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AMERICAN CONGRESS OF REHABILITATION MEDICINE

Archives of Physical Medicine and Rehabilitation

journal homepage: www.archives-pmr.org

Archives of Physical Medicine and Rehabilitation 2016;97:302-15

REVIEW ARTICLE (META-ANALYSIS)

Systematic Review and Meta-Analysis of the Effects of Exercise for Those With Cancer-Related Lymphedema

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Abstract

Objectives: To evaluate the effects of exercise on cancer-related lymphedema and related symptoms, and to determine the need for those with lymphedema to wear compression during exercise.

Data Sources: CINAHL, Cochrane, EBSCOhost, MEDLINE, PubMed, ProQuest Health and Medical Complete, ProQuest Nursing and Allied Health Source, ScienceDirect, and SPORTDiscus databases were searched for trials published before January 1, 2015.

Study Selection: Randomized and nonrandomized controlled trials and single-group pre-post studies published in English were included. Twenty-one (exercise) and 4 (compression and exercise) studies met inclusion criteria.

Data Extraction: Data were extracted into tabular format using predefined data fields by 1 reviewer and assessed for accuracy by a second reviewer. Study quality was evaluated using the Effective Public Health Practice Project Quality Assessment Tool.

Data Synthesis: Data were pooled using a random-effects model to assess the effects of acute and long-term exercise on lymphedema and lymphedema-associated symptoms, with subgroup analyses for exercise mode and intervention length. There was no effect of exercise (acute or intervention) on lymphedema or associated symptoms, with standardized mean differences from all analyses ranging between −0.2 and 0.1 (P values $\geq$.22). Findings from subgroup analyses for exercise mode (aerobic, resistance, mixed, other) and intervention duration (>12wk or $\leq$12wk) were consistent with these findings—that is, no effect on lymphedema or associated symptoms. There were too few studies evaluating the effect of compression during regular exercise to conduct a meta-analysis.

Conclusions: Individuals with secondary lymphedema can safely participate in progressive, regular exercise without experiencing a worsening of lymphedema or related symptoms. However, there is insufficient evidence to support or refute the current clinical recommendation to wear compression garments during regular exercise.

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There is compelling evidence demonstrating the benefits of exercise after cancer, including improvements in quality of life, fitness, function, and potentially survival.[1,2] As a result, regular participation in exercise is promoted and endorsed by major cancer organizations throughout the world, as well as clinical and allied health professional associations.[2] Despite this widespread endorsement of exercise postcancer, many survivors decrease exercise and physical activity levels after treatment and fail to return to precancer levels after treatment.[2-4] A subgroup at particular risk of experiencing a decline in exercise and physical activity are individuals who develop cancer-related lymphedema.[5,6]

Lymphedema is a pathologic swelling of limbs or other body parts associated with pain, heaviness, tightness, and other symptoms.[7] Lymphedema may progress in severity over time from mild pitting edema to severe edema, which may be accompanied by fibrosis and other complications such as cellulitis.[8,9] Cancer-related lymphedema occurs because of obstructed or disrupted lymph flow, which may result from the presence of a tumor, or from trauma or damage to the lymphatic system as a consequence of cancer treatment.[10,11] Lymphedema risk factors related to cancer and its treatment include more extensive surgery (eg, mastectomy vs lumpectomy), more extensive lymph node dissection (eg, axillary lymph node dissection vs sentinel lymph node biopsy), a greater number of positive lymph nodes, a higher stage of cancer, and treatment with chemotherapy or

Disclosures: none.

0003-9993/15/$36 - see front matter © 2016 by the American Congress of Rehabilitation Medicine
http://dx.doi.org/10.1016/j.apmr.2015.09.012

radiotherapy.[12-15] Compared with cancer survivors without lymphedema, those who develop lymphedema report a significantly lower quality of life and are more likely to experience psychosocial effects such as depression, anxiety, frustration, distress, disturbances in relationships, and social avoidance, as well as functional limitations.[16,17] As such, lymphedema also has an adverse and significant societal cost.[18]

Lymphedema is estimated to occur in approximately 20% of breast cancer survivors[14] and between 10% and 40% of gynecologic, melanoma, and head and neck cancer survivors.[19] Previous clinical guidelines for those with lymphedema provided cautionary advice regarding use of the affected limb.[20] This included avoiding strenuous and repetitive exertion of the affected limb, and to wear a compression garment during any bout of exercise.[20-22] Guidelines were based on the principle that repetitive or strenuous use of the affected limb would increase interstitial fluid production and lead to a worsening of swelling.[23] Evidence regarding the role of exercise in cancer-related lymphedema has predominantly focused on upper limb lymphedema, with very limited research involving lower limb lymphedema. Evidence from cohort studies and randomized controlled trials (RCTs) involving women at risk of developing breast cancer treatment–related lymphedema highlights that being physically active is associated with a reduced risk of lymphedema.[14,24-26] Several exercise trials, including at least 1 large RCT, have been conducted over the past decade to assess the effect of exercise for individuals with cancer-related lymphedema. While there exist reviews on exercise and lymphedema, to date these have focused solely on breast cancer survivors at risk of lymphedema (ie, without a clinical diagnosis of lymphedema)[27]; have evaluated treatment strategies to improve quality-of-life outcomes in those with cancer-related lower limb lymphedema[28]; and have evaluated various forms of physical therapy such as passive mobilization and stretching on upper limb pain and range of motion after cancer.[29] Therefore, the purpose of this systematic review and meta-analysis was to summarize evidence from randomized and non-RCTs, and single-group pretest-posttest comparisons of (1) the short- and longer-term effects of acute exercise (ie, single bouts) and exercise training (ie, regular exercise) as well as different exercise modes on cancer-related lymphedema and its associated symptoms; and (2) the effects of wearing compression during exercise in individuals with cancer-related lymphedema.

Methods

Search strategy and selection criteria

This article reports the methods and findings from 2 separate literature reviews. Review 1 identified studies that evaluated the effects of exercise for individuals with diagnosed lymphedema secondary to cancer. Review 2 identified studies that evaluated the effect of compression use during exercise on cancer-related lymphedema. The eligibility criteria were established using the PICO (participants, intervention, comparator, and outcome) framework[30] for review 1 as follows:

List of abbreviations:

CI **confidence interval**
RCT **randomized controlled trial**
SMD **standardized mean difference**

- *Participants:* Studies involving participants with clinically diagnosed, cancer-related upper or lower limb lymphedema were eligible for inclusion. Studies comprised solely of participants considered "at risk" or without a clinical diagnosis of lymphedema were excluded.
- *Intervention:* Studies that included a form of exercise, which was reported as "resistance-based" (ie, weightlifting, resistance exercise, or resistance training), "aerobic-based," or "other exercise" were included. "Other exercise" was considered a form of active exercise that (1) was not specified as aerobic or resistance-based; and (2) did not constitute a component of complete decongestive therapy—based exercise (a common form of lymphedema treatment). Studies that assessed the effects after single bouts of exercise or exercise interventions (eg, ≥4wk of regular exercise training) were included. Acute exercise studies were considered studies in which single bouts of exercise were performed, and the short-term effect on lymphedema was assessed after the bout of exercise (ie, immediately after and up to 72h postexercise). Intervention studies were considered studies that involved more than 1 bout of exercise; that is, they involved regular exercise training (eg, ≥4wk) with lymphedema assessed pre- and postintervention. Studies that involved exercise in addition to other interventions were excluded if the effects of exercise could not be isolated. RCTs, non-RCTs, and single-group pre-post studies were included.
- *Comparators:* Studies comparing exercise with either no exercise; a different mode of exercise, including exercise performed at a different dose or intensity; usual care; or other intervention; and single-group studies with no comparison intervention were included.
- *Outcomes:* Studies involving the assessment of lymphedema (limb swelling) with or without lymphedema-related symptoms of the affected limb—pain, heaviness, and tightness—were included. There were no exclusion criteria on the methods used to assess lymphedema or lymphedema-related symptoms.

Review 2 had the same eligibility criteria as review 1 for participants, intervention, and outcomes. However, for comparators in review 2, studies in which exercise was performed with, compared to without compression, were eligible for inclusion.

Studies were identified through a database search of CINAHL, Cochrane, EBSCOhost, MEDLINE, PubMed, ProQuest Health and Medical Complete, ProQuest Nursing and Allied Health Source, ScienceDirect, and SPORTDiscus. Database searches were limited to peer-reviewed scholarly journal articles published in English before January 1, 2015. To obtain articles meeting the eligibility criteria, a title and keyword search was conducted. Title and keyword search terms for review 1 were "lymphoedema or lymphedema" AND "exercise or physical or aerobic or resistance or training or fitness or strength or weight lifting." Search terms for review 2 were "lymphoedema or lymphedema" AND "exercise or physical or aerobic or resistance or training or fitness or strength or weight lifting" AND "compression."

Data extraction and management

All identified articles using the search strategy were evaluated for inclusion by 1 investigator (B.S.). Eligibility was based on the inclusion and exclusion criteria, which were developed a priori (described above). Articles not meeting eligibility criteria were excluded using several steps. A manual search of reference lists