Title
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Journal
Breast Cancer Research and Treatment, 148(2)

ISSN
0167-6806

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Publication Date
2014-11-01

DOI
10.1007/s10549-014-3171-8

Peer reviewed

Breast Cancer Res Treat (2014) 148:445–453
DOI 10.1007/s10549-014-3171-8

BRIEF REPORT

Upper extremity bioimpedance before and after treadmill testing in women post breast cancer treatment

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Received: 16 August 2014 / Accepted: 13 October 2014 / Published online: 22 October 2014

Abstract Research on the effect of cardiorespiratory (CR) exercise on upper extremity (UE) limb volume is limited in women with breast cancer-related lymphedema (BCRL). The aim of this study was to compare changes in UE volume immediately following a symptom-limited CR treadmill test in women with and without BCRL. As part of a cross-sectional study, 133 women post unilateral BC treatment completed symptom-limited treadmill testing. Bioimpedance spectroscopy (BIS) was used to measure UE resistance before and immediately following treadmill testing. Resistance ratios >1 (unaffected side/affected side) indicate greater volume in the affected limb. T-tests and repeated measures ANOVA were performed to evaluate differences between and within groups. Mean age was 56.2 years (SD 9.4); BMI was 26.13 kg m^{-2} (SD 5.04). For women with previously diagnosed BCRL ($n = 63$), the resistance ratio was 1.116 (SD 0.160) pre-treadmill and 1.108 (SD 0.155) post-treadmill. For women without BCRL ($n = 70$), the resistance ratio was 0.990 (SD 0.041) pre-treadmill and 1.001 (SD 0.044) post-treadmill. Resistance ratios for women with BCRL were higher than those for women without BCRL at both time points (main effect of group: $p < 0.001$). No main effects were found for time ($p = 0.695$). A statistically significant effect was found for the time-by-group interaction ($p = 0.002$). 78 % of the women with BCRL wore a compression garment during testing. Following testing, the women with BCRL demonstrated a non-statistically significant decrease in the resistance ratio, suggesting an immediate decrease in interlimb volume difference. The women without BCRL demonstrated an increase in the resistance ratio.

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Keywords Breast cancer · Lymphedema · Bioimpedance · Cardiorespiratory · Exercise

Introduction

Breast cancer-related lymphedema (BCRL) is the accumulation of interstitial fluid in the breast or upper extremity (UE) as a result of damage to lymph nodes and vessels during breast cancer treatment. This chronic and potentially disabling condition affects more than one in five women treated for breast cancer [1]. Women with BCRL have greater limitations in UE function and self-reported quality of life, as well as lower cardiorespiratory (CR) fitness than women without lymphedema [2–6].

Current recommendations for exercise following breast cancer treatment include gradually progressive resistance exercise and a minimum of 150 min of moderate-intensity or 75 min of vigorous-intensity CR exercise each week [7]. Following breast cancer treatment, women may wish to participate in vigorous CR activities to improve cardiorespiratory fitness. The benefits of exercise during and after cancer treatment in mitigating treatment sequelae [8, 9] and reducing risk of cancer recurrence [10] are well established. Recent evidence supports that gradually progressive UE resistance exercises improve UE strength and function, and are safe for women following breast cancer treatment, including those women with stable UE lymphedema [11, 12]. Moreover, UE resistance exercises may reduce the risk for BCRL in those women without visible evidence of UE swelling [13–16]. Although the evidence is more limited, programs utilizing resistance plus moderate-intensity CR exercises appear safe for women with or at risk for BCRL [16–19]. However, research on the effect of vigorous CR exercise alone (i.e., >80 % of maximal oxygen capacity, VO_2 peak) on UE volume in women with existing BCRL is scarce.

In a randomized controlled trial of women receiving adjuvant chemotherapy for breast cancer, Courneya et al. [20] compared supervised resistance exercise, supervised CR exercise, and usual care in which participants were asked not to begin an exercise program. Participants in the exercise interventions participated in three sessions per week during the period of adjuvant chemotherapy treatment (median duration was 17 weeks, 95 % CI: 9, 24). The CR training intervention consisted of progression from 60 % of maximal oxygen consumption over the first 6 weeks, to 70 % between weeks 7 and 12, to 80 % after week 12, with gradual increase from 15 min in duration to 45 min at week 18 for those still participating at that time. The resistance exercise intervention consisted of two sets of 8–12 repetitions of nine exercises (upper and lower body and trunk) at 60–70 % of their estimated one repetition maximum. Resistance was increased by 10 % when participants completed more than 12 repetitions. Limb volume was assessed with volumetry 1–2 weeks after initiation of chemotherapy (baseline), the midpoint of chemotherapy, and after the intervention (3–4 weeks after the conclusion of chemotherapy). Women were categorized as having lymphedema if they developed >200 ml interlimb volume difference. The percent of women who developed lymphedema after the intervention was 3.7 % in the resistance exercise group, 7.3 % in the control group, and 9.0 % in the CR exercise group. The proportional differences were not statistically significant ($p = 0.381$). However, analyses of the absolute changes in UE volume were not performed, thus the magnitude of change in each group is unknown.

During UE resistance exercises, increased skeletal muscle contraction is thought to improve the lymphatic pumping mechanics and enhance lymph flow in the exercising limb [21]. CR exercises that do not target UE musculature (i.e., walking, jogging, and cycling), therefore, may not provide this same beneficial effect, which could potentially result in excessive fluid accumulation in the UEs, especially for women with impaired UE lymph transport on the side of cancer treatment. The aim of this study, therefore, was to compare UE volume changes, assessed using bioimpedance spectroscopy, in women with BCRL to women without BCRL immediately following a symptom-limited treadmill test (VO_2 peak). We hypothesized that (1) UE volume would increase following treadmill testing, and (2) the affected limb (with lymphedema) would demonstrate the greatest increase in volume compared to the contralateral limb, and to the limbs of the women without lymphedema. Following breast cancer treatment, women demonstrate reduced CR capacity (VO_2 peak) when compared to healthy age-matched norms; women with BCRL have lower CR capacity than the women without BCRL [6]. Since CR fitness has been linked to health outcomes in healthy adults it is essential that health care providers encourage CR exercise with their patients following breast cancer treatment. The results of this study will provide guidance for future randomized clinical trials of vigorous CR exercise training interventions in women post cancer treatment, particularly for women with lymphedema.

Methods

Participants and setting

This was a sub-study of a cross-sectional study that evaluated the impact of BCRL on UE function and overall function [2, 6]. Women were categorized as having or not having BCRL, based on previous diagnosis by a healthcare provider. Women were recruited from the National Lymphedema Network website, San Francisco Bay area hospitals, San Francisco Bay area breast cancer or lymphedema support groups, and breast cancer conferences. Participants were ≥18 years of age, had unilateral breast cancer surgery at least 6 months prior to study enrollment, and were be able to read, speak, and understand English. Participants were excluded if they had current recurrence of breast cancer, current UE infection, lymphangitis, or pre-existing lymphedema. Women were also excluded if they had any absolute contraindications to exercise testing as established by the American College of Cardiology/American Heart Association or the American College of Sports Medicine [22]. All participants attended a single session. Written informed consent was obtained for all participants. This study was approved by the University of California San Francisco (UCSF) Committee on Human

Research and conducted at the UCSF CTSI Clinical Research Center. Women completed a demographic and health status questionnaire.

Cardiorespiratory fitness

Cardiorespiratory fitness was evaluated using symptom-limited treadmill testing. A branching treadmill protocol was used. The participant began walking on the treadmill at a speed determined to be comfortable to them [22]. Exercise intensity was then adjusted by grade (elevation) every 2 min to achieve approximately a 1–2 metabolic equivalent (MET) increment between stages (3.5 ml oxygen per kg body weight per minute—estimated resting oxygen consumption). Exercise intensity was increased until the subject was unable to continue (volitional fatigue) or until there was indication to discontinue the test (i.e., electrocardiographic changes and inappropriate blood pressure response) [22]. A 12-lead electrocardiogram was monitored continuously throughout the test and blood pressure was auscultated at every stage. Ratings of perceived exertion (RPE) were evaluated at the end of each stage (every 2 min) [23]. Oxygen consumption (VO_2) was determined using an open circuit spirometry system (Quinton metabolic cart, Bothell, WA), which was calibrated against known gases before each test. Respiratory gases were analyzed for volume and fractions of oxygen and carbon dioxide, and VO_2 was calculated. Peak VO_2 is expressed in terms relative to body weight (milliliters of oxygen per kilogram of body weight per minute). Maximal oxygen consumption (VO_2 peak) was defined as the highest level of oxygen consumption achieved during the test and was expressed in ml oxygen per kg body weight per minute (ml kg^{-1} min^{-1}). Hemodynamic responses to testing were evaluated at peak exercise levels (i.e., maximal heart rate, maximal blood pressure, and maximal RPE).

Use of compression garment

Consistent with current lymphedema management guidelines [24], women with lymphedema were advised to wear their compression sleeve during the CR treadmill test if that was their usual practice.

Upper extremity volume

Bioimpedance spectroscopy (BIS) was used to evaluate UE volume by assessing the flow of an alternating electrical current over a range of frequencies (4–5 kHz to 1,000 KHz) through body fluids. Resistance measured at low frequencies is a reflection of and inversely correlated to interstitial fluid volume, and can be used as a marker for lymphedema [25]. Resistance ratios are calculated as the resistance of the healthy (unaffected) limb relative to that of the at risk (affected) limb. Higher resistance ratios represent greater volume of the affected limb, relative to the unaffected limb. The Impedimed measurement system (SBF7, Garden City, Australia) was used as described by Cornish et al. [26–28] Electrodes were placed on the dorsum of the hands, wrists, feet, and ankles. The participants were instructed to consume no food or fluids within 1 h, to avoid vigorous exercise within 24 h and to avoid excessive alcohol intake for the 12 h, prior to the study visit. During testing, instructions were given to lie supine for 10 min with no pillows, arms at the sides, and lower extremities flat and slightly abducted. Testing was performed before and immediately following symptom-limited treadmill testing as described above, and two measurements were taken at each time point and averaged to obtain pre- and post-treadmill measurements. Circumferential assessment of the upper extremities was also conducted prior to treadmill testing, using a flexible, non-stretch tape measure, beginning at the ulnar styloid, designated as 0 cm, and at 10 cm intervals proximally to 40 cm. Volume (reported in milliliters) was calculated using the formula for the volume of a truncated cone, $V = 1/12\pi\,\Sigma h\left(C_1^2 + C_1C_2 + C_2^2\right)$,where h is the length of each measured segment and C is the circumference at each end of that segment.

Statistical analysis

Sample size of 120 was calculated a priori, using an alpha of 0.05 and power of 0.80 for the parent BCRL study, based on correlation coefficient of 0.25 for regression analysis. For participant demographic characteristics, means and standard deviations for normally distributed interval data were obtained. Frequencies were determined for nominal and categorical variables. For normally distributed data, paired t tests were performed to evaluate differences in volume before and after treadmill testing. Independent t tests were used to compare outcomes between groups. Analysis of variance (ANOVA) was also performed to evaluate for main effects of time and group and time-by-group interaction. Statistical significance was set at $p < 0.05$. Statistical analyses were performed using SPSS statistical software (version 18, SPSS Inc, Chicago, IL).

Results

One hundred and thirty-three women completed CR fitness testing. 89 % were white and 60 % were working (Table 1). Sixty-three women had been previously diagnosed with lymphedema. None of the women without a prior diagnosis lymphedema demonstrated a greater than 200 ml difference between the affected and unaffected

Table 1 Demographic and clinical characteristics

Characteristics	All participants $N = 133$	Non-lymphedema $N = 70$	Lymphedema $N = 63$	Differences in means (95 % CI)	Sig. (p)[a]
Age (years)	56.27 (9.38)	55.20 (8.82)	57.46 (9.89)	−2.26 (5.47, 0.95)	0.166
BMI (kg m^{-2})	26.13 (5.04)	25.48 (4.65)	26.86 (5.38)	−1.37 (−3.09, 0.35)	0.117
Race, *n* (%)	117 (88.8)	60 (85.7)	57 (90.5)		0.024
White–non Hispanic	10 (7.5)	9 (12.9)	1 (1.6)		
Asian	3 (2.2)	1 (1.4)	2 (3.2)		
Hispanic	3 (2.2)	0	3 (4.7)		
Black					
Dominant hand, *n* (%)	120 (89.6)	64 (91.4)	56 (88.9)		0.880
Right	11 (8.2)	5 (7.1)	6 (9.5)		
Left	2 (1.5)	1 (1.4)	1 (1.6)		
Uses both equally					
Right side affected, *n* (%)	58 (43.3)	28 (40)	30 (47.6)		0.376
Arm volume difference (ml)	90.74 (211.91)	−7.83 (73.14)	200.28 (257.85)	−208.1 (−271.7, −144.5)	<0.001
Years of education	16.66 (2.69)	17.09 (2.47)	16.19 (2.87)	0.895 (−0.021, 1.81)	0.055
Karnofsky score	92.02 (8.42)	92.84 (8.67)	91.13 (8.12)	1.71 (−1.24, 4.64)	0.252
Currently working, *n* (%)	81 (60.4)	40 (57.1)	41 (65.1)		0.402
Exercises on a regular basis, *n* (%)	117 (87.3)	62 (88.6)	55 (87.3)		0.822
Meets ACSM exercise criteria, *n* (%)	46 (34.3)	26 (37.1)	20 (31.7)		0.514
Years since breast cancer diagnosis	6.16 (5.29)	4.92 (4.05)	7.53 (6.14)	−2.62 (−4.38, −0.85)	0.004
Stage of disease at initial cancer diagnosis, *n* (%)	5 (3.8 %)	3 (4.3 %)	2 (3.2 %)		0.646
Stage 0	55 (41.4 %)	32 (45.7 %)	23 (36.5 %)		
Stage 1	61 (45.9 %)	30 (42.9 %)	31 (49.2 %)		
Stage 2	12 (9.0 %)	5 (7.1 %)	7 (11.1 %)		
Stage 3					
Type of breast surgery,	74 (55.2 %)	39 (55.7 %)	35 (55.6 %)		0.985
n (%)	59 (44.4 %)	31 (44.3 %)	28 (44.4 %)		
BCS					
Mastectomy					
Chemotherapy, *n* (%)	91 (67.9 %)	47 (67.1 %)	44 (69.8 %)		0.738
Radiation therapy, *n* (%)	98 (73.1 %)	49 (70.0 %)	49 (77.8 %)		0.309
Radiation to axilla, *n* (%)	32 (23.9 %)	13 (18.6 %)	19 (30.2 %)		0.266
SNB, *n* (%)	86 (64.2 %)	53 (75.7 %)	33 (52.4 %)		0.005
ALND, *n* (%)	99 (73.9 %)	45 (64.3 %)	54 (85.7 %)		0.005
No. of lymph nodes removed	10.60 (7.19)	8.54 (6.46)	12.90 (7.32)	−4.73 (−6.75, −1.99)	<0.001

[a] Independent *t* tests for continuous outcomes, chi^2 for categorical/nominal outcomes

BMI body mass index, *BCS* breast conserving surgery, *SNB* sentinel node biopsy, *ALND* axillary lymph node dissection, *ml* milliliter

limbs (Fig. 1). There was a statistically significant difference in the amount of time since breast cancer diagnosis between the women with lymphedema (7.5 years) and without lymphedema (4.92 years) (−2.62 years, 95 % CI, −4.38, −0.85).

Resistance values and resistance ratios for both UEs from pre- to post-treadmill were compared, as were between group differences in resistance ratio change scores, VO_2 peak, and RPE (Table 2a and b). Reductions in resistance values were seen in both groups in the affected and unaffected limbs ($p < 0.05$). Resistance ratios for the women with BCRL were statistically significantly higher than those for the women without BCRL at both time points ($p < 0.001$). For the women with previously diagnosed BCRL ($n = 63$), resistance ratio pre-treadmill was 1.116 (SD 0.160) and post-treadmill was 1.108 (SD 0.155). This represented a non-statistically significant decrease in the BIS resistance ratio from pre- to post-treadmill

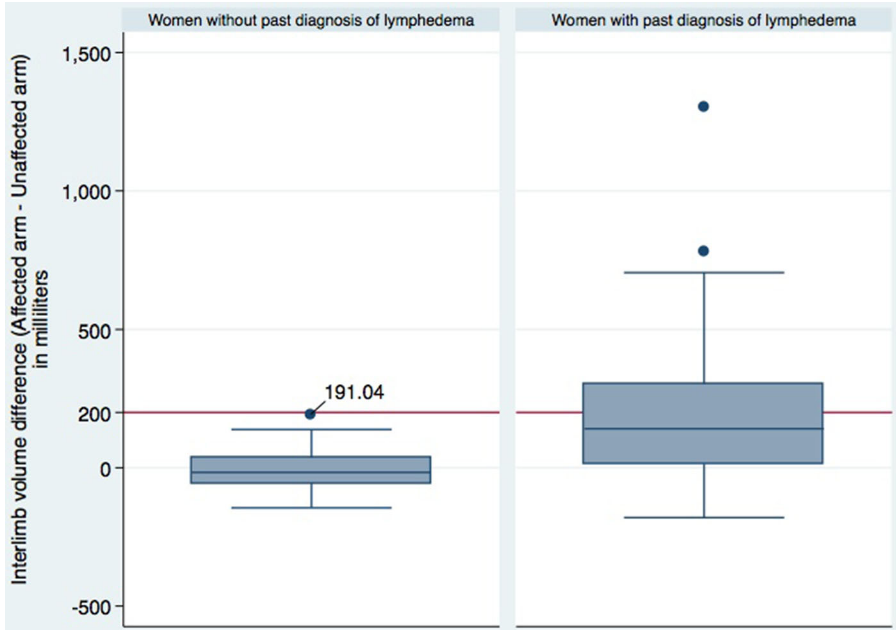

Fig. 1 Differences in interlimb volume in women without and with a past diagnosis of lymphedema

(−0.009, 95 % CI: −0.019, 0.002; $p = 0.097$). For women without BCRL ($n = 70$), pre-treadmill resistance ratio was 0.990 (SD 0.041) and post-treadmill was 1.001 (SD 0.044). This represents a statistically significant increase in the BIS resistance ratio from pre- to post-treadmill (0.011, 95 % CI: 0.004, 0.018; $p = 0.002$). The difference between groups in the change in resistance ratios (−0.009 vs. 0.011) was statistically significant (0.02, 95 % CI: 0.01, 0.03; p = 0.002). ANOVA revealed a statistically significant main effect of group ($p < 0.001$), but not time (0.695). There was a statistically significant group-by-time interaction ($p = 0.002$).

Differences in the change in resistance ratios from pre- to post-treadmill testing between women with BCRL who did ($n = 49$) and did not use compression sleeves ($n = 12$) were not statistically significantly (difference in resistance ratios = 0.026, 95 % CI: −0.0004, 0.051).

Discussion

Our aim was to evaluate and compare changes in UE volume, assessed with bioimpedance spectroscopy, in women with and without BCRL before and immediately after a symptom-limited treadmill test. To our knowledge, this is the first study to do so. As expected, bilateral UE volume increased after the treadmill test in women with and without lymphedema. This was represented as a decrease in bioimpedance resistance values. This finding is consistent with the impact of generalized exercise-induced vasodilation in the UEs, and theoretically reflects increased fluid volume. It was not surprising that the smallest average increase in volume (reflecting the smallest average decrease in resistance) was seen in the unaffected limb of the women without lymphedema. Contrary to our expectations, however, the greatest average increase in volume (reflected by decreased resistance) was seen in the unaffected limb in the women with lymphedema. We hypothesized that the largest increase would be seen in the affected limb in the women with lymphedema. The change in resistance (pre–post-treadmill test) in the affected limbs was similar in both groups. This may be explained in part by the fact that most of the women with lymphedema wore a compression sleeve during the treadmill test (78 %). External support of the limb through compression acts to reduce swelling in lymphedema by limiting blood capillary filtration by elevating interstitial pressure, opposing tissue expansion, and improving the efficiency of the muscle pump in the limb [29]. Our findings suggest a possible benefit from UE compression during the treadmill testing for women with lymphedema; however, because this study evaluated only the immediate change in resistance and after a single symptom-limited treadmill test, the results cannot be generalized to those women with lymphedema participating in ongoing aerobic exercise. Additional studies are needed to formally test and confirm this finding.

Our results support the work of others who found that active exercise while wearing a compression garment reduced affected limb volume in women with unilateral BCRL. Jonsson and Johansson reported results of assessment of a pole-walking regimen in women with BCRL [30, 31]. In their earlier study [30], there was no significant difference in affected limb volume immediately after pole walking or 24 h later compared to baseline. The women

Table 2 Pre–post-treadmill comparisons: (a) all participants and (b) between groups

(a) All participants ($n = 133$)*

	Pre-treadmill	Post-treadmill	Difference pre–post-treadmill (95 % CI)	Significance (p)
BIS (kΩ)				
Unaffected limb	301.93 (40.69)	296.45 (39.93)	5.44 (3.52, 7.36)	<0.001[a]
Affected limb	293.19 (46.51)	286.40 (45.66)	6.80 (5.14, 8.46)	<0.001[a]
BIS resistance ratio				
Unaffected:affected limb	1.0497 (0.12998)	1.0514 (0.1230)	−0.0017 (−0.0079, 0.0045)	0.587[a]
VO_2 peak (ml kg^{-1} min^{-1})		25.55 (6.00)		
Peak heart rate		159.4 (23.3)		
Final RPE (Borg scale 6–20) median (min–max)		18 (12–20)		

(b) Between group comparisons*

	Non-lymphedema group ($n = 70$)				Lymphedema group ($n = 63$)			
	Pre-treadmill	Post-treadmill	Difference pre–post-treadmill (95 % CI)	Significance (p)	Pre-treadmill	Post-treadmill	Difference pre–post-treadmill (95 % CI)	Significance (p)
BIS (kΩ)								
Unaffected limb	303.42 (42.66)	300.00 (42.05)	−3.29 (−0.38, −6.21)	<0.027[a]	299.78 (38.81)	292.16 (37.57)	−7.62 (−5.18, −10.05)	<0.001[a]
Affected limb	308.81 (42.93)	301.73 (41.59)	−6.89 (−4.54, −9.24)	<0.001[a]	277.14 (44.49)	270.51 (44.06)	−6.63 (−4.19, −9.08)	<0.001[a]
BIS resistance ratio								
Unaffected:affected limb	0.990 (0.041)	1.001 (0.044)	0.011 (0.004, 0.018)	0.002	1.116 (0.160)	1.108 (0.155)	−0.009 (−0.019, 0.002)	0.097[a]

	Non-lymphedema group Post-treadmill	Lymphedema group Post-treadmill	Difference between groups (95 % CI)	Significance (p)
Change in BIS resistance ratio	0.011 (0.03)	−0.009 (0.04)	0.02 (0.01, 0.03)	0.002[b]
VO_2 peak (ml kg^{-1} min^{-1})	26.78 (6.58)	24.28 (5.05)	3.57 (0.47, 4.53)	0.016[b]
Peak heart rate	159.5 (20.8)	159.2 (26.0)	0.35 (−7.8, 8.5)	0.931[b]
Final RPE (Borg scale 6–20) median (min–max)	18 (12–20)	18 (12–20)	0	0.987[c]

* Reported as means (SD) unless otherwise noted

[a] Paired samples *t* test

[b] Independent samples *t* test

[c] Independent samples Mann–Whitney *U* test

BIS bioimpedance spectroscopy, *SD* standard deviation, *RPE* rating of perceived exertion, *CI* confidence interval, *VO_2 peak* peak oxygen uptake, expressed in ml oxygen per kg body weight per minutes with lymphedema wore a compression sleeve on the affected UE during the activity. Similar to our study, there was a statistically significant increase in unaffected limb volume immediately after pole walking. In their 2014 study [31], 23 women with unilateral lymphedema participated in an 8 week pole-walking program at 70–80 % of their maximum heart rate. There was a statistically significant reduction in affected limb volume.

A resistance ratio of 1 represents no difference in extracellular fluid volume. As the volume of the affected limb increases, the resistance ratio increases, since the numerator becomes smaller in the resistance ratio calculation. In our study, not surprisingly, women with BCRL had higher average resistance ratios than the women without BCRL both before and after treadmill testing. This is consistent with expectations that the women with BCRL would have greater volume in their affected limb relative to their unaffected limb. In the women without lymphedema, there was a small but statistically significant increase in the average resistance ratio after testing. In contrast, the women with BCRL demonstrated a small and non-significant decrease in resistance ratios. The minimal clinically important difference in bioimpedance resistance values and resistance ratios has not been established, and while the difference in the resistance ratio change scores between groups was small (0.02), it was statistically significant. That we used a continuous measure of volume (bioimpedance resistance and resistance ratios) is a strength of our study. This allowed for greater precision in our estimates of the differences within and between groups.

Limitations

There were important limitations to this study that merit discussion. First, the lymphedema group was determined by prior diagnosis of lymphedema by a health care provider. We were therefore unable to determine the accuracy of that diagnoses. However, between group comparisons of volume differences between those diagnosed with lymphedema and those without support this categorization (Fig. 1). While no women without past diagnosis of lymphedema demonstrated a 200 ml or more difference between limbs, a number of women who had been diagnosed with lymphedema demonstrated volume differences below the 200 ml difference threshold often used to categorize women as having lymphedema [32]. This may be explained, in part, by the fact that many of these women had received education, compression garments, and/or complex decongestive therapy since developing lymphedema.

Duration and degree of lymphedema may influence response to increased lymphatic load. We were not able to report on duration of lymphedema, since date of onset was not systematically recorded. Many women were unable to recall the date of initial lymphedema diagnosis or initiation of lymphedema treatment. Pearson's correlation coefficient was calculated to address the potential association between degree of interlimb volume differences (severity of lymphedema) at baseline, and the changes in resistance ratios following the treadmill test. The correlation was low (−0.0183) and not statistically significant (−0.835).

Most of the women with lymphedema (78 %) wore a compression sleeve during the treadmill test. Differences between those who did and did not wear a sleeve were not statistically significantly different, but this study was not powered for this subgroup analysis. Changes in limb volume in the women with lymphedema were likely influenced by the use of compression garments, and this needs to be considered when comparing volume changes between the women with lymphedema to those without lymphedema, none of whom wore compression garments. We did not attempt to control for the use of compression garments in our analysis. Therefore, those results should be interpreted with caution and clinically meaningful conclusions regarding use of compression garments should not be drawn from those data.

Finally, and importantly, this study examined only the immediate effects of one symptom-limited treadmill test on arm volume in women at risk for or with lymphedema. Therefore, the results cannot be generalized to the cumulative effects of vigorous CR exercise training on UE volume in women with BCRL. The symptom-limited treadmill test is not sustained vigorous activity since grading results in only the last 2–3 min being vigorous (≥80 % VO_2 peak). A single bout of sustained vigorous exercise would be a continuous CR exercise session, ≥20 min at ≥80 % VO_2 peak. Thus, further investigation is needed to substantiate the preliminary findings of this study before recommendations can be made to women regarding the safety of and parameters for sustained vigorous aerobic exercise and its effect on limb volume changes.

Future studies should examine the effects of sustained vigorous CR exercise training on limb volume, utilizing a protocol that includes at least 20 min of vigorous aerobic exercise per session, at least three times per week, over 12 weeks. This protocol is similar to that described by Courneya et al. [20]. Additionally, attention should be paid to the role of compression garments in mitigating volume increases, and continuous measures of volume should be used for greater precision.

Conclusion

Women with BCRL demonstrated lower BIS resistance in their affected limbs, and higher resistance ratios compared to the women without BCRL, both before and after a symptom-limited treadmill test. Women with BCRL also demonstrated a non-statistically significant decrease in the BIS resistance ratio from pre- to post-treadmill, while those without BCRL had a statistically significant increase in the BIS resistance ratio from pre- to post-treadmill.

Cardiorespiratory fitness has been linked to health outcomes in healthy adults; therefore it is essential that health care providers encourage CR exercise with their patients following breast cancer treatment. It is equally important to monitor physical activity with particular attention to women with or at risk for lymphedema. Evidence-based guidelines are needed for exercise prescription and compression garment utilization in women with BCRL, who wish to participate in vigorous CR activities. This study forms the foundation for such investigations by providing evidence that this activity did not appear to be immediately detrimental to UE volume in women with BCRL, and may be beneficial in reducing the volume of the affected limb.

Acknowledgments This research was supported by a grant from the National Institute of Nursing Research (NIH 1R21 NR0101282U) and by NIH/NCRR UCSF-CTSI Grant Number UL1 RR024131. Its contents are solely the responsibility of the author and do not necessarily represent the official views of the National Institutes of Health. Dr. Smoot is partially supported by the Building Interdisciplinary Research Careers in Women's Health (BIRCWH) K12, Grant Number K12HD052163 NICHD/NIH, and by the National Center for Advancing Translational Sciences, National Institutes of Health, through UCSF-CTSI Grant Number KL2TR000143.

Conflict of interest The authors declare that they have no conflict of interest.

Disclosures None.

References

1. DiSipio T, Rye S, Newman B, Hayes S (2013) Incidence of unilateral arm lymphoedema after breast cancer: a systematic review and meta-analysis. Lancet Oncol 14:500–515
2. Smoot B, Wong J, Cooper B, Wanek L, Topp K, Byl N, Dodd M (2010) Upper extremity impairments in women with or without lymphedema following breast cancer treatment. J Cancer Surviv 4:167–178
3. Ridner SH (2005) Quality of life and a symptom cluster associated with breast cancer treatment-related lymphedema. Support Care Cancer 13:904–911
4. Kwan W, Jackson J, Weir LM, Dingee C, McGregor G, Olivotto IA (2002) Chronic arm morbidity after curative breast cancer treatment: prevalence and impact on quality of life. J Clin Oncol 20(20):4242–4248
5. Dawes DJ, Meterissian S, Goldberg M, Mayo NE (2008) Impact of lymphoedema on arm function and health-related quality of life in women following breast cancer surgery. J Rehabil Med 40(8):651–658
6. Smoot B, Johnson M, Duda JJ, Krasnoff J, Dodd M (2012) Cardiorespiratory fitness in women with and without lymphedema following breast cancer treatment. Cancer Clin Oncol 1:21–31
7. Schmitz KH, Courneya KS, Matthews C, Demark-Wahnefried W, Galvao DA, Pinto BM, Irwin ML, Wolin KY, Segal RJ, Lucia A, Schneider CM, von Gruenigen VE, Schwartz AL (2010) American College of Sports Medicine roundtable on exercise guidelines for cancer survivors. Med Sci Sports Exerc 42:1409–1426
8. Battaglini CL, Mills RC, Phillips BL, Lee JT, Story CE, Nascimento MG, Hackney AC (2014) Twenty-five years of research on the effects of exercise training in breast cancer survivors: a systematic review of the literature. World J Clin Oncol 5:177–190
9. McNeely ML, Campbell KL, Rowe BH, Klassen TP, Mackey JR, Courneya KS (2006) Effects of exercise on breast cancer patients and survivors: a systematic review and meta-analysis. CMAJ 175(1):34–41
10. Irwin ML, McTiernan A, Bernstein L, Gilliland FD, Baumgartner R, Baumgartner K, Ballard-Barbash R (2004) Physical activity levels among breast cancer survivors. Med Sci Sports Exerc 36:1484–1491
11. Schmitz KH, Ahmed RL, Troxel A, Cheville A, Smith R, Lewis-Grant L, Bryan CJ, Williams-Smith CT, Greene QP (2009) Weight lifting in women with breast-cancer-related lymphedema. New Engl J Med 361:664–673
12. Cormie P, Galvao DA, Spry N, Newton RU (2013) Neither heavy nor light load resistance exercise acutely exacerbates lymphedema in breast cancer survivor. Integr Cancer Ther 12:423–432
13. Schmitz KH, Ahmed RL, Troxel AB, Cheville A, Lewis-Grant L, Smith R, Bryan CJ, Williams-Smith CT, Chittams J (2010) Weight lifting for women at risk for breast cancer-related lymphedema: a randomized trial. JAMA 304:2699–2705
14. Kilbreath SL, Refshauge KM, Beith JM, Ward LC, Lee M, Simpson JM, Hansen R (2012) Upper limb progressive resistance training and stretching exercises following surgery for early breast cancer: a randomized controlled trial. Breast Cancer Res Treat 133(2):667–676
15. Sagen A, Karesen R, Risberg MA (2009) Physical activity for the affected limb and arm lymphedema after breast cancer surgery. A prospective, randomized controlled trial with two years follow-up. Acta Oncol 48:1102–1110
16. Kwan ML, Cohn JC, Armer JM, Stewart BR, Cormier JN (2011) Exercise in patients with lymphedema: a systematic review of the contemporary literature. J Cancer Surviv 5(4):320–336
17. Portela AL, Santaella CL, Gomez CC, Burch A (2008) Feasibility of an Exercise Program for Puerto Rican Women who are Breast Cancer Survivors. Rehabil Oncol 26:20–31
18. Hayes SC, Reul-Hirche H, Turner J (2009) Exercise and secondary lymphedema: safety, potential benefits, and research issues. Med Sci Sports Exerc 41:483–489
19. Chang CJ, Cormier JN (2013) Lymphedema interventions: exercise, surgery, and compression devices. Semin Oncol Nurs 29:28–40
20. Courneya KS, Segal RJ, Mackey JR, Gelmon K, Reid RD, Friedenreich CM, Ladha AB, Proulx C, Vallance JK, Lane K, Yasui Y, McKenzie DC (2007) Effects of aerobic and resistance exercise in breast cancer patients receiving adjuvant chemotherapy: a multicenter randomized controlled trial. J Clin Oncol 25:4396–4404
21. Reddy NP (1986) Lymph circulation: physiology, pharmacology, and biomechanics. Crit Rev Biomed Eng 14:45–91
22. American College of Sports Medicine: *ACSM Guidelines for Exercise Testing and Prescription, 5th Ed.* 2005: Williams & Wilkins
23. Myers J, Froelicher VF (1993) Exercise testing. Proced implement Cardiol Clin 11:199–213
24. Harris SR, Schmitz KH, Campbell KL, McNeely ML (2012) Clinical practice guidelines for breast cancer rehabilitation:

syntheses of guideline recommendations and qualitative appraisals. Cancer 118(8 Suppl):2312–2324
25. Warren AG, Janz BA, Slavin SA, Borud LJ (2007) The use of bioimpedance analysis to evaluate lymphedema. Ann Plast Surg. 58:541–543
26. Hayes S, Cornish B, Newman B (2005) Comparison of methods to diagnose lymphoedema among breast cancer survivors: 6-month follow-up. Breast Cancer Res Treat 89(3):221–226
27. Cornish BH, Chapman M, Hirst C, Mirolo B, Bunce IH, Ward LC, Thomas BJ (2001) Early diagnosis of lymphedema using multiple frequency bioimpedance. Lymphology 34(1):2–11
28. Cornish BH, Chapman M, Thomas BJ, Ward LC, Bunce IH, Hirst C (2000) Early diagnosis of lymphedema in postsurgery breast cancer patients. Ann N Y Acad Sci 904:571–575
29. Mortimer PS (1990) Investigation and management of lymphedema. Vasc Med 1(1):1–20
30. Jonsson C, Johansson K (2009) Pole walking for patients with breast cancer-related arm lymphedema. Physiother Theory Pract 25:165–173
31. Jonsson C, Johansson K (2014) The effects of pole walking on arm lymphedema and cardiovascular fitness in women treated for breast cancer: a pilot and feasibility study. Physiother Theory Pract 30(4):236–242
32. Armer JM, Stewart BR (2005) A comparison of four diagnostic criteria for lymphedema in a post-breast cancer population. Lymphat Res Biol 3:208–217