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LYMPHEDEMA INCIDENCE, PREVENTION AND TREATMENT (J ARMER, SECTION EDITOR)

Breast Cancer–Related Lymphedema: Personalized Plans of Care to Guide Survivorship

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Abstract

Purpose To present and discuss care domains (oncologic, cardiometabolic, aging, behavioral, environmental) for clinicians when approaching care for a breast cancer survivor at risk for developing breast cancer–related lymphedema (BCRL), as well as survivors who have been diagnosed with BCRL. Assessment using each domain aids in decision-making, yet also identifies barriers to pursuing personalized care for survivors with BCRL.

Recent Findings BCRL occurs from damage to the lymphatics during breast cancer treatment and occurs in approximately 20 to 40% of survivors. Prospective surveillance and early treatment for BCRL are supported in the literature; however, these approaches are frequently not used within evidence-based recommendations.

Summary The five domains can be used to develop a personalized plan of BCRL care. Barriers to pursuing personalized care for survivors with BCRL are identified. Future work in developing evidence-based recommendations is needed to guide clinicians and survivors during prospective surveillance, successful risk reduction, early diagnosis, and treatment of BCRL.

Keywords Breast cancer survivorship · Breast cancer–related lymphedema · Prospective surveillance · Lymphedema risk assessment · Social determinants of health · Cancer survivorship care

Introduction

As addressed throughout this special issue, secondary lymphedema is currently an incurable and chronic condition [1, 2]. The most common form of secondary lymphedema is breast cancer-related lymphedema (BCRL). BCRL occurs from damage to the lymphatic system from cancer treatment and occurs in approximately 20 to 40% of breast cancer survivors [3–6]. Lymphatic system damage can be caused by surgical procedures, radiation to the axilla and chest wall, postoperative infections, and certain chemotherapy agents [1, 7, 8••].

The most common or pronounced symptom of BCRL is often swelling of the arm, chest, or lateral back on the side affected by breast cancer. However, other early symptoms may include a feeling of heaviness in the affected side without a pronounced difference in volume or circumference measurements. As can be imagined, BCRL is a condition that negatively influences breast cancer survivors' quality of life [9–13]. A BCRL diagnosis is also expensive for survivors [14••, 15••, 16] and may affect work engagement and job performance and increase stress [17, 18•].

Although incidence of lymphedema after treatment for breast cancer has declined since the transition to sentinel lymph node biopsies, breast cancer survivors remain at a lifetime risk of developing the condition [19]. Prospective surveillance may expedite a BCRL diagnosis and treatment before progression to a later stage and/or complications occur (e.g., increased swelling and/or pain, decreased mobility, and infection) [20, 21]. Early diagnosis and treatment of BCRL is critical in slowing the progression and decreasing the lifelong burden of the condition [3, 22, 23]. Treatment for BCRL begins with nonsurgical interventions aimed at decreasing swelling (volume), maintaining the health of surrounding tissues (prevention of fibrosis), and preserving or improving mobility.

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The objectives of this case study report are to (1) aid clinicians in developing a personalized plan of care for breast cancer survivors at risk for and those with BCRL and (2) identify knowledge gaps and barriers to BCRL care. Here, we present and discuss care domains (oncologic, cardiometabolic, aging, behavioral; environmental) [24••] that clinicians can consider when approaching care for a breast cancer survivor at risk for developing BCRL, as well as survivors medically diagnosed with BCRL. By assessing each domain, contextual factors that influence BCRL risk reduction, diagnosis, and treatment can be incorporated into survivorship care. Our goal for this report is to highlight the uncertainty in planning BCRL-related care for breast cancer survivors and how this uncertainty can be addressed using the care domains and evidence-based guideline recommendations. Throughout, we use the definition of cancer survivor subscribed to by the National Comprehensive Cancer Network (NCCN) and Oncology Nursing Society (ONS), both of which designate someone as a survivor upon cancer diagnosis [25, 26].

Care Domains

The five care domains discussed below originate from a framework developed by Stout et al. [24••] to inform clinical screening for cancer patients' readiness for and subsequent referrals to increase physical activity. The five domains begin to address the complexity involved in recommending physical activity and exercise for cancer patients and survivors. We believe approaching physical activity and exercise with cancer patients is similar to initiating prospective surveillance and early treatment for BCRL. As with physical activity, readiness and capability for BCRL education, exercises, and risk reduction strategies will vary. That is, a breast cancer survivor who just recently finished with cancer treatment will have a different capacity for BCRL education and risk reduction activities over time. Furthermore, breast cancer survivors are a heterogeneous group, and thus, have varying degrees of risks for developing BCRL. By outlining the five care domains as they correspond to what is known about secondary lymphedema, a personalized approach to BCRL care can be developed.

Oncologic

Five-year survival rates following treatment for breast cancer have risen to over 90% leading to a focus on long-term side effects from treatment and quality of life [3, 27]. All breast cancer survivors carry some lifetime risk for lymphedema, and risk assessment for this domain includes a thorough cancer treatment history. Several oncology treatment–related factors can increase risk of the development of BCRL. The primary risk factor is lymph node dissection [28]. Breast cancer survivors who have had axillary lymph node dissection have been shown to have four times the risk of BCRL than survivors who have had sentinel lymph node dissection [4]. Higher numbers of nodes removed increases the probability of injury to the lymphatic system and/or blockage from disease involvement; thus, there is greater lymphatic compromise.

Radiation therapy to regional lymph nodes also raises the risk of BCRL above the risk for survivors who receive radiation to the breast and chest wall only [28]. Certain chemotherapy agents, such as taxane-based, anthracycline-based, and trastuzumab regimens have been associated with increased occurrences of BCRL [5, 8, 29, 30, 31•, 32]. Thus, it is important for the interdisciplinary health care team to be familiar with the survivor's chemotherapy and full oncologic history.

Cardiometabolic

Cardiotoxicity is recognized as a side effect of chemotherapy agents classified as anthracyclines, taxane-based chemotherapy and targeted therapy drugs such trastuzumab, bevacizumab, lapatinib, sunitinib, and sorafenib [30, 31•, 32–34]. Specific protocols are in place to prevent heart damage due to treatment. For example, according to National Comprehensive Cancer Network (NCCN) guidelines for patients receiving anthracycline chemotherapy, a multi-gated acquisition (MUGA) scan is conducted to ensure an adequate ejection fraction [33, 34]. Baseline echocardiography is also conducted.

Edema can occur with congestive heart failure, and it is important to differentiate between vascular edema and lymphedema. Risk assessment for this domain includes fluid monitoring and assessment of cardiometabolic comorbidities. Although lymphedema usually occurs on the affected side where breast surgery and axillary dissection was performed, if left untreated, it can also be congested into the truncal and neck regions. Hypertension and congestive heart disease may be treated with a beta-blocker, ACE inhibitor, digitalis, and a diuretic. Although these medications can favorably control hypertension secondary to heart disease, there is an association of calcium channel blockers with BCRL development [35]. Furthermore, there is a common misconception that diuretics can decrease the swelling caused by BCRL. Patient factors such as high BMI or post-operative infections can also increase the risk for development of BCRL [5, 31•]. It is a delicate balance to manage BCRL care given a survivor's oncologic and cardiometabolic history.

Aging and Comorbidity

The median age of women diagnosed with breast cancer is 62 years [3]. Paired with the aforementioned 90% 5-year survival rate, breast cancer survivors may live many years navigating the lifelong risks of developing BCRL [3]. Furthermore, upon diagnosis, BCRL is not curable. Initial goals of treatment are to reduce symptom burden as early as possible. With earlier

diagnosis, there is a subsequent reduction in treatment burden, as well; however, due to comorbidities, such as cardiovascular disease, hypertension, or diabetes, survivors over the age of 65 are at risk for delayed diagnosis of BCRL [36].

Risk assessment in the aging domain benefits from prospective surveillance which should include baseline measures and assessment of the survivor's ability to engage in risk-reduction activities, such as specific low-intensity, post-operative exercise or the donning and doffing of compression garments. In addition, the interdisciplinary health care team should be aware of the comorbidities and/or medications that might contribute to the development of BCRL or aggravate a currently manageable stage of BCRL. Certain comorbidities can threaten perhaps already tenuous fluid balances. More sedentary lifestyles with the aging process are common; therefore, ideal weight and BMI become important components to consider. Similarly, the risk of BCRL development should be considered alongside elective or necessary surgeries or procedures that could further damage or compromise the lymphatic system.

Behavioral

There are physiological, psychological, and psychosocial dimensions that are associated with BCRL, all of which correlate to low adherence to performing BCRL self-management regimens [11, 12, 37–40]. Symptom distress and treatment burden are factors contributing to non-adherence [41]. A state of distress often affects the survivor's self-efficacy (the belief that she can affect a situation) and self-regulation (the ability to control factors that interfere with goal achievements). Thus, self-efficacy and self-regulation impact the success of BCRL treatment [42•, 43]. Regardless of the BCRL management regimen, non-adherence undermines treatment resulting in progression of BCRL and increased severity of symptoms [44]. Often, survivors returning to work have decreased self-efficacy in regard to performing like their previous selves. Also, there are perceptions by others that she is no longer able to "pull her weight" and requires accommodations. Isolation from decreased socialization can inhibit feelings of self-worth and well-being [11, 18•]. Knowledge and positive perceptions of self-efficacy and self-regulation are also associated with patient adherence [41].

Of major psychological importance, there is fear of cancer recurrence for all survivors; however, an additional fear is the development of BCRL. Fear can escalate, from a normal level to a clinical level, leading to anxiety, dysfunction, and decreased quality of life [45••]. BCRL education and awareness remain important components of care, as it has been associated with early intervention and adherence [46, 47]. Risk assessment for this domain includes the use of health-related quality of life measures such as the Psychological Adjustment to Illness Scale (PAIS), the Functional Assessment of Cancer Therapy/Lymphedema (FACT+4), or the 36-Item Short-Form Health Survey (SF-36 or SF-12) which can be helpful in establishing baseline behavioral assessments. Follow-up scores could then be used to gauge behavioral factors that contribute to BCRL risk or issues with BCRL management.

Environmental

There are known disparities related to social determinants of health in breast cancer diagnosis, timely treatments, and quality of life during survivorship [48, 49]. The same social determinants of health, such as household income, education level, and access to health care, should be considered alongside the assessments gleaned from the other domains. Inevitably, BCRL diagnosis impacts finances and/or work abilities [14••, 15••, 18•] and quality of life [9, 11, 13, 41]. Risk assessment in this category should incorporate a survivors' environmental and social determinants of health—including access to resources such as a therapist specializing in the treatment of lymphedema and health literacy levels necessary to participate in BCRL education and risk-reduction strategies. Upon BCRL diagnosis, assessment in this domain will also include a survivor's ability to adopt and adhere to self-management and maintenance regimens.

Case Study

A 60-year-old white female, E.M., was diagnosed with Stage IIA invasive intraductal breast ER/PR+ HER2+ cancer of the right breast in 2017. Definitive treatment was a right-modified radical mastectomy with an axillary lymph node dissection after positive sentinel nodes were identified: 4/10 nodes were positive for cancer. Post-op cancer treatment included an adjuvant regimen of doxorubicin/cytoxan followed by paclitaxel plus trastuzumab. E.M. has a history of hypertension and congestive heart failure (CHF) controlled by a thiazide-type diuretic and a calcium channel blocker.

E.M. is divorced and works part-time at a local pet supply store to "get her out of the house and boost her income a little bit." She lives in a condominium where there is a fitness center but does not use it nor participate in any supervised exercise programs. Her daughter is supportive and comes over often to check on her. She has stated in the past that she watches a lot of television and feels "lonesome" some of the time.

E.M. presents today for her 3-year follow-up appointment with her oncologist. On physical exam, E.M. is 5′4″ and weighs 189 lbs. Her BMI is calculated as 32.4. Blood pressure is 126/76, and there is no jugular distention or shortness of breath and no irregularity of the heart on auscultation, such as ventricular gallop. She had recently undergone echocardiography which indicated left ventricular hypertrophy. She reports truncal and right arm edema with no complaints of pain. Duration of edema is stated as "off and on for about 8 months,

but I just thought it was from the surgery and I'm on a water-pill for that." The right arm is visibly larger than the left with circumferential measurement difference of 3%. E.M. states her job requires her to lift heavy objects somewhat frequently, and she has noticed her swelling is increased on the days when she works. Other system reviews were unremarkable.

Discussion—Plan of Care

The five domains are used to guide the assessment of E.M. A physical examination and interview reveal that her cancer treatment history, age, elevated BMI (> 30 = obese), sedentary behaviors, and environment place E.M. as a higher-risk candidate for BCRL. In addition to her hypertension and cardiovascular disease, her physical exam and psychosocial interview place her at risk for additional comorbidities such as diabetes, hypercholesterolemia, and/or depression. E.M. is an exemplar breast cancer survivor who would have benefitted from a prospective surveillance program for BCRL. There were some missed opportunities in E.M.'s survivorship care that could have reduced risk for BCRL emergence and progression to its current stage. Those opportunities include components of a prospective surveillance program such as pre-operative baseline arm measurements, early education, risk-reduction strategies, and non-invasive intervention at the first signs or symptoms of BCRL.

Health care provider knowledge of lymphedema is essential and has been identified by survivors as a barrier to optimal BCRL care [41]. E.M.'s care team (primary care provider and oncologist) could potentially access survivorship recommendations from a number of leading oncological societies including, but not limited to, the American Society of Clinical Oncology (ASCO), the National Comprehensive Cancer Network (NCCN), the National Lymphedema Network (NLN), and the Oncology Nursing Society. E.M.'s primary care provider previously consulted ASCO's guidelines for breast cancer survivorship care [27] which suggest that BCRL prevention and risk reduction are important and should be discussed with survivors but do not necessarily provide clear instruction for continued surveillance. Her primary care provider encouraged E.M. to discuss BCRL risk factors with her oncologist. At her 3-year follow-up appointment, E.M.'s oncologist is familiar with the ASCO and NCCN guidelines for lymphedema care and refers her to physical therapy because she suspects E.M. is describing signs and symptoms of BCRL.

Although the referring physician suspects she has lymphedema, a specialty-trained therapist should be aware of the relationship between the cardiovascular and lymphatic systems and perform her assessment accordingly, including evaluation of congestive heart failure signs and symptoms and a system review [50]. After conferring with the referring physician and taking measurements, the therapist has determined the patient presents with Stage II lymphedema (swelling is not relieved by limb elevation, and there is the presence of tissue swelling and pitting) and prescribes Phase I combined decongestive therapy (CDT) for 1 week. At 1-week follow-up, the lymphedema was reassessed and a custom fitted sleeve was prescribed to wear during the day and another garment for use during sleep. Teaching E.M. to maintain Phase II CDT was critical at this point. Phase II CDT includes self-manual lymphatic drainage, wearing compression garments, performing skin and nail care with observation and applying moisturizer, wearing gloves when there is a possibility for a cut or injury to the skin, and exercises per treatment plan. Per the NCCN guidelines, the therapist also suggested E.M. pursue water-based exercises to help slow lymphedema progression and maintain her current mobility and function. Providing resources that ease barriers to accessibility and/or costs are also important, if applicable.

Survivors should drive the goal-setting process for all of the interventions that contribute to their BCRL management regimen [51]. This includes interventions such as weight management programs and supervised exercise. The therapist monitors E.M.'s weight, mobility, access to resources, and psychosocial/psychological adjustment to BCRL, although BCRL management requires interdisciplinary involvement. Evidence-based guidelines for lymphedema risk reduction, prospective surveillance, treatment, and educative-supportive components are needed to help clinicians prescribe the best plan of patient and family-oriented care [51, 52••].

Clinical Implications

Assessment within each care domain provided a systematic and clear depiction of the lifelong BCRL risks a breast cancer survivor may face. This framework lends an advantage in that it can be used for interdisciplinary assessments to guide plans throughout survivorship. These domains also provide a framework from which uncertainty in BCRL care decisions are identified. What becomes less clear is the plan of care an interdisciplinary health care team should pursue given a survivor's determined risk level [19, 53, 54]. This would be remedied by evidence-based recommendations. For example, an evidence-based recommendation for exercise based on age, comorbidities, and BMI would eliminate guesswork for many survivors and clinicians.

Surveillance, early diagnosis, and treatment of lymphedema remain a challenge for clinicians, health care systems, and cancer survivors [55]. The components of a prospective surveillance program will vary but should include a pre-operative assessment including baseline bilateral arm measures, personalized education, supportive resources, and functional, psychological/psychosocial, and quality of life assessments. Subsequent prospective surveillance visits based on

recommended guidelines can be scheduled with post-operative and oncological visits to decrease patient burden [16, 21, 46, 56, 57]. A 1-month visit followed by quarterly visits would be optimal since approximately 75% of BCRL cases are noted in the first year following breast cancer surgery [58]. The frequent visits would also allow for continued BCRL education and functional, psychological, and psychosocial assessments [16, 21, 47, 56–58].

Conclusion

This case study report illustrates the experience of a woman who is identified to be at increased risk of developing BCRL in her first years of survivorship and who ultimately is given a BCRL diagnosis and referred for treatment after becoming symptomatic. Through a thorough history and risk assessment, each of the five domains is addressed. Her experience is based on present-day standards, processes, and recommendations. As her providers attempt to make a plan of care for her, they must navigate several recommendations and guidelines that (1) may be outdated, (2) do not contextualize the survivor's risk level, and (3) are not guided by evidence-based recommendations. Future work in guideline development with clear protocols and expectations is warranted.

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Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflicts 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.

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