



LITERATURE REVIEW ON BREAST CANCER-RELATED LYMPHEDEMA AND RELATED FACTORS

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SUMMARY

A potential complication that affects a patient's quality of life is breast cancer-related lymphedema (BCRL). Due to lymphatic system failure brought on by breast cancer treatment, it is secondary lymphedema.

This literature review examines 50 articles that are connected to BCRL. Research conducted in the English language between 2017 and 2022 is included. The definition, occurrence, severity, symptoms, risk factors, aspects of quality of life, and total decongestive therapy are all incorporated in this review of BCRL.

The severity of the BCRL is assessed using International Staging Lymphology, 2020 from mild to severe. The documented incidence rates of BCRL in the literature range greatly, between less than 5% and more than 50%. The most significant risk factors of BCRL are related to lymph node surgery, in particular, axillary lymph node excision, and radiation therapy. If BCRL is not properly diagnosed and managed, it could have debilitating, long-lasting and late crippling side-effects of breast cancer treatment. It frequently has a devastating impact on the quality of life in many domains.

To better understand the behaviors and management of lymphedema risk reduction, patients with breast cancer need extra information. To evaluate the effectiveness of complete decongestive therapy as a risk reduction behavior rather than for management and treatment, more study needs be done with a larger sample and longer supervision.

Key words: breast cancer, lymphedema, skin care, treatment, compression

INTRODUCTION

Lymphedema is a common negative side effect of breast Cancer treatment that affects people all over the world (1-3). Breast Cancer-related lymphedema is characterized as a secondary form of lymphedema that develops as a result of lymphatic system malfunction brought on by either the illness itself or breast Cancer treatment modalities such as surgery, radiation, and chemotherapy (4, 5). Lymphedema can be diagnosed using a variety of usually non-invasive methods. Symptoms including growing limb soreness and swelling of the upper extremity girth are commonly used by doctors to diagnose BCRL (4). The most transportable and easily accessible noninvasive methods for determining its presence and extent are only circumferential measurements that evaluate the girth variation between the normal and affected arm. These methods include circumference measurement by humans and machines as well as water displacement for volume changes. Ultrasound, magnetic resonance imaging, photography, and scanning methods are some more non-invasive procedures. It is frequently identified by circumferential measures, which demonstrate a 2-centimeter difference in arm circumference at one anatomical site between the normal arm and the affected arm (6). There are four stages of lymphedema: Stage 0: The lymphatic flow has diminished even if there are no obvious symptoms of the illness, such as swelling. Stage I (mild) refers to pitting edema that is present but reversible, whereas stage II (severe) refers to pitting edema that is irreversible (moderate). When the diseased area becomes enlarged and cannot be treated, elephantiasis is categorized as stage III (severe) (1,6). The BCRL phases are used to determine the severity of

the lymphedema.

Using the keywords "breast Cancer associated lymphedema," "incidence of BCRL," "full decongestive therapy," "skin care," "massage," "exercise," "compression," "BCRL symptoms," "risk factors," and "quality of life" articles were obtained from the PubMed, EBSCO Host, and Google Scholar databases. The word AND was used to combine all of the terms in the research. To raise awareness of this issue, this literature review will examine the 50 published researches in relation to the BCRL's terms. The inclusion criteria compile English-language research from 2017 through 2022. The BCRL is the major topic of this review, along with the aspects that contribute to the issue, such as the definition of BCRL, incidence, severity and symptoms of BCRL, risk factors, quality of life "domains," and comprehensive decongestive therapy. The purpose of this review is to condense the body of knowledge on BCRL and the factors that affect it. The review gives an overview of the prevalence, risk factors, pathophysiology, prevention, and management approaches related to BCRL and includes studies completed up through September 2021. It investigates the psychological effects of BCRL on the patients' quality of life and identifies information gaps to direct future research initiatives.

The article deals with how BCRL can be prevented or treated to a certain extent through education, exercise, lymphatic mapping, and risk-reduction strategies. This section lists the methods for preventing BCRL and lessening its effects, emphasizing the value of early detection and intervention. Also, it examines several therapeutic strategies for BCRL, including manual lymphatic drainage, compression therapy, exercise, surgical therapies, and pharmaceutical interventions. Complete

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decongestive therapy (CDT) is included. It offers an analysis of the merits and drawbacks of these tactics. BCRL has a substantial psychological impact on breast Cancer survivors in addition to having an influence on their physical health. The emotional, social, and psychological effects of BCRL are discussed in this article, including concerns with body image, self-esteem, sadness, anxiety, and sexual function.

INCIDENCE OF BCRL

The excision of the axillary lymph node was specifically associated with early-onset BCRL that manifested in less than a year ($p = .01$), with the peak onset occurring between 6 and 12 months in women who underwent breast Cancer surgery (7). A recent systematic review by Torgbenu et al. found that the incidence rate was 21 percent with a large variance (2020). Less than 5% and more than 50% are the documented incidence rates of BCRL in the literature, respectively (8). This discrepancy happens as a result of various arm volume measurement methods and the absence of clear-cut BCRL diagnostic criteria (9). Furthermore, 63 papers discussing the BCRL were found between 2015 and 2020 according to a review by Champion (10). Depending on the manner and time of the examination, the incidence rates of BCRL ranged from 9 to 39 percent. The incidence of BCRL was 19.5% higher in patients who underwent radiation treatments after having their axillary lymph nodes dissection (ALND) than in those who got either treatment alone (11). However, using sentinel lymph node biopsy (SLNB) rather than ALND has been demonstrated to reduce the incidence of BCRL and limit the scope of axillary lymphadenectomy.

BREAST CANCER RELATED TO LYMPHEDEMA – APPROACH, SEVERITY AND SYMPTOMS

Breast care centers can use the prediction model to assess the likelihood of lymphedema in female patients undergoing ALND surgery. Between January 2008 and May 2018, 504 women who underwent breast Cancer surgery with ALND had their clinical data analyzed (12).

The results support a more cautious surgical approach and highlight the usefulness of weight loss as a preventive measure (12).

Additionally, one should continue participating in a self-management lymphedema education program (SMLEP) for the rest of their lives (13). In addition to reducing upper extremity volume and lymphedema-related symptoms, weight control, meticulous skin care, self-lymphatic drainage (SLD), compression clothing use, and exercise can improve patient compliance and the daily activity level, which impacts the quality of life (14-16).

The length, stage, and severity of the lymphedema were found to be adversely connected with the volume improvements and quality of life improvement by Borman, Yaman (17). One key component that seems to be linked to severe lymphedema is just an increase in the Body Mass Index (BMI), which implies being over-

weight or obesity in patients with BCRL (16).

The physical symptoms of BCRL, a chronic illness, include edema, weight gain, and a limited range of motion (17). Additionally, individuals with BCRL reported worse arm tightness, tingling, heaviness, stiffness, and edema (18). Patients should be taught and educated about the BCRL risk factors for prevention, control, and management in order to avoid modifiable risk factors, take early action to conduct risk-reduction activities, and finish decongestive therapy (CDT) (19).

RISK FACTORS FOR DEVELOPING BCRL

The formation of the BCRL is thought to be connected with a number of risk factors, both related and unrelated to Cancer treatment. A modified radical mastectomy, an infection of the surgical site and the removal of more than 18 axillary lymph nodes were treatment-related variables (6, 20, 21). Lymph nodes with metastatic deposits were substantially more prevalent in patients receiving BCRL (9). Furthermore, it is thought that axillary lymphadenectomy (ALND) poses a larger risk for developing BCRL than sentinel lymphadenectomy (SLND) (22). The primary cause of BCRL is the ALND since it significantly disrupts the lymphatic system. Furthermore, postoperative difficulties were linked to the chance of BCRL (22) and obtaining radiation to localized axillary lymph sites is an example of getting BCRL (8).

Furthermore, the mortality in BCRL patients was negatively impacted by both Lymph-vascular Infiltration (LVI) and Extra-nodal Extension (ENE) of the metastases. Patients who received left-side localization and LVI were four times more likely to experience BCRL advancement. Patients who underwent axillary dissection and had right-arm metastases with ENE were at a greater risk of developing BCRL than those with negative ENT of the metastases (23).

A higher incidence of BCRL was linked to radiation in general for radiotherapy treatment (24). More specifically, when comparing the 2D radiotherapy strategy to the 3D radiotherapy method, the development of lymphedema was statistically strongly connected with the 2D radiotherapy approach ($p < .001$). Patients who received conventional radiation had a considerably higher incidence of BCRL ($p < .001$) compared to those who received hypo-fractionated radiotherapy (8.5%) (25).

Smoking, having a mass index of over 25 kg/m², having a low income, being over 50, being of African American or Hispanic ancestry, and having a higher age all significantly increase the risk of lymphedema (19, 25). Additionally, a review study found that cellulitis and subclinical edema are risk factors with strong supporting data (26). Patients who have more lymph node metastases, weight gain, and a larger circumferential difference (CD) than usual are more likely to experience persistent lymphedema (PLE) (27). All of the aforementioned factors raised the likelihood of getting BCRL. On the other hand, participating in sports, work-

ing out the affected limb, and contacting a doctor right away if there were any signs of infection were all linked to a lower risk of developing BCRL.

QUALITY OF LIFE AND BCRL

The BCRL had an adverse effect on the quality of life (QOL). The patients receiving BCRL reported decreased mobility, life and social functioning, as well as worse lymphedema-specific mental functioning and overall mental health (28, 29). Furthermore, the patients reported a worsening in their assessment of their general health, impairment in their ability to do physical duties, and physical pain (2, 30). The psycho-social issues with BCRL were addressed in a previous study (31). Due to the difficulty of performing their jobs, women with BCRL experienced psychological distress, including anxiety, depression, disturbances of their body image, impaired sexual interest, impaired social functioning, and financial burden (32, 33). This had a significant detrimental effect on their ability to find employment.

Few studies have focused on the sexual experiences of patients who undergo a mastectomy and develop lymphedema (34). The participants who experienced breast Cancer-related lymphedema talked of having unpleasant breast and upper limb sensations, trouble maintaining close relationships, and feelings of decreased sexual arousal. In conclusion, lymphedema patients suffer negative consequences on their sexual function and general quality of life (34). Moreover, ongoing lymphedema treatment for breast Cancer causes problems at work. In addition to experiencing delays in returning to work, BCRL also has an influence on one's ability to perform physically and emotionally at work (35). Survivors claim that personal resilience and adaptation to physical, mental, and employment-related changes are necessary to mitigate the impact of BCRL on the workplace. Throughout the lifecycle, work activities may be maintained and QOL might be improved thanks to modern BCRL management techniques as CDT (35).

UPPER EXTREMITY FUNCTION AND BCRL

The BCRL has a detrimental effect on the use of the upper limbs. While the physical function of the upper extremities and general health status were significantly improved, the BCRL symptom significantly diminished. The patients' ratings for their visual and kinesthetic senses, as well as their disabilities of the arm, shoulder, and hand (DASH) scores, all significantly improved after getting CDT (19, 36). Furthermore, it was observed that after getting CDT during the active phase from a physiotherapist, a total of 37 Turkish women with the diagnosis of BCRL reported a statistically significant decrease in pain and heaviness and an improvement in shoulder mobility.

COMPLETE DECONGESTIVE THERAPY

One of the treatment plans for the management of

BCRL that is most usually suggested is Complete Decongestive Therapy (CDT). It was discovered that CDT is a significant adaptive method for raising QOL. A significant reduction in the size of the afflicted arm was observed in the patients who got CDT. Additionally, while the BCRL symptom significantly decreased, both the health status and upper extremity physical function significantly improved (37). It has been found that BCRL management, which includes CDT, has a favorable effect on QOL domains like physical, emotional, cognitive, social, and role functioning (2, 19).

The best strategy for treating BCRL in its early stages is still complete decongestive therapy (5, 18). It is a demanding program that combines several therapeutic techniques, such as self-lymphatic draining massage, compression clothing, physical activity, and skin care. CDT is used to treat moderate-to-severe lymphedema stages II and III (18).

SKINCARE

Maintaining healthy skin and avoiding infections that worsen BCRL progression are crucial in all stages of CDT as risk-reduction behaviors (17). In addition to checking and palpating the skin, cleansing, moisturizing, and debridement, it involves avoiding sunburn (4). Patients' compliance with skin care self-management was measured by Hamner and Fleming (38). This tool has four categories: skin care, avoiding harm and oppression, lifestyle, and other pressing issues. The findings revealed a lower score for the patients' compliance with skincare, although functional exercise compliance improved (39). The findings revealed a relationship between patient age, educational attainment, views of their condition, and adherence to BCRL risk management practices. Younger patients who had received adequate education and knew enough about BCRL were more likely to follow BCRL risk management practices (14).

Therefore, rather than merely being evaluated once, a patient's comprehension of the advantages of skin care and compliance with instructions should be regularly monitored throughout their lymphedema journey.

EXERCISE

The literature suggests exercise as an adaptive technique to lessen swelling and encourage lymph fluid to depart the swollen area. Early exercise can be a useful tactic in the prevention of BCRL for at least a year after axillary lymph node dissection (27). Exercise is, therefore, an essential component of CDT that has a favorable effect on BCRL development. It improves the physical wellbeing and quality of life of BCRL patients (27). According to a meta-analysis by Panchik, Masco (40), a variety of exercises, such as stretching, yoga, qigong, Pilates, resistance training, and aerobic activity, can safely and effectively assist people who have lymphedema or are at risk of developing it by reducing the severity of its symptoms, such as pain and lymphatic swelling (9, 27, 41).

Patients who are at high risk of BCRL may need to exercise regularly or engage in daily activity that is at least moderately intense (increasing pulse frequency) (12). Early exercise preservation has shown to be a good BCRL prevention treatment for at least a year after axillary lymph node dissection (27). This information was supported by a comprehensive evaluation of eight randomized controlled studies that examined the possible preventive value of exercise on Secondary lymphedema (SL) incidence. It showed that exercising could be a useful trick for avoiding BCRL (11). To determine the effects of weightlifting or resistance exercise on BCRL, a systematic review with 15 researches was undertaken. This proved that BCRL patients or those who are predisposed to the condition could benefit from strength training or weight-lifting when done under supervision because it is secure and effective at reducing arm volume (40). An exercise group (52 weeks; 2 sessions per week of at-home weight training, 180 minutes of weekly walking, and 52 weeks of lifestyle change counseling) and control group were randomly allocated to 351 breast Cancer patients with BCRL in a more recent trial. There were no appreciable BCRL differences between the two groups, according to the study. This is despite the fact that the majority of prior studies have found a beneficial relationship between clinical and at-home physical activity and secondary lymphedema (42, 43).

MASSAGE THERAPY (MANUAL LYMPHATIC DRAINAGE)

Manual lymphatic drainage (MLD) has shown in the literature to minimize stage I lymphedema symptoms and stop BCRL from reaching an irreversible state; as a result, it should be widely used (22). 11 RCTs with a combined total of 1,564 patients were included in a systematic study. Despite the fact that the data do not suggest that MLD can reduce lymphedema volume and improve the quality of life, there is currently strong evidence that MLD significantly lowers discomfort in BCRL patients (30, 44). A double-blind, randomized controlled study involving 194 patients with unilateral BCRL was conducted. All patients had regular CDT and were given the choice of getting conventional, fluoroscopy-guided, or placebo MLD. The participants received therapy for 60 minutes per day for three weeks during the intensive phase, then for 18 sessions totaling 30 minutes over six months during the maintenance phase. Exercise, wearing a compression garment, and performing a self-MLD therapy once a day were all mandated for the participants. The bulk of the outcomes at the level of the arm showed a discernible improvement over time in all three groups, regardless of the form of MLD that was implemented (37, 45). The results of a meta-analysis of randomized control studies showed that when there were more than 20 therapy sessions or when the therapy lasted longer than two weeks, a statistically significant reduction in upper limb volume was achieved. These requirements permit the

recommendation of a manual-lymphatic draining massage for the treatment of BCRL (20).

COMPRESSION THERAPY

Using a prophylactic compression sleeve in the first 12 months after axillary lymph node excision reduces and delays the onset of arm edema, which helps prevent BCRL (46). In addition, using multi-layer compression bandaging or applying compression garment therapy early after breast surgery can slow the onset of BCRL, reduce symptoms, and improve QOL (28).

According to Whitworth et al., proactive care with compression clothing worn for 12 hours a day for one month significantly reduced the incidence of chronic BCRL (21). Based on the evidence in the literature, compression therapy can therefore be used for the treatment and prevention of BCRL.

CONCLUSION

To improve patient outcomes and improve the quality of life for patients, evidence-based risk reduction, preventative, and adaptive techniques like CDT should be used.

Instead of depending exclusively on one CDT domain to halt BCRL from developing and progressing, healthcare providers should take control of it early by inhibiting all domains of CDT functioning. Exercises and compression are employed as preventative strategies in addition to addressing BCRL. In order to determine whether the CDT is more effective as a risk reduction behavior than as a management and treatment strategy, more study with a larger sample and longer monitoring should be carried out.

Declaration of Interests

Authors declare no conflicts of interest.

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