ARTICLE

Balancing Lymphedema Risk: Exercise Versus Deconditioning for Breast Cancer Survivors

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SCHMITZ, K.H. Balancing lymphedema risk: exercise versus deconditioning for breast cancer survivors. *Exerc. Sport Sci. Rev.*, Vol. 38, No. 1, pp. 17–24, 2010. *Lymphedema, a common and feared negative effect of breast cancer treatment, is generally described by arm swelling and dysfunction. Risk averse clinical recommendations guided survivors to avoid the use of the affected arm. This may lead to deconditioning and, ironically, the very outcome women seek to avoid. Recently published studies run counter to these guidelines.* **Key Words:** arm swelling, late effects, survivorship, rehabilitation, quality of life, weight lifting

INTRODUCTION/OVERVIEW

There are more than 11 million cancer survivors alive in the United States today (8). The largest single diagnosis of these survivors is breast cancer, which accounts for more than 2.4 million women or 22% of the total population of survivors (8). In addition, there are approximately 189,000 new breast cancer diagnoses every year, and 89% of these women are expected to live five or more years (3). The improvements in treatment success have created a new set of priorities focused on the issues faced by long-term breast cancer survivors. One common and feared negative side effect of breast cancer treatment is lymphedema. This article provides exercise physiologists and clinicians with an understanding of lymphedema after breast cancer, including a review of lymphatic anatomy and physiology, as well as current risk reduction and treatment guidelines, leading to a review of the potential risks and benefits of upper body exercise. The research on exercise and lymphedema in breast cancer survivors is reviewed, and next steps for research in this area are suggested. The central integrative hypothesis, based on the evidence presented, is that slowly progressive strength training, is as safe, if not safer, than avoiding use of the arm affected by breast cancer treatments for survivors with and at risk for lymphedema. This hypothesis runs 180 degrees counter to current guidance on the Web sites of the American Cancer Society (which includes advice to "use your unaffected arm or both arms as much as possible to carry heavy packages, groceries, handbags, or children") and the Susan Komen Foundation (which includes advice to "avoid lifting or carrying heavy bags, purses, or other objects with the at-risk arm"). It is hoped that this review will contribute to changes in the guidance given to survivors and consequently to assist women with avoiding the unnecessary and inevitable muscle atrophy and reduced function that develops with restricting use of the arm.

Defining Lymphedema, Lymph System Physiology

Lymphedema is defined as a protein-rich accumulation of excess fluid in any body part that has experienced damage to the lymphatics (22). After breast cancer, it is generally characterized by swelling of the hand, arm, breast, or torso on the affected side and is associated with significant physical, functional, psychosocial, and economic burden for those who develop this chronic, progressive, and incurable condition (6,15). Physical morbidities associated with lymphedema include skin changes (29), loss of sensation and limb function, and pain of varying intensity and frequency (22). Significant psychosocial morbidity also has been described in association with lymphedema (15,16). Breast cancer survivors may find lymphedema more distressing than mastectomy as it is less possible to hide the physical manifestation and loss of arm function that negatively affect many aspects of daily life (29).

The functions of the lymph system include transport of proteins (*e.g.*, bacteria, viruses, cancer cells) and to remove excess fat, water, and cellular debris and foreign material

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from the tissues of the body (34). Lymph fluid enters initial lymph collectors that are found in proximity to the arteriovenous anastamoses that serve all systemic tissues. Figure 1 shows an overview of the lymphatic system around the breasts. The type of fluid and molecules that enter the initial lymph collectors differs from what is collected by veins, in part because the openings into the lymph system are larger than the openings into the veins. Therefore, larger molecules (*e.g.*, fat, some proteins, cellular debris, some bacteria and viruses) can only be removed from the tissues through the lymph system. From the initial collectors, lymph fluid moves through lymph vessels that have one-way valves (much like the valves that ensure return of venous blood from the periphery to the heart), eventually reaching lymph nodes. Lymph nodes serve as traps for foreign particles and toxins, to keep harmful materials from entering the blood. In addition, white blood cells in the lymph nodes form antigens to bacteria delivered to the node. Lymph fluid leaves the nodes through efferent vessels to be delivered eventually to the two largest lymph vessels: the right lymphatic duct or the thoracic lymphatic duct. From there, lymph fluid is reintegrated into the first circulation (the cardiovascular circulation) at the point of the right or left subclavian veins. The initial lymph collectors and vessels that serve specific areas of systemic tissue report back to a specific lymph node or set of nodes (34). Therefore, bacteria, proteins, and other materials from a specific body part (*e.g.*, left index finger) are delivered to a specific lymph node that serves that tissue. The arrival of bacteria and cellular debris at a specific lymph node triggers immune system response to the specific tissue served by that lymph node, preventing the development of systemic infection. When nodes are damaged or removed, this immune response system is interrupted, as is the ability to remove excess fluids and large particles from the tissue supported by the particular lymph node removed. If only one node is removed, this means a very small area is impacted. The more lymph nodes removed/damaged, the harder it is for the system to deal with an infection, injury, or inflammatory response. This explains, in part, why the number of nodes removed in curative surgery is associated with risk for lymphedema, as discussed below.

Curative Treatments and Breast Cancer–Related Lymphedema

The goal of curative breast cancer treatment is to remove all cancer cells from the body and, if indicated, to treat systemically in a manner that will reduce the chance of recurrence in a clinically meaningful manner. These treatments generally include surgery, radiotherapy, and various drug therapies. The two types of curative therapies most closely linked to lymphedema risk are surgery and radiotherapy. As the number of lymph nodes surgically removed increases, so does the likelihood that the survivor will develop lymphedema (18). However, there are examples of women who develop lymphedema with as few as two lymph nodes removed (2). A surgical procedure called *sentinel lymph node biopsy* (SLNB) has substantively decreased the incidence of lymphedema compared with the full axillary dissections because fewer nodes are removed with this newer surgical approach. That said, the hypothesis that SLNB completely eliminates lymphedema risk has not been supported.

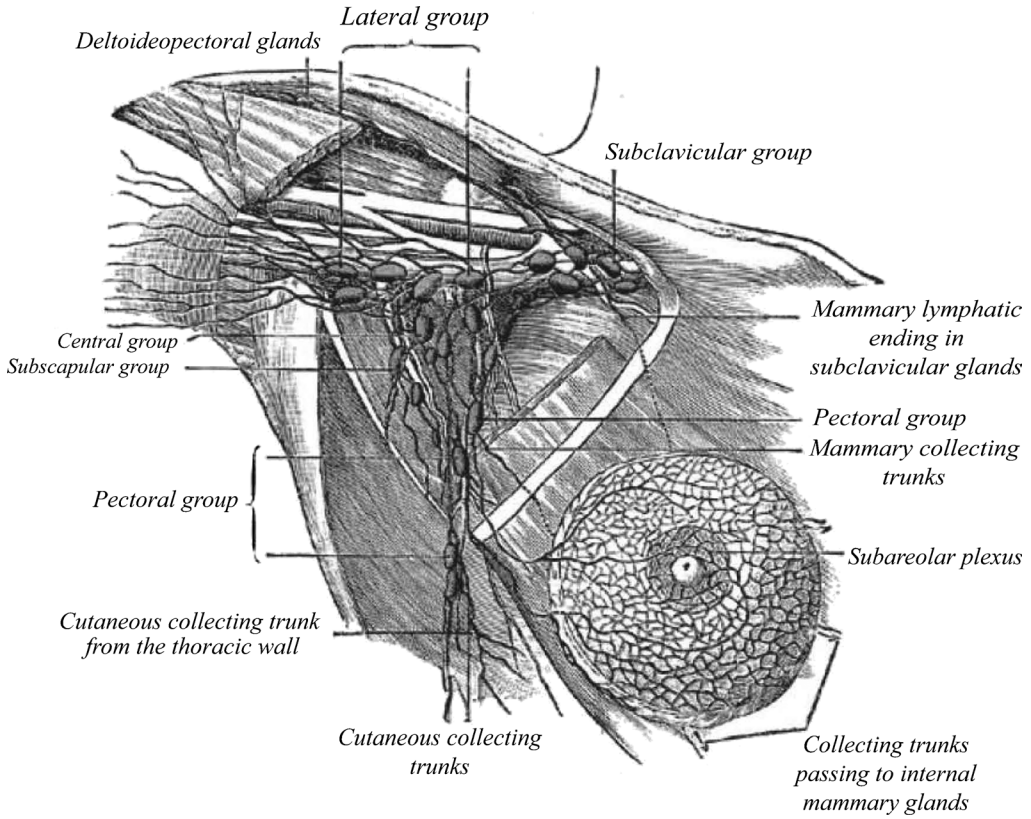

Figure 1. Anatomy of the lymph system of the breast. Originally published in the 20th U.S. edition of Gray's Anatomy of the Human Body, 1918.

One study found 17% of women with SLNB alone (no follow-up axillary dissections) developed grade 1 or higher lymphedema (11). In addition to lymph node removal and trauma to the lymph system resultant to surgery, there is evidence that risk of lymphedema may be increased by as much as 48% among women who undergo radiotherapy compared with those who do not receive radiotherapy (18).

Epidemiology of Breast Cancer–Related Lymphedema: Prevalence and Risk Factors

Prevalence of lymphedema after breast cancer ranges from 6% to 67% in the literature (11), but it is generally stated that the incidence is likely between 20% and 30% (13,28). The wide range of prevalence results from variability in the threshold for diagnosing lymphedema and the length of follow-up. If we estimate 30% of breast cancer survivors that have clinically diagnosed lymphedema, that would mean 720,000 current diagnoses, with 40,000 added each year.

Commonly reported risk factors for breast cancer–related lymphedema include the number of lymph nodes removed/damaged or irradiated as part of curative therapies, as previously noted (18). In addition, women who are obese at the time of breast cancer diagnosis or who gain weight after diagnosis generally have a higher risk of lymphedema (21). Generally, activities that result in injury, infection, or trauma to the affected limb are considered risk factors (*e.g.*, insect bites, cuts, sunburn, or muscle overuse) (25). This is because the lymph system is part of the body's response to handling such tissue challenges. After having been damaged due to curative breast cancer treatments, the lymphatics may be overwhelmed by the natural inflammatory processes used by the body in healing.

Lymphedema Diagnosis and Common Clinical Progression

Lymphedema has traditionally been diagnosed by comparison of limb size (4). The diagnostic threshold has varied in the literature, including 5% interlimb volume differences to 10-cm interlimb circumference differences (4). These approaches have been criticized for exclusion of real cases of lymphedema that are isolated to a specific area of the limb. Even when the specific diagnostic threshold for interlimb swelling differences is not reached, there may be real and meaningful changes in tissue tone and/or texture that result in functional impairments, such as changes in the hands that may make writing difficult (7). A newer set of standard diagnostic criteria addresses this problem by including changes in tissue tone/texture. These criteria, described in detail in Table 1, are included in the National Cancer Institute's document used for grading of common toxicities that are evaluated among patients participating in clinical trials (available online at ctep.cancer.gov/protocolDevelopment/electronic_applications/docs/ctcv20_4-30-992.pdf).

Another key issue in diagnosis of lymphedema is that transient swelling as a result of surgery or radiotherapy that resolves is not the same as lymphedema but may be misdiagnosed as such. There is no generally accepted time line for delineating acute swelling versus chronic lymphedema, but development and/or persistence of symptoms and swelling three months after treatment is commonly used by clinicians.

Finally, survivors report frustration with getting health professionals to refer them to someone with appropriate training and expertise to diagnose lymphedema (15). It is a commonly reported patient experience that surgeons downplay as "normal" a level of arm swelling and symptoms that could benefit from lymphedema treatment (15). This can be quite frustrating, given that earlier diagnosis may improve long-term prognosis and delay progression of this incurable chronic condition (33). Although lymphedema generally would not cause death, minimizing or trivializing the issue is frustrating to survivors, who live with the condition day-to-day, including multiple physical and psychosocial morbidities and the time-consuming and expensive activities required for management and preventing progression.

The majority of breast cancer lymphedema is mild (26). For these women, management of the limb to keep swelling and symptoms minimized is vital to preventing progression to swelling that changes the ability to wear one's clothing and use the arm in activities of daily living (6).

Lymphedema Treatment and Risk Reduction Guidelines

The most widely accepted treatment approach for lymphedema includes multiple elements and is collectively called *complete decongestive therapy*. This comprehensive approach includes manual lymphatic drainage, compression of the swollen limb, exercise, skin care, and patient education in self-care (23). Complete decongestive therapy occurs in two phases. The first phase is intensive and therapist delivered, with a goal of reducing swelling and symptoms. This phase can last from one to 4 wk and may involve as few as two or as many as 20 therapist-delivered treatment sessions. After reaching a plateau of improvement, phase two (*e.g.*, self-care and risk reduction) begins. Depending on the severity of the condition, phase two may include wearing a custom-fitted compression garment during the day, special short stretch compression bandaging at night, exercises, specific skin care guidelines, and after risk reduction practices.

TABLE 1. Common toxicity criteria grading of lymphedema (see (7)).

Grade	Description
1	5%–10% interlimb discrepancy in volume or circumference at point of greatest visible difference; swelling or obscuration of anatomical architecture on close inspection; pitting edema
2	>10%–30% interlimb discrepancy in volume or circumference at point of greatest visible difference; readily apparent obscuration of anatomical architecture; obliteration of skin folds; readily apparent deviation from normal anatomical contour
3	>30% interlimb discrepancy in volume; lymphorrhea; gross deviation from normal anatomical architecture; interfering with activities of daily living
4	Progression to malignancy (*e.g.*, lymphangiosarcoma); amputation indicated; disabling

Other less common lymphedema treatment approaches include use of a pneumatic pump to mechanically simulate manual lymphatic drainage, liposuction, debulking surgery, and pharmacological therapy (30). These approaches may be used in concert with elements of complete decongestive therapy to customize treatment to individual patient needs.

Lymphedema is a chronic condition that requires nearly constant vigilance to avoid allowing the condition to progress, which can cause impaired physical functional ability with the upper body. Most survivors with lymphedema are prescribed a custom-fitted compression sleeve and glove to wear during the day. These garments are similar to the compression support hose used to control swelling from peripheral arterial disease in the lower legs. They must be replaced at least every 6 months, washed according to special instructions, and may cost more than $300. Insurance does not always cover the cost of these garments, which have been shown to be effective in reducing swelling and preventing progression of lymphedema (25).

The risk reduction practices recommended by the National Lymphedema Network (NLN) include skin care (avoiding trauma or injury to reduce infection risk), carefully progressive physical activity with monitoring for symptoms, avoiding limb constriction (*e.g.*, elastic watch bands that leave a mark which might occlude flow of lymph), wearing a compression garment if prescribed, and avoiding extremes of temperature (*e.g.*, avoiding exercise in hot, humid weather) (25). One of the guidelines is to wear gloves while doing activities that may cause skin irritation or injury (*e.g.*, washing dishes, gardening, working with tools). It is possible that women avoid doing some activities with their arms and hands rather than wear gloves, further contributing to lower activity levels and muscular deconditioning.

Exercise guidance from the NLN has been generally risk averse (24). In the absence of evidence, clinicians opted for conservative recommendations, in the effort to protect breast cancer survivors from harm. In the past, the guidelines included recommendations to avoid use of the affected arm, including limiting lifting to less than 5–15 lb. To place this in context, a gallon of milk weighs approximately 8 lb. Women may interpret these recommendations, like the risk reduction guidelines discussed above, in a manner that leads to deconditioning of the affected arm. In turn, this means that average daily activities would require near maximal work of the affected arm, potentially leading to injury and an inflammatory response that may overwhelm the damaged lymphatics, the very outcome women sought to avoid.

Role of Exercise Training

Exercise training could be defined as controlled physiological stress to the body for the purpose of increasing the capacity of the exercised body system to respond to future stresses. The concepts of exercise training effects and specificity of those effects are well described in the exercise science literature. When we challenge our arms in a bout of physical activity to do more work than they are used to doing, the result is adaptation of the specific muscle, circulatory system, and connective tissues used (19). Frequent, repeated bouts of exercise, with appropriate progression of the total work (intensity and/or duration), coupled with adequate rest intervals to allow the adaptations to take place, results in training of the exercised arms such that the maximal and/or sustainable submaximal amount of work capacity of the arms is increased (19). In addition, after exercise training, common daily activities that require lifting will require a lower percentage of maximal effort. As a result, they will be less likely to result in the injuries or inflammatory responses. Unfortunately, little is known about whether the lymphatic system also adapts in response to exercise training (35). For those with lymph system damage, this research is vitally important to understanding whether exercise training results in the development of collateral lymph vessels, as has been observed with the arterial system. It is well established that capillary density increases within the specific muscle beds that are exercise trained. We do not currently know if the same happens with the lymph vessels, in part because methods for examining lymph vessels have not been available (35). Important recent work in this area includes lymphoscintigraphy studies in healthy controls and breast cancer survivors with and without lymphedema (10,17). These studies do not support the hypothesis that exercise training results in increased lymph clearance as measured by lymphoscintigraphy. However, irrespective of what happens with lymph vessels, the positive impact of exercise on our muscular and cardiovascular system seems likely to support improved clearance of lymph from an impaired lymph transport system, including the effect of the muscle pump on venous (and likely lymphatic) clearance.

Cardiac exercise rehabilitation provides an analogy for the potential for exercise to be useful to women concerned about lymphedema, including those with and at risk for the condition. After a myocardial infarction, it is generally accepted that it is useful to gradually, slowly increase the physiological capacity of the damaged body system (the heart) by slowly progressive cardiorespiratory exercise training (1). This training is heavily supervised among those who are most impaired after an myocardial infarction, and as the capacity to do work improves, the level of supervision declines, until gradually, the individual is able to exercise unsupervised. Through cardiac exercise rehabilitation, patients increase the maximal capacity of the cardiorespiratory system to do work, thus decreasing the proportion of maximum capacity required to complete common tasks such as climbing stairs. This exercise training response results in reduced risk of a second cardiac event during exercise, as well as improved function and quality of life (1). The analogous hypothesis for exercise and lymphedema is that by slowly, progressively increasing the physiological stress placed on the affected arm, the body will increase maximal work capacity in the affected limb. Common daily activities such as carrying groceries or lifting children would then require a lower percentage of maximal capacity. If the analogy holds, this should translate into reduced risk for lymphedema onset or worsening due to using the affected arm in day-to-day activities, as well as improved function and increased quality of life.

What is the Empirical Evidence Regarding Exercise and Lymphedema?

Against the backdrop of risk averse guidelines to avoid using the affected arm after lymph node removal as part of treatment,

multiple research studies have examined the effects of exercise training on the limbs of breast cancer survivors with and at risk for lymphedema. More history of the development of the risk averse guidelines and a systematic review of the literature through 2007 are available elsewhere (5). The hypotheses of these studies are all versions of the one stated at the beginning of this article, with a central theme that slowly progressive training may actually be more protective than the inevitable muscle atrophy that results from avoiding use of the affected arm. In this section, we review four key randomized controlled trials that focused on exercise and lymphedema in breast cancer survivors. Table 2 provides a summary of these studies. For the purpose of this review, lymphedema and quality-of-life outcomes from each study are summarized. Below is a brief summary of features of all four of these studies.

Participant description

The sample sizes ranged from 14 (20) to 295 (32) breast cancer survivors. Two of the studies included only women with lymphedema (12,20). The other two (2,32) included women with and at risk for lymphedema. The range of time since diagnosis was approximately 6 months to 15 yr.

Interventions and adherence

Survivors were randomly assigned to a progressive program of weight lifting or a no-exercise control group in all four studies. Two of the studies included an aerobic exercise component, as well. All four studies started with supervised training for at least 8 wk, to ensure all participants learned to do the prescribed exercises safely. The frequency of sessions ranged from 2 to 5 times per wk, and sessions lasted up to 90 min. All interventions included a cardiopulmonary warm-up and cool-down, and stretching. In two of the studies, weight training was limited to the upper body; in the other two studies, exercises for the lower body were included, as well. When reported, exercise adherence was greater than 70%.

Measurements and methods of ensuring safety

Measurements used in each study are described in Table 2 but the table includes arm circumferences and/or water volume measurements in all studies. Intervention elements intended to promote safety included supervision of exercise sessions, requirements to wear compression sleeves during exercise in two of the four studies, and evaluation by a certified lymphedema therapist if participants experienced a change of symptoms that lasted a week or longer.

RESULTS

The results indicate that, with rare exception, there were no increases in arm swelling or worsened symptoms in any of the four studies. There was one woman in the treatment group of the Hayes *et al.* study (12) who experienced an increase in volumes and a substantive "flare-up" of lymphedema symptoms. Her adherence to the intervention was approximately 50%. Within 6 months after the study ended, she was diagnosed with a recurrence of her breast cancer. It is not possible to discern whether the worsening of symptoms was caused by the exercise. The authors note that it also could have been an early signal of the cancer recurrence. The results of the McKenzie and Kalda (20) and Ahmed *et al.* (2) studies, taken together, were pivotal in the 2008 revisions of the NLN guidance regarding exercise for cancer survivors with and at risk for lymphedema to acknowledge that upper body resistive training may be performed, as long as the resistance starts low and progresses slowly and according to symptom response (24). The most recently completed study, the Physical Activity and Lymphedema (PAL) trial (31), also observed that twice weekly strength training reduced, by half, the incidence of lymphedema exacerbations that required physical therapy treatment. The number and severity of lymphedema symptoms also were reduced among the PAL trial participants with lymphedema who did twice weekly progressive strength training, when compared with the control group participants with lymphedema who did not do strength training (31).

Quality-of-life results are available from two of these trials (20,27). Both trials observed improvements in quality of life measures, although these improvements were only significant in one study (27). Within the Weight Training for Breast Cancer Survivors study, participants anecdotally reported improvements in self-perception of elements of body image and relationships, including strength and health, appearance and sexuality, and social functioning (27). This led to the development of a new instrument called the Body Image and Relationship survey (14), which assesses these issues specifically within breast cancer survivors and was administered in the PAL trial. Results on this secondary outcome from the PAL trial are forthcoming.

Summary of Highlighted Studies

Contrary to clinical guidelines that have guided women to avoid use of the arm treated for breast cancer, the studies above indicate that upper body exercise is safe for survivors with and at risk for lymphedema. There is some evidence that quality of life is improved by weight training in breast cancer survivors. Each of the trials excluded women with severe or unstable lymphedema. Hayes *et al.* (12) report that supervision was key to allaying participants' fears that they were potentially harming themselves by exercising. Measurements were frequent to ensure that any changes due to exercise were caught quickly and addressed. It would be inappropriate to interpret the results of these trials as indicating that all breast cancer survivors could begin progressive weight training without any supervision or instruction. All of the reviewed studies included at least 8 wk of supervised sessions to ensure that exercises were performed with proper biomechanics, that the progression of resistance was slow and appropriate. In the PAL trial, changes in symptoms resulted in altered intervention activities until the symptoms were resolved.

In addition to the four reviewed trials, Courneya *et al.* (9) completed a large (N = 242) randomized controlled exercise trial that included a weight-training arm. This trial was conducted during chemotherapy, during the time frame before when it is possible to delineate between the short-term effects of treatment on arm swelling versus chronic lymphedema. For this reason, it is not directly comparable to the four studies reviewed above, each of which took place months after

TABLE 2. Summary of reviewed randomized controlled trials.

Study	Participant Description and Sample Size	Intervention Description	Session Frequency and Duration	Intervention Length; Participant Adherence	Level of Supervision	Measures	Ensuring Safety	Results
McKenzie and Kalda 2003 (20)	All participants 6+ months since breast cancer diagnosis, all had clinically diagnosed lymphedema; *N* = 14, 7 per group	Progressive upper body resistance training, warm-up, cool-down, and stretching all 8 wk, arm ergometry weeks 3–8	Three times weekly, duration not indicated	8 wk; adherence not reported	All sessions supervised	Circumferences, water volume, quality of life	Supervision of exercise, measurements every 2 wk, all women required to wear a compression garment daily and during exercise	No adverse effects on arm volumes, nonsignificant improvement in several quality of life subscales
Ahmed *et al.* 2006 (2)	Survivors with and without lymphedema 4–36 months after end of adjuvant breast cancer treatment; *N* = 46, 23 per group; *N* = 14 with lymphedema, 7 per group	Progressive upper and lower body resistance training, warm-up, cool-down, and stretching all 26 weeks; no upper limit placed on weight lifted as long as there were no symptom changes.	Twice weekly, 60–90 min per session	26 wk; all but one participant attended at least 80% of sessions	Sessions supervised weeks 1–13, continued behavioral support weeks 14–26	Circumferences, symptom survey, quality of life	Supervision of exercise, women given the choice to wear a compression garment or not	No adverse effects on circumferences, nonsignificant improvement in symptoms among women with lymphedema, significant improvement in several quality of life subscales
Hayes *et al.* 2009 (12)	Survivors with clinically diagnosed lymphedema, 6+ months since breast cancer diagnosis; *N* = 32, 16 per group	Weeks 1–2 aerobics only; weeks 3–4 aerobics and water-based resistance training; weeks 5–8 aerobics, water-based resistance training, free weights; weeks 9–12 aerobics and machine-based resistance training	Progressed from 3/week, 20–30 min. per session during weeks 1–4 to 4/week 45+/session during weeks 9–12	12 wk; 88% of women attended at least 70% of sessions	2 of the 3/week sessions supervised weeks 1–4, 1 of 4/week sessions during weeks 9–12	Bioelectrical impedance spectroscopy (BIS), perometry (circumferences)	Supervision of exercise, interim measurements, women given the choice to wear a compression garment or not	No adverse effects on lymphedema outcomes except for one poorly adherent participant.
Schmitz *et al.* 2009 (31,32)	295 breast cancer survivors; 154 1–5 yr since breast cancer diagnosis who were at risk for lymphedema (*N* = 77 each in treatment and control groups); 141 1–15 yr since breast cancer diagnosis who had clinically diagnosed lymphedema (*N* = 71, 70 in treatment, control groups)	Progressive upper and lower body resistance training, "core" training, warm-up, cool-down, and stretching all 52 wk; no upper limit placed on weight lifted as long as there were no symptom changes.	Twice weekly, 60–90 min per session	52 wk; 88% attendance among women with lymphedema; 79% attendance among women at risk for lymphedema	Sessions supervised weeks 1–13, continued behavioral support weeks 14–52	Circumferences, arm volume, BIS, symptom survey, clinical assessment by a certified lymphedema therapist, quality of life	Supervision of exercise, women with lymphedema given custom-fitted compression garments at baseline and 6 months, required to wear them during training. Treatment group participants measured monthly by trainers, all participants measured baseline, 3, 6, and 12 months	Results on 141 women with lymphedema indicate no adverse effects on arm swelling, relative risk 0.47 (95% confidence interval = 0.23–0.97) for lymphedema exacerbations requiring physical therapy treatments, and significant reductions of symptom severity. Results for 154 women at risk for lymphedema not yet published. Quality of life results not yet published.

treatment ended, when the issue of transient swelling due to treatment was no longer an issue. That said, it bears noting that no significant arm swelling was observed in a randomized trial of aerobic exercise or progressive weight lifting versus a no-exercise control group during chemotherapy for breast cancer (9).

Taken together, this evidence supports the safety of weight training in this population. A weight-training program for breast cancer survivors with or at risk for lymphedema should be started in a controlled, supervised setting, somewhat analogous to the approach of initially intensive and then gradually fading supervision of cardiopulmonary rehabilitative exercise after a myocardial infarction.

Next Steps for Research?

What is going on in that arm? Understanding lymphatic structure and function

We currently do not understand the plasticity of the lymphatic system. Physiological studies on lymph system structural and functional changes in response to a single bout of exercise and to exercise training are needed to understand better the results of the studies previously reviewed. The challenge in this work is establishment of a valid, reliable noninvasive method of assessing lymphatic structure and function *in vivo*. Lymphoscintigraphy may be a useful method for this purpose if it can be shown to be repeatable within person on multiple trials and after standardization of measurement protocols. In addition, animal models remain useful, as they did for research on the effects of exercise on cardiovascular structure and function.

Who, what, when, where, and how? Exploring specifics of training safety and efficacy

Breast cancer survivors need to know if the results of the studies above apply to their specific clinical profile. The extent to which compression garments should be worn during exercise, timing after curative treatment (*e.g.*, can women start weeks after surgery or during radiotherapy? Or should they wait until 6 months after treatment?), the differential usefulness of exercise across the clinical progression of lymphedema (primary prevention of lymphedema versus control of clinical progression after diagnosis), and the types of safety monitoring that need to be in place all remain to be explored. Furthermore, women do not want to be limited to the small number of activities that have been studied. Questions about the safety of yoga, Pilates, and other popular physical activities remain to be explored. In addition, none of the above studies have identified the specific elements of the interventions that are truly required to ensure safety. Based on participant concerns voiced in the Hayes' study (12), it seems likely that some supervision may be useful to allay fears, at least at the beginning of a program. Except for one, the studies reviewed used highly trained fitness professionals for intervention delivery. The extent to which it is possible for fitness trainers in commercial and not-for-profit fitness facilities to deliver these interventions with equal effectiveness and safety outcomes is less well established, although the PAL trial used YMCA personal training staff to deliver its intervention.

CONCLUSIONS/SUMMARY

The results of completed studies support the safety of upper-body exercise among breast cancer survivors with and at risk for lymphedema. There is ample evidence that disuse leads to atrophy and decreased maximal and functional capacity of any musculoskeletal tissue. Such decreased capacity might be hypothesized to place the arms of breast cancer survivors concerned with lymphedema at greater risk than a supervised program of slowly progressive exercise training. The physiological and structural response of the lymphatics to this type of training has yet to be completely described. The specifics of all types of upper-body exercise are not yet tested, but several general premises of progressive exercise training seem to hold with this population. Training should start supervised at a low dose and increase according to symptom response and is likely to increase maximal and functional capacity of the affected arm. Future research should include assessment of efficacy and safety of additional modes of exercise popular with breast cancer survivors (*e.g.*, yoga, Pilates) as well as assessment of the timing to start exercise after surgery.

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References

1. Ades P, Green N, Coello C. Effects of exercise and cardiac rehabilitation on cardiovascular outcomes. *Cardiol. Clin.* 2003; 21:435–48.
2. Ahmed RL, Thomas W, Yee D, Schmitz K. Weight training does not increase incidence of lymphedema in breast cancer survivors. *J. Clin. Oncol.* 2006; 24:2765–72.
3. American Cancer Society. Cancer Facts and Figures. Journal [Internet]. 2008 [cited, Available at: http://www.cancer.org/downloads/STT/2008CAFFfinalsecured.pdf, doi. Accessed June 15, 2009.
4. Armer JM, Stewart BR. A comparison of four diagnostic criteria for lymphedema in a post-breast cancer population. *Lymphat. Res. Biol.* 2005; 3:208–17.
5. Cheema B, Gaul CA, Lane K, Fiatarone Singh MA. Progressive resistance training in breast cancer: a systematic review of clinical trials. *Breast Cancer Res. Treat.* 2008; 109:9–26.
6. Cheville AL, McGarvey CL, Petrek JA, Russo SA, Taylor ME, Thiadens SR. Lymphedema management. *Semin. Radiat. Oncol.* 2003; 13:290–301.
7. Cheville AL, McGarvey CL, Petrek JA, Russo SA, Thiadens SR, Taylor ME. The grading of lymphedema in oncology clinical trials. *Semin. Radiat. Oncol.* 2003; 13:214–25.
8. Committee on Cancer Survivorship: Institute of Medicine and National Research Board. *From Cancer Patient to Cancer Survivor: Lost in Translation*. National Academy of Sciences. Washington, DC: National Academies Press; 2006.
9. Courneya KS, Segal RJ, Mackey JR, *et al*. Effects of aerobic and resistance exercise in breast cancer patients receiving adjuvant chemotherapy: a multicenter randomized controlled trial. *J. Clin. Oncol.* 2007; 25:4396–404.
10. Dolan LB, Lane KN, McKenzie DC. Is there enhanced lymphatic function in upper body trained females? *Lymphat. Res. Biol.* 2008; 6:29–38.
11. Francis WP, Abghari P, Du W, Rymal C, Suna M, Kosir MA. Improving surgical outcomes: standardizing the reporting of incidence and severity of acute lymphedema after sentinel lymph node biopsy and axillary lymph node dissection. *Am. J. Surg.* 2006; 192:636–9.
12. Hayes SC, Reul-Hirche H, Turner J. Exercise and secondary lymphedema: safety, potential benefits, and research issues. *Med. Sci. Sports Exerc.* 2009; 41:483–9.

13. Hinrichs CS, Watroba NL, Rezaishiraz H, *et al.* Lymphedema secondary to postmastectomy radiation: incidence and risk factors. *Ann. Surg. Oncol.* 2004; 11:573–80.
14. Hormes JM, Lytle LA, Gross CR, Ahmed-Saucedo RL, Troxel AB, Schmitz KH. The Body Image and Relationships Scale (BIRS): development and validation of a measure of body image in female breast cancer survivors. *J. Clin. Oncol.* 2008; 26:1269–74.
15. Johansson K, Holmstrom H, Nilsson I, Ingvar C, Albertsson M, Ekdahl C. Breast cancer patients' experiences of lymphoedema. *Scand. J. Caring Sci.* 2003; 17:35–42.
16. Kwan W, Jackson J, Weir LM, Dingee C, McGregor G, Olivotto IA. Chronic arm morbidity after curative breast cancer treatment: prevalence and impact on quality of life. *J. Clin. Oncol.* 2002; 20:4242–8.
17. Lane KN, Dolan LB, Worsley D, McKenzie DC. Upper extremity lymphatic function at rest and during exercise in breast cancer survivors with and without lymphedema compared with healthy controls. *J. Appl. Physiol.* 2007; 103:917–25.
18. Lee TS, Kilbreath SL, Refshauge KM, Herbert RD, Beith JM. Prognosis of the upper limb following surgery and radiation for breast cancer. *Breast Cancer Res. Treat.* 2008; 110:19–37.
19. Magel JR, McArdle WD, Toner M, Delio DJ. Metabolic and cardiovascular adjustment to arm training. *J. Appl. Physiol.* 1978; 45:75–9.
20. McKenzie DC, Kalda AL. Effect of upper extremity exercise on secondary lymphedema in breast cancer patients: a pilot study. *J. Clin. Oncol.* 2003; 21:463–6.
21. Meeske KA, Sullivan-Halley J, Smith AW, *et al.* Risk factors for arm lymphedema following breast cancer diagnosis in black women and white women. *Breast Cancer Res. Treat.* 2009; 113:383–91.
22. Mortimer PS. The pathophysiology of lymphedema. *Cancer.* 1998; 83: 2798–802.
23. National_Lymphedema_Network_Medical_Advisory_Committee. Topic: Treatment. Journal [Internet]. 2006 [cited 2008 (September 17)]. Available at: http://www.lymphnet.org/pdfDocs/nlntreatment.pdf, doi:http://www.lymphnet.org/pdfDocs/nlntreatment.pdf. Accessed August 10, 2006.
24. National Lymphedema Network Medical Advisory Committee. Topic: Exercise for Lymphedema Patients. Journal [Internet]. 2008 [cited 2008 (September 17)]. Available at: http://www.lymphnet.org/pdfDocs/nlnexercise.pdf, doi:http://www.lymphnet.org/pdfDocs/nlnexercise.pdf. Accessed March 2008.
25. National Lymphedema Network Medical Advisory Committee. Topic: Lymphedema Risk Reduction Practices. Journal [Internet]. 2008 [cited 2008 (September 17)]. Available at: http://www.lymphnet.org/pdfDocs/nlnriskreduction.pdf, doi:http://www.lymphnet.org/pdfDocs/nlnriskreduction.pdf. Accessed March 2008.
26. Norman SA, Localio AR, Potashnik SL, *et al.* Lymphedema in breast cancer survivors: incidence, degree, time course, treatment, and symptoms. *J. Clin. Oncol.* 2009; 27:390–7.
27. Ohira T, Schmitz KH, Ahmed RL, Yee D. Effects of weight training on quality of life in recent breast cancer survivors: the Weight Training for Breast Cancer Survivors (WTBS) study. *Cancer.* 2006; 106:2076–83.
28. Ozaslan C, Kuru B. Lymphedema after treatment of breast cancer. *Am. J. Surg.* 2004; 187:69–72.
29. Petrek JA, Pressman PI, Smith RA. Lymphedema: current issues in research and management. *CA Cancer J. Clin.* 2000; 50:292–307; quiz 308-11.
30. Rockson SG. Diagnosis and management of lymphatic vascular disease. *J. Am. Coll. Cardiol.* 2008; 52:799–806.
31. Schmitz K, Ahmed RL, Troxel A, *et al.* Weight lifting in women with breast cancer-related lymphedema. *N. Engl. J. Med.* 2009; 361:664–73.
32. Schmitz KH, Troxel AB, Cheville A, *et al.* Physical activity and lymphedema (the PAL trial): assessing the safety of progressive strength training in breast cancer survivors. *Contemp. Clin. Trials.* 2009; 30:233–45.
33. Stout Gergich NL, Pfalzer LA, McGarvey C, Springer B, Gerber LH, Soballe P. Preoperative assessment enables the early diagnosis and successful treatment of lymphedema. *Cancer.* 2008; 112:2809–19.
34. Szuba A, Rockson SG. Lymphedema: anatomy, physiology and pathogenesis. *Vasc. Med.* 1997; 2:321–6.
35. Zawieja D. Lymphatic biology and the microcirculation: past, present and future. *Microcirculation.* 2005; 12:141–50.