

Best-Practice Guidelines in Assessment, Risk Reduction, Management, and Surveillance for Post-Breast Cancer Lymphedema

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Abstract Breast cancer-related lymphedema (LE) is a progressive, chronic disease that affects millions of cancer survivors and primarily results from surgical lymphatic vessel and/or node removal and radiation therapy. Patient support and education in the importance of early detection is essential in helping health care providers detect lymphedema early, when there is the best chance of preventing progression. Improved imaging and surgical techniques have reduced the incidence of LE; however, effective risk-reduction and treatment have historically lacked the level of evidence necessary to

standardize effective treatment. The purpose of this article is to report an extensive review of literature, including highlighted multidisciplinary studies within the past 3 years, in order to update best-practice guidelines in assessment, risk reduction, management, and surveillance for post-breast cancer lymphedema.

Keywords Breast cancer · Lymphedema · Practices · Risk reduction · Management · Surveillance · Lymphatic · Combined decongestive therapy · Complementary · Manual lymphatic drainage · Exercise · Compression garment · Intermittent pneumatic compression pump · Limb volume

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Introduction

Secondary lymphedema (LE) is a chronic, progressive, and debilitating condition estimated to affect over 11.4 million American cancer survivors who are at risk of developing LE in their lifetimes [1, 2]. LE is the abnormal accumulation of lymph in the interstitial spaces leading to persistent swelling of the affected regions, resulting in several symptoms and sequelae [2]. Breast cancer survivors are at lifetime risk for developing LE: occurrence is from 41 % to 94 % within 57 months, depending on the measurement tools and defining criteria; however, it can present with onset ranging from early in the post-operative period to beyond 30 years post-treatment [2, 3, 4]. Among breast cancer survivors, the most common causes of secondary LE are lymphatic vessel and/or node removal and radiation treatment [4]. LE symptoms have been shown to adversely affect survivorship after breast cancer treatment [5].

Although the definition of LE has not been standardized, a common definition is swelling of the affected limb which is greater than the baseline (pre-operative) measurement *or*

compared with the unaffected limb [6••]. Multiple longitudinal studies provide evidence that limb volume and its appearance may fluctuate over time with LE emerging as transient, chronic, mild, or severe [3•, 4]. However, the presence of initial transient swelling in the early post-operative phase has been associated with later LE development [7]. Identification of swelling during the post-operative phase provides an opportunity for early intervention which may theoretically preempt progression to a chronic edematous state.

With an aging population of breast cancer survivors, education should include LE risk-reducing and rehabilitative strategies with management support [8••]. According to the theoretical model of elderly cancer survivorship by Bellury et al. [9], age alone is a risk factor for cancer diagnosis and treatment-related sequelae, for example, LE. Risk factors for breast cancer survivorship have been categorized as:

1. personal-modifiable (e.g., BMI, physical activity);
2. personal-nonmodifiable (e.g., age, gender);
3. age-specific (e.g., cognition);
4. cancer-specific (e.g., treatment type, metastasis); and

5. baseline health status (e.g., frailty) [9].

A conceptual model of the biopsychosocial factors affecting post-breast cancer LE is depicted in Fig. 1 [8••].

Diagnosis and Assessment

History and Examination

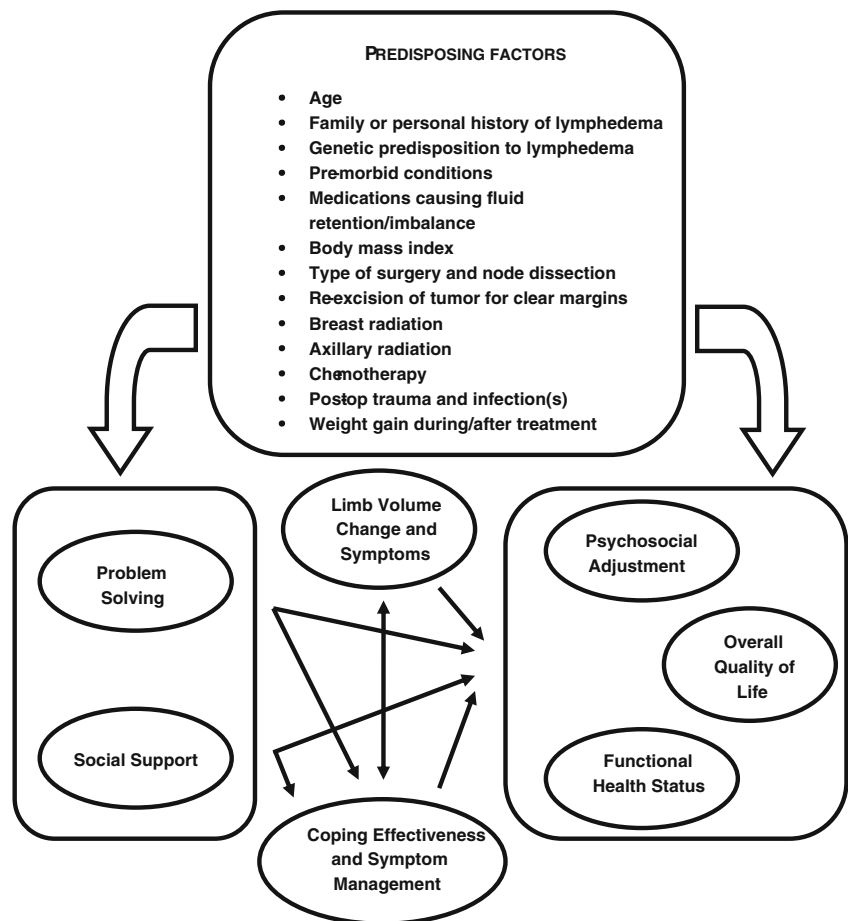
Detection and management of LE starts from clinical assessment and includes:

- cancer history, including primary and adjuvant cancer treatment(s);
- assessment of the anatomy, function of the lymphatic system, and physical manifestations; and
- LE staging determination [6••].

For a patient presenting with a swollen upper extremity, clinical, lymphatic, and venous system evaluation (with appropriate imaging) should be conducted. Consideration of duplex ultrasonography, to rule out deep venous thrombosis, and computed tomographic scanning, to rule out

Fig. 1 Conceptual model of biopsychosocial factors affecting post-breast cancer lymphedema. Adapted from Armer et al. [8••].

Rehabilitation concepts among aging survivors living with and at risk for lymphedema: a framework for assessment, enhancing strengths, and minimizing vulnerability. *Top Geriatr Rehabil* 2012;28(4):260–8



cancer recurrence (which is known to precipitate and exacerbate LE) may be warranted [6••, 8••].

Imaging

Several imaging modalities are available for assessment of the anatomy and function of the lymphatic system. Lymphoscintigraphy (LS) is the accepted standard for LE assessment [6••]. Lymphoscintigraphy utilizes a nuclear tracer, 99m-technetium, which is injected intradermally into the hand for lymphatic system uptake. Tracer imaging enables depiction of lymphatic anatomy and flow and can highlight pathologic changes because of lymphatic obstruction [10, 11]. Direct contrast lymphography has largely been replaced by lymphoscintigraphy as the imaging method of choice, because of the complexity of the procedure and associated risk of pulmonary embolism [5]. Despite this, lymphography may be useful for pre-operative assessment of complex lymphatic anatomy [5]. Indocyanine green (ICG) infrared fluorescent imaging is also used for imaging the lymphatic system in select research centers in the United States [12–16]. Magnetic resonance imaging (MRI) using gadolinium tracers has also been used outside the United States; however, intradermal injection of gadolinium lacks FDA approval for intradermal injection of gadolinium [6••, 17]. Ultrasound can be useful for assessing venous system changes, defining tissue spaces, and detection fluid accumulation [6••].

Assessment Tools

Objective limb volume (LV) measurement is used to detect increased swelling and to monitor changes over time [6••]. The exact method is not as important as using a standard, reproducible method consistently over time [6••].

- Water displacement remains the accepted standard for measurement of LV; however, this method is limited by its cumbersome nature, hygiene concerns, and difficult implementation [18, 19].
- Circumference tape measurement at designated landmarks, using a nonstretch tape measure, is the most common method for assessing LV change. It is not prohibited by limb mobility and size and is reproducible if done correctly using a standardized procedure [6••, 20]. Both limbs are measured at identified anatomical landmarks to monitor for changes over time [6••]. Circumference measurement is inexpensive, but time-consuming, and requires rigorous training to achieve reliable and accurate measurement [18].
- Perometry (Juzo, Cuyahoga Falls, OH, USA) uses infrared light and opto-electronic sensors to calculate LV from the three-dimensional silhouette of the limb [18,

21]. Perometry is efficient in time and hygienic, enabling measurement even of limbs with wounds, because no equipment touches the skin of the arm. The instrument is costly, however, particularly for smaller clinics. In a longitudinal study of breast cancer survivors, LV change from pre-operative baseline through 57 months post-surgery was assessed by use of four commonly cited diagnostic criteria (2 cm circumferential change, 200 mL perometry limb volume change, 10 % perometry limb volume change, and signs and/or symptoms) [3•]. Investigators reported that the 2 cm criteria resulted in the highest estimation of LE, followed by the 200 mL perometry criteria, with 10 % limb volume change by perometry and symptom report resulting in the lowest estimation [3•, 22].

- Fluid content can be measured by use of bioelectrical impedance spectroscopy (BIS) which measures extracellular fluid on the basis of resistance to a small electrical current [23–25]. BIS seems to be more sensitive than traditional diagnostic methods in potentially detecting early LE changes before physically measurable changes in LV are observed [6••, 26].
- Tissue texture is an important assessment characteristic that should be assessed in LE patients because of the skin's increased susceptibility to injury and infection [6••]. With LE progression, the limb tissues develop a fatty and fibrotic quality and subsequently become resistant to compression [6••, 27]. Tonometry has been used to measure tissue compressibility and its correlation with limb swelling; however, standard procedures have not been established and reliability remains an issue [23, 27].

Classification

Historically, there has been no international consensus on the definition of LE or the staging data used to reflect LE severity [6••]. In 2009, the International Society of Lymphology (ISL) published an updated consensus documenting the clinical staging and severity system on the basis of objective physical examination findings (Table 1) [28].

Risk Reduction

Absolute prevention is not yet fully possible in breast cancer-related LE; however, advances in cancer diagnostic imaging and surgical techniques have reduced the risk of LE and newer tools and techniques have enabled earlier detection of subclinical LE. In addition, early implementation of risk-reduction strategies may improve outcomes by preventing progression and sequelae of LE [29].

Methods to reduce development of LE are largely operative or physical, and include the following:

Table 1 Clinical staging and severity according to the International Society of Lymphology Consensus Document. Data reproduced with permission of Lymphology [28]: International Society of Lymphology.

The diagnosis and treatment of peripheral lymphedema. Consensus document of the International Society of Lymphology. Lymphology 2009, 40:49–57

Clinical stage	Description
0	Subclinical stage in which swelling is not seen despite underlying changes in the lymphatic system
I	The initial stage of swelling which can be transient and where simple elevation can alleviate swelling
II	Swelling is constant and pitting without resolution using elevation
III	The tissue has become hard and fibrotic with associated skin changes
Severity	Based on volume differences between affected and contralateral limb in unilateral presentation mild (<20 % increase) in limb volume, moderate (20–40 % increase), or severe (>40 % increase)

Operative Methods

Sentinel Lymph Node Biopsy (SLNB) vs. Axillary Lymph Node Dissection (ALND)

Earlier breast cancer detection has enabled use of less invasive surgical procedures to assess and treat the regional lymph nodes [6••]. In a systematic review, Sanghani et al. [30] reported ALND does not have any survival benefit compared with no dissection for patients with *negative* sentinel lymph nodes. The American College of Surgeons Oncology Group (ACOSOG) Z0011 trial ($n=813$) reported there is no benefit to performing ALND among patients with clinical T1 or T2 breast cancer with 1 or 2 positive (microscopic disease) SLNs who are treated with breast conservation, whole breast irradiation, and systemic therapy. At a median of 6.3 years follow-up, SLNB alone remained equivalent to ALND [31].

Axillary Reverse Mapping

A newer technique has been proposed to identify and make a distinction between the breast-draining and arm-draining lymphatic channels and nodes. This technique avoids disruption of lymphatic vessels draining the arm at the time of SLND or ALND. Although this technique is promising for reducing LE incidence, long-term follow-up studies have not been conducted and there has been controversy regarding the oncologic safety of this procedure [6••, 32, 33].

Lymphatic–Venous Anastomosis (LVA)

This operative technique uses injection of blue dye into the upper arm to identify lymphatic channels at the time of ALND to create connections between these channels and the venous system in an attempt to preserve lymphatic drainage of the affected limb [34]. Data from a one-year follow-up study show that patients who underwent ALND and LVA did not develop LE as evidenced through LS [35]. Longer follow-up and randomized control trials (RCTs) are needed to determine the true effectiveness in preventing LE.

Physical Methods

Early detection and intervention remain the primary strategy for reducing the incidence of chronic LE [6••, 29]. Because a lower incidence of LE is associated with contemporary surgical techniques, it is expected that breast cancer-related LE incidence will decrease further as more is learned from lymphatic preservation research with breast cancer treatment. Physical risk-reduction recommendations should take LE incidence into consideration and recognize the benefit–risk ratio when proposing particular risk-reduction regimens to patients [6••].

Promising findings have emerged from studies suggesting noninvasive approaches to reducing the occurrence of LE in at-risk survivors [36]. Stout Gergich et al. [37] reported, after an early pilot study, that LE incidence may be successfully reduced by using accurate assessment techniques and early intervention with compression garments. Recent data show that early physiotherapy after breast cancer surgery, including ALND, may be effective in reducing LE risk for at least 1 year [38]. Post-operative swelling has been associated with later LE development [7]. Awareness of an initial episode of transient swelling provides an opportunity for early intervention which may theoretically preempt progression to a chronic state. Finally, a growing body of evidence suggests that exercise does not exacerbate or trigger secondary LE [39, 40].

Management

Complete Decongestive Therapy

Complete decongestive therapy (CDT), also called complex lymphatic therapy, has long been the standard of care in the treatment of acute and long-term management of breast cancer-related LE [4, 41••, 42–44]. The primary components of CDT recognized by the Medicare Evidence Development and Coverage Advisory Committee (MEDCAC) in 2009 include:

1. manual lymphatic drainage (MLD);
2. compression bandaging (CB) and/or garments (CG);

3. exercise;
4. skin care; and
5. sequential pumps.

CDT is usually initiated as two phases, intensive CDT, indicated for moderate to severe LE, and modified CDT, for mild or moderate LE [42].

In a systematic review of literature evidence for CDT therapy published from 2004 to 2011, reviewers recruited by the American Lymphedema Framework Project (ALFP) rated 26 eligible studies [41••]. They found that CDT as a combination of intervention procedures, and MLD and CB as individual components, were effective in reducing lymphedema [8••]. Despite the limited number of RCTs, CDT continues to be viewed as effective in reducing LE, although the relative contribution of each of the individual components affecting the efficacy of CDT is not well understood [8••]. CDT should be administered by a specialty-trained therapist with the objective of reducing swelling and fibrosis in the affected area. Patient training in life-long LE self-management practices should also be included [4, 41••, 43, 45•].

After intensive CDT, self-maintenance may include self-MLD, daytime compression garments, night-time bandaging, exercise, skin care, and nutrition. Wearing properly-fitted compression garments enables management of swelling and preservation of skin integrity [41••, 42, 43]. For frail patients with LE who may not tolerate high levels of compression, modification of compression bandaging with an alternative non-elastic compression device (e.g., Velcro closure) should be considered [8••]. Although the level of evidence in the literature regarding compression garment use during exercise is “moderate” [41••], experts recommend the use of a compression garment during exercise [43].

Manual lymphatic drainage involves light, lymphatic massage to move lymph fluid from the extremity to a more central (proximal) region of the body where lymphatic flow is not impaired [41••]. Induced muscle contractions increase lymphatic and vascular flow throughout the body and thereby reduce lymphatic stasis and LE symptoms [4, 41••, 46]. Survivors have different physical and cognitive limitations; therefore, individualized, supervised exercise programs should be developed by a multi-disciplinary rehabilitation team to create a safe, appropriate regimen [47].

Patient education regarding proper skin care management is an essential component of CDT which reduces the risk of exacerbating LE because of inflammation and infection. Self-maintenance instruction should include hygiene, moisturizing, sunscreen, and avoidance of constriction from blood pressure cuffs or tourniquet application [43, 48]. Additional patient education should also include nutritional information and strategies to promote optimum weight management as another means of preventing LE development and progression [48, 49].

Few recommendations exist in the literature for LE management in the palliative care setting. Beck et al. [50•] conducted a systematic review of the published literature from 2004 to 2011 regarding the evidence of LE management in palliative care and summarized five eligible studies using the Oncology Nursing Society (ONS) Putting Evidence into Practice (PEP) guidelines [51]. They concluded that CDT, MLD, and compression bandaging are categorized as “effectiveness is not established,” but note that no adverse findings were reported [50•]. On the basis of these findings, it is suggested that CDT, MLD, and compression bandaging are of potential benefit in LE symptom control and improved quality of life for LE patients receiving palliative care for symptom management in advanced disease, for example recurrent breast cancer.

Surgical Management

Cormier et al. [52••] conducted a systematic review of the literature from 2004 to 2010 pertaining to the surgical treatment of LE. Twenty identified studies met the inclusion criteria and were categorized as excisional/debulking, lymphatic reconstruction, or tissue transfer. Excisional procedures remove fibrofatty tissue that has formed secondary to sustained lymphatic fluid stasis. Procedures include debulking, liposuction, and amputation and should be considered only when standard LE treatment, for example, CDT, has failed. Lymphatic reconstruction is a microsurgical technique for reconstruction or bypassing of obstructed lymphatic channels which is performed to improve lymphatic drainage. These procedures can include anastomoses from the lymph vessels to veins, lymph nodes to veins, or distal to proximal lymphatics using lymphaticovenular anastomosis (LVA). Tissue-transfer procedures involve transferring lymph tissue into a congested area with anastomosis of lymphatic vessels in order to reestablish lymphatic flow. The largest LE volume reduction was associated with excisional procedures (91.1 %), followed by lymphatic reconstruction (52.9 %), and, last, tissue transfer procedures (45.6 %) [52••].

It is noted that most of these surgical procedures will require lifelong compression garment use to maintain post-operative results [52••]. Findings regarding surgical procedures are difficult to generalize because of lack of high-level evidence and the need for surgical vs. non-surgical studies with larger sample sizes. Although no adverse events were reported in the studies reviewed, patient teaching should include awareness that these surgical procedures can be associated with significant risks, as with any surgical procedure, including infection, delayed wound healing, and stricture and/or occlusion of newly created anastomoses [52••].

Intermittent Pneumatic Compression (IPC) Therapy

Several early systematic reviews exist pertaining to the use of IPC therapy for LE management. Previously, in a review

by Moseley et al. [53], IPC was identified as the most likely therapeutic modality to facilitate large volume reductions in the treatment of LE. Conversely, Rinehart-Ayres et al. [54] reported there was no evidence to suggest that use of an IPC pump offers more benefit than arm care and hygiene practices, nor does evidence support one type of IPC pump regimen over another. However, a recent study confirmed by NIR fluorescence imaging reported lymphatic function improvement for four of six subjects after use of an advanced programmable IPC with a segmented sleeve and calibrated gradient processor versus a less advanced older version of the device [12].

Because of the lack of consensus regarding recommended IPC treatment conditions or frequency, Feldman et al. [55] conducted a systematic review of peer-reviewed studies from 2004 to 2010. Findings indicate that although IPC devices are reportedly well-tolerated in low to moderate pressure ranges and seem to be safe for home use, no clear guidelines for compression levels and frequency emerged from the literature. They concluded that IPC may be appropriate as part of a supervised multi-modality approach for home-based LE management for some patients.

Exercise

Schmitz et al. [56•] report that at 6 years post-diagnosis, 57 % of survivors ($n=287$) experienced one or more late effects of breast cancer treatment amenable to rehabilitative intervention (exercise). Furthermore, a systematic review by Kwan et al. [57••] of studies of exercise and LE care published from 2004 to 2011 concluded that breast cancer survivors may safely engage in an instructed, supervised exercise regimen throughout their survival, including during treatment. They drew attention to six RCTs [19, 58•, 59•, 60–62] and one cross-over study [63] which furnished “highly-likely-be-effective” evidence there is very little risk of development or exacerbation of upper extremity LE as a result of resistance exercise [57••]. The physical activity and lymphedema (PAL) studies by Schmitz et al. [57••, 58•, 59•] were cited as innovative studies revealing that slow, progressive resistance weight-lifting exercise is likely to be effective in reducing risk of LE symptoms and progression, and in increasing overall strength of survivors post-ALND. Preliminary studies examining aerobic and resistance combination exercises also report no increase in LE, and seem safe [39, 64, 65].

In the review by Kwan et al. [57••], the reported range of LE incidence among intervention participants was 13 % at 2 years [19], 17 % at 10 to 38 months [60], 30 % at 18 months [39], and 17 % at 2–6 years post-diagnosis [58•]. It should be noted that the incidence of LE was higher in control groups than in the intervention groups [19, 58•, 61, 62]. Rehabilitative and exercise intervention have been

shown to benefit breast cancer survivors with LE; however, programs must be structured according to the abilities of each patient with close monitoring by qualified therapists to ensure safety and standardization [66, 67]. Additional research is needed to offer recommendations regarding compression garment use during exercise [57••].

Complementary and Alternative Medicine (CAM)

Complementary and alternative medicine (CAM) is widely used as a means to achieve health and well-being. Breast cancer patients use CAM more often than patients with other types of cancer because of treatment side effects and problems continuing after treatment [68]. Wanchai et al. [68] found that among Thai survivors, CAM information is obtained through peers and only one-third of Thai breast cancer survivors report sharing information about CAM usage with their physicians, because of their fear of a negative response.

Studies to evaluate the effectiveness of CAM in reducing LE are usually based on self-report and results are variable [69]. A growing body of literature offers evidence that the practice of mindfulness-based stress reduction (MBSR) improves quality of life and reduces psychological distress [70]. The use of aqua lymphatic therapy (ALT) to manage LE has also been reported, with favorable results. Investigators noted ALT adherence was higher—78 % compared with <30 % adherence to compression bandages and/or garments, self-massage, and special exercise [71]. Recent pilot data suggest that yoga, acupuncture and/or moxibustion, and Tai Chi breathing with arm exercises seem safe [72–75]; however, additional large-scale studies are needed to determine the effect of CAM therapy in LE symptom management.

Psychosocial and Economic Considerations

It is well-established that recurrence of breast cancer is the greatest fear among survivors, followed by fear of developing LE [6••, 76]. Investigators from the United Kingdom found that at least 78 % of patients with LE reported lost work time, with 9 % suffering a negative job status outcome [77]. Shih et al. [78] reported that two-year medical insurance claim costs for US breast cancer survivors with LE (\$23,164) were nearly double those for survivors without LE (\$14,875). Patients with LE were twice as likely to have lymphangitis or cellulitis, contributing to a more advanced condition and compounding medical costs [78]. These findings indicate that financial issues for cancer survivors with LE extend beyond insurance coverage and rehabilitation costs [8••, 78, 79].

Data suggest that breast cancer survivors experience chronic psychological distress associated with symptoms, beginning at pre-diagnosis (biopsy) and extending throughout the

post-treatment period [79]. Survivors with LE often report poor physical function, physical self-image, and quality of life, and social isolation leading to persistent psychological distress [80–82]. Fu et al. [81] conducted a systematic review of 23 published studies from 2004 to 2011 on the psychosocial effect of LE and reported that poor psychosocial and social well-being are prevailing findings among survivors with LE.

Surveillance

Surveillance for LE signs and symptoms starts with obtaining a focused patient history regarding swelling of the at-risk limb and other areas of the body potentially affected by cancer treatment [8••]. Regular anthropometric and symptom assessment beginning pre-operatively through the post-operative period and at three-month intervals thereafter for at least the first year post treatment provide the best opportunity to monitor LE [8••]. Early detection provides the best chance to preventing progression [6••]. Routine LV measures during follow-up visits in a busy clinical practice setting are feasible, efficient [38, 83], and should be included in standard surveillance practices [84••]. Triage for further assessment is recommended when symptoms (e.g. sensation of heaviness and/or observed swelling) or girth and/or volume measures increase.

Awareness of predisposing factors, for example, high BMI, weight gain after breast cancer treatment, post-operative swelling, post-operative seroma, infection, and LE family history (Fig. 1), can be used to guide individualized education and support in developing LE risk-reduction behavior. Irrespective of the method used to assess LV, it is important that the approach selected be consistently applied at regular intervals, for example pre and post-operatively, quarterly (for 12 months), semi-annually (for 1–3 years), and then annually, thereafter. Such assessment, accompanied by education on self-monitoring, provides optimum opportunity for early detection and intervention.

Stout et al. [85••] suggest that objectives for a prospective surveillance model for breast cancer survivors should include:

1. promotion of monitoring for functional and physical impairment commonly associated with breast-cancer treatment;
2. provision of education about early signs and symptoms of LE and the importance of early detection;
3. referral for rehabilitation and exercise intervention when physical limitations are identified; and
4. promotion and support of physical activity, exercise, nutrition, and weight-management behaviors throughout survival.

These recommendations are supported by Schmitz et al. [67] and Binkley et al. [86•] who also advocate a

multidisciplinary prospective surveillance approach in the management and treatment of adverse effects of breast cancer treatment.

An additional component of an effective surveillance program is the involvement of researchers in developing minimum data sets (MDS) to create, organize, and disseminate up-to-date clinical research data and measure patient outcomes nationally and worldwide. Under the oversight of Chi-Ren Shyu, Director of the University of Missouri Informatics Institute, and with National Library of Medicine funding, an internet-based information technology system has been designed and tested as a means of collection and transfer of data which will be used to update best practices with new research at regular intervals [87].

Surveillance programs should include a patient-related component with:

- pre-operative assessment of, and measurements on, all breast cancer patients requiring surgical treatment;
- education and supportive regimens tailored to each patient relevant to prevention and early detection of LE;
- ongoing monitoring for, and assessment of physical impairment, beginning with breast cancer treatment and continuing throughout recovery and survivorship;
- referral to resources and implementation of self-care management regimens for patients who have developed breast cancer-related LE; and
- opportunities for clinical trials and programs to assess psychosocial and social well-being.

A research component of the surveillance plan should include support for ongoing development of the MDS system. As a minimum, at each visit, the clinicians should assess for symptoms of heaviness and/or observed swelling. Self-report of symptoms is sufficient to initiate referral for further assessment by an expert in this area.

Conclusion

These guidelines are provided using the latest information available from published reports and experts in the field. These recommendations are synergistic with the new multidisciplinary model proposed by the National Accreditation Program for Breast Centers (NAPBC) for early detection of physical impairment with the objectives of:

- promoting monitoring of common post-treatment physical impairment;
- introducing rehabilitation and exercise intervention when issues are identified; and
- encouraging and supporting physical activity throughout breast cancer patients' diagnosis, treatment, recovery, and survivorship [88].

Despite the authors' desire to define clear, agreed-upon practices, data are still limited in many areas because of the lack of large replicated trials. Diagnosis and assessment methods are available which should be utilized in standardized fashion to follow patients and their treatment [89••]. Newer detection methods and increased attention to survivorship are likely to shorten the time to initial diagnosis and thereby improve patient outcomes. In addition, continued improvement in cancer diagnosis and treatments are also likely to reduce incidence. Finally, a good range of treatments is available for patients with LE. Hopefully, an increase in the number of high-level studies will promote research on determination of the best treatment(s) for each patient, leading to optimum quality of life.

Conflict of Interest J.M. Armer declares that she has no conflict of interest.

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M. Bernas declares that he has no conflict of interest.

P. Ostby declares that she has no conflict of interest.

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- Of importance
- Of major importance

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