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Treating Breast Cancer-Related Lymphedema

Early detection, aggressive treatment and rigorous education are critical to improving BCRL-patient outcomes and quality of life

Lymphedema is swelling from the pathological accumulation of protein-rich lymph fluid in the interstitial space in soft tissue. Though lymphedema may be inherited, far more frequently it is acquired from obstruction of, or damage to, the lymphatic system. Lymphedema is chronic, progressive and incurable. Early detection and treatment are essential to stop or slow the progression of lymphedema and effectively manage its symptoms.

Though prevalence estimates vary widely, in part because lymphedema diagnosis criteria and measurement techniques are inconsistent,¹ the disease is thought to affect more than five million Americans and remains a major health problem in the United States. Literature reviews attest to the pain, loss of function, profound psychological distress, and damage to social life and career endured by lymphedema patients.^{2,3} Lymphedema, and cancer-related lymphedema (CRL) specifically, is also a major driver of healthcare costs.^{4,5}

One of the most common etiologies of lymphedema in Western countries is cancer treatment² and breast cancer-related lymphedema (BCRL) accounts for a large subset of CRL patients. Women living in the United States have a 12.4 percent lifetime risk of breast cancer,⁶ and 40 percent of survivors will acquire lymphedema following surgery and/or radiation therapy involving the axillary lymph nodes.⁷ Reported BCRL prevalence is steadily increasing.⁵

BCRL usually presents as swelling in tissue ipsilateral in relation to the breast cancer. Often seen in the arm, BCRL may also produce swelling in other tissue with lymphatic drainage to the axilla, including the hand, shoulder, breast and chest.⁸

The lymphatic system

Lymph originates from capillary filtration, the process in which blood pressure drives water and its component proteins, nutrients, cells and debris through the permeable walls of capillaries into the interstitial spaces in tissue. Lymphatic capillaries interlaced through the interstitial space are solely responsible for collecting this protein-rich fluid and returning it, via collecting lymphatic vessels, to the vascular system.⁹ Every day, 2 to 4 liters of lymph fluid reenter the bloodstream through the lymphatics into the subclavian veins.¹⁰

In addition to their circulatory function, the lymphatics are essential to host defense. Because lymphedema impacts immune function as well as fluid balance it can lead to a progressive spiral of chronic inflammation, recurrent infection, and fibrosis, which results in further lymphatic damage, worsening symptoms and increasing susceptibility to infections.¹¹ Lymph nodes concentrate, filter and detoxify lymph fluid of pathogens, damaged cells, cellular debris, viruses, bacteria and toxins; produce lymphocytes; and defend the body with specialized immune cells when lymph composition communicates a threat of infection.¹² Though lymphatic vessels and lymph nodes may facilitate the metastatic spread of cancer, under the right conditions they may also defend against cancer through immune response targeting malignant cells.¹²

Historically, some clinicians have withheld lymphedema treatment from cancer patients out of fear that compression therapy could promote the dissemination of cancer cells through the lymphatic system. Cancer research has found this fear to be unfounded and that treatments such as manual lymphatic drainage should not be withheld from patients with metastasis.¹³⁻¹⁵

BCRL risk factors

Though a multitude of potential BCRL risk factors remain in dispute, from a surgical standpoint risk increases with the number of axillary lymph nodes removed.¹⁶ Nodal irradiation (radiation treatment to the axilla/ underarm) after axillary surgery^{17,18} and obesity/elevated body mass index (BMI)¹⁷ are also risk factors for development of the disease. Age, family history, repeated surgeries, local infection, hypertension, medication and many other factors may also influence lymphedema risk.¹⁹

Though breast cancer survivors are at lifelong risk of developing lymphedema, 80 percent of BCRL first occurs within two years of cancer diagnosis.⁷ Routine follow-up patient examinations are essential to detect lymphedema early and initiate treatment to halt its progression. Rigorous patient education is also needed to support patient surveillance, risk-reduction steps and, when lymphedema is diagnosed, compliance with therapy.

Detection and diagnosis

The progressive nature of lymphedema makes it imperative for clinicians to diagnose lymphatic impairment as early as possible, a step shown to improve outcomes.²⁰

During the initial development of BCRL, measurable volume changes are often absent.¹ The earliest indicators include stiffness, pain, numbness, tightness in the fingers, limb fatigue or weakness, and other functional symptoms that precede visible swelling. These symptoms may begin months or even years before detectable changes in limb volume occur.¹ Post-treatment patient education should emphasize the importance of recognizing these early signs of lymphedema. It should also include risk-reduction precautions (Fig. 1).

Swelling is the hallmark of lymphedema onset, and diagnosis can often be readily determined based on clinical history and physical examination.²¹ Examination includes comparative girth and/or limb-volume measurements of ipsilateral and contralateral limbs, assessment of edema buildup based on pitting (Fig. 2) and observance of skin changes. When possible, BCRL patients should receive baseline limb assessments prior to surgery, as well as periodic assessments for at least one year and preferably longer after surgery.²²

Pitting signifies that filtration of lymph has overwhelmed lymphatic transport, resulting in accumulation of fluid in the limb.¹² Pitting that quickly resolves may be present as early as ISL Stage 1; by early stage 2 pitting does not resolve with elevation. Clinicians should initiate lymphatic treatment at these stages to stimulate lymph flow and debulk the limb, as prolonged swelling and accumulation of protein-rich lymph damages fragile lymphatic vessels²³ and can create an immunocompromised district in the affected area.¹¹ Early-stage skin changes (e.g., dermatitis) and chronic inflammation reflect compromised local immunity and can give way to worsening complications, including recurrent infection (e.g., cellulitis) and progressive fibrosis.¹¹ Loss of pitting in lymphedema's latter stages marks structural changes, including deposition of fat and fibrosis, which are irreversible.¹⁶

Before initiating lymphedema therapy, clinicians should determine whether lymphedema is primary or secondary, and follow established protocols for evaluating comorbid conditions. A host of conditions such as lipedema, venous obstruction, heart failure, obesity, liver disease, hypertension or kidney failure may cloud the clinical picture.²¹ Regardless of etiology, however, all chronic edema indicates impaired lymph drainage.¹²

A variety of imaging techniques are available to aid diagnosis and staging.²⁴ Recently, bioimpedance spectroscopy (BIS) measurement of fluid retention has emerged as a promising clinical tool for detecting early lymphatic impairment.²⁵

Treatment and management

Diagnosis of lymphedema should be followed by complete decongestive therapy (CDT) aimed at stimulating the lymphatics and reducing limb volume.²⁶ CDT, administered by a certified lymphedema therapist, includes manual lymphatic drainage to promote lymph flow and use of multilayer bandaging combined with exercise to amplify lymphatic vessel contractions and increase lymphatic efficiency.²⁷ CDT may involve as much as 6 weeks of treatment administered 3–5 days per week. The goal at this acute stage of treatment is to reduce limb volume to the greatest extent possible prior to fitting the patient with a compression garment intended to help preserve therapeutic gains. Clinicians must avoid the common error of fitting patients with compression garments before initiation of CDT, or as a stand-alone treatment, since static compression alone is ineffectual for reducing limb volume.¹⁰

The reduction phase of treatment is followed by the maintenance phase, in which patient-directed lymphedema management at home takes a leading role. Patients must understand that lymphedema is chronic and may worsen without vigilant, lifelong attention to symptoms, skin changes, treatment regimens and risk-reduction steps. Patients can also combat lymphedema proactively. Weight reduction has been shown to reduce BRCL,²⁸ and while evidence of the efficacy of exercise to reduce symptoms is mixed,²⁹ gradually increasing exercise in accordance with prescribed therapy appears to be safe and potentially beneficial for lymphedema patients.¹

Patient compliance to therapy, which historically has been low, is the greatest obstacle to successful treatment.^{30,31} Numerous studies have reported that BCRL patients find the self-care modalities prescribed by lymphedema clinicians, including compression sleeves and bandage wrapping, to be burdensome, uncomfortable and detrimental to quality of life.^{32–34} Methods to improve patient adherence to BCRL self-care are clearly needed.³⁴

Pneumatic compression devices

Pneumatic compression devices (PCDs) can be an adjunct to CDT in the reduction phase of treatment and have demonstrated substantial value for improving BCRL lymphatic circulation,³⁵ reducing limb volume,^{36,37} lowering healthcare expenditure,⁵ and improving patient-reported symptoms and quality of life³⁷ during the maintenance phase of at-home BCRL care.

Advanced PCDs (APCDs, denoted by HCPCS Code E0652) are more adjustable than simple PCDs (SPCDs, HCPCS Code E0651), and allow users to fine-tune the degree and location of compression to concentrate on specific areas and modify pressure to comfortable levels. APCDs are associated with improved edema reduction³⁸ and reduced healthcare costs³⁹ compared with SPCDs.

Research has shown that APCDs benefit patients with BCRL and other forms of CRL. In a 2015 study,⁴⁰ use of an APCD (the Flexitouch® system, Tactile Medical, Minneapolis, MN) was associated with steep reductions in healthcare costs and rates of cellulitis in CRL patients. Flexitouch use has been shown to improve lymphatic function³⁵ and maintain or reduce limb volume³⁷ in BCRL patients. It is also associated with high levels of BCRL patient compliance.³⁷

Clinician skepticism of the value of PCDs for lymphedema therapy may be based on outdated evidence. A 2003 systematic review⁴¹ conducted on behalf of the Centers for Medicare and Medicaid Services (CMS) found mixed evidence of the effectiveness of PCDs for treatment of venous-related lymphedema and leg ulcers. However, this review did not distinguish between specific PCDs and relied on evidence dating as far back as 1975. Recent

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evidence published in the *Journal of Vascular Surgery* showed that use of the Flexitouch APCD combined with conservative therapy was associated with major, statistically significant reductions in phlebolymphe­dema-related costs compared with conservative therapy alone, SPCDs and other APCDs.³⁹

Surgical options

Surgical options for lymphedema are either ablative or physiologic.⁴² In ablative procedures, edematous and fibrotic tissues above the deep fascia are removed either through wide resection (historically) or through suction-assisted lipectomy. These procedures are conducted on late-stage, non-pitting lymphedema-affected limbs as a palliative measure to debulk fat, which can constitute >90 percent of excess limb volume at Stage 3,⁴³ and improve limb function.

Lymphaticovenular anastomosis (LVA) and vascularized lymph node transfer (VLNT) are physiologic microsurgie­ries intended to restore lymph flow from the affected limb when other therapies have been inadequate in improving symptoms. These procedures have shown positive results in properly selected patient populations.⁴²

Although these treatments may improve lymphedema, they are not a cure, and proper patient selection is critical to outcome. Not all patients are candidates for surgery, and poor patient selection may worsen the patient's condition. Referral to a surgeon with expertise in treating lymphedema patients is important to determine candidacy.

Low awareness: a clinical problem

Despite its high prevalence and potentially devastating effects, BCRL and other forms of lymphedema are widely misunderstood, overlooked and underdiagnosed in medical practice.³⁴ This gap in care is often attributed to lymphedema's status as an "orphan disease" that does not fall into any single medical specialty. In an informal physician survey, Dr. Stanley Rockson of Stanford University found that many respondents had received just 15 minutes of instruction on the lymphatics in medical school.⁴⁴ BCRL patients continue to express frustration over low awareness among healthcare providers of lymphedema and its care guidelines, a lack of treatment protocols during hospitalization, and even the failure of providers to recognize lymphedema as a chronic disease.⁴⁵

Given low awareness among clinicians, it's not surprising that BCRL patients are generally poorly educated on lymphedema.⁴⁶ This is especially troubling because education has been linked to improved patient compliance with lymphedema management,⁴⁷ more frequent practice of risk reduction behaviors,^{48,49} significantly fewer reported symptoms,⁵⁰ and improved patient outcomes.⁵⁰

Though breast cancer care providers commonly entrust BCRL care to lymphedema therapists, there is a clear need for physicians and nurses to assume greater stewardship of the disease, beginning with an open, evidence-based dialogue with patients, supplemented with written information (Fig. 3).

Conclusion

BCRL is common in the United States and represents a serious and costly healthcare problem often overlooked in medical care. The keys to managing BCRL are early detection, early and aggressive treatment, and strict lifelong patient compliance to at-home self-directed therapy and surveillance. Whereas intervention at the earliest stages of lymphatic impairment may halt or even reverse lymphedema progression, failure to confront lymphedema until the non-pitting stage results in irreversible structural limb damage and a potential spiral of worsening complications. Use of APCDs combined with conservative therapy has been shown to stimulate the lymphatics, maintain or reduce limb volume, and reduce CRL healthcare costs. Increased clinician awareness of lymphedema, a prerequisite of improved patient education and treatment, may represent the most immediate opportunity to improve outcomes and quality of life for BCRL patients.

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Key points

- BCRL is a common and expensive healthcare problem in the U.S. and can have a devastating impact on patient quality of life
- The keys to halting BCRL progression and managing the disease are early detection, aggressive treatment and strict patient compliance with self-care
- Progression of lymphedema beyond the pitting stage leads to permanent structural damage to the affected limb and can initiate a spiral of worsening complications related to immune dysfunction and continuing lymphatic damage
- Use of PCDs, especially APCDs, as an adjunct to therapy has been demonstrated to improve lymphatic function, reduce limb volume and symptoms, and lower healthcare costs
- Surgical options may be beneficial to some lymphedema patients, but poor patient selection may worsen their condition
- Awareness of lymphedema and its treatments among healthcare providers remains low and patient education inadequate. Improving awareness and education are critical to improving patient outcomes

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FIG. 1: BCRL RISK-REDUCTION PRECAUTIONS

Excerpted from www.breastcancer.org. Patients should review the entire list of recommendations.

Protect your skin:

- Moisturize daily to keep skin supple
- Keep your hand and arm clean, but don't use harsh soaps
- Wear protective gloves for activities that could stress the limb or injure the skin
- Don't get manicures that cut or overstress the skin around the nails
- Don't allow the skin of your at-risk arm or hand to be pierced or pressured for any reason: for example, injections, blood draws, intravenous lines, vaccines, and blood pressure

Protect your arm and hand from overuse, trauma, or too much pressure:

- Be cautious about suddenly lifting something heavy
- Be careful when you start tackling [repetitive] activities such as scrubbing, mopping or raking
- Use sunscreen
- Avoid taking unusually hot baths or showers
- Don't apply heating pads or hot compresses
- Avoid carrying heavy objects or shoulder bags on your at-risk arm
- Avoid wearing tight watches, bracelets, or rings on your affected hand or arm
- Avoid wearing clothing that has tight sleeves or that restrains movement
- Avoid exercises that put great pressure on the arm until you and your therapist determine what your arm can handle and how to build up its strength

FIG. 2: THE ISL STAGING SYSTEM

Stage 0: Latent—swelling not yet evident

Stage I: Early fluid accumulation subsides with limb elevation; pitting may occur

Stage II: Elevation alone rarely reduces swelling; pitting is manifest

Late Stage II: Pitting may or may not occur as excess fat and fibrosis supervene

Stage III (lymphostatic elephantiasis): Usually non-pitting; skin changes are prominent; further deposition of fat and fibrosis; warty overgrowths

The International Society of Lymphology. The diagnosis and treatment of peripheral lymphedema: 2016 consensus document of the international society of lymphology. *Lymphology*. 2013;49(4):170–84.

FIG. 3: PATIENT EDUCATION ON LYMPHEDEMA: KEY POINTS

- Verbal and written pretreatment education on the risk of lymphedema should be introduced into discussion of breast cancer treatment options; written material should be culturally sensitive and evidence-based.
- Post-treatment education should stress the importance of recognizing early signs of lymphedema, include information on hand and arm precautions, and offer practical advice for avoiding situations associated with lymphedema risk. Advice should be offered about what to do if these situations are encountered (i.e., a wound on the affected arm).
- Patients who develop lymphedema should be evaluated comprehensively by experienced professionals and be fully informed about treatment options, management of acute lymphedema, and self-maintenance of stable but chronic forms of lymphedema.

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