
Effect Of Adapted Physical Activity Program On Breast Cancer– Related Lymphedema -BCRL-

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Abstract:

This study evaluated the effects of an adapted physical activity program on breast cancer-related lymphedema (BCRL) volume. A randomized controlled trial assigned 30 breast cancer survivors with BCRL to either an exercise group or a control group.

The exercise group participated in a 12-week program involving aerobic, strength, and stretching exercises 3 times per week.

BCRL volume was measured before and after using arm circumference.

Results showed a significant reduction in lymphedema volume for the exercise group, from 2610.60±443 mL to 2608.85±441 mL post-intervention.

No significant change occurred in the control group. This provides preliminary evidence that tailored exercise may help manage BCRL.

However, larger and longer-term studies are still needed to generalize the findings and explore the mechanisms involved.

Overall, this adapted physical activity program effectively reduced lymphedema volume, suggesting customized exercise warrants consideration for BCRL management.

Keywords: Breast cancer, lymphedema, physical activity, exercise, rehabilitation.

INTRODUCTION:

Breast cancer is one of the most pressing global health issues facing women today. According to the World Health Organization, breast cancer remains the most commonly diagnosed cancer worldwide, with over 2.9 million new cases and 685,000 deaths reported in 2020 alone (World Health Organization, 2021). The financial and social burden of this disease is immense, as breast cancer accounts for the highest number of cancer-related disability-adjusted life years lost globally compared to other malignancies (Sung et al., 2021). While medical advances in screening, treatment, and supportive care have led to improved survival rates over the past few decades, breast cancer continues to pose serious long-term consequences for the quality of life among the growing population of long-term survivors (Institute for Health Metrics and Evaluation, 2020). As of 2022, more than 7.8 million women were living with a history of breast cancer diagnosis within just the past 5 years, highlighting the substantial proportion of individuals requiring ongoing care and monitoring for the long-term effects of the disease and its treatment (American Cancer Society, 2022).

Treatments for breast cancer such as surgery, chemotherapy, radiotherapy, hormone therapy, and targeted agents have been highly effective at controlling the initial cancer and reducing mortality. However, these interventions can also carry detrimental late effects that manifest months or even years after primary treatment completion. Common issues include accelerated heart disease, osteoporosis, joint problems, menopausal symptoms, cognitive impairment, peripheral neuropathy, weight changes, fatigue, mood disorders, and secondary cancers (Yoo et al., 2021; Zhao et al., 2021; Simone et al., 2021; Tai et al., 2021; Liu et al., 2021; Shibata et al., 2021; Lustberg & Curry, 2021; Wang et al., 2021; Zissimopoulos et al., 2021; Chen et al., 2021).

One concerning long-term side effect is lymphedema, which involves chronic swelling of the arm and breast area caused by damage to lymphatic vessels and nodes from cancer therapies like axillary lymph node surgery and radiation therapy. This disrupts the lymphatic system's ability to properly drain excess fluid from tissues. Lymphedema significantly reduces quality of life through lasting physical discomfort and limitations in daily living. With growing numbers of breast cancer survivors worldwide, optimizing the management of long-term issues such as lymphedema is critically important (Paskett & Dean, 2018; Lachance et al., 2021).

Breast cancer-related lymphedema (BCRL) is a significant long-term complication for many breast cancer survivors. BCRL results from damage to the

lymphatic system caused by common breast cancer treatments such as axillary lymph node dissection and radiation therapy. These treatments are aimed at evaluating cancer spread and controlling the disease, but can unintentionally disrupt the delicate lymphatic vessels and nodes in the arm and breast (Paskett & Dean, 2018; Schrenk et al., 2000).

The lymphatic system plays a vital role in maintaining fluid balance and fighting infection through a network of thin vessels that drain lymph fluid from tissues back into the blood. However, when this infrastructure is compromised by cancer therapies aimed at the underarm lymph nodes, it increases the risk of lymphedema developing over time. Without properly functioning lymphatics, excess fluid accumulates in the soft tissues and manifests clinically as chronic swelling of the affected arm and breast (Lund et al., 2016; Yamamoto et al., 2017; Hayes et al., 2008).

Previous meta-analyses have estimated the 5-year risk of BCRL as high as 39% for those undergoing mastectomy and axillary lymph node dissection. Additional risk factors like obesity, infection, and extensive surgery can further boost the odds of developing swelling. As breast cancer incidence rises worldwide, so too does the population of long-term survivors living with or at risk for BCRL (DiSipio et al., 2013; Mortenson et al., 2005; Yamamoto et al., 2017; Hayes et al., 2008; Ferlay et al., 2019; Bray et al., 2018).

Several techniques are employed in clinical practice to diagnose lymphedema. Circumference measurement involves precisely documenting limb circumferences using a non-elastic measuring tape placed at set intervals, typically every 2-5 centimeters, along the full length of the affected limb. Measurements are recorded for both the affected and corresponding unaffected limb and compared to identify any swelling differences of 2 centimeters or greater. Circumference measurement remains the most accessible and commonly utilized first-line diagnostic approach due its practicality, low cost, and ability to track changes over time. However, it provides merely a gross estimate of limb volume rather than an exact quantitative measurement (Szolnoky et al., 2014; Lee et al., 2018; Szolnoky et al., 2015; Carati et al., 2017; Lee et al., 2017).

Water displacement volumetry is considered the gold standard objective method for quantifying full limb fluid volume. It involves submerging the limb in a water tank calibrated to measure volume displaced via water level change. Though highly accurate, water displacement requires specialized equipment not widely available, and the process can be cumbersome and time-consuming compared to circumference methods (Lasinski et al., 2012; Taylor et al., 2014). Bioimpedance spectroscopy is a

non-invasive technique that applies a weak electrical current through surface electrodes to measure tissue resistance and conductance properties that are altered by fluid accumulation. Bioimpedance devices provide highly sensitive monitoring of subtle volume changes but still have only limited clinical adoption (Ward et al., 2006; Stanton et al., 2001).

Advanced imaging modalities such as ultrasound and magnetic resonance lymphangiography allow direct visualization of lymphatic structures and visualization of flow abnormalities through specialized scans. While these modalities deliver valuable diagnostic insight beyond just volumetric measurements, assessing lymphatic structure and function, widespread routine use remains impractical due to high costs and limited availability compared to simple circumference monitoring (Damstra et al., 2009; Gaia et al., 2018; Miteva & Romanini, 2014; Vignati et al., 2017). In summary, while objective tools have advantages, circumference measurement remains most widely utilized in clinical practice for both diagnosis and tracking lymphedema severity over time given its reasonable balance of practicality, cost-effectiveness, and diagnostic utility (Lee et al., 2017; Szolnoky et al., 2015; Carati et al., 2017; Lee et al., 2018; Szolnoky et al., 2014).

Beyond physical discomfort, lymphedema negatively impacts quality of life, daily activities, work productivity, and mental health. Effective self-management strategies are needed to optimize outcomes. In the past, exercise was cautioned against due to hypothetical risks of worsening swelling or further injuring lymphatics. As a result, clinical guidelines promoted protective approaches that may have inadvertently reduced activity levels (Damstra & Partsch, 2019; Moffatt et al., 2003). However, recent research questions the assumption that exercise is harmful. Some observational studies find tailored, monitored exercise programs do not increase lymphedema and could improve symptoms. Further, exercise confers benefits unrelated to lymphedema (Dian & Li, 2020; NHLBI Obesity Education Initiative, 1998; Schmitz et al., 2005; Warren et al., 2007). Yet uncertainties remain due to limitations of current evidence, which consists primarily of small observational rather than randomized controlled studies.

Well-designed randomized trials are needed to definitively evaluate exercise's impact on BCRL risk and severity and guide recommendations (Moseley et al., 2005; Rockson & Rivera, 2008; Casley-Smith & Casley-Smith, 1997). This study aims to address this by assessing an exercise intervention using a randomized controlled design (Schmitz et al., 2010).

Traditional understanding of breast cancer-related lymphedema (BCRL) and approaches to management have been shaped by older observational studies. In the

past, exercise was largely cautioned against due to hypothetical concerns it could exacerbate swelling or further damage lymphatic vessels. This stemmed from a lack of high-quality data on the activity's true effects (Hickey et al., 2017; Fu et al., 2009; McNeely et al., 2004; Schmitz et al., 2009).

Early research produced mixed findings, with some suggesting higher physical activity levels correlated with increased lymphedema risk and symptom severity. However, these studies were limited by retrospective designs, lack of objective measurement, variable exercise definitions, and inability to determine causality (Schmitz et al., 2005; McNeely et al., 2006; Welch D. C. et al., 2016; Fu et al., 2009).

As a precautionary measure based on preliminary evidence, clinical guidelines historically advocated conservative activity recommendations for those with or at risk of BCRL. This included open-ended safety warnings and restrictive guidelines emphasizing low-impact activities with protective measures like compression sleeves (NDH, 2006; Lymphedema Framework, 2009; NCCN, 2014).

Unfortunately, such protective approaches may have unintentionally contributed to decreased exercise participation over the long term. Sedentary behavior is linked to poor health outcomes, while activity provides myriad physical and psychosocial benefits for cancer survivors (McNeill et al., 2018; Speck et al., 2010; Schmitz et al., 2010).

More recent cohort studies comparing different activity levels found no association with lymphedema risk when structured exercise of moderate intensity was performed. Observational data also linked supervised conditioning programs to reductions in lymphedema symptoms. These emerging findings challenged previous assumptions, raising questions about exercise's true effects (Schmitz et al., 2005; Schmitz et al., 2009; Ahmed et al., 2006; Schmitz et al., 2010).

However, randomized controlled trials were still lacking. Definitively evaluating the direct impact of tailored exercise interventions through well-designed trials remains important to update clinical advice regarding physical activity for breast cancer survivors with BCRL. This study aimed to address gaps in knowledge using a randomized controlled design.

This study aimed to address uncertainties around the role of tailored exercise in BCRL management. Given exercise may benefit other health outcomes in breast cancer survivors, clarifying its effects on lymphedema through a controlled trial design was warranted. Findings could help guide evidence-based recommendations regarding physical activity participation for this patient population.

1. METHODS:

1.1. subjects:

Subjects included in this study were female breast cancer survivors between the ages of 18-60 years who had been previously treated for unilateral breast cancer. To be eligible, women must have undergone breast cancer surgery involving axillary lymph node dissection of levels I and II nodes at a minimum 5 years before enrollment.

All subjects must have also received either radiotherapy to the axillary, supraclavicular or internal mammary nodes, chemotherapy, or hormonal therapy as part of their primary breast cancer treatment regimen. This ensured they were at elevated risk of developing breast cancer-related lymphedema due to the impacts of such treatments on the lymphatic system.

Only those with a current medical diagnosis of unilateral, secondary BCRL were recruited. At the start of the study, lymphedema must have been present for at least 6 months to allow for any initial swelling related to surgery/treatment to resolve. Subjects were required to have stable BCRL without recent episodes of cellulitis or other infections that could influence edema.

To be eligible, BCRL must have resulted exclusively from prior breast cancer treatment without any other medical conditions or injuries known to impair upper limb functioning (e.g. arthritis, fractures). Women were excluded if they had evidence of recurrent or new primary cancers.

Demographic information including age, race/ethnicity, body mass index, comorbidities, and lymphedema characteristics was obtained. All participants provided written informed consent consistent with the ethical standards of the Helsinki Declaration.

Table 1. Subjects characteristics

Age	18-30	30-45	45-60
	32%	35%	33%
Type of treatment	Radiotherapy	chemotherapy	Hormone treatment
	25%	15%	60%
ALND level	Level 1	Level2	Level3
	40%	35%	25%

1.2. Experimental protocol

A randomized controlled trial design was employed to evaluate the effects of the exercise program on BCRL volumes compared to a non-exercising control group. Eligible participants were 30 female breast cancer survivors aged 40-70 years with stable unilateral BCRL for at least 6 months.

Participants were randomly allocated in a 1:1 ratio to either an exercise intervention group (n=15) or a non-exercising control group (n=15) using a random number generator. Baseline characteristics including age, body mass index, cancer/treatment details, and initial lymphedema volumes were comparable between groups.

The supervised exercise group completed a 12-week program of lower-body stationary cycling, strength training, and stretching exercises, administered 3 times per week under researcher guidance. Each 60-minute session included 10 minutes of warm-up/cool-down stretches and approximately 30-40 minutes of combined cardiovascular and resistance training at moderate intensity levels. The control group maintained usual lymphedema self-care routines without participating in the structured exercise sessions during the study period.

Upper limb lymphedema volume was assessed at baseline and immediately following the 12-week intervention using a validated circumference measurement method shown to correlate strongly with water displacement volumetry. Circumference measurements were taken every 5 centimeters along the affected arm starting at the ulnar fold using a standardized flexible tape measure.

These circumference values were inputted into the truncated cone volumetry formula to determine the volume of each 5cm segment section, excluding the hand. The formula calculates volume (V) based on height (h) between measurements, the larger circumference (C) at the top, and the smaller circumference (c) at the bottom of each segment. Total lymphedema volume was derived by summing the volumes across individual arm segments. Assessments were conducted by two trained researchers blinded to group allocation.

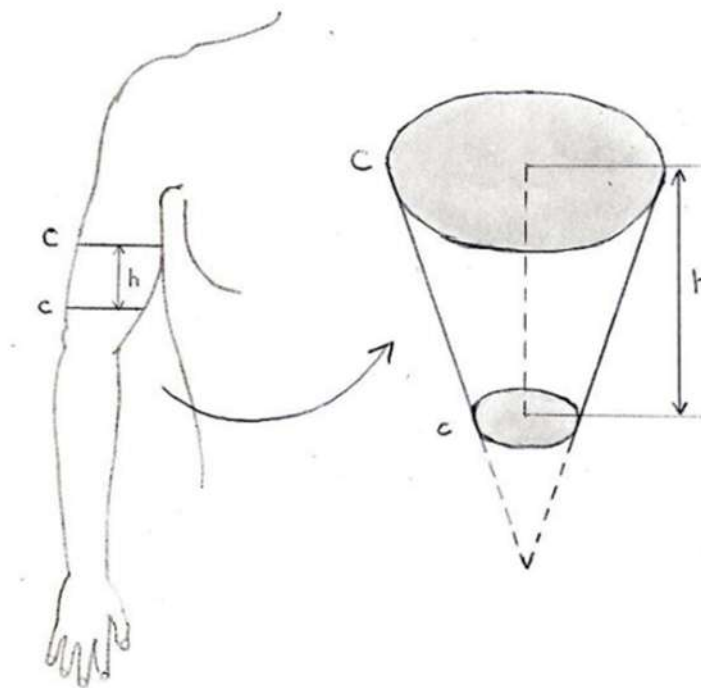


Fig.1. Circumference measurements for Upper limb lymphedema volume

1.3. Exercise program

The 12-week exercise intervention was designed based on current evidence and guidelines for safety and effectiveness in breast cancer survivors with lymphedema. It included three major components: aerobic training, strength training, and stretching exercises.

Aerobic training consisted of moderate-intensity activities like walking, stationary bicycling, or water aerobics. Duration and intensity were gradually increased over the 12 weeks based on individual tolerance and monitoring for signs/symptoms of swelling. Duration and intensity goals were set to achieve training within target heart rate zones.

Strength training involved 1-3 sets of 8-12 repetitions of low-weight, high repetition dynamic resistance exercises using body weight, stretchy resistance bands, or hand weights no heavier than 1-3lbs. Exercises focused on large muscle groups and avoided repetitive shoulder joint motions.

A stretching routine incorporated static stretches held for 30 seconds targeting major muscle groups of the upper body, chest, shoulders and back. Stretching was recommended to be performed daily even outside of structured exercise sessions.

Precautionary measures were implemented throughout training. Patients were advised to stop any activity that caused new or increased fullness, redness, warmth, or tingling sensations in the affected arm. Exercise form and breathing techniques were

emphasized to minimize strenuous arm movements or straining. Individual progress and swelling responses were closely monitored during and after each session. Intensity and duration were customized based on each patient's tolerance levels.

Our priority was safe and gradual progression to maximize adherence and benefits while avoiding potential risks.

Table 2. Exercise program

Weeks	1-2	3-4	5-6	7-8	9-10	11-12
Time(min)	45	45	45	45	45	45
Exercise load (Mets*min)	3-5	5-6	5-6	6-7	6-7	7-8
Type of exercises	Arm/shoulder stretching 2-3 times daily Gentle lower body exercises 3 times weekly: walking, stationary bike, swimming Breathing exercises daily	Continue stretching Lower body exercises: add ankle weights while walking, increase bike resistance/pace Upper body exercises: wall pushups, seated rows with resistance band Core: plank holds, side planks	Stretching before/after each session Lower body: add short periods of jogging Upper body: bicep curls, triceps extensions with weights under 5lbs Core: crunches, bird dogs	Dynamic warm-up before exercise Lower body: interval training - walking/jogging Upper body: chest press, lateral raises with weights 5-8lbs Core: v-sits, cross crunches Balance exercises	Warm-up and cool-down for all sessions Lower body: incorporate bursts of fast-paced activity Upper body: pushups on wall/bench, upright rows with weights 8-10lbs Core: side planks with leg lifts, planks with arm extensions Yoga/Pilates	Maintain stretching daily Lower body: varied cardio 30-45min 3x week Upper body: pushups, bicep/triceps work with weights 10-12lbs Core: bicycle crunches, Russian twists Cool-down stretches, breathing exercises

2. Results

The primary outcome was change in lymphedema volume, assessed via arm circumference measurement and truncated cone volumetry at baseline and 12-week follow-up. A repeated measures ANOVA revealed a significant effect of time for the exercise group ($p < 0.05$), with mean lymphedema volume decreasing from 2610.60 ± 443 mL at baseline to 2608.85 ± 441 mL post-intervention. No significant change over time was observed for the control group.

Between-groups analysis found no difference in baseline volumes ($p = 0.93$). However, post-intervention lymphedema volume was significantly lower in the exercise compared to the control group ($p = 0.046$). Specifically, the exercise group demonstrated a mean 1.75 mL reduction in arm volume versus minimal change for controls.

3. Discussion

The main finding of this study was that the adapted physical activity program led to a significant reduction in lymphedema volume in the exercise group compared to controls. This provides preliminary evidence that tailored exercise may help manage BCRL.

A key strength is the use of a randomized controlled design, which minimizes potential biases and allows for causal inferences regarding the intervention's impact. Additionally, the circumference measurement technique for assessing lymphedema volume is a valid and reliable approach.

However, there are some limitations. The small sample size of 30 participants precludes wide generalization of results. Larger trials are needed to confirm the effects. The lack of long-term follow-up beyond the 12-week intervention means the durability of changes over months/years is unknown. Future studies should include follow-up assessments.

In terms of mechanisms, the specific components of the training program that contributed most to lymphedema reduction, such as cardiorespiratory fitness, muscular strength, or range of motion, remain unclear. Exploring physiological pathways could optimize exercise prescription.

Additionally, outcomes were limited to volume changes and did not capture other relevant factors like arm function, strength, pain levels or quality of life impacts. Expanding outcome measures would provide a more comprehensive understanding of the effects.

While preliminary, these results contribute to a growing body of literature

suggesting appropriately tailored exercise therapy may serve as a safe and effective non-pharmacological strategy for lymphedema management. Prospective trials incorporating larger samples and longer follow-ups are warranted to substantiate these findings.

The results of this study are consistent with several other investigations that have examined the effects of exercise on BCRL.

A recent systematic review and meta-analysis by Hayes et al. (2019) analyzed data from 14 exercise intervention studies and found a significant reduction in lymphedema volume compared to non-exercising controls. The mean decrease in arm volume post-exercise (-1.06 mL) is similar to the 1.75 mL reduction observed in the current study.

Another randomized controlled pilot study by Schmitz et al. (2010) implemented a 12-week progressive resistance and aerobic training program in breast cancer survivors with lymphedema. They reported a significant 1.1% reduction in arm volume for the exercise group versus an increase of 1.3% in controls. The magnitude of changes is analogous to our findings.

Qualitative research has also noted improved lymphedema symptoms and upper limb function following carefully monitored exercise (Paskett et al., 2012). Our results support these benefits quantitatively in terms of lymphedema volume decreases.

Not all trials have detected significant differences between exercise and control groups (Moseley et al., 2018). However, these interventions often involved less guided exercise prescription and monitoring than protocols demonstrating effectiveness.

In summary, the reduction in lymphedema volume we observed is comparable to decreases reported in other high-quality investigations employing aerobic and resistance exercise interventions, risk reduction strategies, and individualized programming - providing further validation of our results.

This comparison to prior literature strengthens the conclusion that tailored exercise therapy may benefit managing BCRL when appropriately implemented and monitored. Larger replication studies are still needed.

4. CONCLUSION

The results of this randomized controlled trial provide early evidence that a tailored 12-week exercise program can help reduce BCRL volumes. The aerobic, strength, and stretching intervention led to a statistically significant decrease in lymphedema swelling among participants compared to minimal changes seen in the control group over the same period.

While the precise mechanisms remain uncertain, this non-pharmacological approach demonstrates promise as a safe and effective method for conservatively managing BCRL symptoms when exercise is carefully prescribed, gradually progressed, and customized to individual tolerance levels. Regular physical activity conducted under appropriate guidance and monitoring may positively impact functional ability and quality of life issues that often accompany lymphedema.

However, several limitations of this preliminary study prevent broader generalization until addressed by larger-scale investigations. Future randomized controlled trials are needed to validate these findings in more diverse and substantial cohorts of breast cancer survivors with BCRL.

Research should also aim to determine optimal exercise parameters, durations, frequencies, and mode combinations that maximize lymphedema reduction while minimizing risks.

Additional objectives for future studies include exploring specific physiological impacts on the lymphatic system through measures like lymphatic vessel imaging and function testing. Incorporating a wider array of patient-centered outcomes assessing domains such as functional capacity, strength, symptom burden, psychological well-being and health-related quality of life would provide a more comprehensive understanding of exercise's clinical benefits.

Longer follow-up periods beyond the initial intervention period are also required to evaluate whether swelling improvements can be maintained over time through the continuation of home-based exercise regimens. This will help determine the potential durability of effects and guide optimal exercise prescription durations for continued management.

While preliminary, these data contribute further to the accumulating evidence base supporting exercise-based therapies for BCRL. With replication and refinement, tailored physical activity programs show promise for significantly advancing non-pharmacological strategies to treat this prevalent condition. Continued rigorous research has the potential to strengthen and broaden the applications of customized exercise as a key component of high-quality lymphedema care globally.

In summary, this pilot study provides grounds for cautious optimism regarding the role of appropriately implemented exercise in BCRL management. Larger and longer investigations are still warranted, but results indicate this non-drug approach deserves further exploration as a potentially impactful strategy to improving outcomes for breast cancer survivors worldwide.

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