CE

Diagnosis and Treatment of Edema and Lymphedema in the Cancer Patient

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Abstract

Background: Lymphedema occurs commonly in cancer survivors. It is crucial to properly assess cancer patients in order to distinguish lymphedema from general edema and to initiate evidence based treatment.

Purpose: To provide evidence based recommendations for screening, evaluating, and treating lymphedema and to establish the role of the nurse in the care of patients with lymphedema.

Methodology: Comprehensive overview with narrative literature review of evidence based lymphedema diagnosis and treatment.

Findings: Cancer-related edema represents numerous complex conditions. A variety of interventions are needed to address prevention, early detection, patient education, and effective treatment.

Conclusion: Lymphedema treatment is complex and multimodal, and is provided by an interdisciplinary team of properly trained professionals. Nurses play a major role in evaluating, treating and educating patients on the signs and symptoms of cancer-related edema and patient self-management.

Clinical Implications: Evidence-based assessment and treatment should be initiated early to improve outcomes and quality of life in patients with cancer-related lymphedema.

Keywords: Cancer survivors; complete decongestive therapy; compression; edema; lymphedema.

Introduction

Edema is a common symptom that can be caused by abnormality in many organ systems. Lymphedema is a specific form of edema that occurs commonly in cancer survivors, occurring in approximately 15% of all cancer survivors (Cormier, Davidson, Xing, Evans, & Armer, 2006), but more frequently in certain cancers such as breast, melanoma, head and neck, and gynecologic cancers. For example, breast cancer-related arm lymphedema occurs in approximately 34% of women after axillary node surgery (Hayes, Rye, Battistutta, & Newman, 2010) and breast lymphedema among 50% after lumpectomy and radiation (Degnim et al., 2012). Lower extremity lymphedema after groin dissection for melanoma is estimated to be 41.9% (Renner et al., 2017) and as high as 60% among patients with head and neck cancer (Deng, Ridner, Dietrich, et al., 2012). Lymphedema is also persistent: After gynecologic cancer surgery, 58% of women exhibit clinically significant lymphedema 8 years after surgery (Graf et al., 2013). Lymphedema is associated with decreased health-related quality of life (Ahmed, Prizment, Lazovich, Schmitz, & Folsom, 2008; Hormes et al., 2010; Morgan, Franks, & Moffatt, 2005)

The patient undergoing cancer treatment has many potential causes of edema. It is important to properly assess the patient with cancer-related edema in order to distinguish lymphedema from general edema and to initiate evidence-based treatment. Beyond assessment, nurses play a crucial role in educating patients on signs and symptoms of progression of lymphedema and its complications (Deng, Fu, et al., 2015; Radina, Armer, & Stewart, 2014), providing resources for self-care and performing the care coordination that is critical to an effective team approach for this complex patient population.

Pathophysiology of Lymphedema

Edema is a general term referring to enlargement of a body part from fluid engorgement regardless of the etiology, whereas lymphedema is edema that is specifically caused by an abnormality of the lymphatic system. Primary lymphedema results from abnormal development

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of the lymphatic system. Secondary lymphedema occurs as a result of damage or disruption of a previously normal lymphatic system. In developed countries, the most common cause of secondary lymphedema is cancer treatment. The patient with cancer may have had lymph node resection, surgical disruption of lymphatic vessels, or radiation therapy to lymph nodes and lymphatic vessels. Any of these procedures alone or in combination can lead to lymphedema.

The lymphatic system is a part of the vascular system. Together the lymph vascular and cardiovascular systems function to create homeostasis in the body's fluid regulation. The cardiovascular system is a closed loop of vessels leading to and from the heart, but by contrast, the lymphatic system is an open system of vessels, absorbing interstitial fluid at the level of the blood capillaries. When this fluid enters the lymph vessel, it becomes lymph. Lymphatic vessels carry lymph fluid, macromolecules, immune cells, and lipids (chyle) from the interstitium to lymphoid organs, including lymph nodes, to process and destroy foreign material. Purified fluid is returned to the cardiovascular system by unidirectional flow through the lymphatic vessels.

Surgical lymph node removal is a common cause of lymphedema, but it may be caused by lymphatic vessel damage from excessive tissue pressure, inflammation, and radiation fibrosis. Lymphatic vessel damage reduces the ability of lymph vessels to contract, leading to lymphatic valvular insufficiency and backflow with progressive overdistention of lymphatic vessels. The pressure in the overdistended lymphatics increases, and this is known as lymphatic hypertension. Lymphatic fluid backs up and becomes stagnant in the interstitial tissue matrix, which is known as lymph stasis. Tissue damage from lymph stasis and lymphatic inflammation leads to a vicious cycle of lymphatic pump failure. The affected body parts become progressively and irreversibly more swollen, heavy, inflamed, fibrotic, and with increase in adipose tissue (Harvey, 2008; Ryan, 1995).

Lymph stasis is clinically observed as progressive inflammation and build-up of thick fibrofatty tissue in the dermis of the skin and subcutaneous tissue with or without erythema. Upon palpation, lymphedema is firm and has a nonliquid feel. In its later stages, lymphedema changes from a doughy-like feel to a harder texture and becomes thick and nonpitting. Edema that feels like soft, mobile fluid usually is not lymphedema and may be from cardiovascular or other medical causes.

Excision of or damage to lymph nodes or vessels above the clavicle may lead to lymphedema of the oral cavity, larynx, and pharynx internally and of the face, head, and neck externally. The axillary lymph nodes drain the skin of the chest, arm, and trunk on the ipsilateral side of the node basin above the waist and below the clavicle anteriorly and posteriorly. Removal of lymph nodes and damage to lymph vessels in the axillary distribution can lead to lymphedema of any of the structures of the chest, upper back, and arm. Removal of pelvic and para-aortic lymph nodes and damage to lymph vessels in the abdomen and pelvis from radiation may cause lymphedema of the lower abdomen, external genitalia, buttocks, and legs as well as internal linings of pelvic organs including bladder and vagina. Removal of inguinal lymph nodes may lead to ipsilateral leg swelling.

Diagnosis of Lymphedema

The diagnosis of lymphedema is primarily by history, clinical assessment (staging), and patient-reported outcome measures (PROMs). An important component of diagnosis of lymphedema is to confirm that the edema is truly of lymphatic origin; thus, diagnostic tests and imaging may be needed (International Society of Lymphology, 2016) subsequent to initial clinical diagnosis. Differential diagnosis of new onset edema in an individual with cancer should include ruling out central or peripheral venous thromboembolism, cellulitis, pathologic fracture, cancer recurrence, a second primary cancer, and metastatic spread of cancer. Other potential causes of lymphedema in cancer patients are listed in Table 1.

History

A thorough history must be taken from a patient with cancer who develops edema. The history should review the patient's cancer treatment, including cancer stage at diagnosis, cancer stage at the present time, surgical interventions, extent and location of lymphadenectomy,

Table 1 Potential causes of edema in cancer patients

Lymphedema: Removal of damage to lymph nodes and/or vessels by radiation or surgery
Drugs: Taxanes (M. J. Lee, Beith, Ward, & Kilbreath, 2014; Park et al., 2014), corticosteroids, calcium channel blockers, zolendroic acid, gemcitabine (Curtis, Hong, Gucalp, & Calvo, 2016), and gabapentin (Keeley, 2012)
Tumor: Solid tumor or bone metastasis causing enlargement of tissues, or tumors infiltrating lymph vessels
Venous: Thrombosis in any part of the body or venous valvular incompetence in the lower extremities
Hypoproteinemia
Heart failure
Thyroid failure
Rheumatologic/orthopedic conditions, including aromatase inhibitor or chemotherapy-induced arthropathy and tendinitis, exacerbation of prior degenerative joint disease or injury including pathologic fracture
Hepatic disease
Renal disease
Cachexia

locations and types of radiation, all chemotherapy agents used in the past and presently, complications of treatment including venous thromboembolism (and interventions such as thrombectomy or thrombolysis), and surgical infections. The effectiveness of management interventions that have been attempted, including medications such as diuretics and anticoagulants, surgical decompression of seroma or hematoma, and use of compression wraps and stockings/sleeves, should be evaluated and documented.

The pattern and timing of swelling are important in the differential diagnosis of cancer-related edema. Acute edema requires an urgent evaluation, whereas chronic lymphedema is not a medical emergency but warrants further investigation. Lymphedema is usually local and unilateral and begins distally before progressing proximally, but there are exceptions. Lymphedema progression is generally slow and indolent and may cause symptoms of discomfort and heaviness but does not present with frank pain.

Staging

Lymphedema is staged with two parameters: (1) the status of tissue fibrosis (usually by palpation) and (2) the size of the affected part (usually by a tape-measured calculation of the limb volume). At the bedside, palpation plus tape-measured circumference at consistent locations can be used to monitor changes. Education of the patient in the rationale for ongoing monitoring of tissue fibrosis and watching for changes in the size or configuration of the affected part is important.

The most commonly accepted lymphedema clinical staging is from the Consensus Document of the International Society of Lymphology and has three clinical stages (International Society of Lymphology, 2016). Stage 0 represents subclinical lymphedema; stages of clinical edema range from Stage 1 (reversible, with mild or no pitting) to Stage 3 (progressive dermal overgrowth and increasingly firm, nonpitting fibrofatty). Stages are defined in Table 2. A volume severity index (as shown in Table 3) is the most common way to document the size of the affected limb and should be used along with soft tissue staging. Minimal volume increase is commonly considered 5%–20%, moderate is 20%–40%, and severe is >40% above a baseline. At the bedside, when percentage volume calculations are unavailable, tape measurements at consistent points on the extremity can be used. A 2-cm difference of the involved side over the uninvolved side is considered clinically relevant (Armer, Stewart, & Shook, 2009). Documentation of edema should clearly state the stage and circumference (or calculated volume severity index when available) in order for ongoing monitoring of the condition. At the bedside, monitoring of daily weight should also be done because large changes in body weight are usually from other medical causes and may mimic lymphedema with changes in limb size and tissue tension.

Table 2 Staging by tissue fibrosis (International Society of Lymphology [ISL], 2016)

ISL Stage	Description
Stage 0	Subclinical (latent) with potential to progress to become clinically evident
Stage 1	Mild soft pitting that reverses with elevation
Stage 2	Pitting +, subcutis fibrofatty deposits, architectural distortion, elevation does not reverse
Stage 3	Warty dermal overgrowths, severe architectural distortion, nonpitting due to hardness

Table 3 Volume to pair with tissue staging (International Society of Lymphology, 2016)

Volume Severity (Increase Over Baseline or Uninvolved Extremity)	Percentage Above Baseline
Minimal	5–10
Mild	10–20
Moderate	20–40
Severe	>40

Patient-Reported Outcome Measures

Thorough lymphedema diagnosis and assessment includes patient-reported symptoms and lymphedema-related distress assessed using a patient reported outcome measure (PROM). Studies of breast cancer patients reporting symptoms of lymphedema reveal that other types of pain, especially neuropathic pain, can be mistaken for lymphedema (Bulley et al., 2013). Patient self-report of stiffness, numbness, weakness, tingling, and loss of range of motion has been positively correlated with objective measures of arm swelling in the breast cancer population (Hayes, Janda, Cornish, Battistutta, & Newman, 2008). Therefore, it is important to treat the symptoms the patient is reporting, which may be multifactorial (Ridner & Dietrich, 2015). Swelling itself may be the lesser concern or nonexistent. The fear of lymphedema leads to anxiety in cancer patients that may be alleviated by treating other sources of pain misinterpreted as lymphedema (Sackey et al., 2015) and ensures that other diagnoses such as venous thromboembolism, cellulitis, or cancer recurrence are not missed

The effect of lymphedema on the patient's life is dependent upon the patient's vocation and usual activities. Studies have shown that patient symptoms often bring the condition of lymphedema to medical attention. The discomfort associated with lymphedema, along with the alteration of body image and daily function, can cause severe distress (Teo, Novy, Chang, Cox, & Fingeret, 2015). The National Comprehensive Cancer Network (NCCN)

Survivorship Guideline (Version 1.2016; NCCN, 2016c) uses patient self-report of pain symptoms as the symptom for referral to lymphedema rehabilitation services (Bulley et al., 2014; Tsauo, Hung, Tsai, & Huang, 2011). PROMs should be over an extended period of time, 2–6 years after completion of primary cancer treatment (Gärtner et al., 2010; Sackey et al., 2015). Early symptoms are more intense, and the symptom burden often reduces over time (Gärtner et al., 2010; Kopec et al., 2013). Those patients with prolonged symptom burden are at risk for loss of employment, depression, increased medical costs, and loss of ability to perform daily life tasks and recreation (Sackey et al., 2015; Teo et al., 2015). Nurses utilize PROMs to evaluate the impact of the condition, educate patients, and advocate interventions to address the condition holistically to other disciplines on the patient's care team.

The World Health Organization's Classification of Functioning, Disability and Health, known as the ICF (World Health Organization, 2001), assesses the activity restriction and participation limitation imposed upon an individual from an impairment. A Lymph-ICF (Devoogdt, Van Kampen, Geraerts, Coremans, & Christiaens, 2011) was constructed for breast cancer-related lymphedema consisting of five domains: physical function, mental function, household activities, mobility activities, and life/social activities. An ICF set for breast cancer has also been developed (Brach et al., 2004), again reflecting that a variety of conditions cause posttreatment morbidity in the upper quadrant that, in combination, have functional and social/emotional impact on health-related quality of life. A number of PROMs have been developed for use in breast cancer-related lymphedema (BCRL) so that the clinician can select one that is most compatible with their setting and patient population (Bulley et al., 2014; Coster, Poole, & Fallowfield, 2001; Pusic et al., 2013; Ridner & Dietrich, 2015). Some tools have also been developed for lower extremity cancer-related lymphedema or both upper extremity (UE) and lower extremity (LE) lymphedema (Carter et al., 2010; Keeley et al., 2010; Weiss & Daniel, 2015). Because there is no recognized clinical method for detecting breast, genital, or head and neck lymphedema, a PROM must be utilized to identify and follow patients for these entities (Deng et al., 2013, 2016; Deng, Ridner, Aulino, & Murphy, 2015; Deng, Ridner, Murphy, & Dietrich, 2012; Flores, Eden, & Galantino, 2015).

Diagnostic Tests

In addition to history, staging, and PROM assessment for differentiating between lymphedema and general edema, addition of laboratory and imaging may be used to confirm the clinical diagnosis.

Laboratory Tests

In the cancer patient with edema, review of prior pertinent laboratory and imaging evaluations should be undertaken, especially thyroid, liver, and renal function tests; echocardiogram; and the most recent computed tomography or positron emission tomography scans. Pertinent missing laboratory tests and imaging should be ordered. Be aware that positron emission tomography scans exclude the long bones of the extremities, so swelling in the extremities of patients with known metastatic disease, multiple myeloma, or primary bone tumors should prompt additional imaging of the extremity for tumor enlargement or pathologic fracture.

Imaging

Lymphoscintigraphy is used to image the peripheral lymphatic vessels and has been the primary imaging technique for lymphatic dysfunction (Gloviczki et al., 1989; Szuba, Shin, Strauss, & Rockson, 2003; Ter, Alavi, Kim, & Merli, 1993; Yuan et al., 2006). Lymphoscintigraphy provides a functional assessment of lymphatic pumping, stasis, and obstruction that guides treatment and determines prognosis for expected outcome of treatment (Hwang et al., 2007; B. B. Lee & Laredo, 2011; B. B. Lee, Laredo, & Neville, 2011; Pecking, Albérini, Wartski, Edeline, & Cluzan, 2008). Because edema is a symptom that may be transient or treatable and the differential diagnosis of edema in cancer patients is complex, the lymphoscintigraphic evaluation of lymphatic function is a part of the evaluation and management of chronic lymphedema. Lymphoscintigraphy is used for imaging extremity lymphedema but is not useful for trunk, head, and neck lymphedema that are mainly clinically diagnosed. Lymphoscintigraphy is widely available in institutions with nuclear medicine radiologists and where cancer is treated because the technique utilizes the same equipment as that used for identification of the sentinel lymph node for surgery.

Doppler ultrasound studies of the upper and lower extremities and central venous imaging with contrast enhanced magnetic resonance, computed tomography, or venography to rule out venous thromboembolism should also be done as part of the lymphedema diagnostic workup. Reducing venous hypertension, if present, eliminates strain on the lymphatic system and may, in and of itself, reduce or reverse associated lymphedema and help to differentiate lymphedema from other types of edema (Czerniec, Ward, Meerkin, & Kilbreath, 2015; Gardner et al., 2014; Gjorup, Hendel, Klausen, Zerahn, & Hölmich, 2017; Gjorup, Zerahn, & Hendel, 2010; Johnson, DeSarno, Ashikaga, Dee, & Henry, 2016; Suehiro et al., 2014, 2016; White et al., 2014). In addition, soft tissue ultrasound can be used to stage lymphedema in the face, chest, and trunk where

volume measurements cannot be taken. Ultrasound and MRI also help distinguish when lymphedema has converted to primarily fibrofatty tissue with minimal fluid component that can explain why some patients become refractory to compression. The combination of lymphatic imaging, soft tissue imaging, and vascular imaging is helpful for differentiating edema from lymphedema in cancer patients (Tassenoy, De Strijcker, Adriaenssens, & Lievens, 2016; Tassenoy et al., 2006) and guiding a treatment plan.

Management of Lymphedema

Recommended lymphedema management strategies differ according to whether the lymphedema is considered to be early or preclinical lymphedema or clinically evident lymphedema.

Management of Early or Preclinical Lymphedema

A patient identified as at risk for lymphedema or having signs of development of lymphedema should be referred to a qualified rehabilitation professional, a certified lymphedema physical therapist (PT) or occupational therapist (OT), or cancer rehabilitation physical medicine and rehabilitation physician. These clinicians are qualified to determine if the patient needs further diagnostic workup and if lymphedema therapy (Complete Decongestive Therapy [CDT]) is indicated prior to getting a compression garment. Early intervention with a Compression Class 1 sleeve has been shown to be beneficial for preclinical or Stage 1 breast cancer-related lymphedema to potentially reverse early volume increase (Dayes et al., 2013; Soran et al., 2014; Stout Gergich et al., 2008). Because fluctuations in volume are known to occur naturally after axillary lymph node dissection, some will reverse spontaneously, but this remains a risk for later development of arm lymphedema (Armer, 2005; Kilbreath et al., 2013). Therefore, treatment should be implemented when subclinical or early lymphedema is detected but not assign a diagnosis of lymphedema. The mislabeling of early preclinical volume increases as clinical lymphedema creates significant unnecessary anxiety among patients and costly overtreatment with unnecessary decongestive therapy. The objective of early screening for lymphedema is to reduce anxiety by identifying more at-risk individuals and following them through the critical period. The fear of lymphedema after breast cancer treatment is very high so accuracy of diagnosis, staging, and stratification of treatment is both cost-effective and patient-centered (McLaughlin et al., 2013). There is an opposite risk in the current lack of rigor in accurately staging and stratifying lymphatic insufficiency to the detriment of clinical outcomes for patients with more severe lymphedema, that is, greater than Stage 1. Clinicians unfamiliar with the continuum of lymphatic dysfunction may erroneously conclude that compression garments are equivalent to decongestive therapy in patients with Stage 2 and higher lymphedema. Patients with greater than Stage 1 lymphedema should be treated with CDT (Lasinski et al., 2012).

Management of Clinically Evident Lymphedema

Management of clinically evident lymphedema differs between hospital and outpatient settings. In the inpatient setting, initial nursing care focuses on basic comfort care with absorbent pads, compression bandage wraps, and skin care while evaluating all of the causes for eventual definitive treatment and as temporizing measures to reduce edema in preparation for more definitive diagnosis. Inpatient nurses who identify and manage edema and lymphedema play a key role in discharge planning to ensure that patients are referred to a certified lymphedema PT or OT. Certified lymphedema therapists have specialized training in CDT, the gold standard for lymphedema treatment (see section below).

Compression

Initially, compression therapy prioritizes edema reduction through ACE wrapping or, if tissues are fibrotic, with inelastic or short-stretch bandages (International Society of Angiology, 2003). This initial medical management strategy is aimed at reducing fluid volume yet avoiding harmful constriction from elastic bandages, stockings, or sleeves until longer-term management is undertaken. Thus, compression is often begun in the inpatient setting. Weeping from fluid tension under the skin can be managed by placing absorbent pads under compression bandage wraps and changing frequently to prevent skin maceration. Barrier creams or topical antibacterial agents should be used if dermatitis is present. Meticulous skin care with gentle washing and patting dry reduces the likelihood of cellulitis and should be continued until the weeping and dermatitis clears. Patients and family members should be instructed in these gentle cleaning and wrapping techniques. When certified lymphedema PTs and OTs are available in the hospital setting, they may be consulted for appropriate bandaging recommendations.

After initial wrapping has been undertaken, transition to prescription compression according to the patient's diagnosis and severity of edema (Moffatt et al., 2006, 2009) may begin. The amount of compression delivered to the lymphedematous tissues differs widely with various fabrics and is associated with the amount of lymphedema reduction achieved, so the amount of compression of various fabrics must be considered when prescribing garments and bandages (International Society of Angiology, 2003).

For lymphedema patients, the ideal garment has a low pressure at bed rest and a high pressure when upright and moving (Partsch, 2005). This dynamic is best achieved with an inelastic fabric that allows the action of the contraction of muscles to propel stagnant interstitial fluid toward the central circulation replacing the action of ineffective lymphatics. Short-stretch (inelastic) bandages are superior to long-stretch (elastic) bandages in the reduction and maintenance lymphedema. Flat knit (inelastic) seamed garments are able to apply compression to firm areas of lymphedema as compared to circular knit (elastic) garments that can compress softer edema but may constrict limbs with variable shape or firmer lymphedema. It is important to note that circular knits deliver more pressure to the distal and narrower parts of the limb whereas flat knit garments deliver more uniform gradient so that patients requiring higher-compression class garments may have better results with flat knit garments that do not constrict at narrow parts of the limb. There must be no constriction from a compression garment as constriction from a compression garment creates a tourniquet effect, leaving indentation of the tissues, areas of rubbing, or abrasion that could lead to skin breakdown and risk for cellulitis. When compression garments are ill-fitting, the patient can be referred to a lymphedema therapist or custom garment fitter for more options.

Compression classes and pressures are not standardized. As a result, the clinician must read the label or box for the compression classification of the specific garment and check the fit of the garment on the patient to be sure it is effective. Nurses working with patients who have edema or lymphedema should assist the patient in making sure the garment has a correct fit and should verify upon delivery of new garments or wraps that the fabric and fit are those prescribed by the provider.

Complete Decongestive Therapy

The standard treatment for Stage 2 extremity lymphedema is CDT, an outpatient treatment that combines PT/OT lymphedema treatment techniques with patient self-management. Complete Decongestive Therapy consists of Phase I, the clinical reductive phase, and Phase II, the maintenance or self-management phase (Lasinski et al., 2012). Complete Decongestive Therapy, as a multimodality therapy, has demonstrated effectiveness for reducing limb volume (Devoogdt, Van Kampen, Geraerts, Coremans, & Christiaens, 2010) when treatment is sustained/maintained into Phase II self-care (Boris, Weindorf, Lasinski, & Boris, 1994; Finnane, Janda, & Hayes, 2015; Ko, Lerner, Klose, & Cosimi, 1998; Koul et al., 2007; Ochalek, Gradalski, & Szygula, 2015). Complete Decongestive Therapy is also highly effective for lymphedema of the face, jaw, chin, and neck associated with head and neck cancer (Smith et al., 2015). Standard Phase I CDT uses short-stretch (inelastic) compression bandages and therapist-applied manual lymphatic drainage to reduce the size of the affected body part. Standard Phase II CDT requires therapist-recommended compression garments to maintain the reduction. Usually after a course of CDT, flat knit (inelastic) compression maintenance garments are recommended to be worn day and night. Complete Decongestive Therapy should be performed by qualified therapists who have completed training as certified lymphedema therapists because bandaging and manual lymphatic drainage use specific techniques that require training and practice. The certified lymphedema therapists should recommend the type of Phase II compression garment prescribed. Complete Decongestive Therapy achieves the greatest volume reduction when started early in the disease before the limb becomes excessively large (Forner-Cordero, Muñoz-Langa, Forner-Cordero, & DeMiguel-Jimeno, 2010; Haghighat et al., 2013). Patient adherence to compression bandages in Phase I is a predictive factor for the overall success of CDT (Forner-Cordero et al., 2010).

Pneumatic Therapy

Pneumatic compression devices currently available for the treatment of lymphedema are known as intermittent pneumatic compression (IPC) devices. The devices used for lymphedema treatment are not the same as the vasopneumatic devices used on hospitalized patients for prevention of venous thromboembolism. For the treatment of lymphedema, the inflated pneumatic cuff has to overcome tissue resistance and elevated pressure in dilated lymphatics. The therapeutic peak inflation pressure in the absence of fibrosis is about 30–60 mm Hg and is well tolerated in most patients. Intermittent pneumatic compression therapy for lymphedema reduction or maintenance appears to be effective and well tolerated as a part of a multimodality treatment approach along with compression garments, but its effectiveness as a stand-alone therapy is questionable. Prescribing and treating clinicians must specify the type of IPC device and how the patient is to use it with a compression garment in order to achieve clinical benefit (Feldman et al., 2012).

Self-Care and Exercise in Cancer-Related Lymphedema

Patients undergoing lymphedema therapy are usually given a regimen of self-care strategies to maintain or improve their lymphedema, but aside from maintenance compression garments, there is little evidence supporting use of self-care strategies. Self-care strategies may include

compression bandaging, resistive or aerobic exercise, self-applied manual lymphatic drainage, IPC devices, elevation of the affected extremity, and weight management. Lymphedema self-care can be burdensome and expensive. Brown and colleagues evaluated adherence to self-care interventions over 12 months in patients with breast cancer-related lymphedema who participated in a weight lifting intervention (Brown et al., 2015). Only 28% of participants meticulously adhered to prescribed self-care interventions; adherence had no significant relationship to lymphedema volume at 12 months. However, participants who performed weight lifting twice a week had a 53% reduction in need for repeat lymphedema treatment. Medical professionals prescribing self-care interventions for patients and nurses educating patients on lymphedema care should be mindful of the time, energy, and financial implications of self-care to patients, particularly when evidence for many interventions is scant. Because lymphedema is a chronic condition, regular follow-up with a lymphedema clinician is important to evaluate for progression. Lymphedema self-care modalities should be only those demonstrated effective, allowing patients more time to focus on exercise, weight management, and wellness.

The role of exercise in lymphedema has been well studied. Numerous studies have shown that exercise does not cause lymphedema in susceptible populations or exacerbate lymphedema in patients with a confirmed diagnosis of lymphedema (Brown, John, Segal, Chu, & Schmitz, 2013; Buchan, Janda, Box, Schmitz, & Hayes, 2016; Cormie, Galvão, Spry, & Newton, 2013; Cormie, Pumpa, et al., 2013; Di Blasio et al., 2016; Keilani, Hasenoehrl, Neubauer, & Crevenna, 2016; Kwan, Cohn, Armer, Stewart, & Cormier, 2011; McKenzie & Kalda, 2003; Paskett et al., 2017; Schmitz et al., 2009, 2010; Singh, Disipio, Peake, & Hayes, 2016). A weight lifting intervention among patients at risk for lymphedema showed that those who participated in weight lifting had a reduced chance of developing lymphedema (Schmitz et al., 2010), whereas a small study of Nordic walking suggested benefit for prevention of lymphedema (Di Blasio et al., 2016). Although exercise for prevention of lymphedema has not been conclusively demonstrated (Cavanaugh, 2011; Paskett et al., 2017), the health benefits to cancer survivors are clear. Health professionals should counsel patients with lymphedema and those at risk for lymphedema to exercise (McLaughlin, DeSnyder, et al., 2017). The specific exercise prescription with respect to type of exercise, intensity, and length of intervention should be individualized and prescribed by a qualified health professional who understands the difficulties with adherence to exercise after cancer treatment (Kirkham et al., 2018; van der Leeden et al., 2018), especially within the setting of lymphedema management. The NCCN Guideline for Survivorship (NCCN, 2016a) lists lymphedema as a condition for which patients should receive medical evaluation and referral to a cancer rehabilitation clinician (physiatrist or physical therapist) for individualized recommendations for lymphedema-related exercise precautions and modifications. The guideline also suggests that high body mass index is a risk factor for developing secondary lymphedema (Clark, Sitzia, & Harlow, 2005; Swenson, Nissen, Leach, & Post-White, 2009). Thus, nurses should counsel patients on measures they can take to reduce body fat, specifically diet and exercise, to decrease risk of developing lymphedema.

Some patients have difficulty exercising in compression garments. Patients with uncomfortable, ill-fitting, or constricting garments are less likely to enjoy and adhere to exercise guidelines (Gho, Munro, Jones, & Steele, 2014a, 2014b). For patients with confirmed lymphedema, studies are inconclusive as to whether patients with lymphedema should wear compression garments while exercising (Singh et al., 2015, 2016), but generally accepted current practice holds that compression should be worn during exercise. Some patients may be able to remove their garments briefly for exercise provided they have well-managed lymphedema and are scrupulously adherent to wearing garments as prescribed when not exercising. Patients who experience difficulty in exercising due to lymphedema should be referred to a lymphedema therapist and custom garment fitter to assist in finding individual exercise garments that are comfortable and meet their requirements for lymphedema management. There is no evidence that at-risk patients without evidence of clinical lymphedema should wear compression garments during exercise to prevent lymphedema.

Prevention for the Cancer Patient at Risk for Lymphedema

Screening

Oncology and rehabilitation nurses have a primary role in screening for and educating patients on early identification of cancer-related lymphedema. Clinicians, including nurses, in outpatient and inpatient settings need to establish collaborate practice within their institutions to determine roles that will ensure compliance, communication, and care navigation for cancer patients to access screening and early treatment for lymphedema. Of particular importance is the sharing of data from outpatient to inpatient settings during care transitions to monitor for early changes suggesting development of lymphedema.

Screening practices for cancer-related lymphedema are most fully developed with respect to breast cancer. Breast cancer-related lymphedema is associated with significant morbidity and cost (Shih et al., 2009). Patients who have undergone lymphadenectomy for melanoma, gynecologic cancer, and head and neck cancer also have significant morbidity and distress from lymphedema, so increasing attention is being paid to early diagnosis and treatment for these groups as well (Beesley, Janda, Eakin, Obermair, & Battistutta, 2007; Deng et al., 2013; Purcell, Nixon, Fleming, McCann, & Porceddu, 2016; Spillane, Saw, Tucker, Byth, & Thompson, 2008). An Expert Panel for the American Society of Breast Surgeons recommends that all breast cancer patients with a risk of lymphedema receive education and specific information about risk of lymphedema on their Survivorship Care Plan (McLaughlin, Staley, et al., 2017). For breast cancer-related lymphedema, the NCCN guidelines also state that patients treated for invasive breast cancer must have follow-up to "educate, monitor and refer for lymphedema management" (NCCN, 2016b).

There is no consensus on method for screening for BCRL (Armer et al., 2013; Blaney et al., 2015). Regardless of the measurement tool used, screening for breast cancer-related lymphedema requires a preoperative baseline measurement for maximal accuracy (Sun et al., 2016). There is general agreement that the highest risk of developing BCRL of the arm is in patients who have undergone axillary surgery and the time course of highest incidence is within the first 2 years after surgery (Armer et al., 2009). Screening for early unilateral lymphedema may use bioimpedance spectroscopy, which has established thresholds guiding points at which intervention may be initiated (Ward, Dylke, Czerniec, Isenring, & Kilbreath, 2011). The threshold at which lymphedema remains reversible has not been empirically established, yet clinical experience has demonstrated that early Stage 1 and subclinical lymphedema have the greatest opportunity for reversibility. Studies with indirect volume measures indicate that it is reasonable to consider early BCRL threshold at approximately 5% limb volume increase (Cormier et al., 2009; Specht et al., 2013). Early BCRL of low volume has a tendency to progress (Bar Ad et al., 2012; Mahamaneerat, Shyu, Stewart, & Armer, 2008), so interventions to reverse or reduce BCRL should be undertaken with a low volume of increase (Johansson & Branje, 2010). Screening programs are typically undertaken for 2 years postoperatively for optimal outcome and cost-effectiveness (Bilir, DeKoven, & Munakata, 2012; Chance-Hetzler et al., 2015; Stout et al., 2012).

Because most institutions currently rely on tape measurement arm circumferences for diagnosis and treatment of BCRL, it is reasonable to utilize this modality for early detection of clinically evident lymphedema when other methods are not available or when patients do not meet criteria for other methods (Chance-Hetzler et al., 2015). Tape measurements cannot detect subclinical lymphedema; however, the detection of early clinical lymphedema is a worthy endeavor because treatment of early clinical lymphedema has been shown to reduce or eliminate progression of the condition (Dayes et al., 2013; Stout Gergich et al., 2008).

There is no consensus on screening for lymphedema in patients at risk for lower extremity, genital, breast, or head/neck lymphedema. In these populations, early education and implementation of a patient-reported outcome tool in the oncology setting is key. Nurses involved in the care of cancer patients must collaborate across service lines and across disciplines to implement early education, PROM tools, and early referral to lymphedema clinicians for all at-risk populations. Any patient, regardless of tumor type, who has had lymphadenectomy or radiation to lymphatic structures may develop lymphedema. High-risk populations should have specific clinical pathways for education and early referral for lymphedema.

As noted above, the success of prophylactic interventions has not been empirically supported in any cancer population, but evidence does support the effectiveness of early intervention (Stage 1 or Early Stage 2, before the onset of fibrosis), so screening, early detection, and treatment referral are critically important to reduce lymphedema-related morbidity. Furthermore, screening programs provide the opportunity for nursing education and lifestyle management around weight management, exercise recommendations, and referral to cancer rehabilitation physical medicine and rehabilitation physicians, PTs, and OTs who specialize in recovery from the side effects of cancer treatment.

Lymphedema Risk Reduction Practices

When discussing lymphedema risk reduction practices with patients, it is important to differentiate the use of *risk reduction* practices designed to prevent lymphedema from *lymphedema precautions* intended to minimize trauma and cellulitis in those who already have lymphedema. Lymphedema risk reduction practices are predicated on the belief that lifestyle factors and controllable physical factors play a role in triggering onset of secondary lymphedema in susceptible individuals. The use of practices for prevention of breast cancer-related lymphedema in the at-risk population is controversial. The practices with the greatest controversy are air travel, needle sticks, venipuncture, and blood pressure cuffs. Several studies have shown that air travel is not a risk factor for the

development of BCRL so the routine use of compression sleeves on airplanes to prevent lymphedema after axillary node dissection is generally considered not to be required (Ferguson et al., 2016; Graham, 2002; Kilbreath et al., 2010; Mak et al., 2009; Showalter et al., 2013). Similarly, there is no definite association between development of lymphedema and venipuncture (Ferguson et al., 2016; Showalter et al., 2013) or taking a blood pressure on the side of axillary node removal (Ferguson et al., 2016; Mak et al., 2009; Showalter et al., 2013). There are, however, anecdotal reports of lymphedema manifesting clinically after these incidents, and because the published studies have limitations, it is impossible to be certain that there is no risk. Rather than a uniform approach, the American Society of Breast Surgeons Expert Panel recommends individually tailored education on risk-reducing practices for patients (McLaughlin, DeSnyder, et al., 2017). Nurses working in hospitals should become aware of any hospital policies at their institutions relative to blood pressures and venipunctures in patients with a history of lymph node dissections. In an emergency when time is of the essence, the overriding concern should be reversing a critical situation. Nurses should assess for swelling after procedures on at-risk limbs so that prompt treatment can be undertaken at the earliest opportunity.

When counseling the individual patient regarding prevention of lymphedema by utilizing risk reduction practices, the clinician should strive to stratify risk and reduce unnecessary anxiety in populations at low risk (McLaughlin et al., 2013). For some patients, the risk may be high enough to warrant taking a more aggressive approach to risk reduction. The fear of lymphedema, body image concerns, and financial cost of wearing compression garments when the risk of lymphedema is low should be determined individually and inform development of the individualized treatment plan. Studies have shown that patients who have had sentinel lymph node dissections can safely choose to be exempt from following standard risk reduction practices (McLaughlin et al., 2013). However, because of the limitations of current research, most clinicians recommend the patient use the uninvolved side, if any, for venipuncture and blood pressures or, alternatively, to use the side with the lowest number of lymph nodes removed for procedures when possible. If patients wish to wear a compression sleeve or stocking on a plane for prophylaxis, they should obtain the garment well in advance of the trip and wear it several times to make sure it does not constrict. If sleeves are worn for prophylaxis on a plane, it is recommended to wear a gauntlet to prevent hand swelling if the sleeve becomes tight at the wrist during periods of low cabin pressure.

There is general lack of consensus on patient risk reduction practices, and the topic engenders a great deal of emotion among proponents on all sides of the issue. The reality is that the lack of evidence for specific risk reduction practices and the seeming randomness of the development and progression of clinical lymphedema may have more to do with the phenotypic and genotypic predisposition to the condition. When the lymphatic system is already under stress from the pathophysiologic factors of inflammation and fibrosis, an environmental trigger may add to the lymphatic load and uncover a process that was inevitable. As early detection and physiologic prevention become more scientifically sophisticated, clinicians will be better able to provide patients with personalized recommendations regarding risk reduction measures according to the patient's status and available research on these measures.

For prevention of lymphedema, the most significant development in reducing the risk of developing lymphedema has been limiting the use of lymph node dissection for staging (McLaughlin et al., 2008). Studies have shown that the number of lymph nodes removed and postoperative infections are the most significant risk factors for the later development of lymphedema (Bevilacqua et al., 2012; Tsai et al., 2009; Ugur et al., 2013). The incidence of arm lymphedema in patients undergoing sentinel lymph node biopsy is significantly less than patients undergoing standard axillary node dissection.

Regarding patients with confirmed lymphedema, precautions are recommended to decrease the risk of excessive fluid build-up, infection, or trauma in an already lymphedematous limb. Patients with lymphedema should avoid trauma and skin breakdown to the lymphedematous body part. When surgical interventions or procedures are necessary on a lymphedematous body part, preprocedure lymphedema treatment and postprocedure management must be implemented with the involvement of a lymphedema specialist, either a certified lymphedema therapist or physical medicine and rehabilitation lymphedema specialist.

Discussion: Future Considerations for Diagnosing and Treating Cancer-Related Lymphedema

Cancer-related lymphedema has a complex pathophysiology, and the thresholds for detection and for initiating and discontinuing intervention have not been conclusively determined. Future research should seek to establish biomarkers and molecular, pharmacological, and immune system treatments for the underlying pathophysiology of the disease. Clearly there is a point at which the proliferative, inflammatory destruction of healthy lymphatic vessels leads to irreversibility and progression of the disease. Research on clinically evident lymphedema clearly shows that early detection at lowest volumes improves long-term outcomes. The point at which subclinical lymphedema must be treated and

how aggressively requires additional research to develop evidence-based treatment guidelines.

There is sufficient evidence to recommend that, after ruling out and treating comorbid edemas, the treatment of clinical lymphedema by properly trained professionals, using accepted techniques, improves outcomes and quality of life in patients with cancer-related lymphedema. Because of the complexity and the multimodality treatment for lymphedema, a team approach to care is of the highest importance to optimal patient care. Lymphedema is best managed with a team approach involving nonsurgical physician and physician-extender specialists such as nurse practitioners, certified lymphedema therapists (PT/OT), nurses in oncology or rehabilitation with an interest in lymphedema, cancer exercise specialists, and surgeons working within the established framework of lymphedema clinicians (Damstra, 2012). Nurses have important roles at every level of care for cancer-related edema ensuring best practice treatment, patient and family education, support, care coordination, and advocacy for this complex patient population.

Conflict of Interest

The author declares no conflict of interest.

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