A Randomized Trial on the Effect of Exercise Mode on Breast Cancer–Related Lymphedema

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ABSTRACT

BUCHAN, J., M. JANDA, R. BOX, K. SCHMITZ, and S. HAYES. A Randomized Trial on the Effect of Exercise Mode on Breast Cancer–Related Lymphedema. Med. Sci. Sports Exerc., Vol. 48, No. 10, pp. 1866–1874, 2016. Purpose: Breast cancer–related lymphedema is a common and debilitating side effect of cancer treatment. This randomized trial compared the effect of progressive resistance- or aerobic-based exercise on breast cancer–related lymphedema extent and severity, as well as participants’ muscular strength and endurance, aerobic fitness, body composition, upper-body function, and quality of life. Methods: Women with a clinical diagnosis of stable unilateral, upper-limb lymphedema secondary to breast cancer were randomly allocated to a resistance-based (n = 21) or aerobic-based (n = 20) exercise group (12-wk intervention). Women were assessed preintervention, postintervention, and 12 wk postintervention, with generalized estimating equation models used to compare over time changes in each group’s lymphedema (two-tailed P < 0.05).

Results: Lymphedema remained stable in both groups (as measured by bioimpedance spectroscopy and circumferences), with no significant differences between groups noted in lymphedema status. There was a significant (P < 0.01) time–group effect for upper-body strength (assessed using four to six repetition maximum bench press), with the resistance-based exercise group increasing strength by 4.2 kg (95% confidence interval [CI] = 3.2–5.2) postintervention compared with 1.2 kg (95% CI = −0.1 to 2.5) in the aerobic-based exercise group. Although not supported statistically, the aerobic-based exercise group reported a clinically relevant decline in number of symptoms postintervention (−1.5, 95% CI = −2.6 to −0.3), and women in both exercise groups experienced clinically meaningful improvements in lower-body endurance, aerobic fitness, and quality of life by 12-wk follow-up. Discussion: Participating in resistance- or aerobic-based exercise did not change lymphedema status but led to clinically relevant improvements in function and quality of life, with findings suggesting that neither mode is superior with respect to lymphedema effect. As such, personal preferences, survivorship concerns, and functional needs are important and relevant considerations when prescribing exercise mode to those with secondary lymphedema. Key Words: PHYSICAL ACTIVITY, ARM SWELLING, BREAST CANCER, STRENGTH TRAINING, CARDIOVASCULAR FITNESS

Breast cancer–related lymphedema is estimated to occur in 21% of survivors (9). This potentially chronic condition results after an alteration to the lymphatic system due to cancer and its associated treatments. In early stages, lymphedema is predominantly characterized by an increase in interstitial fluid, with changes in composition, such as deposition of adipose and fibrotic tissues, reflecting lymphedema progression (13). The presence of lymphedema is typically associated with a range of additional adverse symptoms such as swelling, heaviness, and pain (27); physiological and psychosocial effects, including impaired immune function (15), distress, depression, anxiety, and social inhibition; and decreased quality of life (23). A compelling body of research clearly demonstrates that participation in regular exercise is an effective approach to counteract cancer-related morbidity and to improve function and quality of life (11,33), and it may also improve survival (18,24). However, its role in lymphedema prevention or management is less well defined.

In the past, women considered at risk of, as well as with confirmed, lymphedema postbreast cancer were advised to limit physical activity and use of the affected arm (26). This recommendation was based on the premise that use or overuse would increase lymph load and therefore increase one’s risk of developing or exacerbating the condition. However, evidence from cohort studies suggested that physical inactivity (rather than regular physical activity) increased upper-body impairments, including lymphedema (30,32). There is also new evidence available from several trials (14,38), including one large randomized controlled trial (31), which supports progressive, initially supervised exercise as safe, and potentially beneficial, for lymphedema.

To date, the focus of exercise interventions evaluated in lymphedema cohorts has been resistance-based exercise (either alone or in combination with aerobic-based exercise). This may be because skeletal muscle pumping stimulates
lymph flow (12), and resistance-based exercise is the most effective exercise mode for training the muscular system. However, lymph flow is also supported via the cardiovascular system through blood circulation (21) and respiration, which compresses and decompresses the abdominal cavity (25), stimulating lymph flow back to the heart. The optimal exercise mode for training the cardiorespiratory system is aerobic-based exercise. Therefore, depending on the importance of the musculoskeletal versus cardiorespiratory systems in aiding the lymphatic system, it is plausible that resistance- and aerobic-based exercises could have different effects on lymphedema.

Gaining a greater understanding of how each exercise mode affects lymphedema, as well as other health-related outcomes, such as fitness and quality of life, will improve exercise prescription guidelines relevant to this specific breast cancer cohort. Therefore, the purpose of this work was to compare the effects of resistance- and aerobic-based exercises on breast cancer–related lymphedema, as well as aerobic and muscular fitness, body composition, upper-body function, and quality of life.

METHODS

Subjects

Eligible participants were females 18 yr and older with a history of nonmetastatic breast cancer; had completed breast cancer treatment, except hormone therapy/aromatase inhibitors; had a clinical diagnosis of unilateral upper-limb lymphedema; had no medical conditions that would limit exercise participation; and had not undertaken more than 75 min of moderate- to vigorous-intensity resistance- and/or aerobic-based exercise per week in the past 3 months (equivalent of ≤50% of intervention exercise prescription). Baseline exercise was assessed during an initial telephone interview with the potential participant, used to assess eligibility. Women were asked about their typical activity levels, both planned (exercise) and incidental (general physical activity). Follow-up questions were used as needed to get a clear picture of what activity each woman was doing, how often and regularly, and what intensity this was typically at. On the basis of this conversation, exclusions were made for women who reported exercise levels exceeding 75 min of moderate- to vigorous-intensity resistance- and/or aerobic-based exercise per week in the past 3 months, with no exclusion criteria for general physical activity. It must be highlighted that exercise participation was tracked separately from physical activity participation (which included exercise), using the Active Australia survey (3), with no exclusion criteria related to overall physical activity levels. Exclusions were made for those with lymphedema restricted to the breast or trunk and unstable lymphedema, defined as follows: 1) needing intensive lymphedema therapy within 3 months before study entry, 2) experiencing a lymphedema-related infection requiring use of antibiotics within 3 months before study entry, or 3) requiring a notable change in activities of daily living due to exacerbation of lymphedema within 3 months before study entry (31).

Potential participants were recruited from private and hospital-based physiotherapy and occupational therapy practices that provide lymphedema treatment, via local lymphedema groups, and a preexisting database of women with lymphedema interested in being informed of future research studies, held at the Queensland University of Technology. After a telephone screening, eligible participants were sent a survey collecting information on demographic, medical, and lymphedema-related variables, as well as self-report outcome measures, to be completed and returned at baseline assessment. Written informed consent was obtained from all participants, and ethical approval for this study was obtained from the Research Ethics Unit at the Queensland University of Technology (approval no. 1300000103) and Metro South Human Research Ethics Committee, Brisbane, Australia (approval no. HREC/13/QPAH/306).

Study design. This study was a randomized two-group exercise trial comparing the effect of participation in resistance- versus aerobic-based exercise with a 1:1 allocation. Baseline, postintervention (12 wk), and 12-wk follow-up (24 wk) assessments were conducted at Queensland University of Technology, Brisbane, Australia. Supervised, one-on-one exercise sessions were conducted at the participant’s home or other participant-selected location (e.g., local fitness center or park). Participants were randomly allocated (computer-generated numbers) to a resistance- or aerobic-based exercise group using a stratified, blocked (blocks of two) approach. Stratification was based on the stage of lymphedema (stage 0/1 or stage 2/3). The same researcher completed randomization, assessments, and exercise sessions.

Intervention. The exercise interventions used in this study were based on a program previously developed for use in a large-scale randomized controlled trial involving women with breast cancer–related lymphedema (31). To ascertain equivalence in exertion between the two groups, METs of tasks were used to quantify exercise amount, and the revised Borg RPE scale was used to prescribe and monitor intensity. Participants in both groups were instructed to undertake 150 min of supervised and unsupervised exercise (resistance or aerobic based) each week (Table 1), at a MET level of 3 to 3.5 (weeks 1–6), increasing to 5 in weeks 7–12.

All exercise sessions included a 5-min warm-up and cooldown period, incorporating light aerobic-based exercise and stretching. The resistance-based exercise group completed a full-body strength training program, including chest fly, triceps kickback, squat, curl ups, bent-over row, bridging, wall push-up, bicep curls, calf raises, shoulder press, external rotation, and forward lunge. The initial six exercises were introduced during week 1, with one new exercise introduced weekly, for a total of 12 exercises by week 7. Free weight exercises were initially performed using weights of less than 1.5 kg. For weeks 1–4, participants performed two sets of 10–12 repetitions, with weight increased once the
participant was able to complete the assigned number of sets and repetitions. Weight increase was based on what was needed to maintain an RPE of 11–13 so as to achieve a MET level of 3–3.5. For weeks 5–12, participants performed two sets of 8–10 repetitions, with weight increased once participants correctly and safely performed assigned sets and repetitions, so as to maintain an RPE of 12–14 and MET level of 5. For those in the aerobic-based exercise group, a range of exercises were permissible (e.g., walking/jogging, cycling, and swimming) depending on personal preference and ability and available resources. To ensure supervision remained constant, the researcher participated in sessions when necessary (e.g., cycling and walking), ensuring that pace was maintained as needed to reach the desired intensity. Aerobic exercise was progressed throughout the 12-wk intervention to maintain the same intensity and MET level as undertaken by the resistance-based exercise group. Women in both groups were instructed to maintain their normal lymphedema management (e.g., manual lymphatic drainage and compression garment) during the 24-wk study timeframe. In addition, participants decided whether they wore a compression garment during exercise from prior advice given by their lymphedema therapist or personal preference.

**Outcomes. Primary outcome.** Lymphedema status was assessed using two objective measures, specifically bio-impedance spectroscopy (BIS) and circumference measurements, and via self-report. Multifrequency BIS (SFB7; ImpediMed, Brisbane, Australia) measures the impedance of extracellular fluid. When the impedance ratio between the untreated and the treated sides is 3 SD or more from the normative mean, lymphedema is diagnosed (39). Circumference measures were assessed according to the Australasian Lymphedema Association’s national standards (4), with modification made to distance between measurements (5 cm rather than standard 10 cm). Circumference measurements were then used to determine interlimb difference in percentage ([affected arm total circumference − unaffected arm total circumference] / unaffected arm total), with an interlimb difference of ≥5% considered clinically relevant (15). The validated Norman lymphedema survey was used as the self-report assessment of upper-limb lymphedema and was used to collect information on the frequency and severity of 14 lymphedema-associated symptoms (including swelling and pain) for the past 3 months (28). Participants were asked whether they experienced any lymphedema symptoms and, if yes, the severity and frequency of these symptoms. A clinically significant change was defined as a shift of one unit in overall number or severity of symptoms (31). The stage of lymphedema was determined using the International Society of Lymphology scale, ranking lymphedema from stage 0 to stage 3 based on clinical presentation, which takes into account whether the lymphedema is pitting or nonpitting (non-pitting lymphedema denotes lymphedema characterized by deposition of fatty tissue and fibrosis, rather than excess extracellular fluid) (19).

**Secondary outcomes.** Lower-body muscular endurance was assessed using a squat test. Participants completed as many body weight squats (i.e., no additional weight held) as possible, until fatigue or when correct form could no longer be maintained. Upper-body muscular strength was assessed in three ways: a 4– to 6-repetition maximum bench press (using an initial 10-kg bar with 2.5- or 5-kg weight progression based on ease of performance) (20) and two isometric tests using a shoulder and arm dynamometer (100 kg; TTM, Tokyo) and a handgrip dynamometer (100 kg, Smedley’s, TTM) (6). Aerobic fitness was assessed using the 6-min walk test, based on guidelines of the American Thoracic Society (2). Dual-energy x-ray absorptiometry was used to measure body composition (fat and lean mass) using a Lunar Prodigy Advance (GE Healthcare, Wisconsin, USA) and the same analysis software (enCORETM 2011 Version 13.6; GE Healthcare, Wisconsin, USA) for all testing. A total body scanning mode was used, with two partial scans conducted and results combined for participants that exceeded the scanning width (37). Self-reported upper-body functioning was assessed using the Disabilities of the Arm, Shoulder and Hand questionnaire (5), whereas quality of life was measured using the Functional Assessment of Cancer
Therapy-Breast + 4 (FACT-B + 4) (8). Program adherence and reasons for missed sessions were also recorded using exercise logs for supervised and unsupervised exercise sessions.

Statistical analysis. Continuous variables were approximately normal and were therefore described using mean and 95% confidence intervals (CI), and categorical variables were described using proportions and n values. Data were analyzed on an intention-to-treat basis, regardless of intervention compliance. To incorporate the longitudinal nature of the data, generalized estimating equation models with an independent working correlation structure were used. Between-group analyses included comparing change from baseline to 12 wk, baseline to 24 wk, and 12 wk to 24 wk in the resistance- versus aerobic-based exercise groups. Within-group analyses assessed change over time. Statistical significance level was set at $P < 0.05$, and analyses were performed using Microsoft Excel and IBM SPSS statistics version 21.0 software.

Sample size calculations were based on a primary alternative hypothesis: greater benefits in lymphedema will be observed in participants in the resistance-based exercise group compared with the aerobic-based exercise group by 24 wk. A clinically relevant between-group difference was defined as $\geq 0.2$ units difference in the impedance ratio for BIS or a change of $\geq 5\%$ interlimb difference for circumference measurements (13, 26). Calculations, based on 80% power, allowing for a combined 20% attrition and noncompliance rate, suggested a total sample size of 40 was needed to detect clinically relevant differences in BIS or circumference change.

RESULTS

Group Characteristics

From the 103 women assessed for eligibility, 45 women enrolled in the study and 41 completed baseline assessment,
TABLE 2. Baseline demographic, medical, and lymphedema-related characteristics.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Overall (n = 41)</th>
<th>RES (n = 20)</th>
<th>AER (n = 21)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (95% CI), yr</td>
<td>56.0 (52.8–59.2)</td>
<td>58.5 (54.2–62.8)</td>
<td>53.7 (48.9–58.5)</td>
</tr>
<tr>
<td>Employment status</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not working</td>
<td>17 (41.5)</td>
<td>9 (45.0)</td>
<td>8 (38.1)</td>
</tr>
<tr>
<td>Paid employment</td>
<td>24 (58.5)</td>
<td>11 (55.0)</td>
<td>13 (61.9)</td>
</tr>
<tr>
<td>Education</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High school only</td>
<td>13 (31.7)</td>
<td>6 (30.0)</td>
<td>7 (33.3)</td>
</tr>
<tr>
<td>Undergraduate degree</td>
<td>11 (26.8)</td>
<td>6 (30.0)</td>
<td>5 (23.8)</td>
</tr>
<tr>
<td>Postgraduate</td>
<td>7 (17.1)</td>
<td>2 (10.0)</td>
<td>5 (23.8)</td>
</tr>
<tr>
<td>Further study (other)</td>
<td>10 (24.4)</td>
<td>6 (30.0)</td>
<td>4 (19.0)</td>
</tr>
<tr>
<td>Total physical activity*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sedentary</td>
<td>5 (12.2)</td>
<td>3 (15.0)</td>
<td>2 (9.5)</td>
</tr>
<tr>
<td>Insufficient</td>
<td>16 (39.0)</td>
<td>9 (45.0)</td>
<td>7 (33.3)</td>
</tr>
<tr>
<td>Sufficient</td>
<td>20 (48.6)</td>
<td>8 (40.0)</td>
<td>12 (57.1)</td>
</tr>
<tr>
<td>Body mass index, mean (95% CI), kg m⁻²</td>
<td>29 (27–32)</td>
<td>30 (26–33)</td>
<td>29 (26–32)</td>
</tr>
<tr>
<td>Months post-BC diagnosis, mean (95% CI)</td>
<td>56 (43–70)</td>
<td>57 (38–76)</td>
<td>56 (35–77)</td>
</tr>
<tr>
<td>Adjuvant treatment (yes)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chemotherapy</td>
<td>38 (92.7)</td>
<td>19 (95.0)</td>
<td>19 (90.5)</td>
</tr>
<tr>
<td>Radiation therapy</td>
<td>36 (87.8)</td>
<td>18 (90.0)</td>
<td>18 (85.7)</td>
</tr>
<tr>
<td>Hormone therapy</td>
<td>24 (58.5)</td>
<td>13 (65.0)</td>
<td>11 (52.4)</td>
</tr>
<tr>
<td>Comorbidities⁶</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>4 (9.8)</td>
<td>1 (5.0)</td>
<td>3 (14.3)</td>
</tr>
<tr>
<td>1–3</td>
<td>27 (65.9)</td>
<td>14 (70.0)</td>
<td>13 (61.9)</td>
</tr>
<tr>
<td>3–3</td>
<td>10 (24.4)</td>
<td>5 (25.0)</td>
<td>5 (23.8)</td>
</tr>
<tr>
<td>Stage of lymphedema</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>22 (53.7)</td>
<td>11 (55.0)</td>
<td>11 (52.4)</td>
</tr>
<tr>
<td>2</td>
<td>19 (46.3)</td>
<td>9 (45.0)</td>
<td>10 (47.6)</td>
</tr>
<tr>
<td>Time with lymphedema</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Months, mean (95% CI)</td>
<td>39 (28–51)</td>
<td>41 (25–58)</td>
<td>38 (20–55)</td>
</tr>
<tr>
<td>Lymph node removal</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sentinel node biopsy only</td>
<td>20 (48.8)</td>
<td>8 (40.0)</td>
<td>12 (57.1)</td>
</tr>
<tr>
<td>Axillary node dissection</td>
<td>19 (46.3)</td>
<td>11 (55.0)</td>
<td>8 (38.1)</td>
</tr>
<tr>
<td>No lymph nodes removed</td>
<td>2 (4.9)</td>
<td>1 (5.0)</td>
<td>1 (4.8)</td>
</tr>
<tr>
<td>Lymphedema on dominant side</td>
<td>17 (41.5)</td>
<td>8 (40.0)</td>
<td>9 (42.9)</td>
</tr>
<tr>
<td>Lymphedema presentation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Recurrent/fluuctuates²</td>
<td>15 (36.6)</td>
<td>5 (25.0)</td>
<td>10 (47.6)</td>
</tr>
<tr>
<td>Garment use during exercise</td>
<td>15 (36.6)</td>
<td>6 (30.0)</td>
<td>9 (42.9)</td>
</tr>
</tbody>
</table>

Values are presented as n (%), unless otherwise indicated.

RES, resistance-based exercise group; AER, aerobic-based exercise group; BC, breast cancer.

⁶Based on Active Australia survey; included exercise, as well as participation in physical activity other than exercise; sedentary (no physical activity), insufficient (<150 min or ≥150 min and less than five sessions), and sufficient (>150 min and five sessions or more).

⁷Comorbidities = heart attack, angina, other heart problems, high blood pressure, high cholesterol, stroke, diabetes, asthma, chronic bronchitis, emphysema, stomach or duodenal ulcers, migraine, osteoporosis, rheumatoid arthritis, depression, cancer besides breast, and other medical conditions.

⁸Remaining participants ‘stable and persistent.’

with common reasons for not participating outlined in Figure 1. Three participants in the aerobic-based exercise group dropped out after baseline testing and randomization, with two of these women completing data collection assessments and therefore included in intention-to-treat analyses.

Personal (age, living arrangement, education, and health insurance), medical (months after breast cancer and cancer treatment), and lymphedema-related characteristics (time, location, presentation, who diagnosed, and routine treatment) of study participants (n = 41) were similar to those who were unable to participate (n = 23) (data not shown). The resistance- and aerobic-based exercise groups also reported similar characteristics at baseline (Table 2). There were clinically relevant differences in baseline physical activity levels (which included exercise, as well as participation in physical activity other than exercise) between groups, whereby 40% of participants in the resistance-based exercise group self-reported sufficient activity levels, compared with 57% in the aerobic-based exercise group. In addition, one in four women in the resistance-based exercise group reported recurrent/fluuctuating lymphedema (i.e., mild changes in subjective swelling or other symptoms but not meeting criteria of “clinically unstable” previously defined [31]), compared with one in two in the aerobic-based exercise group.

Overall, 35 women (92%) completed 75% or more of supervised exercise sessions. The remaining three participants had rates of 50% (resistance-based exercise group), 56%, and 69% (aerobic-based exercise group), with lower adherence of these participants attributable to non-study-related injury, family illness requiring travel, or work commitments. Median adherence to exercise during the 12-wk follow-up period (period from the 12- to 24-wk assessment) was equivalent between groups, and indicated participants typically achieved 150 min or more of weekly moderate- to vigorous-intensity exercise.

Changes in lymphedema status. Overall, the interaction effect between time and group was not statistically significant for lymphedema status or associated symptoms, demonstrating that there were no differences between groups or over time in lymphedema or lymphedema-associated symptoms (Table 3). However, the aerobic-based exercise group reported a clinically meaningful decline in the number
of lymphedema-related symptoms from baseline to 12 wk (−1.5, 95% CI = −2.6 to −0.4). There was a trend for symptom severity declines in both groups by 12 wk. Intrarater reliability for circumference measures (correlation) was high, with $r = 0.97$.

### Changes in objectively measured outcomes.

There was a significant time–group effect for upper-body strength (Table 4); both groups showed improvements in upper-body strength over time, although improvements were greater in the resistance-based exercise group compared with the aerobic-based exercise group (5.1 kg, 95% CI = 3.8–6.4, vs 1.7 kg, 95% CI = 0.9–2.5, respectively; $P < 0.01$). Clinically meaningful increases were observed in both groups for lower-body endurance (more than nine squats) between baseline and 24 wk for the resistance-based exercise group (12.4, 95% CI = 9.6–19.7, and 14.0, 95% CI = 7.3–20.6, respectively). Clinically meaningful within-group improvements were also observed on multiple FACT-B + 4 subscales, with increases in physical well-being reported by the resistance- and aerobic-based exercise groups, and increases in the breast cancer subscale observed in the aerobic-based exercise group (data not shown for remaining subscales).

### Lymphedema symptoms.

Increased swelling, heaviness, and/or aching were reported by the majority of participants during the 12-wk intervention (72%), which they attributed to hot, humid weather (majority of intervention was conducted during summer months). Three women reported increased swelling and/or aching attributed to stress and fatigue (not exercise related), with no change in lymphedema treatment. Two women reported increased swelling after flights and increased garment use ($n = 2$) and self-massage

![Table 4](image-url)

**Table 4. Secondary objective outcomes at baseline, 12 wk, and 24 wk.**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Baseline (T1)</th>
<th>12 wk (T2)</th>
<th>24 wk (T3)</th>
<th>$P$</th>
<th>ΔT2 – T1 scores</th>
<th>ΔT3 – T1 scores</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean (95% CI)</td>
<td>Mean (95% CI)</td>
<td>Mean (95% CI)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aerobic fitness (6MWT, m)</td>
<td>529.3 (489.4 to 567.2)</td>
<td>542.8 (504.3 to 581.2)</td>
<td>562.9 (529.4 to 596.4)</td>
<td>0.02</td>
<td>14.4 (13.2 to 20.2)</td>
<td>34.6 (10.4 to 58.8)</td>
</tr>
<tr>
<td>RES</td>
<td>554.4 (514.6 to 594.1)</td>
<td>542.8 (504.3 to 581.2)</td>
<td>581.3 (540.1 to 622.5)</td>
<td>0.01</td>
<td>14.7 (8.1 to 23.6)</td>
<td>26.9 (3.1 to 50.7)</td>
</tr>
<tr>
<td>Lower body endurance (no. squats)</td>
<td>23.7 (18.0 to 29.3)</td>
<td>33.1 (24.4 to 41.7)</td>
<td>36.1 (26.2 to 45.9)</td>
<td>0.75</td>
<td>9.4 (1.7 to 17.0)</td>
<td>12.4 (3.4 to 21.4)</td>
</tr>
<tr>
<td>RES</td>
<td>33.6 (24.0 to 43.3)</td>
<td>43.0 (27.4 to 58.6)</td>
<td>42.5 (23.8 to 61.2)</td>
<td>0.01</td>
<td>9.4 (0.3 to 18.4)</td>
<td>8.9 (3.5 to 21.2)</td>
</tr>
<tr>
<td>Upper body strength (4–6RM, kg)</td>
<td>16.3 (14.9 to 17.7)</td>
<td>20.6 (19.1 to 22.0)</td>
<td>21.4 (19.9 to 22.9)</td>
<td>&gt;0.01</td>
<td>4.2 (3.2 to 5.2)</td>
<td>5.1 (3.8 to 6.4)</td>
</tr>
<tr>
<td>RES</td>
<td>17.3 (15.5 to 19.0)</td>
<td>18.5 (17.0 to 20.0)</td>
<td>18.9 (17.5 to 20.4)</td>
<td>0.25</td>
<td>1.2 (0.1 to 2.5)</td>
<td>1.7 (0.9 to 2.5)</td>
</tr>
<tr>
<td>Body fat (%)</td>
<td>45.0 (40.2 to 49.9)</td>
<td>45.3 (41.1 to 50.0)</td>
<td>45.2 (40.9 to 48.6)</td>
<td>0.94</td>
<td>0.5 (0.1 to 1.1)</td>
<td>0.2 (1.2 to 1.7)</td>
</tr>
<tr>
<td>RES</td>
<td>44.9 (42.0 to 47.8)</td>
<td>45.4 (42.7 to 48.2)</td>
<td>45.5 (42.8 to 48.1)</td>
<td>0.69</td>
<td>0.3 (0.2 to 0.7)</td>
<td>0.4 (1.3 to 0.4)</td>
</tr>
<tr>
<td>Lean body mass (kg)</td>
<td>40.6 (38.4 to 42.9)</td>
<td>40.9 (38.5 to 43.3)</td>
<td>40.2 (37.9 to 42.5)</td>
<td></td>
<td>0.6 (0.3 to 1.1)</td>
<td>0.4 (1.3 to 0.6)</td>
</tr>
<tr>
<td>RES</td>
<td>39.8 (37.6 to 42.1)</td>
<td>40.4 (38.1 to 42.7)</td>
<td>39.5 (37.4 to 41.5)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

RES, resistance-based exercise group; AER, aerobic-based exercise group; 6MWT, 6-min walk test; RM, repetition maximum.

* $P < 0.05$.
TABLE 5. Secondary self-report outcomes at baseline, 12 wk, and 24 wk.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Baseline (T1)</th>
<th>12 wk (T2)</th>
<th>24 wk (T3)</th>
<th>ΔT2 — T1 scores</th>
<th>ΔT3 — T1 scores</th>
</tr>
</thead>
<tbody>
<tr>
<td>Upper-body function (DASH)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RES</td>
<td>18.8 (12.4 to 25.1)</td>
<td>15.6 (8.3 to 22.9)</td>
<td>15.2 (8.9 to 21.5)</td>
<td>0.50</td>
<td>-3.2 (-6.7 to 0.3)</td>
</tr>
<tr>
<td>AER</td>
<td>17.8 (10.7 to 24.9)</td>
<td>12.3 (6.8 to 17.8)</td>
<td>14.8 (8.1 to 21.6)</td>
<td>-5.5 (-11.1 to 0.2)</td>
<td>-3.6 (-6.9 to -0.2)</td>
</tr>
<tr>
<td>QoL (FACT-B + 4) total</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RES</td>
<td>97.2 (88.8 to 105.6)</td>
<td>107.2 (97.9 to 116.5)</td>
<td>111.8 (102.6 to 121.1)</td>
<td>0.54</td>
<td>10.0 (6.2 to 13.9)</td>
</tr>
<tr>
<td>AER</td>
<td>104.4 (96.5 to 112.3)</td>
<td>117.6 (108.9 to 126.2)</td>
<td>118.4 (108.4 to 128.3)</td>
<td>13.2 (6.7 to 19.7)</td>
<td>14.0 (7.3 to 20.6)</td>
</tr>
<tr>
<td>Physical well-being</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RES</td>
<td>15.5 (13.9 to 17.0)</td>
<td>23.8 (22.2 to 25.4)</td>
<td>23.5 (21.7 to 25.3)</td>
<td>0.98</td>
<td>8.3 (7.1 to 9.5)</td>
</tr>
<tr>
<td>AER</td>
<td>15.7 (14.0 to 17.3)</td>
<td>24.1 (22.3 to 25.8)</td>
<td>23.6 (21.1 to 26.1)</td>
<td>8.4 (6.7 to 10.1)</td>
<td>8.0 (5.7 to 10.2)</td>
</tr>
<tr>
<td>Breast cancer subscale</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RES</td>
<td>22.2 (19.1 to 25.2)</td>
<td>22.6 (19.3 to 25.9)</td>
<td>24.6 (21.3 to 27.9)</td>
<td>0.36</td>
<td>0.4 (-1.3 to 2.2)</td>
</tr>
<tr>
<td>AER</td>
<td>25.1 (21.9 to 28.3)</td>
<td>27.7 (24.7 to 30.7)</td>
<td>28.5 (25.8 to 31.3)</td>
<td>2.6 (0.0 to 5.3)</td>
<td>3.4 (0.2 to 6.5)</td>
</tr>
</tbody>
</table>

RES, resistance-based exercise group; AER, aerobic-based exercise group; DASH, Disabilities of the Arm, Shoulder, and Hand; QoL, quality of life.

(n = 1) as a result. No increase of lymphedema-related symptoms was directly attributed to exercise participation.

DISCUSSION

Neither resistance- nor aerobic-based exercise significantly improved objective lymphedema status. There was a trend for the aerobic-based exercise group to report fewer lymphedema-related symptoms after the intervention, with this trend not observed in the resistance-based exercise group. Conversely, resistance-based exercise was associated with significantly greater improvements in upper-body strength, with this change not observed in the aerobic-based group. Both resistance- and aerobic-based exercise modes led to equivalent improvements in muscular endurance, aerobic fitness, and quality of life. Improvements were primarily maintained during the 12-wk unsupervised follow-up period. No exercise-related adverse events or lymphedema exacerbations were reported during the trial or follow-up.

Results from this trial suggest that although resistance- or aerobic-based exercise does not improve objectively measured lymphedema, it may play a role in prevention of progression and reduction in number and/or severity of symptoms.

These findings are consistent with the larger Physical Activity and Lymphedema trial, where women reported a significant reduction in number of symptoms after a 12-month exercise intervention, compared with usual care (31). On the basis of our results, however, declines in lymphedema-associated symptoms (either number or severity) can occur within 12 wk of commencing regular resistance- or aerobic-based exercise. This is clearly relevant to those with lymphedema, as past research suggests changes in symptoms may be equally important to, and possibly more important than, changes in objective lymphedema measurements (10).

Improvements in muscular strength and endurance and aerobic fitness were observed in the resistance- and/or aerobic-based exercise groups, with no change in body composition seen in either group. Strength improvements are consistent with findings reported by others after low- and high-load strength training (n = 62) (7), as well as 6 months (1) and 12 months (31) of progressive resistance-based exercise.

However, our study is the first to assess muscular strength and endurance, and aerobic fitness outcomes in women with breast cancer–related lymphedema after participation in an aerobic-only exercise intervention. Although previous studies that compared resistance- and aerobic-based exercises also suggest both exercise modes (34,40) may produce clinically meaningful improvements in aerobic fitness, they did not involve women with breast cancer–related lymphedema. Strength and fitness declines are common after breast cancer (16), and in particular those with breast cancer–related lymphedema (35). Thus, these findings are particularly relevant and suggest that women can expect improvements in subjective lymphedema and functional well-being after participation in either resistance- or aerobic-based exercise.

In contrast to our objective upper-body function findings, there was no clinically meaningful change observed in self-reported upper-body function (Disabilities of the Arm, Shoulder and Hand questionnaire) after participation in the resistance- or aerobic-based exercise intervention. Conversely, both exercise groups reported clinically relevant improvements in overall quality of life (FACT-B + 4; ≥7). Minimal improvement in upper-body function may have been due to high upper-body function at baseline, leaving little room for improvements. Similar to previous research (7,22), changes in the physical well-being domain drove quality-of-life improvements in both groups. This suggests quality-of-life benefits from exercise may be primarily related to improvements in physical issues such as lack of energy, feeling ill, or nausea. Resistance- and aerobic-based exercises appear useful to counteract quality-of-life and upper-body functioning declines common in breast cancer survivors with lymphedema (23).

Intervention adherence was high, with 92% of participants attending 75% or more of supervised sessions, similar or higher to rates in other exercise interventions involving women with breast cancer–related lymphedema (7,31). However, the finding that six participants reported follow-up adherence levels of 50% or less highlights that some individuals may need continued or more gradual decline in supervision (e.g., drop to once every fortnight then once every month), or peer encouragement, to increase their self-efficacy to exercise and move into the “maintenance”
stage of behavior change (29). Maximizing exercise adherence is necessary if it is to form an effective long-term treatment strategy for lymphedema. The findings from our study suggest that the majority of women were able to maintain fitness and quality-of-life gains from an initially supervised component, benefits that may be available for all women if adherence barriers are individually addressed.

Interpretation of findings must consider several limitations. The main limitation of this work was the absence of a control group, which would have allowed assessment of potential bias due to concomitant lymphedema treatment effects. In addition, it would have provided valuable information on the effects of weather on lymphedema (study primarily conducted during summer, a time when lymphedema is often at its worst) (36). Nonetheless, qualitative comments from participants highlighted that lymphedema was stable during the exercise program, despite ordinarily being unstable (worse) during summer. In addition, although characteristics of participants were similar to individuals who did not participate, it is likely a response bias exists. Only 12% of participants were sedentary at baseline, and the absence of medical conditions that could impede their capability of participating in moderate-intensity exercise was an inclusion criteria. Therefore, it is possible that the intervention effects (positive or negative) on the outcomes measured in this study were difficult to observe. The lack of blinding during randomization, assessments, and supervised exercise sessions (all conducted by the same researcher) is another limitation of this study. However, uniformity in assessments and intervention conduct, as well as inclusion of objectively assessed outcomes, minimized potential bias introduced by nonblinding.

Strengths of this study included a comprehensive objective and subjective assessment of lymphedema, making findings relevant to women with early- or later-stage lymphedema (although of note, all but one woman in the study had interlimb difference of <20%). Further, evaluation of a wide variety of patient-relevant physical and psychosocial health outcomes were also included and intention-to-treat analysis (which was adequately powered for the primary outcome) was undertaken. Further, the study included a 12-wk unsupervised follow-up period, providing valuable information on longer-term exercise uptake and self-maintenance.

In conclusion, no statistically significant or clinically relevant differences in objectively measured lymphedema were found between resistance- and aerobic-based exercises. In addition, both modes produced improvements in muscular and aerobic fitness and quality of life, even in a cohort with 49% of participants reporting sufficient physical activity levels at baseline. As each woman diagnosed with breast cancer has different survivorship concerns (e.g., strength loss and reduced quality of life), the results of this study suggest that at least in the clinical setting, the prescription of exercise mode can be individualized toward improving specific physiologic concerns, without adversely affecting lymphedema. Once this foundation is established, programs can be modified to optimize a woman’s recovery and longer-term function, health, quality of life, and survival. In the research setting, these findings can be used to guide the development of exercise interventions to be evaluated in an effectiveness trial or as part of dissemination research.

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