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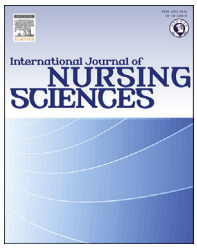

Review

Breast cancer-related lymphedema: A literature review for clinical practice

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ABSTRACT

Lymphedema is the swelling of soft tissues as a result of the accumulation of protein-rich fluid in extracellular spaces. Secondary lymphedema is precipitated by an event causing blockage or interruption of the lymphatic vessels. Secondary lymphedema is a potential complication that may affect the quality of life of patients treated for breast cancer. Life-long risk factors of post-breast cancer lymphedema are related to the extent of axillary node involvement, type of breast surgery, and radiation therapy. These factors decrease lymphatic drainage and increase stasis of fluids in the areas of skin and subcutaneous tissues that drain to regional lymph nodes. Breast cancer-related lymphedema can involve the arm and hand, as well as the breast and trunk on the operative side. Clinical symptom assessment and circumferential measures are widely used to evaluate lymphedema. Treatment of lymphedema associated with breast cancer can include combined modality approaches, compression therapy, therapeutic exercises, and pharmacotherapy.

Contents

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1. Introduction

Breast cancer has been the focused of many studies because it significantly affects both in developed and developing countries worldwide. In 2012, about 1.7 million women worldwide were diagnosed with breast cancer and 521,900 cases died from this disease [1]. The American Cancer Society reported that approximately 231,840 new cases of invasive breast cancer are expected to be diagnosed among women in the USA in 2015; this organization also predicted that 60,290 new cases of in situ breast cancer and 40,290 breast cancer deaths would occur in 2015 [2]. The 5-year relative survival of women diagnosed with breast cancer has increased from 80% in the 1950s to 89% today relative to age-matched women without the disease [2].

Although breast cancer treatments, including surgery, radiotherapy, chemotherapy, and hormonal therapy, have improved patient outcomes, these techniques cause patients to potentially suffer substantial adverse effects [3]. One complication of these treatments is lymphedema, a chronic health problem, troublesome to both patients and health professionals. Lymphedema describes a set of pathological conditions, in which protein-rich fluid accumulates in soft tissues because of interruption of lymphatic flow [4]. Lymphedema is most commonly found in the extremities but can also be found in the head, neck, abdomen, lungs, and genital regions [5]. Although the incidence of breast cancer-related lymphedema (BCRL) remains unclear because of differences in diagnostic criteria, the different characteristics of the patients and their inadequate follow-up delayed the developments in treatment of the disorder [6]. The overall incidence of upper extremity lymphedema ranges from 8% to 56% 2 years post-surgery [7]. The incidence of breast and truncal lymphedema has been rarely reported. Jeffs [8] reported a 13% incidence of breast/truncal lymphedema in 168 patients. This study was conducted to refresh the understanding of nurses and public health personnel on breast cancer-related lymphedema.

This article is divided into 55 parts, which include pathophysiology of lymphedema, risks and causes of lymphedema, diagnosis of lymphedema, treatment of lymphedema, and nursing implications.

2. Pathophysiology of lymphedema

The lymphatic system maintains fluid balance in tissues, fights infection, and assists in removal of cellular debris and waste products from extracellular spaces. Under normal conditions, the lymphatic system is involved in production of immune cells and antibodies, destruction of red cells, and lymph transport. The lymphatic system is divided into superficial and deep layers, which are connected by perforating vessels. The lymphatic system is assumed to function independently [5]. The superficial transport lymphatic vessels lie in subcutaneous tissues to provide drainage for the skin and subcutaneous tissues; moreover, deep transport lymphatic vessels lie near deeper blood vessels to provide drainage from muscles, tendon sheaths, nervous tissues, periosteum, and most joint structures [5]. Lymph from the lower body below the diaphragm and the left side of the body above the diaphragm is transported by the thoracic duct, which is the largest lymph vessel in the body. The thoracic duct empties into the left venous angle, which is formed by the left subclavian and left jugular veins. Lymph from the right side of the body above the diaphragm is transported by the right lymphatic duct, which empties into the right venous angle formed by the junction of the right subclavian and right jugular veins [9].

Fluids normally diffuse into interstitial spaces at the arteriolar end of the capillary and filter back into the capillary at the venular end. Up to 90% of fluids filtered into the interstitium from capillaries are reabsorbed into the venous side. The remaining 10% (or more) of fluids and proteins are removed from the interstitium by small, terminal (one-way) lymphatic vessels [10]. The normal outward flow of fluids slightly exceeds the inward flow, and the net filtrate enters the lymphatics and drains back into the bloodstream. This process creates stable interstitial pressure. If large molecules accumulate, such as in obstructed lymph transport because of axillary treatment, sufficient effective osmotic pressure develops and causes excessive fluids in the interstitial space [9]. This protein-rich swelling condition is called lymphedema.

3. Risks and causes of lymphedema

Lymphedema that develops after breast cancer treatment is thought to be related to the extent of axillary node involvement, type of breast surgery, and radiation therapy. These factors lead to decreased lymphatic drainage and stasis of fluids in the skin/tissue areas that normally drain to the axilla; these areas include ipsilateral breast, chest, lateral and posterior upper trunk, arm, and hand [10]. The lymphatic vessels in the radiation field are constricted after radiation because of the resultant fibrotic tissue constriction in the vessels [11]. In addition, radiation damages cells within the nodes, wherein high dose of radiation may be directed to eradicate malignant cells. Radiation compromises lymph node function and can cause a certain degree of lymphedema [11]. Cancer surgery also results in superficial scarring that inhibits lymphatic flow across the scar tissue, leading to lymphatic fluid collection proximal to the scar [19]. Moreover, local infection after surgery or radiation contributes to the development of

lymphedema because it increases the volume of fluids and cellular components in the tissues and thus potentially exceeds the transport capacity in an altered lymphatic system [11]. These sources of damage inhibit the lymphatic system to transport the normal amount of fluids and proteins from the affected area [11]. Other factors, such as obesity and recurrent cancer, also increase the risk of patients to develop lymphedema [12]. Additional individual predisposing factors associated with risk for lymphedema development must be further investigated [12,13].

4. Diagnosis of lymphedema

Clinicians do not universally agree on what measurement and criteria define lymphedema. However, lymphedema is commonly diagnosed when a 2 cm difference or more in arm circumference at a single anatomic level measured or a 200 ml limb volume difference between the affected and non-affected limbs is observed [4]. Lymphedema is classified as stage I, II, or III and quantified as mild, moderate, or severe. Stage I lymphedema pits on the application of pressure but reverses with limb elevation. Stage II lymphedema no longer pits on pressure because of excess fat deposition and tissue fibrosis and no longer reverses with elevation. Stage III lymphedema is characterized by progressive swelling with trophic skin changes, including papules, warts, skin folds, tissue bulges, and often open draining wounds, leading to severe impairment in mobility and high risk of infection [14].

Diagnosis of lymphedema requires a detailed medical history and physical examination [15]. Based on patient's medical history, patients with breast cancer and lymphedema may report symptoms, such as sensation of arm fullness and mild discomfort. These symptoms are manifested in the early stages of the condition. Joint immobility, pain, and skin changes are noted frequently in the later stages of lymphedema. Such changes may include pitting of tissues, increased thickness of skin folds, and enlargement of the affected limb [15]. The history of the present illness should determine when the onset of symptoms occurred, duration of symptoms, any triggering events, and the attempted treatments [14,15]. Moreover, the history should include information on past operation, postoperative complications, radiation treatment, interval from radiation or surgery to the onset of symptoms, intervening variables in the presence or severity of symptoms, history of trauma or infection, and current medications [15].

Physical examination techniques include water displacement volumetry, sequential circumferential arm measurement, infrared laser perometry, and tissue bioelectrical impedance spectroscopy [15,16]. However, the most common methods in determining volume in clinical practice are water displacement and circumferential measurements [15,16].

The most frequently-used method is tape measurement of arm circumference 10 cm below and 10 cm above either on the olecranon or the lateral epicondyle; this method can be easily applied and involves low cost to the patient. Although circumferences may appear to be a simple measure, control of intra- and interrater-reliability is difficult [16].

Water displacement is considered the "gold standard" for volumetric measurements and incorporates volumetric measurements of the hand or foot in the total limb volume measurement [16]. Although water volume method is accurate, this technique does not provide information on the shape of the extremity, cannot be used with open wounds, and can be time-consuming and cumbersome to perform [15,16].

Three other less commonly used clinical measures are adopted in this study. A perometer is an optoelectronic device used to rapidly, hygienically, and accurately calculate volume calculation and works similarly to a computer-assisted tomography but uses infrared light instead of X-rays [16,17]. Tonometry measures tissue resistance instead of volume and determines the extent of tissue fibrosis [18]. At early lymphedema, bioelectrical impedance spectroscopy is used to measure tissue resistance to electrical current to evaluate extracellular fluid volume that may not be detectable with tape measure or visual inspection [16].

Other quantitative measures involve radiological imaging studies, such as computed tomography, magnetic resonance imaging, ultrasonography, lymphoscintigraphy, and lymphangiography [15,19]. Both computed tomography and magnetic resonance imaging show a distinctive honey-comb pattern within the lymphatic system; this pattern can differentiate lymphedema from other potential cancer-related causes of edema, such as deep vein thrombosis [19]. Lymphangiography was used extensively in the past as an imaging technique but is associated with inflammation, scarring, and atrophy of lymph vessels, resulting in impaired lymph transport capacity [19]. Lymphoscintigraphy is a method of injection of a radioactive tracer into the subdermal region of the affected limb combined with monitoring with a gamma camera; this technique is preliminary used to predict patients with increased risk for lymphedema after axillary treatment [19]. Lymphoscintigraphy can identify pathways of lymphatic drainage, dermal backflow, collateral lymph channels, number of lymph nodes, and clearance times of radiopharmaceutical agents [19].

In conclusion, lymphedema diagnostic methods vary. Each method presents its own appropriateness for application in clinical practices. For example, water displacement method is the most reliable ("gold standard") method for measuring edematous arms and legs but is not practical for patients with wounds. Circumferential measurement is a simple and low cost technique but cannot directly calculate limb volume and is subject to inter- and intra-rater reliability issues. The high cost of perometry limits its application, although it can calculate limb volume quickly and accurately. Finally, biopedance can detect subclinical swelling but has ongoing costs for disposable electrides; radiological imaging may not be practical because of their high costs unless causation and management require further investigation. Consequently, assessment method needs to be carefully selected depending on clinical and research settings as well as targeted patient outcomes.

5. Effect of lymphedema

Lymphedema is a chronic condition that has a lifelong effect on the quality of life of cancer survivors. Previous studies

reported that the presence of lymphedema was associated with decreased quality of life, particularly in physical functioning, such as functioning in a domestic environment in the long term [20–22]. Kwan, Jackson, Weir, Dingee, McGregor, and Olivotto [23] reported that patients with lymphedema presented decreased quality of life compared with survivors without lymphedema. In addition, lymphedema confers tremendous physical, psychological, social, spiritual, and emotional costs on breast cancer survivors with this chronic condition [24,25]. Although swelling or edema within the tissue is not in itself painful, stretching of nerve fibers within the skin, presence of a localized infection, or fluid collection that causes compression on top of a nerve bundle can result in significant discomfort and disability. Following the onset of limb swelling, the patient is predisposed to infection, cellulitis, and lymphangitis, which are sometimes followed by life-threatening septicemia [26]. Armer, Radina, Porock, and Culbertson [27] pointed out that "aching," "heaviness," "tightness," and "pulling" are adjectives commonly used by patients to describe their discomfort that may be present before visible signs of swelling are noticed. Moreover, pain can be significant and troublesome for individuals with BCRL. For example, Paskett and Stark [28]indicated that about 72% of the respondents report pain in addition to edema. Moreover, when asked in what ways lymphedema interfere with particular aspects of daily living, women most often report that clothing and appearance are negatively affected by the condition, followed by effect on daily routine and activities [28]. Furthermore, one of the major problems identified by women is the necessity to wear compression sleeves; they described this experience as ugly, terrible, un-feminine, and uncomfortably warm, particularly in summertime because of the need to conceal their arms by wearing special clothing [29].

6. Treatment of lymphedema

Treatment of lymphedema associated with breast cancer can include combined modality approaches, compression therapy, therapeutic exercises, and pharmacotherapy [19].

Complete decongestive therapy (CDT), a multi-modality approach, is the "gold standard" for lymphedema treatment. This therapy includes various techniques, such as manual lymphatic drainage (MLD), external compression garments and bandages, skin care, and exercises guided by specially-trained therapists [5,19]. CDT includes two phases. In Phase I, acute management is performed in an out-patient clinical setting. This phase aims to reduce the size of the extremity, reverse any distortion in the shape, soften the subcutaneous tissue, and improve the overall health of the skin [5]. On average, this phase consists of a 4-week program of manual lymphatic drainage, multi-layer short-stretch compression bandaging, exercise, and proper skin and nail care [19]. Phase II is conducted at home by the patient and/or family and involves continued proper skin care and exercise, simple (or self-) manual lymphatic therapy, and use of a compression sleeve and glove during the day and compression bandaging at night [19]. This phase aims to maintain the achievements of the first phase and requires life-long commitment by the patient [5].

Compression therapy includes compression bandages or compression garments, which assist the muscle pump in the area to be compressed to mobilize lymphatic fluid [19]. The use of pneumatic compression therapy is widely debated. This form of therapy can reduce swelling and may be indicated as adjunctive therapy when self-MLD is difficult for the patient. However, this technique can lead to a displacement of fluid elsewhere in the body with the possibility of future problems [5].

Skin and nail care is essential to prevent infection [5]. Skin care includes keeping the extremities clean and dry, applying pH-neutral moisturizer to prevent chapping, and protecting exposed skin with sunscreen. Moreover, as much as possible, patients should avoid any puncture wounds, such as injections and blood-drawing on the at-risk/affected limbs. In addition, patients should avoid using razors that may cause skin injury in the affected area [30].

Therapeutic exercises are a recognized component of lymphedema management and include remedial exercises with the garment or bandage in place to facilitate lymphatic flow through repeated contraction and relaxation of muscles [19]. Exercise involving the affected arm, shoulder girdle, and trunk may be beneficial in controlling lymphedema. Although some clinicians have recommended avoidance of rowing, tennis, golf, skiing, squash, racquetball, or any vigorous, repetitive movements against resistance, no published evidence from rigorously-conducted studies suggests that these activities promote or worsen lymphedema [31].

Manual lymphatic drainage is a delicate massage technique that stimulates lymph vessels to contract frequently and directs and channels lymph and edema fluids toward adjacent lymphatic vessels [16]. The pressure applied is very gentle, and the movements are slow to correspond with naturally slow, rhythmic lymphatic pulsations [16]. Multi-layered low-stretch compression bandaging is applied immediately after manual lymph drainage. Bandages are wrapped from the fingertips to the axilla in layers to create high pressure gradient at the most distal part of the limb that gradually decreases proximally [32]. In mild edema, in Stages I and II, a compression garment may be used instead of bandages [24]. Proper fit and function of a compression garment are essential and need to be tailored to the individual. An ill-fitting compression garment is worse than no compression at all. In this case, "one size does not fit all."

7. Nursing implications

Lymphedema, associated with swelling and pain, is a significant problem among breast cancer survivors. As such, nurses should understand this complex problem to inform their breast cancer patients of the lifelong risk of developing this complication [10]. To reduce/prevent lymphedema, nurses should educate breast cancer survivors to follow self-care regimen for controlling symptoms and avoiding exacerbation; recommendations include performing daily skin care, wearing gloves during activities to prevent skin breaks, preventing injury in the affected side, preventing muscle strain, and promoting lymph drainage (i.e., elevate the affected arm,

engage in regular, light aerobic exercise daily, maintain optimal body weight, and wear a well-fitted compression garment when traveling by air) [25]. In addition, the current best practice management for lymphedema, including compression either by garments, bandages or sleeve, manual lymphatic drainage, massage, exercise, and skin care, should be explained to deal with lymphedema effectively [16]. With increasingly brief hospital stays associated with breast cancer treatment, nurses should teach patients how to reduce risk or cope with lymphedema; this information can make a difference in patient recovery and should be reinforced in the outpatient setting during survivorship follow-up [33]. When patients understand the pathophysiology of their condition, they can devise creative ways to deal with the manifestations of the disease or problem-solve a way to include lymphedema management into a schedule that maintains function as long as possible [34]. Until further research is conducted and science discovered methods to reduce risk for lymphedema, patient education is the best tool that health professionals can use to reduce risk of developing this condition or decreasing its severity [10].

Lymphedema management among breast cancer survivors is based on results from case studies, clinical experience, and anecdotal information. However, this information is less understood and needs further study [31]. As a result, further rigorous studies must be performed. Currently, much of the focus of education deals with recommendations for risk reduction that are not yet based on empirical evidence. Future research is therefore needed on risk-reduction strategies in women at risk because of breast cancer treatment [32,35]. In addition, future research should address the influence of patients' level of accurate understanding on lymphedema and their choices of effective and appropriate treatment techniques to better understand the needs of patients with lymphedema [32,35,36]. Johansson, Holmstrom, Nilsson, Ingvar, Albertsson, and Ekdahl [29] pointed out that "future research needs to focus on coping strategies and how they can be strengthened in the women with lymphedema." In addition, the relationship of exercise in women with lymphedema is not completely clear. Hence, additional research is needed to address this interaction [37]. Furthermore, breast cancer patients are at a lifetime risk of developing lymphedema and need more education and counseling about their condition. Further research is needed to develop an educational and counseling component that will improve patient knowledge and understanding of lymphedema. Moreover, a previous study reported that women with lymphedema travel in different places to find help [38]. During this wandering period, they might obtain useful information and secondary gain but they might also lose more than they gain because of time and money wasted. Studies should also address health-seeking behavior of patients that might be different in various societies. Future research should focus on identification of barriers regarding lymphedema management in breast cancer survivors with different cultural and ethnic backgrounds by using phenomenological approaches [39].

8. Conclusion

Lymphedema in breast cancer survivors is a relatively common condition that remains under-recognized by health care providers. Patients with upper extremity, breast, or truncal edema secondary to breast cancer therapy experience a substantial degree of functional impairment, psychological morbidity, and diminished quality of life. Lymphedema management aims to prevent the progression of the disease, reduce edema, maintain edema reduction, alleviate symptoms, prevent infection, improve patients' mobility and ability to perform activities of daily living, and improve overall psychological well-being [5]. Nurses are key members of the health care team who need to know what lymphedema is and how to manage it. Therefore, nurses must be trained to assess emergence and progression of lymphedema, as well as to educate patients throughout their treatments for appropriate individualization of management planning. For example, during the peri-operative period, nurses can educate patients regarding risk-reduction strategies as well as signs and symptoms of lymphedema. In addition, further education and rigorous clinical trials are needed to address the importance of early recognition and management of lymphedema after breast cancer treatment. A prospective surveillance program integrated into the clinical setting is recommended as the emerging standard of care.

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