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Are post-operative preventative measures effective in breast cancer-related lymphedema? A systematic review

Abstract

Breast cancer-related lymphedema (BCRL) is one of the most debilitating complications of breast cancer therapy. Many of the current approaches to preventing BRCL are based solely on anecdotes and insufficient evidence. This systematic review aimed to determine the effectiveness of post-operative BCRL preventive measures. The preferred reporting items for systematic reviews and meta-analysis guidelines were used in this review. Four databases (EBSCO CINAHL, EBSCO MEDLINE, EBSCO AMED, and Cochrane) were searched from 2012 to 2021. Studies were screened following preset inclusion and exclusion criteria. Joanna Briggs Institute (JBI) checklist and the Oxford Centre for Evidence-Based Medicine Hierarchy of Evidence (OCEBM) were used to critically appraise and evaluate the level of evidence of eligible studies. Out of the 470 articles screened, 29 were eligible for review. The articles were classified into six categories based on risk behaviors. Venipuncture, blood pressure measurements, and air travel had no strong evidence to be correlated with remission or exacerbation of BCRL ($p > 0.05$). There was a strong correlation between obesity and exacerbation or onset of lymphedema ($p < 0.05$). Physical activity and resistance training had high-quality evidence in preventing BCRL. Most studies were of moderate evidence level. There is limited evidence for post-operative precautions — like venipuncture, air travel, blood pressure measurements, and lifting heavy loads as risk factors for BCRL in patients with breast cancer. Empirical information regarding post-operative suggestions given to patients with BCRL will help to limit potentially harmful practices and enhance psychosocial health.

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Keywords: Breast cancer, lymphedema, risk factors, precautions, guidelines

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Introduction

According to the International Agency for Research on Cancer (IARC) statistics published by the World Health Organization (WHO) in 2020, breast cancer is one of the most frequently diagnosed cancers in women, accounting for approximately 24.5% of all cancers and nearly 15.5% of all cancer-related deaths in women [1]. Despite the fact that significant progress and advancements have been achieved in the last decade to combat the mortality linked with the condition [2], there still appears to be considerable morbidity associated with breast cancer. These morbidities are heterogeneous [3, 4] and may involve physical ailments such as pain [5], loss of range of motion, and functional activity restrictions [6] in addition to a plethora of psychological implications [7], depending on the type of management or if resection is being considered, the type of surgery [8].

Surgical management is the primary intervention for patients with breast cancer, and it is the first modality of therapeutic potential in most cases [8]. Patients diagnosed with breast cancer in the United Kingdom (UK) often receive one of the following surgical procedures: breast-conserving mastectomy, mastectomy with sentinel lymph node dissection, or axillary lymph node dissection. Alternatively, they could also undergo a mastectomy [9]. Over the past four decades, the advancements in early detection, diagnostic methods, and surgical approaches have been pivotal in doubling the five-year cancer survival rate in the UK [10], additionally, improving the disability-adjusted life years in the population [11]. Even though these treatments have improved patient outcomes, they are associated with considerable adverse effects. These adverse effects might be acute, such as superficial and deep wound infections [12, 13], seromas [13, 14], necrosis [13], and pain [15], or might precipitate later in the form of breast cancer-related lymphedema (BCRL) [16].

Breast cancer-related lymphedema is a chronic debilitation [17] and feared [18] complication post--breast cancer surgery. Even though the etiology of lymphedema is poorly understood, its pathophysiology is generally accepted to be initiated by mechanical damage to the lymphatic system, which in turn encourages protein accumulation in the tissues and ultimately results in fibrosclerosis. This edema further disrupts the metabolic processes in the interstitium and facilitates increased inflammatory reactions [19]. As a result of this accumulation of fluid, the breast, trunk, or upper extremities of the surgically altered side become edematous and swollen [20]. Whilst swelling is a symptom that many people have reported experiencing, it is typically accompanied by other symptoms such as pain, tenderness, heaviness, numbness, soreness, stiffness, and fatigue [21]. Likewise, these manifestations are not only restricted to physical ailments but have been recognized as being multifactorial [22] causing severely altered and poor quality of life [23]. Most patients with BCRL have reported depression, anxiety, body image issues, altered psychological quality of life [24], and feeling handicapped [25]. BCRL can also further predispose patients to infections, cellulitis, and further deterioration of health.

The incidence of lymphedema is difficult to evaluate due to the different definitions, populations, and measurement methodologies, but the reported incidence varies from 3% to 42.2% [26–30]. A meta-analysis conducted in 2013 of 72 incidence studies and 13 risk factor studies found that one in five survivors of breast cancer will develop BCRL [31]. Furthermore, Ribeiro Pereira et al. [13] in a 10-year prospective observational study said that the incidence of lymphedema increases from 13.5% in two years to 41.1% in 10 years [13]. Lymphedema has been linked to several risk factors; however, only a handful of them are supported by solid evidence from scientific studies. These factors broadly can be classified into three groups: treatment-related factors, disease-related factors, and patient- and clinical-related factors [32]. Some commonly mentioned risk predictors include factors like the performance of mastectomy [31], axillary lymph node dissections [33] (ALND), obesity, age [26], and post-operative complications [13]. A substantial correlation was observed between the frequency of BRCL in individuals who had received radiation therapy or chemotherapy to the same arm, had a body mass index (BMI) of more than thirty, had suffered post-operative seroma, or were diagnosed with advanced disease [13].

In BCRL, a total inter-limb volume difference of 200 mL between an at-risk arm and the contralateral unaffected limb is considered clinically significant [31]. The traditional methods of measurement include girth measurements using tape and volumetric assessment of the limb using water displacement, in comparison to the non-operated side [34]. These measurements even though are extremely cost-effective, easy to perform, reliable, and immensely popular [35–37] have low sensitivity and consistency, high inter-rater variability, standardization difficulties, and varying diagnostic thresholds. This was not suitable for an early diagnosis necessitating the need for more sensitive tools. The perometer [38] and bio-impedance spectrometry (BIS) [39] are two of the few newly developed, well-validated, and efficient measuring techniques that have gained favor in clinical and research contexts in recent years. An experimental study by Svensson et al. [21]

reported that the BIS had a sensitivity of 76% and a specificity of 93%, demonstrating clinically significant and compelling positive (10) and negative (0.3) likelihood ratios.

Despite the lack of a cure for BRCL [40], early treatment and diagnosis are among the best approaches to slow disease advancement [41]. Patients with lymphedema frequently air grievances with their diminished ADL and recreational autonomy [26, 42]. Treatment for lymphedema continues to be poor and predominantly palliative [43] with the goal of delaying advancement or avoiding incidence rather than treating the condition. Due to this, most patients require lifetime treatments, such as manual lymphatic drainage procedures and the wearing of compression wear, to prevent lymph fluid from accumulating or draining into the affected limb [44]. Despite all this, the vast majority of patients remain concerned about their illness progression [45]. Moreover, because these therapies are inefficient, time-consuming, expensive, and unpleasant, their compliance remains exceedingly low [46]. There is a significant void in our understanding of lymphedema, and the molecular process responsible for it is poorly understood [46]. Current guidelines based on current scientific evidence, the most common way to treat it has been to counsel patients right after surgery about potential causes, preventative exercises, and early detection strategies. However, many of the current approaches of preventing lymphedema are based solely on anecdotal and inadequate scientific research. Hence, the purpose of this review is to highlight the scientific evidence supporting or disproving the current advice offered immediately following surgery to prevent lymphedema.

Methods

The protocol for this review was registered with the National Institute of Health's International Prospective Register of Systematic Reviews (CRD42022364643). The Preferred Reporting Items for Systematic Reviews (PRISMA) 2020 guidelines [47] were followed in this review. The 27-item checklist was used to ensure transparency, accuracy, and replicability of the review [48]. The PRISMA flow chart for the study is presented in Figure 1. The search results were extracted

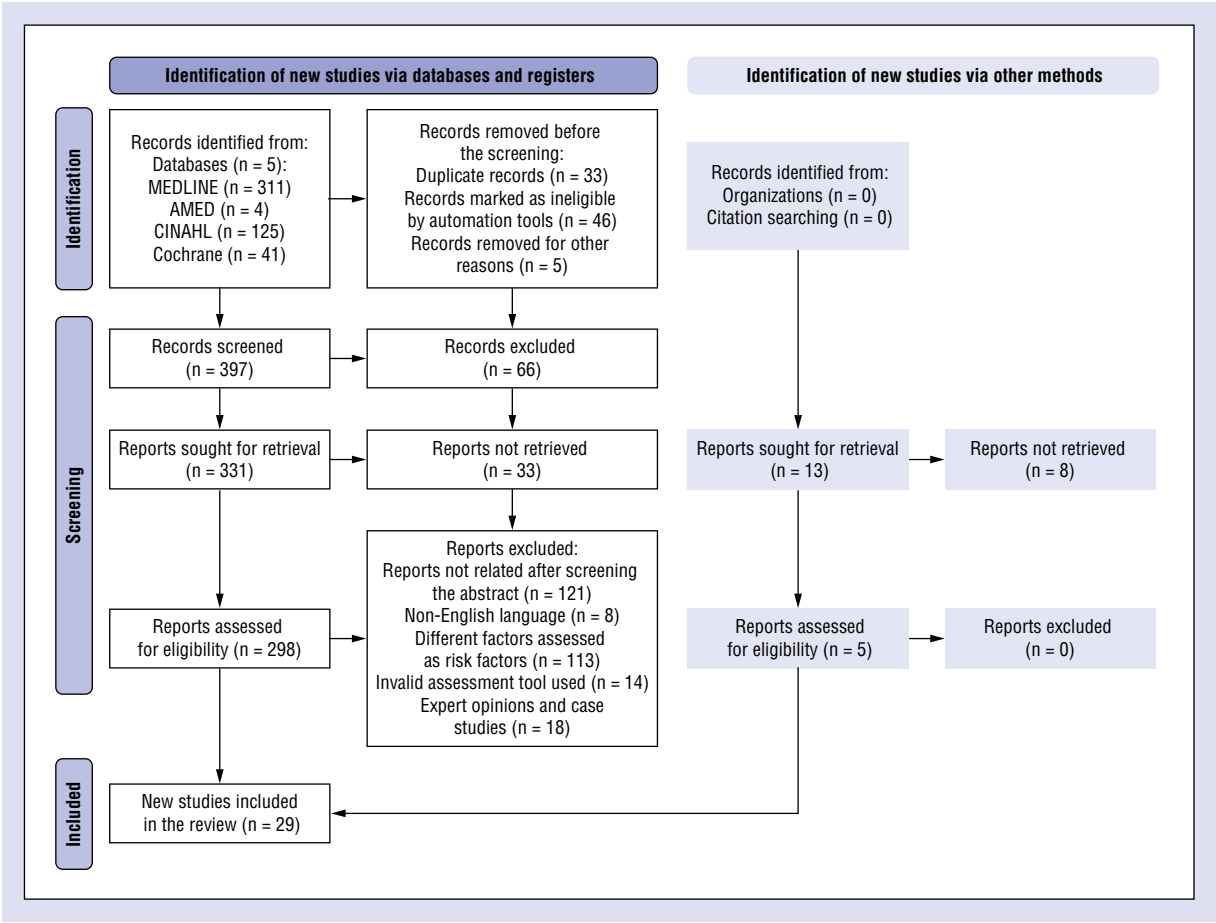

Figure 1. PRISMA flowchart for the study [50]

Table 1. Inclusion criterion and exclusion criteria

	Inclusion	Exclusion
Study design	Experimental, prospective, and retrospective studies Full text available 2012–2021	Case studies, conference papers, animal studies, anecdotal & expert opinions
Participants	Patients undergoing breast cancer surgery	Lower extremity edema, axillary web syndrome, and other co-morbidities in conjunction with BRCL that could potentially impact the results Primary lymphedema
Intervention	Preventative measures, post-operative recommendations, on-treatment-related risk factors	Solely looking at Racial or age factors, the effect of chemotherapy, radiation therapy, or any other treatment-related effects
Outcome measures	Measure of lymphedema	Studies assessing QoL or ROM only

BRCL — breast cancer-related lymphedema; ROM — range of motion; QoL — quality of life

into Zotero, duplicates were eliminated, and the titles and abstracts of each article were evaluated against the exclusion criteria manually. The inclusion of articles was contingent upon the availability of full-text articles and fulfillment of elements listed in Table 1. Additionally, references to the chosen articles and review papers were examined to identify any missing or relevant publications. The Populations, Interventions, Comparison, Outcomes, and Study Design (PICOS) premise served as the foundation for the search approach.

Individual search strategies were used for each of the electronic databases chosen for the review. The databases were EBSCO CINAHL, EBSCO MEDLINE, EBSCO AMED, and Cochrane. Each bibliographic database's standards of syntax were taken into account when the search strategy was formulated, which used a combination of regulated preset Medical Subject Heading (MeSH) [49] phrases and free terms employing the Boolean operators (*i.e.*, OR and AND). The MeSH terms used in the review include breast neoplasm, lymphedema, mastectomy, Resistance training, and obesity (Appendix 1 — complete search terms). Also, the references of the articles found were checked to identify potentially relevant articles that could have been missed in the initial search. Only publications in the language English were considered from the year 2012 onwards, considering this review as an update on the systematic review by Cemal et al. [43].

Randomized controlled trials, observational studies, and retrospective and prospective studies that investigated the risk factors linked with lymphedema, or the preventative measures advised and their effects on lymphedema were included in this review. Patients with breast cancer who may or may not have developed lymphedema of the upper extremity were included in the study. The clinical outcome of interest included lymphedema status. This is normally expressed as a relative change in the limb volume as measured by weight-adjusted volume change, water displacement, funnel method, perometry, bioimpedance spectrometry, or relative circumference. Studies that did not quantify lymphedema were excluded from the review. Also omitted were studies that focused primarily on measures of range of movement or quality of life. To preserve the quality of the evaluated papers, case studies, expert opinions, and conference papers were excluded from the search. Table 1 shows the inclusion and exclusion criteria of the review [50].

Two reviewers (PV and CM) extracted data on the participant demographics, study type, methodology, and results from the eligible studies. A third reviewer (TG) arbitrated any dispute with respect to the inclusion and exclusion of studies in the review. The screened studies were evaluated for the level of evidence using the OCEBM Hierarchy of Evidence 2009 [51] and then critically appraised using the Joanna Briggs Institute (JBI) checklist Supplementary Table 1. Most studies measured lymphedema using various techniques ranging from truncated cone measurements to perometry. The gold standard though stands to be water displacement volumetric measurements [52]. These obtained data were manually classified into categories and then used to construct review Tables.

Results

The literature search yielded 481 papers, of which 29 fulfilled the review's inclusion criteria. The descriptives of the studies are presented in Supplementary Table 2. The results of the quality appraisal of these studies are shown in Supplementary Table 3. Based on the appraisal, 44.8%, 51.7% and 3.5% of the included studies are individual randomized controlled trials

(RCTs) (1b), individual cohort studies (2b), and case series (with or without comparison — 4) respectively.

These studies were further analyzed by categorizing them into five thematic groups based on the preventive measures that are commonly advised for post-operative patients as recommended by the National Lymphedema Network (NLN) [53], and Macmillan Cancer Support (MCS) [54]. These are 1) avoidance of venipuncture, surgical interventions, and cuts in the ipsilateral arm, 2) avoidance of air travel and donning compression garments when flying, 3) maintain healthy BMI, 4) avoid repetitive movements or loading of the ipsilateral arm, 5) avoid extreme of temperatures and heat, and 6) avoid blood pressure measurements and limb constriction (Supplementary Table 4–7).

Avoidance of venipuncture, surgical interventions, cuts in the ipsilateral arm

This literature search revealed three prospective, three retrospective, and two observational studies. Between 2005 and 2014, a significant prospective analysis of patients was carried out, including patients receiving treatment for breast cancer. The goal of the study was to determine whether arm volume and blood samples, injections, and cuts were related in a cohort of patients who were being screened for lymphoedema using Perometer. At every follow-up appointment, patients were asked to report the number of blood draws, injections, or cuts. The authors suggested that burdensome restrictions need to be reformed and updates made in accordance with the finding that there was no significant correlation between the two at 24 months [55].

A similar study by Asdourian et al. [56] conducted a comprehensive prospective study on the correlation between lymphoedema and the commonly acknowledged lifestyle risk factors in patients with bilateral breast cancer surgery. The study recruited 332 patients and followed up regularly to screen them for lymphoedema. This is one of the studies that looked at patients without the availability of a control arm. In this study, most of these patients had no choice when exposed to venipuncture or injections. The authors of the study found no significant association between blood draws and lymphoedema even after up to two years of follow-up with the patients. They then concluded that the lack of evidence should cast doubt on the current guidelines and encouraged further investigation to individualize the guidelines given to patients. Supporting the results of these studies was a prospective cohort study conducted by Kilbreath et al. [57] in 2016 on 450 patients, evaluating the bioimpedance and arm circumference in patients pre-operatively and post-operatively at regular follow-up periods. The study showed no significance between arm trauma, medical procedures, and lymphoedema in the "at-risk arm". While the study did find a statistically significant odds ratio association between needle punctures and lymphoedema, it is important to keep in mind that the wide confidence interval observed could have resulted from several confounding factors.

In addition to caution against venipuncture and injections, there has been much debate about whether or not surgical procedures should be conducted on such patients, and whether or not the benefits would be worth the risk of causing lymphoedema [58]. A survey of health professionals to evaluate whether hand surgery is contraindicated in patients after axillary node dissection revealed that approximately 60% of breast surgeons and 10% of breast care nurses agreed with the statement and advised against ipsilateral arm surgery [59]. The present review of the literature showed two observational and two retrospective studies that refuted these claims.

To evaluate the effect of elective hand surgery on patients who had undergone breast cancer surgery, Baltzer et al. [60] and Naranjo et al. [61] conducted a retrospective analysis on 103 and 3724 patients respectively, who underwent surgery without a history of lymphoedema. Out of the 103 and 7896 patients recruited in the studies, only four patients in both studies developed lymphoedema. The studies found no significant difference concerning the number of IVs placed or the site of placement to be relevant. The studies also did not find surgery to be a risk factor for the development or aggravation of lymphoedema.

Olsha et al. [62] conducted an observational study on three patients with end-stage kidney failure who needed hemodialysis access in the ipsilateral arm in 2012. Even after 2–76 months, none of the participants developed lymphoedema, according to the study. A comparable study conducted in 2015 by Gunnoo et al. [63] studied 32 patients suffering from carpal tunnel syndrome, one of the most common debilitating morbidities seen in up to 12% [64] of breast cancer surgery patients, from pre-operative through post-operative. The study discovered that, while there was a transitory rise in limb volume immediately following surgery, by 33 months the amount had decreased and was stable, with no local problems noted.

Despite the lack of controlled experiments in the field, due to ethical limitations posed, this review has managed to find higher-quality evidence to support the conclusions drawn by Cemal et al. [43]. The reviewed literature also gives us enough evidence

to challenge the long-held beliefs regarding the use of the ipsilateral arm for venipuncture, withholding of elective surgeries on the ipsilateral side, and other intravenous procedures on the "at-risk arm". The author suggests that considering the growing body of research that does not support a cause-and-effect link between skin puncture carried out by trained professionals and infection as seen in the literature it is impractical to avoid the use of the ipsilateral arm for intravenous application and surgery.

Avoidance of air travel and donning compression garments when flying

Showalter et al. [65] recruited 295 individuals who were at risk for developing lymphoedema as well as those with stable lymphoedema as part of a prospective sub-analysis of an RCT. All participants in the trial were instructed to wear compression garments throughout. The purpose of the study was to measure the volume and circumference of the arm to quantify arm edema and link it with air travel. There was no significant association found between traveling to different altitudes and lymphoedema. Similar findings were found in prospective large cohort studies conducted by Ferguson [55] and Kilbreath [57] in 2015 and 2016, respectively. Large sample numbers were utilized in these investigations, and both univariate and multivariate analyses to identify the effect of variables on the identified risk factors. These studies also revealed no association between the number of flights, flight duration, or wearing of compression garments and lymphoedema.

Another prospective study conducted in 2022 as part of a prospective analysis of a parent RCT by Koelmeyer et al. [66] suggested no correlation between the number of flights taken with or without compression garments. The author further also goes on to say that caution regarding the prescription of prophylactic compression garments is not warranted considering no actual benefit was observed in the study. Liu's [67] study conducted a 10-year follow-up of patients with breast cancer, assessing lymphoedema status by the Norman telephone questionnaire. The questionnaire was found to have a sensitivity of 0.86–0.92 in patients with moderate lymphoedema and a specificity of 0.90 [68]. Logistic regression on different lifestyle variables showed no association between air travel and the occurrence of lymphoedema.

A study conducted in Australia by Czerniec et al. [69] in 2016 was an experimental study that challenged the cellular pathophysiology for the occurrence or exacerbation of edema during air travel. Women with unilateral BRCL participated in the study and underwent routine extracellular fluid and arm volume measurements over a period of six months. The author recorded a weather-related barometer dip of 930 hPa that occurred during the trial but wasn't connected to any extracellular fluid movement upon evaluation. Hence, it should be noted that cabin pressures are typically lower than this and shouldn't result in the cellular alterations postulated. The findings of the literature evaluation indicate that only a negligible proportion of patients were adversely impacted and that air travel is not related to an aggravation of symptoms. Also, with the improvement of technology newer aircraft can maintain higher cabin pressures [70], so air travel shouldn't be a concern for patients post–axillary dissection. In addition, no evidence was identified for the prophylactic use of compression garments in these patients.

Maintain a healthy body mass index

Paiva et al. [71] conducted a descriptive observational cross-sectional study on 100 patients who had had a mastectomy and were enrolled for hospital-based physiotherapy intervention. A logistic regression analysis of the study's sample found that patients who gained weight over time had four times the likelihood of developing lymphoedema compared to those with a normal BMI. The authors also highlighted that the risk of lymphoedema rose by a factor of six if the patient was obese before surgery.

The incidence of BCRL and its relationship to patient and therapy variables like obesity should be understood for the sake of patient education and early risk identification. A study by Nguyen et al. [72] in 2017 found that in a cohort of 1794 patients a higher incidence of BRCL and associated morbidity in patients with BMI of more than 30 kg/m^2. A prospective study on 2164 patients concluded similar findings in 102 patients who developed lymphoedema in the group. The author also noted almost 35.9% of patients who were obese developed lymphoedema. Greene et al. [73] conducted an experimental, controlled study on 67 individuals, splitting them into two groups: those with a healthy body mass index and those with a high BMI. Obesity was found to be a strong predictor of infections, hospitalizations, and increased limb volume in the population. In addition to this, Leray et al. [74] discovered that there was no significant influence of age or weight fluctuations on the severity of lymphoedema and that the only factor that was related to it was the patient's body mass index (BMI) at the time the condition first developed.

Adding on to the existing evidence is also a prospective study conducted by Armer et al. [75] recruiting 468 patients involved in a three-year follow-up study. Using both univariate and multivariate analyses,

the authors of this paper discovered that patients with breast cancer who were overweight or obese were more likely to get symptomatic lymphoedema than patients who were not.

Avoid repetitive movements or loading of the ipsilateral arm

In the last decade, many authors have looked at the gradual introduction of resistance training to both a group at risk of incident lymphoedema and a group with manifest lymphoedema at risk of aggravation. Hayes et al. [76] conducted an RCT to compare the effect of weightlifting interventions on lymphoedema outcomes and found that irrespective of the diagnostic criterion used, no effect of exacerbation or onset was seen. Similar effects were reported in individuals recruited by Kilbreath et al. [77] when upper limb progressive resistance training was begun 4–6 weeks post-operatively for patients who underwent axillary lymph node dissection or sentinel node biopsy. In addition, Kilbreath et al. [78] also conducted a single-blinded trial in 2020 to investigate the efficacy of exercise training *vs.* a control group. The paper indicated that combining resistance and aerobic exercise is safe for women with lymphoedema, and initial findings demonstrated that it was effective in lowering the severity and volume of the disease. To further strengthen the evidence, Anderson et al. [79] in 2012 conducted an RCT on moderately customized exercise programs that demonstrated better quality of life, physical function, and no detrimental effect on arm volume. Imposing similar results was also a study by Ammitzbøll [80] and Simonavice [81] looking at the effect of resistance training in patients after breast cancer surgery. These studies on the effect of resistance training on breast cancer patients following surgery found comparable outcomes indicating progressive resistance training and moderate intensity resistance training to be safe for the group of patients in the investigation. In addition, no aggravation of symptoms or severity was noted.

Very few studies have studied the acute response of women with BCRL performing resistance exercises with the affected arm and, more significantly, whether exercise response differs with light or heavy lifting. This provides crucial information on the response of a lymphedematous arm to varying weights, which may then be transferred onto functional activities. Cormie et al. [82] conducted a cross-over trial of 60 patients to find the acute characteristics of lymphedema with exposure to heavy lifting and light lifting. Familiarization and washout time was given to all patients recruited. The research revealed that there was no variation in volume or circumference in individuals immediately after exercise, 24 hours later, or 72 hours later. There was also a decline in pre-exercise volume after 72 hours of heavy-load exercise. Along the same lines, Bloomquist [83] found that 149 patients recruited to study the effects of heavy load training had no development of BRCL after the intervention.

Avoid extreme temperatures and heat

The current review of literature found three distinct articles on the topic. Showalter et al. [65] and Kilbreath et al. [57] in their prospective studies looking at risk factors associated with lymphoedema found that there was no significant effect of exposure to extreme temperatures. Showalter et al. [65] 64 reports significance was only noted between patients who had used the sauna, and having a cut in the arm. Li et al. [84] conducted an experimental study looking at the efficacy and safety of far infrared radiation in patients with lymphoedema. The study was conducted on 32 patients, 11 of whom had lymphoedema. The results of the study showed radiation in the extracellular fluid and limb circumference with no occurrence of any adverse effects.

Avoid blood pressure measurements and constriction of the limb

This literature search revealed 6 studies. Asdourian [56] and Ferguson [55] conducted a prospective study on patients with 327 and 332 patients respectively, measuring their exposure to speculated risk factors. Both studies came to the same conclusion that there was no significant exacerbation of new-onset lymphoedema stimulated by the blood pressure measurement. A similar study conducted by Liu et al. [85] also cited that of the 866 patients recruited 299 had taken blood pressure readings in the ipsilateral arm. The article concluded that no significance of statistical value was found between the two. Another prospective cohort study conducted to gauge the relation between blood pressure measurements and onset of Lymphoedema was by Showalter et al. [65], who recruited patients at risk of developing lymphoedema. The study found no correlation between the frequency of sphygmomanometer measurements and the onset of lymphoedema.

There is transference of the proposed theoretical basis of lymphoedema into other treatment methods such as surgery, which may require the use of a tourniquet. The patients are often advised against hand surgery due to the cumulative risk of tourniquet use and the surgery wound itself. To address this factor better Gunnoo [63] conducted an observation study

on breast cancer patients undergoing carpal tunnel syndrome surgery and found that there was no statistically relevant relation between tourniquet use and exacerbation of lymphoedema. These findings can also be extrapolated from the retrospective study by Baltzer [60] on elective hand surgery and tourniquet use. All studies suggested that avoidance of blood pressure measurement on ipsilateral was not requisite. Furthermore, it is also to be noted that most therapies for lymphoedema are focused on compression, like pneumatic compressions, and compression garments which further puts the theory underpinning the guidelines in question [86]. Although the results from the review even though are mostly retrospective and prospective, in patients with the highest risk [80], blood pressure measurement did not show any exacerbation.

Discussion

Breast cancer-related lymphoedema is one of the most dreaded complications that can occur following breast cancer surgery [6]. The varied etiology [87] and unpredictability are frequently cited as reasons for the excessive adoption of risk-reducing actions. However, due to superior visualization techniques in place and artificial intelligence programs paving the way for better risk-predicting algorithms, there has been a substantial rise in the available information regarding the lymphatic system over the last decades. Unfortunately, despite the vast available literature pool and increased evidence, there appears to be a significant delay in implementing these into real-world scenarios.

The National Lymphoedema Network in its risk reduction practices states that "If possible, avoid punctures such as injections and blood draws [53], which is similar to recommendations given by many such organizations including the Lymphoedema Support Network [88] or the Macmillan Cancer Support Foundation [89] to name a few. This is arguably the most popular prophylactic intervention prescribed for individuals at risk of developing lymphoedema, and it is based on the assumption that these wounds may lead to infections [90], and consequently cause the development or worsening of lymphoedema. Additionally, a survey conducted by LeVasseur et al. [91] to understand the perception of patients regarding risk factors for lymphoedema found that 75% of patients cited blood drawing as a contributing factor for lymphoedema. The author suggests that considering the growing body of research that does not support a cause-and-effect link between skin puncture carried out by trained professionals and infection as seen in the literature it is impractical to avoid the use of the ipsilateral arm for intravenous application and surgery Historically, the evidence behind this recommendation dates back to the early 19th century, where Halsted proposed that the swelling of the arm (elephantiasis chirurgica) [92] seen in patients after mastectomy was a result of the infection caused due to the blockage of lymphatic and venous channels due to infection of the primary closure of the wound. Further development came in 1992, when Brennan [93] published a case associating BCRL with a needle stick in a patient who acquired LE 30 years after surgery, after using a needle prick to assess sugar levels. Unfortunately, most evidence that supported this thought was anecdotal and with poor scientific quality based on case studies or with very limited information vital information is needed to establish causation [94].

To understand the practice patterns and familiarity with breast cancer recommendations among members of the medical fraternity, the American Society of Breast Surgeons conducted a survey in 2020 [87]. According to the survey, over 60% of respondents advise patients to "avoid venipuncture, injection, or blood pressure measures", and 35.6% suggested wearing compression clothing as a preventative strategy when flying. The survey's analysis indicated some critical information on the breast care team practices and the lack of updating. A similar survey [95] conducted in 2018 on 490 practicing doctors in France found similar value, with almost 22% advocating for avoidance of sport in the arm. Even though the majority of members in both studies claimed to educate and screen at-risk patients, best practice standards were largely neglected. Most recommendations given by them have already been updated and largely refuted in most guidelines [22].

Most patients with a history of axillary lymph node dissection are advised against air travel, and even if they do, it is increasingly recommended that they take flights of shorter durations and wear compression garments throughout the journey. Due to the relatively rapid change in pressure and the prolonged decreased cabin pressure, it is hypothesized that air travel will worsen or cause lymphoedema by possibly increasing fluid retention and consequently pooling of blood in the limbs [96]. Implementation of research findings to clinical practice has been a slow process and is popularly known to have a wide gap [97]. Historically, the risk factor was first noted in a few case studies that highlighted the occurrence of lymphoedema after air travel and quoted anecdotal incidence rates in at-risk patients. This was followed by many introducing the donning of compression garments to prevent this occurrence. This literature search found six studies;

four prospective, one cross-sectional, and one experimental study where contradictory evidence to these beliefs was reported.

Obesity is a key documented lymphoedema risk factor supported by high-quality data. Numerous studies have found that obesity can increase the likelihood of subsequent lymphoedema following lymphatic vascular injury. Even as early as 1957 [98], it was recognized that the higher the patient's weight, the greater the likelihood that the individual would develop lymphoedema after breast cancer therapy. A case-control study [99] conducted in 2013 on Chinese women after breast cancer surgery stated that patients who were overweight or obese had a relative risk of 1.35 times compared to people with normal BMI. The results of the study were further supported by a study by Konishi et al. [100] in 2022 stating that a direct relationship exists between the increase in BMI and the increase in hazard ratios of lymphoedema in the population. The reviews were able to corroborate high-quality evidence that links obesity to the worsening and onset of symptoms of lymphoedema by considering the articles reviewed. Having this information at hand can make early surveillance much easier, which in turn can improve patient outcomes.

For a long time, patients have been advised against carrying a baby, doing heavy housework, lifting heavy bags, or exercising excessively on the ipsilateral side [85]. Historically, this recommendation dates back to 2001, when Petrek et al. [101] retrospectively observed a cohort of 923 women and stated 51 women were classified as having "at-risk occupation", which is one that involved heavy lifting. This claim can be refuted by a seminal work around the same time by McKenzie [102] on breast cancer patients who participated in the dragon boat race. This was chosen due to the strenuous and repetitive activity in the upper limb required to paddle the boat. The training intensity could be easily varied according to individual capabilities. The article noted no exacerbation of symptoms in the population. This study was eye-opening and formative towards the effect of exercise on lymphoedema. Most guidelines and precautions have been updated in this regard because of the wide high-quality evidence backing. This review found research conducted after the previous systematic review. The findings from the current review significantly add to the body of evidence showcased by Cemal et al. [43] showing that progressive resistance training with heavy weights is safe, and not just for the regular populace but also for those who are susceptible to developing lymphoedema.

The National Lymphoedema Network (UK) [53] risk reduction guidelines state that caution has to be taken when exposing the arm to temperatures above or below room temperature. The recommendations also go on to say that "topical heat may or may not have a positive or negative effect on lymphoedema". These ambiguous instructions may make it more challenging for the breast care team to provide appropriate recommendations to patients and may further add to the perplexity that already exists. The initial studies that covered the usage of heat exposure to lymphedematous limbs actually found a therapeutic effect rather than a negative one. These studies were done by Chinese researchers who looked at the usage of microwave therapy or heat therapy for patients with filarial limbs [84]. These studies showed positive results in almost 2/3rd of the large sample size spanning over 1000 patients. Inferring from the review, recommendations should be aimed at maintaining antiseptic measures when in the presence of a wound and using a sauna. No other restrictions have any relevant evidence base to be included in practice.

Most recommendations currently list blood pressure measurement as one of the "avoid if possible" risk factors due to the inability to find high-quality evidence that says otherwise. The initial theoretical principle is assumed to be derived from an article published in the 1940s [103] that posited increased venous pressure causing damage to the lymphatic system and further increasing lymph production [101], causing swelling of the limb. Recently many researchers have included and measured the occurrence of blood pressure measurement in their lymphoedema risk assessment studies. Although, the results from the review are mostly retrospective and prospective, in patients with the highest risk [78], blood pressure measurement did not show any exacerbation. Hence, the author recommends that limiting the recommendation would help reduce health-related anxiety and disturbance to normalcy in these patients.

The current systematic review aimed at increasing this awareness and reviewing the current pool of evidence, built upon the only systematic review conducted in the field by Cemal et al. [43] even though the previous review was methodologically imperfect, the authors have tried to be systematic and approach the topic using the PRISMA guidelines for a more robust review that will drive holistic care. The review also intended to help patients and healthcare workers distinguish the risk factors from the persistent myths surrounding lymphoedema. Even though risk factor guidance is largely helpful, unsubstantiated

claims can create unnecessary health anxiety and restrictive behaviors in patients [104]. Even though RCTs for many suggestions in the literature analysis were not discovered, it is crucial to acknowledge the ethical difficulty [105, 106] in performing RCTs for many of the guidelines cited, therefore well-designed prospective cohort studies should be acceptable.

As increased attention has been focused on patient education, overwhelming amounts of recommendations and guidelines have been distributed in the form of patient information pamphlets and expert opinions on how to prevent lymphoedema following breast cancer surgery by different government and non-government organizations worldwide. The NLN, MCS, the Royal College of Nurses, the Royal College of Anesthetists, and Breast Cancer Care UK are all examples of such gatekeeping and propagating organizations in the United Kingdom. Even though most guidelines have been regularly reviewed in accordance with research-based findings, most restrictions that have been disproved are still not completely refuted but are coveted by "if possible avoid". In sum from this study, good quality prospective evidence was discovered with a significant number of participants that used univariate and multivariate analysis to determine the importance of these factors. According to the majority of these papers, limiting recommendations on venipuncture, trauma, and surgery generate undue health anxiety [107] and are not required to be given to everyone if performed with appropriate expertise and sterile precautions. Similarly, the author also found good quality evidence to refute the precautionary measures concerning blood pressure measurements, limb constriction, air travel, and prophylactic use of compression garments in patients without lymphoedema. In addition, for guidelines with an existing evidence base, the author attempted to identify papers that might be deemed updates that considered a broader range of patient populations. This was evident in advice regarding weightlifting and keeping a healthy body mass index. The studies identified were experimental trials of good quality that indicated a substantial association between various BMI categories and lymphoedema. The evidence also helped shed some light on the guidelines for lifting heavy weights causing an acute precipitation of lymphoedema [108].

Several limitations impact the generalizability of findings and their clinical consequences. A few non-English studies were excluded from this systematic review since only articles written in English were considered. In addition, publications for which full-text papers could not be retrieved were excluded from the study. The absence of standardization in the measurement of lymphoedema in subjects and the diverse methodology of the studies were significant shortcomings of the review.

Conclusions

Even though there is a large amount of research and guidelines concerning precautionary measures, there is a lack of standardization universally regarding these recommendations, resulting in the implementation of unnecessary practices with additional cost, time, quality of life, and physical and psychological implications. There is limited evidence for post-operative precautions — like venipuncture, air travel, blood pressure measurements, and lifting heavy loads as risk factors for BCRL in patients with breast cancer. Empirical information regarding post-operative suggestions given to patients with BCRL will help to limit disadvantageous practices and enhance psychosocial health. The recommendations with regard to venipuncture, air travel, blood pressure measurements, and lifting heavy loads should be individualized to patients at risk with the goal of maximizing quality of life beyond the treatment of breast cancer. Care should be taken when exposed to extreme temperatures, and emphasis should be placed on maintaining a healthy body weight and being physically active.

Article information and declarations

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Author contributions

All authors contributed significantly to this review. PV and CM were involved in the conceptualization, methodology, and drafting of the original and final manuscripts. PV and CM were involved in data curation and analysis; TG acted as the third review and participated in formal analysis; AO, MHG, and FF were involved in the review and drafting of the final manuscript. All authors have read and approved the manuscript for publication.

Conflict of interest

The authors declare no competing interests.

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Supplementary material

The Supplementary Material for this article (Appendix 1, Supplementary Tables 1–7) can be found online at https://journals.viamedica.pl/palliative_medicine_in_practice/article/view/101961.

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