

**Breast Cancer-Related Lymphedema: The Effects of Exercise, Nutrition, and Current
Approaches to Treatment**

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Abstract

Breast cancer is a disease that effects thousands of women each year in the US. Breast cancer survivors are among the largest group of cancer survivors, with more people living with cancer-related conditions than ever before. Breast cancer treatments from surgery, chemotherapy, and radiation may often lead to the development of health conditions such as lymphedema.

Lymphedema is a chronic condition where swelling of the upper limb occurs after post-operative mastectomy from breast cancer. Lymphedema effects many aspects of the patient's quality of life, functional capabilities, and health. While many studies have been done on lymphedema and the standard treatment involving Complete Decongestive Therapy, there is still much research to be done in the realm of nutrition, exercise physiology, and preventative measures after cancer treatment. The focus of this paper will encompass all of the current research involved with cancer-related lymphedema such as the mechanism of the condition, effects of exercise, nutrition, current treatment methods, and the psychosocial aspects. The purpose of this paper was to compile the most current research of these topics within breast cancer-related lymphedema. The overall finding is that significantly more research is necessary to improve knowledge on BCRL preventative measures and address the psychosocial concerns associated with patient barriers to treatment. Emphasis of research should include educational programs within the cancer treatment model, continuing education for healthcare providers, and BCRL treatment interventions in order to improve patient outcomes.

Keywords: breast cancer, lymphedema, nutrition, exercise, therapy, psychosocial

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The National Cancer Institute reports that the five-year survival rate for breast cancer is approximately 90% from the years 2009-2015 [14]. More women than ever before are surviving breast cancer years after diagnosis. With continuous improvements in research, technology, and treatments, the likelihood of survival after breast cancer is stronger, however this also means that more people are living with health conditions that may have developed as a result of cancer treatments. Lymphedema is one such condition which can occur in patients who have undergone procedures that may have compromised the lymphatic system in the process. The problems associated with breast cancer-related lymphedema, (BCRL), involve chronic swelling of the ipsilateral upper extremity on the side where the cancer treatment has taken place.

BCRL can be a significant concern to patients in remission. The purpose of this paper is to explore the most recent research that goes beyond standard lymphedema management in order to establish the direction of future research that may benefit patients affected by this condition. With the goal of improving quality of life, the major topics discussed will be the mechanism of BCRL, what the current research studies find on the effects of Complete Decongestive Therapy, and what research has been done with exercise, nutrition, and the psychosocial aspects of lymphedema. The paper will conclude with areas of the field that are still not fully understood and address issues surrounding patients' barriers to successful treatment that will warrant further investigation.

The Development of BCRL and Associated Risk Factors

It is estimated that 1 in 5 breast cancer patients will develop secondary lymphedema after treatment [11]. In breast cancer-related lymphedema, (BCRL), the connection between the upper extremity lymphatic system and treatment procedures that involve lymph node removal, (such as a lumpectomy, mastectomy, or lymph node biopsy) or radiation treatments that target lymph nodes (Regional Nodal Irradiation), may put the patient at risk for developing lymphedema due to the possibility of damage to the regional lymph system [15, 26]. Jeffs et. al noted that 20% of women who have had axillary node dissection may develop swelling of the limb [15]. BCRL is a type of secondary lymphedema that can develop in stages. Initial signs are often asymptomatic or Stage 0, and then progress to reported feelings of heaviness or paresthesia in the affected limb and visible swelling. In more advanced stages of lymphedema, skin break down can occur.

While other types of secondary lymphedema can occur in areas of the body such as the face, groin, and lower extremities, BCRL primarily affects the upper extremity of the ipsilateral side. BCRL may also affect the breast or chest region where the treatment was rendered and may spread throughout the upper trunk region to the upper limb and hand. This persistent swelling can impede the joints associated with the region and cause issues such as decreased shoulder mobility and impact other functional aspects. Other concerns associated with lymphedema are skin infections such as cellulitis that may occur in areas where edema persists [8].

Lymph fluid is a protein-rich substance that the body filters via the lymphatic system. Lymph vessels exist to pump the lymph out of the interstitial region and towards the thoracic duct in the direction of the heart under normal conditions [28]. The normal exchange of fluids follows Starling's Law, which describes the exchange of fluid from the pre-capillary arteriole to

the post-capillary venules due to the pressure gradient, with lymph vessels being responsible for the return of most of the fluid to the venous system [17, 27]. BCRL occurs as a result of the disruption of these conditions due to mechanical insufficiency of the lymphatic system. The lymph volume remains the same, however the rate of flow has been decreased due to loss of function from removed or compromised lymph nodes. The system is unable to process the lymph flow at a normal rate, thus leading the gradual accumulation of fluid into the interstitium resulting in lymphedema [7]. The high protein content of lymph fluid in the interstitial space creates a condition where bacteria can thrive, increasing the risk of cellulitis [1]. The presence of excess lymph over a prolonged period of time can also alter the integrity of the skin, leading to symptoms such as pitting edema, skin breakdown and the proliferation of wounds. The inflammatory process is exacerbated with BCRL and can create a cycle of inflammation, swelling, and infection. These conditions can be life threatening if not addressed and may develop months or even years after the breast cancer procedure. BCRL often does not subside without treatment.

A systematic study by Visser et. al [28] found that there may be a genetic component to the development of lymphedema. The study discovered 18 specific gene mutations that were present among patients diagnosed with BCRL. The association between these genetic variations and women who developed lymphedema after breast cancer surgery may indicate that there is a possible subset of women who may be more at risk for lymphedema than others undergoing the same treatment. While there is not yet a clear indicator that the 18 genes found in the study are directly the cause of BCRL, this does confirm that more research into the genetic component of lymphedema is warranted, with the possibility that future genetic testing can be an option for patients undergoing cancer treatment.

Complete Decongestive Therapy: The Current Standard for Treatment

The current gold standard treatment for any type of lymphedema, including the association with breast cancer, is a treatment known as Complete Decongestive Therapy (CDT) [2, 9, 24]. CDT is a mechanical treatment approach that involves improving the flow of lymph by manually massaging the affected area of swelling (manual lymphatic drainage or MLD), decreasing the limb circumference or effected regions by applying gradient compression wrapping or wearing compression garments, and activating the skeletal muscle pump through exercise [11]. When combined as part of a holistic approach to therapy, each treatment has been shown to have a positive effect on patient outcomes in reducing limb volume, improving lymphatic flow, and increasing the patient's functional capacity.

While CDT has been shown to have a positive impact on BCRL patients [2, 20, 23] some of its challenging aspects is adherence to the treatment and the high costs of compression bandaging and garments. In a study [5] that compared BCRL patients with BC patients who did not have lymphedema, health costs for BCRL patients were seven times higher. Most health insurances do not fully cover compression supplies, which may put further financial strain on patients. Boyages et. al [5] found that lack of both insurance and financial support for treatment services and compression sleeve costs caused some patients to discontinue care. The cascading effect of non-compliance can be due to financial constraints, psychosocial factors, and inadequate healthcare support [24]. This emphasizes the importance of continued research in accessible interventions such as exercise, nutrition, and patient/provider education in the realm of lymphedema therapy.

The Current Landscape on the Effects of Exercise

Exercise has been shown to improve lymphatic pump rate and in general, improve circulation. Initially, patients who had undergone mastectomy for breast cancer were strongly discouraged to participate in any resistance type exercise on the affected limb as it was believed that this would actually stress the lymph system, therefore exacerbating symptoms [1, 20]. Recent studies have shown that this dated belief was actually detrimental to patient outcomes, leading to fear-avoidance behaviors against exercise and increased sedentary behaviors in patients [3]. In a systematic review, Nelson found that 2-3 days of progressive resistance exercise training at moderately high intensities safely improved strength in BCRL patients without exacerbating lymphedema [20].

In a systematic review on the effects different modes of exercise had on specifically BCRL, Baumann et. al compiled the literature on studies published between 2003-2016 to provide a comprehensive look at exercise-based treatments for BCRL patients [2]. Out of 822 studies, 11 were selected for the review. Resistance training, swimming/aquatic therapy, gravity resistive exercise, yoga, and even non-conventional forms of exercise such as Qi Gong and Tai Chi were analyzed. The review found that 4 of the 11 studies found a decrease in upper extremity circumference and limb volume and 6 found noticeable improvements in subjective data. There were no reports of negative side effects in any of the studies, providing further evidence that exercise, regardless of the mode can be a beneficial intervention in the treatment of BCRL. While there were significant positive outcomes reported in these studies, Baumann et.al. note that the studies which had a beneficial impact on limb volume and size had some component of resistance exercise to them [2].

Increasing evidence supports the safety of progressive resistance training [2, 20, 29] and research on other exercise modes is ongoing to isolate the specific effects they may have on

BCRL patients. In a study by Bloomquist et. al, there was no significant difference between resistance and aerobic exercise in reported subjective symptoms between the two groups studied [2]. Furthermore, both groups had subjective reports of decreased symptoms of pain, heaviness, and improved function and range of motion. At the end of the trial, the resistance group reported increased strength while the aerobic group reported fewer symptoms. Subjective reports in the study show that there is minimal difference in the superiority of aerobic and endurance activities in the prescription of exercise to the BCRL patient. As both modes of exercise had positive outcomes in the study, exercise can be considered adaptable to the individual and can include a blend of both resistance and aerobic activity.

While improving lymphatic flow to decrease symptoms of limb discomfort and improve function may be considered as the main role of exercise in BCRL, other modes of exercise may provide different benefits such as improved emotional and cognitive well-being. In a recent study [25], the positive effects of yoga as an intervention in 40 women with BCRL showed that while there were limited effects on limb volume, the psychological and cognitive benefits on decreased pain symptoms were considerable. Pasyar et al. [25] indicated that when compared to a control group that had standard treatment, BCRL patients that practiced yoga combined with diaphragmatic breathing for eight weeks had improved physically, emotionally, and mentally. In addition, the study found that the intervention group had decreased symptoms of pain, fatigue, and insomnia compared to the control group. When yoga was implemented as a treatment intervention for patients who were risk for BCRL, Mazor et. al found that an eight-week yoga program had significant positive outcomes for strength, moderate outcomes for upper limb range of motion, and insignificant outcomes for limb volume [18].

While both the Mazor and Pasyar studies [18, 25] provided evidence that yoga is a safe intervention that can provide physical and psychological benefits for those who may be affected by lymphedema after breast cancer, both studies contained a small sample size and only observed the short-term effects. Further research is necessary to determine if yoga can be a beneficial long-term intervention for BCRL. It is important to add to the body of research in order to determine other safe modes of exercise that go beyond strengthening and delve further into the other multi-factorial aspects of lymphedema, which ultimately impact the patient's quality of life.

Exercise Combined with Compression

Within the CDT model, patients are encouraged to wear compression garments while exercising to further promote the effects of both. While this may seem like an effective way to gain more favorable results, patient compliance must be considered as the role of compression garments is still inconclusive. Omar et al. found that low-intensity resistance exercise was beneficial for the reduction of symptoms associated with pain and feelings of heaviness in the limb. Additionally, resistance exercise improved shoulder mobility and function, regardless of whether the patient performed the exercises while wearing a compression sleeve [23]. This evidence is significant because one of the challenges for patient compliance is independent care, particularly donning compression garments. In one qualitative study, Jeffs et. al. [15] found that some of the barriers to adherence to wearing a compression sleeve were negative self-image, difficulty with donning, and discomfort. The decreased burden of worrying about compression while exercising makes the task more accessible to the patient, which may improve their motivation to care.

Aquatic Therapy

There is limited research on the effects of aquatic therapy in relation to lymphedema treatment. In a small pilot study done on individuals with lower extremity lymphedema, bioimpedance tests revealed lower global extracellular fluid and a significant decrease in limb volume one hour after the interventions, however it was not indicated how long the effects lasted [10]. In a study specifically done on BCRL patients looking at slow versus quick speed of aquatic exercise, Deacon et. al [9] determined that slow exercise combined with diaphragmatic breathing had immediate positive results on limb circumference, however the effects only lasted an hour. In a meta-analysis review, five studies aquatic therapy as an intervention for upper extremity lymphedema, Yeung et. al concluded that there were no significant beneficial outcomes over land-based therapy [31]. While the existing research does show that it can be a safe intervention, (no exacerbation of symptoms were reported in any of the studies), there needs to be more research with larger sample sizes when it comes to determining the benefits of aquatic therapy for BCRL.

Exercise as a Preventative Measure

The significance of the research that has been done on BCRL have been important in determining that exercise is safe for these patients and will not increase symptoms associated with the condition. Although the evidence that supports exercise for lymphedema is increasing, there is still limited data on how exercise, if any, can prevent lymphedema after breast cancer treatment. In a study done on resistance training specifically to prevent upper extremity lymphedema in the first year after surgery, there was no indication that progressive resistance was effective as a preventative measure [1]. This study adds to the growing body of evidence that resistance training continues to promote positive and beneficial side-effects (such as

decreased pain, decreased symptoms of heaviness in the affected limb, increased strength and range of motion) for BCRL patients.

The effects of physical activity are considered to have a positive impact on patient with lymphedema overall. The benefits of possible limb reduction, increased strength, flexibility, and psychological benefits continue to outweigh any previously believed risk of exacerbating the condition. While studies have shown these positive outcomes, more studies are warranted to look into the possible protective mechanisms, if any exist, that exercise may have in the prevention of lymphedema. Studies involving larger sample sizes and a variety of exercise modes need to be continued in order to grow the evidence of exercise as an intervention, and more specifically look at the appropriate dosage for patients of varying stages and conditions.

Effects of Supplements and Diet on BCRL

In research that looks at the nutritional aspects of BCRL, intake of medium chain triglycerides (MCT) may have a positive effect on BCRL. A random controlled study conducted on ten women who had a mastectomy after breast cancer diagnosis divided the group of women into a control group that underwent physical therapy consisting of MLD, massage, and skin care and then another group that had the same therapy with the addition of MCT intake for four weeks [22]. The control group had used long chain triglycerides as a fat source. While both groups demonstrated decreases in symptoms of heaviness, pain, and overall discomfort related to upper limb lymphedema, the MCT group showed more of a significant decrease in limb circumference, volume, and heaviness compared to the control group [22]. The theory behind the increased reduction in limb volume and clinical symptoms in the MCT group may be actually the lack of LCT in the diet. MCT fatty acids are absorbed and do not accumulate in the lymphatic system. Due to the accumulation of LCT in the lymphatic system with mechanical insufficiency,

this could indicate that diets that include LCT such as corn or vegetable oil may not be ideal for BCRL patients and that MCTs would be a better fat source. While this signifies a correlation between MCT intake and lymphedema reduction, newer research on this aspect of nutrition has yet to be seen.

Another aspect of nutrition involves the ingestion of probiotics. In a recent pilot clinical trial, a 10 week supplementation of symbiotics in conjunction with a diet consisting of high antioxidant rich foods and weight reduction diet, had a mild positive impact on decreasing limb volume in BCRL patients compared to those in the study who took a placebo [19]. While the research on the effect probiotics have on lymphedema is emerging, it is known that obesity and chemotherapy are two factors that may contribute to the reduction of important enzymes or probiotics that yield antioxidant properties. Navaie et. al reveal that certain gene expressions of these enzymes may also be regulated by probiotics [19] indicating further research on genes may be beneficial as to how enzymes have an effect on BCRL survivors. This may lead to a better understanding of the proper dosing when it comes to probiotic supplementation. Another study regarding supplementation is the effects of oral or intravenous use of sodium selenium [13]. Selenium is a mineral that has antioxidative properties, however in this study it was determined that it worked by decreasing inflammation in subjects by targeting the immune system. Han et. al concluded that selenium was considerably successful in decreasing the effects of BCRL and led to a downscaling of lymphedema stages when compared to the control group [13].

The research regarding the nutritional and dietary effects of lymphedema on humans is extremely limited, however some studies on diet and lymphatics in the animal model have primed the landscape for further research into a better understanding of lymphedema and the lymphatic system. In a study done on rats, Nikpey et. al examined the effects of a high sodium

diet (HSD) and hypertension on the lymphatic system [21]. The researchers found that although blood pressure and skin tissue had higher osmolality in the rats who were on an HSD, the lymph and deeper dermis were similar between the HSD and control group. The study indicated that there may exist an osmotic gradient in which the skin tissue and kidney have separate control mechanisms that may not directly impact the lymph system [21]. While reducing sodium is generally a healthy recommendation for most people, this study underlies that the nutritional links, regarding sodium rich foods and lymphedema are not yet fully understood.

Gousopoulos et. al discovered that a high fat diet (HFD) given to mice were surgically induced to have lymphedema was not the main factor for increased symptoms related to lymphedema in mice without obesity [12]. While it has been previously determined that there is a correlation between obesity (caused by HFD) and impaired lymphatic flow [12], the Gousopoulos study revealed that mice who were not obese but fed a HFD did not experience any more increase in fibrosis or adipose tissue compared to the control group. This may indicate that a diet can consist of some healthy fats without further exacerbating symptoms of lymphedema. Furthermore, the link between inflammation and lymphedema indicates that a diet rich in omega-3's may have anti-inflammatory benefits to patients [7].

The association between obesity and lymphatic impairment stipulate the importance of healthy weight loss in order to minimize the effects of the disease [7, 30]. As obesity rates continue to rise in the U.S. population [7], the risks associated with BCRL complications such as impaired lymphatic function, increased inflammation, potential for cellulitis, and physical impairments can become more prevalent as both cancer survival rates and obesity continue to increase [30]. The need for further studies is imperative as more people may have the potential to develop these conditions. Due to the limited knowledge on the effects of sodium, fats, and

antioxidants, continued research in nutrition and supplementation is required in order to make more clearly defined dietary recommendations for people living with lymphedema.

Psychosocial Aspects of BCRL

The psychosocial aspects of lymphedema can impact treatment, and involves a spectrum of issues ranging from emotional, social, and psychological. Since BCRL is a lifelong condition, patients may not be prepared for the long-term treatment and self-care associated with it [24]. Complete Decongestive Therapy and lymphedema management involves patient compliance and motivation in order to be effective. According to Ostby et. al, psychological, physical, emotional, and psychosocial components can all create a barrier to effective treatment [24]. Furthermore, a lack of confidence in provider knowledge and education on lymphedema treatment can also be a barrier to patients.

An online survey by the Breast Cancer and Knowledge Study was used to determine BCRL knowledge and referral practices among 887 practitioners. The survey revealed that only 36.2% of primary care physicians referred BCRL patients for treatment [24]. Furthermore, Ostby et. al found that websites dedicated to the topic of lymphedema was a primary source of information for 76% of patients, followed by medical professionals. This may indicate that lymphedema patients are not getting adequate information after BC treatment and are seeking information independently. In a study that focused on patients' perspective of treatment barriers, Ostby et. al revealed that most of the subjects did not receive any information about lymphedema until after they developed symptoms and sought medical care [24]. The findings in this study indicate that the major barriers of BCRL treatment include patient education and awareness, in addition to self-efficacy and social support. Addressing any barriers to patient treatment are critical to early interventions and long-term success.

Since a large portion of lymphedema care must be patient-driven, self-efficacy is an important factor to patient success. In the study by Ostby et. al, it was determined that in order for independent management to be effective, adequate follow-up support by providers and therapists was crucial. According to the study, patients believed that having a good support system aligned with early intervention success and long-term compliance to care.

Conclusion: Further Necessary Research

As cancer treatments and survival rates continue to improve, more people will likely be at risk for secondary lymphedema. According to Rebegea et. al, breast cancer survivors who have previously undergone axillary node dissection have a 16% chance of developing lymphedema years after the surgery [26]. While this number may seem insignificant, it is possible that there is a number of unreported cases due to patients not seeking medical care for lymphedema symptoms. Due to lack of awareness or knowledge, patients may not recognize early or even middle stage symptoms, as noted by Borman and Ostby [4, 24], which indicates that there could be a greater number of BC patients affected by lymphedema than is realized. In a 2016 study, Borman et. al found that out of 180 women admitted to a lymphedema treatment center, only 35 reported being given any information on lymphedema after their breast cancer surgery [4]. This finding elucidates the need for more patient and healthcare provider education on the risk factors associated with breast cancer surgery, symptoms, and treatment options. The consequences of not recognizing early stage lymphedema can lead to decreased prognosis, increased medical complications associated with lymphedema, and higher treatment costs to both patients and health insurances.

The bodies of research featured in this writing reflect the limited studies that have been done to further understand BCRL. Further research is necessary to provide a better understanding

of how obesity effects lymphedema, what types of diet and nutrition provide the best outcomes for these patients, and what types of modalities provide the greatest reduction and relief of symptoms. As more women have the potential to develop complications associated with BCRL, patient education immediately provided, even prior to surgery will be beneficial. It is clear from the compilation of studies and articles discussed in this paper that significantly more research with larger sample sizes is necessary to improve knowledge on BCRL preventative measures and address the psychosocial concerns associated with patient barriers to treatment [4, 5, 24]. This should involve more emphasis on educational programs within the cancer treatment model, continuing education for healthcare providers, and expanding research on interventions that are necessary to the continued success and best possible outcomes for breast cancer survivors.

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