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# Evidence Summary: Single modality management of lymphoedema: Exercise

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## QUESTION

What is the best available evidence on the effectiveness of exercise regimens in managing lymphoedema?

## SUMMARY

Exercise is generally useful as a component in multimodal, complex lymphoedema therapy, implemented in conjunction with consistent elevation, compression therapy and manual lymph drainage of the affected limb(s). This evidence summary is focused on the evidence specific to exercise when used as the primary intervention for treatment to reduce lymphoedema. Most of the studies exploring exercise are conducted with women following breast cancer surgery to investigate whether exercise exacerbates post-surgical swelling. The trials are generally small but consistently show no increase in lymphoedema associated with exercise regimens<sup>1-7</sup> (Level 1.a and Level 1.c evidence). Some larger trials have demonstrated reduction in lymphoedema associated with resistance training<sup>6, 7</sup> (Level 1.c evidence); however, systematic reviews do not show any significant benefit<sup>1, 2</sup> (Level 1.a evidence). Women can undertake upper body aerobic exercise and resistance training following breast cancer surgery under the direction of a qualified practitioner<sup>1, 2</sup> (Level 1.a evidence). There is both a need for good quality trials to determine whether doing so is associated with decreasing arm swelling and research to determine effective treatment of lower limb lymphoedema.

## BACKGROUND

Lymphoedema is a form of chronic, progressive oedema in which there is significant, persistent swelling of a limb or other body region due to excess and abnormal accumulation of protein-rich fluid in body tissues. This fluid contains a range of inflammatory mediators and adipogenic factors.<sup>8-12</sup> The lymphatic system is unable to manage the volume of accumulated fluid.<sup>9</sup>

Lymphoedema occurs due to primary, secondary or mixed causes. Primary causes are described as congenital (e.g. an inherited disorder such as Milroy's disease), praecox (onset at puberty, e.g. Meigs' disease) or tarda (sudden onset no apparent cause).<sup>13-15</sup> Secondary causes arise from direct damage or trauma to the lymphatic system such as injury, surgery or radiotherapy (usually related to treatment of breast cancer), or parasitic invasion.<sup>14-16</sup> Lymphatic filariasis (also called elephantitis) is a cause of secondary lymphoedema in endemic areas primarily in Africa and Asia.<sup>11, 17</sup> Mixed lymphoedema describes lymphoedema arising from decompensation or failure of the lymphatic system associated with other disease or conditions, including but not limited to obesity, immobility, venous disease or lipoedema.<sup>14, 15, 18</sup>

Without management, lymphoedema may lead to:<sup>9, 19</sup>

- progressive swelling,
- superficial tissue changes — increasing adiposity and fibrosis
- physical and functional limitations,
- increased risk of chronic infection,
- lymphorrhoea (leaking of lymph fluid),
- pain and discomfort, and
- reduced ability to undertake activities of daily living (ADLs).

There is mixed opinion on the relationship between exercise and lymphoedema. Studies are primarily conducted in women following breast cancer treatment. The research on this topic is designed to test two competing hypotheses:

- That lymphoedema is a potential adverse outcome associated with exercise. This theory suggests that exercise undertaken after breast cancer surgery to address other issues (e.g. to improve shoulder range of motion), may interfere with regeneration of the lymph system following surgery and lead to lymphoedema, especially if commenced too early or via an overly intensive regimen.<sup>1, 3, 20</sup>
- That an exercise regimen can reduce oedema and other signs and symptoms associated with lymphoedema. Resistance exercise training (RET) is thought to improve function capacity and strength, and increase lymph flow by stimulating muscle contraction via the pumping effect.<sup>2</sup>

## TYPES OF EXERCISE

The high resistance regimens explored in the research included upper and lower body exercises with increasing weight resistance and repetitions over time. Participants generally progressed by the smallest possible weight increment (e.g. 5%) after being able to complete between 10 and 20 repetitions over two consecutive sessions. Other exercise regimens primarily focus on improving range of movement and/or aerobic fitness<sup>1, 5, 21, 22</sup>. Aerobic-based exercise increases cardiovascular function and could stimulate lymph flow back to the heart, thereby reducing swelling<sup>3</sup> (1.c evidence). Some of the studies focused on benefits of water-based exercise.<sup>5, 22</sup> Water-based exercise is primarily resistance exercise, with the water acting as the resistive force.<sup>22</sup> The hydrostatic pressure, which increases in deeper water, may also enhance lymph flow.<sup>22</sup> (1.c evidence)

Participants were supervised by experienced trainers in many studies,<sup>4, 6, 7, 23</sup> sometimes in a group setting.<sup>1, 5, 22, 24</sup> Other studies provided home-based videos for solo exercise. These different models may influence concordance and outcomes. (Level 1.a evidence and 1.c evidence).

In many of the studies participants wore compression garments, but only while performing exercise.<sup>6, 7</sup> One study found that there was no difference in severity of symptoms between women who did or did not wear compression therapy while engaging in aerobic or progressive resistance-based exercise programs.<sup>25</sup> (Level 1.d evidence)

## CLINICAL BOTTOM LINE

### Effectiveness in reducing oedema

- Data pooled from three RCTs found that there was no significant difference between incidence of lymphoedema at 6 to 8 months between women who commenced exercise in the early post-operative weeks following breast cancer surgery compared to women who delayed exercise (odds ratio [OR] 1.24, 95% confidence interval [CI] 0.45 to 3.41,  $p$ =not significant). Some studies showed a small to moderate increase in wound drainage and increase in wound duration of one day<sup>1</sup> (Level 1.a evidence).
- A narrative systematic review concluded from the results of seven RCTs that resistance training was not associated with increase in lymphoedema in women who had undergone breast cancer surgery. The authors concluded that difference in results between the studies arose from the different methods used to measure oedema, different regimens and different length of the trials, with longer trials more likely to demonstrate effect<sup>20</sup> (Level 1.a evidence).
- One very small randomised controlled trial (RCT) in women with breast cancer-related lymphoedema ( $n=6$  in exercise group,  $n=19$  controls) found no difference in arm volume after three months of high resistance exercise. Compression garments were worn by 25% of participants<sup>4</sup> (Level 1.c evidence).
- A larger RCT ( $n=141$  study group,  $n=70$  control) with women with breast cancer-related lymphoedema who participated in an upper and lower body resistance exercise regimen for 12 months found approximately 11% of participants experienced an inter limb volume difference of 5% or greater, but this was not significantly different (12%,  $p=1.0$ ) when compared to the control group<sup>6</sup> (Level 1.c evidence).
- In another large RCT ( $n=154$  participants,  $n=75$  controls) investigating an upper and lower body resistance exercise regimen for women with breast cancer-related lymphoedema found those engaged in the exercise program had a lower rate of arm volume increase compared with women in the control (11% participants versus 17% of participants,  $p=0.04$ )<sup>7</sup> (Level 1.c evidence).
- An RCT compared a resistance exercise program to an aerobic program for post-surgical women with breast cancer. After participation in the 12 week programs, both groups showed significant reductions over time in

oedema ( $p=0.01$  for resistance group,  $p=0.02$  for aerobic group) measured using bioimpedance spectroscopy, with no significant difference between the groups ( $p=0.91$ )<sup>3</sup> (Level 1.c evidence).

- A small RCT ( $n=29$ ) investigating the effects of water exercises for improving range of movement found no significant difference in lymphoedema measured at 8-week follow-up using perometry ( $p>0.05$ ) and bioimpedance spectroscopy ( $p>0.05$ ) between the water exercise group and control group with no specified exercise regimen<sup>5</sup> (Level 1.c evidence). Expert clinicians suggest that the shoulders should be below the water when exercising for hydrotherapy to be beneficial (Level 5c evidence).
- Improvement in limb circumference and volumetric measures of lymphoedema were observed after 8 weeks of participating in a home-based progressive resistance training program in women who had undergone breast cancer surgery at least 1.5 years before engaging in the program. The outcome may have been a result of normal improvement with time<sup>24</sup> (Level 2.d evidence).
- A water-based program, performed for 45 minutes in a weekly group session for 12 weeks was associated with significant reductions in upper limb volume for women with breast cancer-related surgery. Exercises consisted of self-massage, distal movement of the upper limb and “dog paddle”. There were significant reductions in mean arm volume between pre- and post-session measurements ( $p=0.02$  for first session and  $p<0.01$  for last session). However, there was no significant difference in mean arm volume compared with a control group not engaging in exercise ( $p=0.87$ ). None of the women experienced limb infection from engaging in water-based exercise<sup>22</sup> (Level 1.c evidence).

### Effectiveness in improving function

- A meta-analysis of three studies showed significant improvement in shoulder flexion at 4 to 6 weeks associated with commencing range of motion exercise early following breast cancer surgery, compared with delaying exercise (mean difference [MD] 12.12, 95% CI 0.35 to 23.88,  $p=0.04$ ). Two studies showed this significant difference persisted to 6 months (MD 3.53, 95% CI 0.60 to 6.47,  $p=0.02$ ) while the third study showed the significant difference was no longer present at 24 months (MD 3.00, 95% CI  $-0.65$  to 6.65,  $p=0.11$ )<sup>1</sup> (Level 1.a evidence).
- A number of RCTs conducted with women with breast cancer-related lymphoedema showed significant improvements in functional outcome measures associated with upper and lower body resistance exercise regimens. One study showed improvements in strength, including grip strength, chest press and leg press<sup>4</sup> A second reported significant improvements in leg and bench press strength ( $p<0.001$  for both)<sup>6</sup> and a third found improved leg press ability ( $p=0.02$ ) and bench press ability ( $p<0.001$ ).<sup>7</sup> Another study showed greater increase in upper body strength associated with resistance training compared with aerobic training ( $p<0.05$ ) after 12 weeks.<sup>3</sup> (Level 1.c evidence)

- There was significant improvement in shoulder flexion ( $p \leq 0.001$ ) but not in abduction ( $p = 0.32$ ) or external rotation ( $p = 0.007$ ) for women undertaking water exercises compared to a group with no exercise. This study was small with follow-up measures taken at 8 weeks.<sup>5</sup> (Level 1.c evidence)

### Effect on tissue

- To investigate effects of progressive resistance training on muscle and subcutaneous tissue, an RCT was conducted in 32 women following breast cancer surgery. Women participating in the progressive resistance training ( $n = 16$ ) showed increased muscle thickness ( $p = 0.025$ ) and decreased subcutaneous tissue thickness ( $p = 0.02$ ) on ultrasound investigations conducted at 8 weeks compared to women who did not engage in exercise ( $n = 16$ ). There was also a significant change in both distal and proximal circumferences of the affected limb at 8 weeks in the exercise group ( $p < 0.05$ )<sup>23</sup> (Level 1.a evidence).

## CHARACTERISTICS OF THE EVIDENCE

This evidence summary is based on a structured database search combining search terms describing lymphoedema and exercise. The evidence comes from:

- Experimental designs<sup>1-7, 10, 20, 22, 23, 25</sup> (Level 1 evidence)
- Quasi-experimental designs<sup>24</sup> (Level 2 evidence)
- Observational-analytical designs<sup>16</sup> (Level 3 evidence)
- Observational-descriptive designs<sup>18</sup> (Level 4 evidence)
- Expert opinion and bench research<sup>8, 9, 11-15, 17, 19, 21</sup> (Level 5 evidence)

## BEST PRACTICE RECOMMENDATIONS

Women who have lymphoedema associated with breast cancer treatment can engage in high resistance exercise regimens without significant exacerbation of lymphoedema symptoms. (Grade B recommendation)

Commencing exercise in the early post-operative weeks is not associated with increased incidence of lymphoedema compared with delaying onset of exercise. Wound drainage may increase with earlier exercise, and wounds may take slightly longer to heal. Weigh the risks of early exercise against benefits of attaining adequate shoulder range of motion to undertake adjuvant cancer therapy (e.g. ability to position arm appropriately for radiation therapy). (Grade B recommendation)

Exercise should be conducted under the supervision of a qualified practitioner. (Grade B recommendation)

## RELATED EVIDENCE SUMMARIES

JB1 11559 Lymphedema: classification

JB1 11562, 11564, 11870, 11871: Lymphedema: methods of objective assessment

JB1 11560 Lymphedema: subjective assessment

JB1 12998 Managing lymphoedema: complex lymphedema therapy

JB1 12921 Single modality treatment of lymphedema: manual lymphatic drainage

JB1 12096 Single modality treatment of lymphedema: pneumatic compression therapy

JB1 13918 Managing lymphoedema: laser therapy

JB1 13567 Prevention of filariasis

JB1 13568 Treatment of filariasis

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<sup>1</sup>: Sibbald RG, et al. *AdvSkin Wound Care* 2011;24(2): 78-84

