–related LE (mean time since treatment, 43 months; mean duration of LE, 88 months)	10 women treated for unilateral breast cancer with LE (United Kingdom)	Skin thickness (ultrasound), LV (perometer), and arm circumference	Skin thickness was better correlated with arm LE than subcutaneous thickness; thickness measured by high-frequency ultrasound was simple and reliable method of diagnosing LE
Perometry	Armer[11]	Breast	Prospective longitudinal cohort study including self-report assessments, face-to-face interviews, and anthropometric measures; patients observed preoperatively to 12 months postdiagnosis	118 women newly diagnosed with stages I to IV breast cancer	LVC as measured by arm circumference, perometer, and self-report of heaviness or swelling	Methods (and criteria) of diagnosing LE were not uniform; 10% LVC by perometer was most conservative; 2-cm difference (circumference) was most liberal
	Spillane et al[12]	Melanoma	Cross-sectional study of patients with melanoma who received surgical treatment on lower limbs	66 patients who had undergone inguinal or ilioinguinal dissection (Australia)	LVC as measured by arm circumference, water displacement, and perometer	Lower LVC (≥ 15%) by perometer and increase in sum of circumferences (≥ 7%) indicate lower limb LE
Bioimpedance	Gaw et al[13]	Upper and lower limbs (not limited to oncology patients; primary and secondary LE)	Cohort study of healthy women, women with unilateral arm LE, and women without unilateral leg LE	89 participants (65 controls, 12 each with arm and leg LE; Australia)	Limb impedance ratio and L-Dex score	Low frequency (< 30 kHz) impedance measurements provided reliable early detection of LE
	Ward et al[14]	Breast	Cohort study of healthy women and women with unilateral LE	45 women with LE and 21 healthy controls (Australia)	Bioimpedance indices (impedance ratio and L-Dex score) and interlimb volume changes (perometer)	Bioimpedance indices highly correlated with LVC measured by perometry ($r = 0.926$); appropriate alternative to perometry

(continued on following page)

Table 1. Diagnostic Methods for Cancer-Related LE (continued)

Method	Study	Site	Design	Participants	Outcome Measures	Findings
Arm circumference	Taylor et al[15]	Breast	Cohort study of healthy women, women who had undergone surgical treatment for breast cancer and developed LE, and women who had undergone surgical treatment for breast cancer and did not develop LE	19 women with LE, 22 LE-free women, 25 healthy controls (Australia)	LV calculated from arm circumference measurements and water displacement	Volumes calculated by both means were reliable ($r = 0.97$ to 0.99 for circumference; $r = 0.94$ to 0.98 for water displacement); volumes from circumferences based on anatomic landmarks, although larger than volumes for water displacement, were valid ($P < .001$)
	Armer[11]	Breast	Prospective longitudinal cohort study including self-report assessments, face-to-face interviews, and anthropometric measures; patients observed preoperatively to 12 months postdiagnosis	118 women newly diagnosed with stage I to IV breast cancer	LVC as measured by arm circumference, perometry, and self-report of heaviness or swelling	Methods (and criteria) of diagnosing LE were not uniform; 10% LVC by perometer was most conservative; 2-cm difference (circumference) was most liberal
	Spillane et al[12]	Melanoma	Cross-sectional study of patients with melanoma who received surgical treatment on lower limbs	66 patients who had undergone inguinal or ilioinguinal dissection (Australia)	LVC as measured by arm circumference, water displacement, and perometry	Lower LVC (≥ 15%) by perometer and increase in sum of circumferences (≥ 7%) indicate lower limb LE
Self-report	Czerniec et al[16]	Breast	Cohort study of women with and without unilateral LE	33 women with LE; 18 women without LE (Australia)	LE measured by self-report, bioimpedance, perometry, and arm circumference	Bioimpedance, perometry, and circumference assessments were highly reliable ($ICC_{2,1}$, 0.94 to 1.00) with high concordance (r_c, 0.89 to 0.99); self-report was moderately correlated with these ($r = 0.65$ to 0.71) and moderately reliable ($ICC_{2,1}$, 0.70)
	Armer[11]	Breast	Prospective longitudinal cohort study including self-report assessments, face-to-face interviews, and anthropometric measures; patients observed preoperatively to 12 months postdiagnosis	118 women newly diagnosed with stage I to IV breast cancer	LVC as measured by arm circumference, perometry, and self-report of heaviness or swelling	Methods (and criteria) of diagnosing LE were not uniform; 10% LVC by perometer was most conservative; 2-cm difference (circumference) was most liberal

Abbreviations: ALND, axillary lymph node dissection; L-Dex, LE index; LE, lymphedema; LV, limb volume; LVC, limb volume change; MRI, magnetic resonance imaging.

Although these references relate specifically to breast cancer, the results might be generalizable to other cancers as well.

Water displacement was once considered the gold standard for LE diagnosis because of its affordability and excellent reliability and validity.[8] However, other technologies, such as lymphoscintigraphy, perometry, and bioimpedance (Table 1), although more costly, provide equally reliable and valid limb volume measurements with greater ease and patient comfort. Although research examining the use of lymphoscintigraphy to assess cancer-related LE is sparse, one study of patients with primary and secondary LE in both limbs reported that quantitative lymphoscintigraphy yielded an accurate estimation of lymph transport capacity,[9] and high-frequency (20 MHz) ultrasound was significantly correlated with degree of swelling (as measured by arm circumference) and duration of LE in a small study[10] of patients with breast cancer.

Perometry using infrared light beams also offers a reliable and convenient method of assessing limb volume.[57] Armer et al[51] characterized arm LE in patients with breast cancer by a 200-mL limb volume change (LVC) or a 10% LVC between arms or within the same arm before and after treatment. A 10% difference in limb volume was a more conservative definition compared with a 200-mL LVC, because only 8% of the sample had LE at 6 months postsurgery, and 21% met the criterion at 12 months (compared with 24% and 42%, respectively, for the 200-mL criterion). Spillane et al[12] defined LE as a difference $\geq$ 15% in lower limb volume.

Perhaps the newest, but most costly, method of detecting changes in limb volume is bioimpedance, which could also be important for the identification of subclinical swelling.[58,59] In one study of patients with cancer- and non–cancer-related LE, bioimpedance offered an adequate differentiation between arm and leg ratio of impedance for patients both with and without LE,[13] and it highly correlated with arm volume differences measured by perometry ($r = 0.926$).[14]

LE can also be assessed with a simple tape measure. Assessing limb circumference assumes a cylindrical shape, which is usually not the case, and trends toward estimating slightly higher volumes (by as much as 5%) compared with water displacement.[15] Armer et al[51] characterized arm LE as having at least a 2-cm difference between affected and unaffected limbs at any point in time, offering the most liberal definition among methods compared. Unfortunately, high variability has been reported among measurers,[11] whereas circumferences in relation to anatomic landmarks were more reliable, valid, and accurate than those circumferences based on distance from fingertips.[15] In assessing lower limb LE in patients with melanoma, Spillane et al[12] defined LE as $\geq$ 7% increase in the sum of circumferences of specific points along the limb.

Researchers and clinicians frequently assess LE, in part, by self-report. Self-reported symptoms of pain, heaviness, or swelling were moderately reliable among a sample of patients with breast cancer ($ICC_{2,1}$, 0.70),[16] and Armer et al[51] reported prevalence of LE by self-report at 19% at 6 months and 40% at 12 months postsurgery for breast cancer treatment. Self-report has also correlated moderately with physical measurements of bioimpedance and perometry ($r = 0.65$ to 0.71).[16]

Treatment of LE

Currently, LE cannot be cured; it can only be managed, with the goal of decreasing limb size and maintaining it, preventing complications, and improving limb function and overall well being.[60] This can be accomplished through the development of comparable lymph flow pathways or improved function of existing pathways. Therapies evaluated to date include complex physical therapy, low-level laser therapy (LLLT), pharmacotherapy, and surgery (Table 2). Complex physical therapy (including complete decongestive therapy) consists of MLD, exercise, nonelastic wrapping, use of compression garments, and skin care. Badger et al[52] reported a significant reduction in upper and lower limb volume with use of bandaging plus an elastic compression garment compared with wearing the garment alone in a study of patients with cancer- and non–cancer-related LE. Although compression garments prevent reaccumulation of fluid after decongestive treatments and are well tolerated by patients, proper fit is crucial for effectiveness, and garments need to be replaced every 3 to 6 months.

LLLT was effective in reducing limb volume, extracellular fluid, and tissue hardness in one third of patients with breast cancer with LE 3 months after treatment, although two cycles had to be administered to produce the desired effect.[53] Similar results were reported among patients with breast cancer with LE who received one cycle of treatment in a separate study.[54] Conversely, pharmacotherapy has received little attention recently, perhaps because few options offer long-term solutions.[61] Selenium, however, shows promise as a cost-effective, nontoxic anti-inflammatory agent.[61] In a randomized, placebo-controlled, double-blind study, patients with squamous cell carcinoma of the oral cavity who had undergone recent surgery with bilateral neck dissection reported significantly less swelling postsurgery after treatment with sodium selenite during the perioperative period.[50]

Surgical treatment for LE seems to be restricted to patients in whom other attempts at treatment were unsuccessful or are impractical. Surgical approaches either remove lymphedematous tissue or use microsurgery for anastomosis,[62] but research examining the use of surgery as treatment for cancer-related LE is sparse. One study of patients with cancer- and non–cancer-related LE reported that 83% of patients who underwent reconstructive lymphatic microsurgery demonstrated a significant improvement in limb volume, with an average follow-up of $>$ 10 years.[55] Continued monitoring showed similar results 3 years later.[56]

Effects of LE on QOL

The impact of LE on QOL ranges from subtle to drastic, and sequelae include frustration, distress, depression, and anxiety, especially in regard to body image.[63] These effects extend into social ramifications like role function and social support as well as pain and disability.[63] Breast cancer survivors reported the effects of LE (ie, swelling, pain, poor body image) threatened their occupations, social life, hobbies, and activities[64] as well as their physical and mental QOL.[65] Compared with breast cancer survivors without LE, those with LE had a 9% higher probability of scoring one point lower on the QOL scale and a 29% higher probability of reporting poorer health during the 5-year period after surgery.[66] In a cohort of breast cancer survivors, those who reported persistent swelling had significantly lower QOL on the Functional Assessment of Cancer Therapy–Breast total score and Short Form–12 physical and mental health subscales.[65]

Hormes et al[67] suggested the total number of arm symptoms (ie, not just swelling or LE severity) is important when assessing QOL in breast cancer survivors, because pain in the affected arm correlated with poor QOL outcomes, regardless of swelling. Ridner et al[68] asserted that greater attention should be paid to instruction on LE

Table 2. Treatment Approaches for Cancer-Related LE

Approach	Study	Site	Design	Participants	Outcome Measures	Findings
Complex physical therapy	Badger et al[52]	Upper and lower limbs (not limited to oncology patients; primary and secondary LE)	RCT; intervention (18 days of MLB followed by elastic compression garment for 21 weeks) *v* control (elastic compression garment for 24 weeks)	90 women with unilateral LE of upper or lower limb at least 12 months post-treatment for disease (United Kingdom)	LVC	LVC for MLB plus garment was significantly greater compared with garment alone ($P = .001$); mean LVC for MLB plus garment, 31% *v* mean LVC for garment alone, 15.8%
LLLT	Carati et al[53]	Breast	Double-blind, placebo-controlled, randomized, single crossover trial (placebo *v* one cycle LLLT *v* two cycles LLLT; patients observed for 3 months)	61 women with LE (Australia)	LVC, upper body extracellular fluid distribution, dermal tonometry, and range of limb movement	After two cycles of LLLT, significant LV reduction observed at 1 and 3 months post-treatment ($P < .05$); extracellular fluid index significantly reduced at 3 months post-treatment ($P < .05$); significant softening of tissues in affected upper arm ($P < .05$); no effect on range of limb movement
	Ahmed Omar et al[54]	Breast	Double-blind, placebo-controlled, randomized trial (placebo *v* active LLLT three times per week for 12 weeks)	50 women with LE (Egypt)	Arm circumference, shoulder mobility, and grip strength	Significant LVC in active LLLT group compared with control group at 8 and 12 weeks post-treatment ($P < .05$); similar improvements observed in shoulder mobility and grip strength at 12 weeks for LLLT group ($P < .01$)
Pharmacotherapy	Zimmermann et al[50]	Oral cavity	Double-blind, placebo-controlled, randomized, prospective trial (oral *v* IV administration of sodium selenite for 21 days surrounding operative period; patients observed for 2 weeks postsurgery)	20 patients (18 men, two women) with squamous cell carcinoma in oral cavity who had undergone surgery with bilateral neck dissection (Germany)	Distance and circumference measurements of tragus, nostrils, corner of mouth, and tip of chin	Sodium selenite significantly reduced LE after surgical treatment for oral and maxillofacial tumors ($P < .05$); most appropriate within 2 weeks after surgery when manual lymphatic decongestion therapy is not practical
Surgery	Campisi et al[55]	Upper and lower limbs (not limited to oncology patients; primary and secondary LE)	Longitudinal study of patients diagnosed with LE who were treated with microsurgical techniques over 30 years	1,500 patients with peripheral LE treated with microsurgical techniques (Italy)	LVC measured by lymphoscintigraphy and water displacement	LVC significantly improved (> 75% excess volume reduction) in 83% of patients after mean follow-up of 10 years
	Campisi et al[56]	Upper and lower limbs (not limited to oncology patients; primary and secondary LE)	Cross-sectional study of patients diagnosed with LE who were treated with microsurgical techniques over 30 years	1,800 patients with peripheral LE treated with microsurgical techniques (Italy)	LVC measured by lymphoscintigraphy and water displacement	LVC significantly improved (mean excess volume reduction, 67%) in 83% of patients after mean follow-up > 10 years

Abbreviations: LE, lymphedema; LLLT, low-level laser therapy; LV, limb volume; LVC, limb volume change; MLB, multilayer bandaging; RCT, randomized controlled trial.

self-care practices, because those who reported more breast cancer–related LE symptoms spent more time engaged in self-care practices but reported poorer QOL. These self-care practices, however, have never been evaluated in studies to assess their ability to prevent LE.[68]

DISCUSSION

LE is a adverse effect of cancer treatment. Estimates of the exact incidence and prevalence are not well established, especially for cancer sites other than the breast. Problems with concise definitions and measurement techniques have hindered obtaining good estimates, as have poor recognition of LE by health care providers and patients. The causes are better defined and center on patient characteristics (eg, obesity at diagnosis) and treatment modalities (eg, ALND). Prevention strategies are untested; however, there is some evidence supporting exercise. The sequelae of LE are many, including poorer QOL and body image, interference with social functioning and job performance, and increased health care costs.[64,65,69] Treatments, mainly with compression and MLD, are somewhat effective if started early when symptoms first appear and if maintained. The risk for LE does not disappear, although it is reduced, as the time since initial cancer diagnosis increases.

This review has identified many areas related to LE that require additional research. First, most research on LE has focused on breast cancer survivors.[62] Because patients with other types of cancer (eg, gynecologic, urologic, and head and neck) are susceptible to LE, the magnitude and impact of this problem in a variety of cancer sites need to be determined. Second, consensus on a definition of LE, including the best measurement tool, needs to be obtained. Self-report has a place in perhaps early recognition of symptoms of LE and should be considered. Moreover, patients should be informed about signs and symptoms to be aware of and report them, thus enabling treatment to start early, when intervention is most successful, and the sequelae of LE are not as deleterious.[64] Proper and prompt treatment for patients with early signs of LE should be a priority, which suggests that access to qualified providers must be facilitated. The capacity of the provider workforce to accommodate this need is not well known.

Prospective assessment of limb volume at regular checkups could also assist in detecting early-stage LE as another vital sign obtained and assure follow-up for any swelling found. Because the effects of LE have an impact on QOL and social as well as physical functioning, treatment should include psychosocial support and counseling. Lastly, although some studies have demonstrated the increased health care costs attributed to LE diagnosis,[69] no studies have collected data on the ability of patients to get needed care once diagnosed with LE. Anecdotal reports of lack of insurance coverage for compression garments and/or physical therapy visits suggest other reasons for worsening of symptoms and poorer psychologic outcomes.

Overall, the evidence to date points to several conclusions. LE is an unwelcome consequence of cancer treatment, and patients and health care providers should be aware of the signs, symptoms, and risk factors for LE. Access to proper and prompt treatment should then be a priority, and barriers to this care (ie, cost, availability of certified provider) should be removed. More research is urgently needed on causes and ways to prevent and treat LE. Finally, consensus on definition of LE and ways to easily assess swelling must be adopted to identify early-stage cases and quantify the magnitude of the problem across all cancer sites. This last point will become increasingly important in obtaining resources to pay for and treat all instances appropriately and reduce sequelae of this adverse effect of cancer treatment.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

The author(s) indicated no potential conflicts of interest.

AUTHOR CONTRIBUTIONS

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