

## Randomized Controlled Trial of Weight Training and Lymphedema in Breast Cancer Survivors

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### ABSTRACT

#### Purpose

Lymphedema is a common condition that breast cancer survivors face. Despite a lack of supporting evidence from prospective observational studies, occupational and leisure time physical activity are feared to be possible risk factors for lymphedema onset or exacerbation. We examined effects of supervised upper- and lower-body weight training on the incidence and symptoms of lymphedema in 45 breast cancer survivors who participated in the Weight Training for Breast Cancer Survivors study.

#### Methods

Participants were on average 52 years old, 4 to 36 months post-treatment, and had axillary dissection as part of their treatment. Thirteen women had prevalent lymphedema at baseline. The intervention was twice-a-week weight training over a period of 6 months. Lymphedema was monitored at baseline and 6 months by measuring the circumference of each arm, and by self-report of symptoms and clinical diagnosis.

#### Results

None of the intervention-group participants experienced a change in arm circumferences  $\geq 2.0$  cm after a 6-month exercise intervention. Self-reported incidence of a clinical diagnosis of lymphedema or symptom changes over 6 months did not vary by intervention status ( $P = .40$  and  $P = .22$ , respectively).

#### Conclusion

This is the largest randomized controlled trial to examine associations between exercise and lymphedema in breast cancer survivors. The results of this study support the hypotheses that a 6-month intervention of resistance exercise did not increase the risk for or exacerbate symptoms of lymphedema. These results herald the need to start reevaluating common clinical guidelines that breast cancer survivors avoid upper body resistance activity for fear of increasing risk of lymphedema.

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### INTRODUCTION

Increasing attention is being devoted to the unique treatment-related conditions that breast cancer survivors face,<sup>1</sup> such as lymphedema. Of the approximately two million breast cancer survivors in the United States,<sup>2</sup> 200,000 to 400,000 are thought to have clinically diagnosed lymphedema; 49% of survivors self-report symptoms of lymphedema, with or without a clinical diagnosis.<sup>3,4</sup>

In breast cancer survivors, lymphedema is a chronic and progressive swelling of the arm, shoulder, neck, or torso from physical disruption or compression of the axillary lymphatic channels from surgery or radiation therapy; there is a synergistic effect of axillary dissection and radiation therapy on lymphedema risk.<sup>5,6</sup> Axillary therapy<sup>6,7</sup> is hypothe-

sized to induce damage interrupting lymph transport, such that lymph volume exceeds transport capabilities,<sup>6</sup> eventually leading to abnormal accumulation of tissue protein, edema, and chronic inflammation within the arm.<sup>8</sup> Other risk factors may play a role in lymphedema development, given that even sentinel node biopsy has been associated with a 0% to 6% risk of lymphedema.<sup>9</sup> Lymphedema may develop at any time from initial treatment to 20 years later.<sup>4</sup>

Risk factors for lymphedema are poorly characterized. In addition to axillary treatment, arm infection, injury, and elevated body mass have been positively associated with lymphedema.<sup>4,10-12</sup> Occupational and leisure time physical activity are feared as possible risk factors; however, no form of physical activity has been associated with lymphedema in prospective research.<sup>4</sup> Preliminary evidence from

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three small studies that observed no increases in lymphedema symptoms from exercise<sup>13-15</sup> stands in contrast to clinical guidelines that warn breast cancer survivors against vigorous, repetitive, or excessive upper body exercise.<sup>13</sup> These guidelines are problematic. Exercise protects against chronic disease<sup>16-19</sup> and may help women regain strength, function, and range of motion after treatment. Further, exercise may help women return to activities enjoyed before cancer and to feeling physically and psychologically empowered after cancer treatment.<sup>20-23</sup>

We hypothesized progressive weight training would not increase the incidence of or exacerbate symptoms of lymphedema in survivors of recent breast cancer. To examine these hypotheses we used data from the Weight Training for Breast Cancer Survivors (WTBS) study, a randomized controlled trial designed to determine the effects of twice-a-week weight training on several outcomes in breast cancer survivors (who were 4 to 36 months postadjuvant therapy);<sup>24</sup> lymphedema measures were a secondary aim of this trial. A recent review included increases in arm-circumference measurement by at least 2 cm, on the arm ipsilateral to breast cancer treatment minus the contralateral arm, as one of several thresholds for clinical diagnosis;<sup>7</sup> we used this threshold, as well as self-reported diagnosis and symptoms, to evaluate our hypotheses.

## METHODS

The WTBS study included a 6-month randomized controlled intervention. The full study design is described in detail elsewhere.<sup>24</sup> After baseline measures were complete, participants were randomly assigned into intervention and nonintervention control groups, using a blocked randomization procedure that balanced participants by age and baseline body fat percentage.<sup>24</sup>

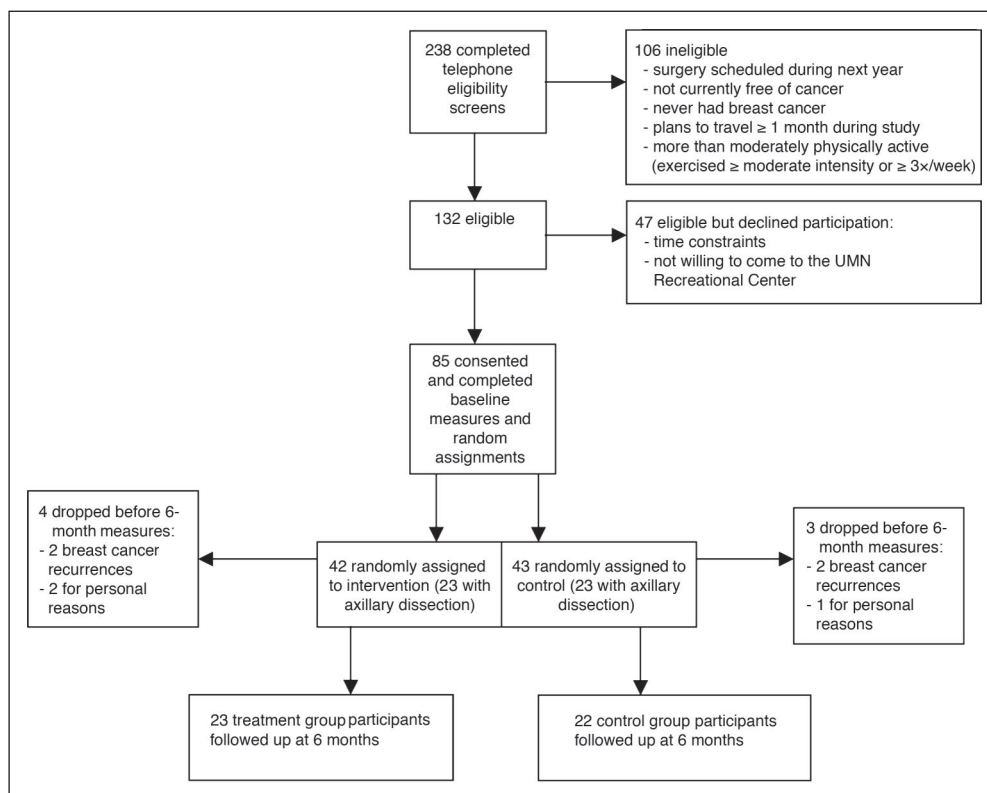
The flow of participants from recruitment is illustrated in Figure 1. Recruitment of participants, exclusion, and eligibility criteria have been described.<sup>24</sup> Briefly, 85 women were recruited from breast cancer survivors living in the greater Minneapolis-Saint Paul, MN metropolitan area between October 2001 and June 2002. After dropouts and loss to follow-up, 78 women completed baseline and 6-month measures. These analyses include the 45 women who had axillary node dissection beyond sentinel node biopsy as part of their breast cancer treatment.

This study and all protocols were approved by the University of Minnesota (Minneapolis, MN) and Park Nicolett Health Care System (St Louis Park, MN) committees for protection of human subjects in research. All participants gave signed informed consent.

### Weight Training Intervention

The weight training intervention, which took place at the University of Minnesota Recreational Center, has been described.<sup>24</sup> Briefly, for the first 3 months of weight training, participants met twice-a-week with an American College of Sports Medicine certified fitness professional. During the first 3 months, participants met in groups of four, to ensure adequate instruction in safe and effective performance of warm-up, weight training, cool down, and stretching exercises. From months 3 to 6, participants exercised in pairs, on their own, with continued access to the fitness trainers.<sup>24</sup> Participants were instructed to refrain from purposeful changes in diet (aside from normal seasonal variation) and exercise habits outside the intervention.<sup>24</sup>

**Weight training exercises.** Nine common exercises were performed using variable resistance machines and free weights, targeting muscles of the arms, back, chest, buttocks, and legs.<sup>24</sup> For the upper body, participants started with no weight or half-pound wrist weights for each exercise. If there were no lymphedema-related symptoms by the next session, the weight was increased by the smallest available increment for each exercise. For the lower body, participants lifted the most weight they could lift in each exercise, eight to 10 times for each set of repetitions. Participants increased to three sets for each exercise over the first 2 to 3 weeks of exercise. Women were taught



**Fig 1.** Flow of participants through the study. UMN, University of Minnesota.

stretching exercises to increase range of motion. Sessions lasted approximately 60 minutes.

**Additional guidelines regarding lymphedema.** All participants and staff had access to the University of Minnesota Medical Center lymphedema clinic for questions or concerns regarding lymphedema; two lymphedema specialists served as staff consultants. Only one participant consulted with these specialists directly, on one occasion. Participants were queried for symptoms before the intervention and were monitored regularly with arm-circumference measurements at exercise sessions and measurement visits. Women with known diagnosed lymphedema followed the guidance of their lymphedema specialist regarding whether or not to wear compression garments during and after exercise sessions. Participants were encouraged to continue lymphedema self-care therapy (eg, wrapping, massage, manual lymph drainage) during the study. Adherence to this therapy was monitored at measurement visits.

**Measurements.** Before study enrollment, participants completed the Physical Activity Readiness Questionnaire<sup>25</sup> to assess whether exercise was advisable, and obtained from their physician written permission for participation, specifics of breast cancer diagnosis (date, stage, and tumor grade), and of breast cancer treatment (surgery, radiotherapy, chemotherapy, and number of axillary nodes removed).

Other measurements were taken at baseline and 6 months. Physiological and survey measures were taken at the University of Minnesota General Clinical Research Center at least 48 hours after exercise, between 6:30 and 11:00 AM, after a 12-hour fast, and between 5 and 11 days after starting menstrual flow for menstruating participants ( $n = 14$ ). Staff taking measurements were blinded to patients' random assignments.

**Lymphedema measurements.** Lymphedema was measured three ways: with arm-circumference measurements, self-report of diagnosis, and self-report of symptoms. Arm-circumference measurements were taken on both arms at the level of the metacarpophalangeal joints (MCP), just distal to the ulnar styloid process (US), 10 cm distal to the midpoint of the lateral epicondyle (DLE), and 10 cm proximal to the midpoint of the lateral epicondyle (PLE). During measurements, participants lay prone, with their arms at their sides and elbows straight. A cloth measuring tape was placed around the arm so that there was no slack and no indentation of the tissue. This protocol was modified from Harris et al.<sup>13,26</sup> Participants who wore compression sleeves removed them 1 hour before measurements were taken. The mean of two measurements was used. The outcome measure was the calculated difference in each circumference measure between the ipsilateral and contralateral arms.

A validated survey measured self-report of lymphedema diagnosis, symptoms, and treatment over the last 3 months.<sup>27</sup> This survey had a specificity of 0.90 and sensitivity of 0.86 to 0.92 for diagnosing lymphedema (difference in arm circumferences  $> 2$  cm), compared with clinical assessment by a physical therapist with training in lymphedema.<sup>27</sup> Symptoms of lymphedema included whether or not a participant had noticed that her hand, lower arm, or upper arm on the side of the cancer was larger than the side of the opposite arm, and if the difference was mild, moderate, or severe. Additionally, other symptoms included altered fine motor function, puffiness, swelling, and/or pain of the hand or arm.

A participant was a self-reported "incident" case of lymphedema if she self-reported a clinician diagnosis of lymphedema at 6 months but not at baseline; she was a self-reported "prevalent" case if she self-reported a clinician diagnosis of lymphedema. A participant was considered to have lymphedema symptoms if she reported any lymphedema symptoms in the survey.

**Additional measures.** Body composition measures, injury assessment, medication use, demographic, and dietary intake methods have been described.<sup>24</sup> The Baecke Questionnaire assessed participant physical activity outside of the intervention.<sup>28</sup> Upper and lower body strength was assessed by one-repetition maximum (1RM) tests, as described.<sup>24</sup>

### Statistical Analysis

These analyses included the 23 intervention-group and 22 control-group women with axillary dissection who completed baseline and 6-month measures. There were 26 women who had sentinel node biopsy ( $\leq$  four nodes removed) and six women without any axillary dissection; these are not included in these analyses. SAS (SAS/STAT User's Guide, version 6, 1990; SAS Institute, Cary, NC) was used for all analyses.

Baseline variables were compared by intervention group using  $t$  tests for continuous variables (with Scatterthwaite approximation if variances were indicated as heterogeneous) and  $\chi^2$  tests (or Fisher's two-sided Exact tests) for categorical outcomes.

We examined changes in self-report diagnosis and symptoms of lymphedema. Proportions of new self-reported diagnoses or change in symptoms from 0 to 6 months in the intervention and control groups were compared with  $\chi^2$  tests (and Fisher's two-sided Exact tests). For incident lymphedema, women without baseline prevalent lymphedema were included in the denominator. For symptoms, all participants were included in the denominator, regardless of whether or not lymphedema was present at baseline. Mean change in 1RM strength and the differences between ipsilateral arm and contralateral arm circumference measures from 0 to 6 months were assessed using  $t$  tests and linear regression. Potential confounders were added to individual models in a stepwise fashion and retained if they changed the regression estimate by at least 10%. Covariates that were examined but not included in final models included baseline lean mass, number of lymph nodes removed, cancer stage, baseline age, sport and leisure activity scores from the Baecke, adherence to the intervention, whether or not women had received (yes/no) specific breast cancer treatments (radiation, surgery), time since diagnosis, and time since treatment. Final models included baseline body fat percentage, change in 1RM strength, and change in body fat percentage and lean mass. Plots of circumference measurements included baseline ipsilateral arm minus contralateral arm circumference differences, which were plotted against change in circumference differences over 6 months. Statistical tests and corresponding  $P$  values were two-sided; a  $P$  value of less than .05 is reported as statistically significant.

Power calculations were developed to determine the smallest detectable differences in ipsilateral arm circumferences and 6-month change in ipsilateral minus contralateral arm circumference differences at all four circumference measurement sites. These calculations, based on trial data and therefore posthoc, assumed a sample size of 23 per group, 80% power, and a two-sided  $t$ -test with type 1 error set at .05. Results of these calculations indicated detectable differences ranging from 0.36 to 1.43 cm for ipsilateral arm circumferences and from 0.28 to 0.71 cm for comparison of ipsilateral minus contralateral arm circumference differences, over a period of 6 months. Assuming change of 2.0 cm is clinically relevant,<sup>7</sup> the sample size was adequate.

## RESULTS

Baseline characteristics were distributed similarly in the intervention and control participants in these analyses (Table 1). There was a statistically, but not clinically, significant between-group difference in the ipsilateral minus contralateral circumference measures of the ulnar styloid process.

**Adherence.** All but one intervention-group participant attended at least 80% of exercise sessions.<sup>24</sup> Adherence did not vary by baseline lymphedema prevalence. Further evidence of adherence is seen with changes in strength in the intervention versus control group (Table 2). The small increases in strength observed in the control group may be attributed to learning the exercises during strength tests.

**Circumference measurements.** Group mean changes for the four circumference measurement differences were less than 2 cm over 6 months (Table 3). Plots of ipsilateral minus contralateral arm circumference differences reveal that only one participant (control group) experienced a clinically significant ( $\geq 2$  cm) circumference measurement change over 6 months at the distal and proximal lateral epicondyle measurements (Figs 2A to 2D).

**Self-reported incidence of lymphedema.** At 6 months, two of 16 women in the intervention group and one of 16 women in the control group self-reported the onset of lymphedema since baseline. These

**Table 1.** Baseline Values by Intervention Status (of all participants who completed baseline and 6-month measures)

	Intervention (n = 23)		Control (n = 23)		P
	No.	%	No.	%	
Age, years					.98
Mean	52.3		51.7		
SD	7.7		7.5		
Self-report clinical diagnosis of lymphedema at baseline	7	30.4	6	26.1	.63
Self-report symptoms of lymphedema at baseline	10	43.4	7	30.4	.43
Lymphedema by circumference measure difference > 2 cm at baseline	4	17.4	4	17.4	.95
Time since first breast cancer diagnosis, months					.73
Mean	22.3		21.9		
Range	6.9-42.9		10.7-57.1		
Breast cancer stage					.40
DCIS	1	4.4	1	4.4	
Stage I	6	26.1	7	30.4	
Stage II	13	56.5	13	56.5	
Stage III	3	13.0	2	8.7	
Time since last breast cancer treatment session, months					.99
Mean	13.4		13.4		
Range	4.6-31.7		4.0-37.3		
% Treatment					
Radiation	17	73.9	17	73.9	.99
Chemotherapy	20	87.0	20	87.0	.99
Axillary dissection	23	100	23	100	.99
No. of lymph nodes removed					.76
Mean	14.9		15.4		
SD	6.3		5.5		
Adjuvant treatment					
Tamoxifen	19	82.6	17	74.0	.47
Raloxifene	0	0.0	0	0.0	
Anastrozole	1	4.3	2	8.7	.55
Letrozole	0	0.0	1	4.3	.31
None	3	13.0	3	13.0	.96
Postmenopausal at baseline	21	91.3	18	78.3	.24
Energy intake, Kcal/d					.75
Mean	1,594		1,432		
SD	559		599		
Leisure Activity Score, units					.78
Mean	2.6		2.6		
SD	0.5		0.5		
Sport Physical Activity Score, units					.92
Mean	3.2		3.2		
SD	0.6		0.6		
Body fat, kg					.92
Mean	31.6		31.2		
SD	11.5		11.8		
Body fat, %					.92
Mean	44.2		43.7		
SD	8.4		8.6		
Lean mass, kg					.90
Mean	38.1		37.9		
SD	5.2		4.9		
Total body mass, kg					.93
Mean	72.3		71.7		
SD	15.3		15.0		
Height, cm					.73
Mean	163.1		164.2		
SD	6.5		6.0		
BMI, kg/m <sup>2</sup>					.97
Mean	27.1		26.5		
SD	4.9		4.9		

(continued on following page)

**Table 1.** Baseline Values by Intervention Status (of all participants who completed baseline and 6-month measures) (continued)

	Intervention (n = 23)		Control (n = 23)		P
	No.	%	No.	%	
MCP difference, cm*					.16
Mean		-0.01		-0.1	
SD		0.6		0.5	
US difference, cm*					.02
Mean		0.02		0.1	
SD		0.4		0.7	
DLE difference, cm*					.17
Mean		0.2		0.4	
SD		0.9		1.1	
PLE difference, cm*					.94
Mean		0.3		0.5	
SD		1.2		1.1	

Abbreviations: SD, standard deviation; DCIS, ductal carcinoma in situ; BMI, body-mass index; MCP, metacarpophalangeal joint; US, ulnar styloid process; DLE, 10 cm distal to the lateral epicondyle; PLE, 10 cm proximal to the lateral epicondyle.

\*Circumference measurement differences calculated by subtracting the ipsilateral from the contralateral arm circumference at each measurement level.

incidence rates were not statistically different ( $P = .40$ ). Additionally, one control participant who was not included in these analyses (she had only two lymph nodes removed) developed lymphedema by 6 months.

**Symptoms of lymphedema.** From baseline to 6 months, three control-group participants versus no intervention-group participants reported an increase in lymphedema symptoms ( $P = .22$ ). All women who self-reported a diagnosis of lymphedema at baseline or 6 months reported symptoms (data not shown).

The results of all analyses presented were essentially unchanged when analyses were repeated including all 78 women who completed baseline and 6-month measures.

## DISCUSSION

The findings from WTBS are consistent with the hypotheses that twice-a-week progressive weight training does not increase the onset of or exacerbate lymphedema in recent survivors of breast cancer. During the 6-month trial, neither the incidence of lymphedema nor the onset of lymphedema symptoms varied in the intervention-group versus control-group participants; further, none of the intervention-group participants experienced an increase in any ipsilateral minus

contralateral circumference measurements of  $\geq 2$  cm. The control-group participant who experienced an increase of more than 2 cm in the difference of ipsilateral minus contralateral arm circumference measurements at 6 months had diagnosed lymphedema at baseline. At baseline, she reported that she actively followed lymphedema self-care therapies (wrapping, wearing a sleeve, and manual lymphatic drainage); at 6-month measures, she reported that she had stopped following these practices. Other participants with prevalent lymphedema at baseline did not experience increases in circumference measurements over the intervention.

Although incidence of lymphedema was similar in the intervention and control groups in WTBS, four participants were diagnosed with lymphedema over 6 months. Three of these four women had more than 22 lymph nodes removed as part of their breast cancer treatment; by contrast, one participant (in the control group) had two lymph nodes removed. This participant was not included in the analyses because she had not had axillary dissection beyond sentinel node biopsy. However, she highlights the fact that even women with sentinel node biopsy are at risk for lymphedema. Increased awareness of lymphedema symptoms due to study participation may have introduced bias into the study and encouraged some participants to seek a clinical diagnosis. It is possible that the natural course of lymphedema

**Table 2.** Mean 1RM Strength (in pounds) Over 6 Months of Strength Training

Variable Name	Baseline			6 Months			$\Delta$ 0-6 Months		P*
	No.	Mean	SE	No.	Mean	SE	Mean	SE	
Leg Press									
Intervention	23	214.8	9.8	23	296.6	10.2	81.8	10.2	< .0001
Control	23	218.5	9.6	22	238.9	9.9	20.3	9.8	
Bench Press									
Intervention	23	50.7	2.7	23	83.0	2.8	32.3	2.4	< .0001
Control	23	56.1	2.7	22	63.0	2.7	6.9	2.3	

Abbreviation: 1RM, one repetition maximum test.

\*P value from two-sided tests for comparing the changes in the intervention group to the changes in the control group over the 6-month randomized controlled trial, adjusted for baseline body fat percentage and change in body fat percentage and lean mass.

**Table 3.** Mean Arm Circumference Changes Over 6 Months of Strength Training

Variable Name	Baseline			6 Months			Δ 0-6 Months		P*
	No.	Mean	SE	No.	Mean	SE	Mean	SE	
<b>MCP</b>									
Ipsilateral MCP									
Intervention	23	19.25	0.21	23	19.41	0.21	0.16	0.09	.26
Control	23	19.30	0.21	22	19.32	0.21	0.02	0.09	
Contralateral MCP									
Intervention	23	19.27	0.20	23	19.35	0.20	0.09	0.08	.37
Control	23	19.40	0.20	22	19.39	0.20	-0.01	0.08	
Ipsilateral minus contralateral MCP†									
Intervention	23	-0.01	0.12	23	0.06	0.12	0.07	0.07	.70
Control	23	-0.10	0.11	22	-0.07	0.11	0.03	0.06	
<b>US</b>									
Ipsilateral US									
Intervention	23	16.24	0.23	23	16.37	0.23	0.13	0.11	.89
Control	23	16.25	0.23	22	16.40	0.23	0.15	0.11	
Contralateral US									
Intervention	23	16.26	0.21	23	16.39	0.21	0.13	0.10	.91
Control	23	16.12	0.21	22	16.24	0.21	0.12	0.10	
Ipsilateral minus contralateral US†									
Intervention	23	-0.02	0.12	23	-0.02	0.13	0.00	0.08	.77
Control	23	0.13	0.13	22	0.17	0.13	0.03	0.09	
<b>DLE</b>									
Ipsilateral DLE									
Intervention	23	24.57	0.57	23	24.80	0.57	0.24	0.25	.53
Control	23	24.26	0.57	22	24.28	0.56	0.01	0.23	
Contralateral DLE									
Intervention	23	24.36	0.51	23	24.44	0.56	0.08	0.19	.98
Control	23	23.88	0.52	22	24.28	0.57	0.08	0.18	
Ipsilateral minus contralateral DLE†									
Intervention	23	0.20	0.21	23	0.36	0.21	0.16	0.17	.37
Control	23	0.38	0.20	22	0.32	0.19	-0.06	0.16	
<b>PLE</b>									
Ipsilateral PLE									
Intervention	23	31.18	0.84	23	31.73	0.84	0.55	0.36	.39
Control	23	30.79	0.84	22	30.89	0.83	0.11	0.36	
Contralateral PLE									
Intervention	23	30.84	0.79	23	31.24	0.79	0.40	0.34	.95
Control	23	29.23	0.77	22	30.61	0.78	0.37	0.33	
Ipsilateral minus contralateral PLE†									
Intervention	23	0.34	0.22	23	0.50	0.23	0.15	0.18	.18
Control	23	0.55	0.23	22	0.29	0.22	-0.26	0.17	

NOTE. Includes women with axillary dissection beyond sentinel lymph node biopsy.

Abbreviations: US, ulnar styloid; MCP, metacarpophalangeal joints; DLE, 10 cm distal to the lateral epicondyle; PLE, 10 cm proximal to the lateral epicondyle.

\*P value from test for comparing the changes in the intervention group to the changes in the control group over the 6-month randomized controlled trial.

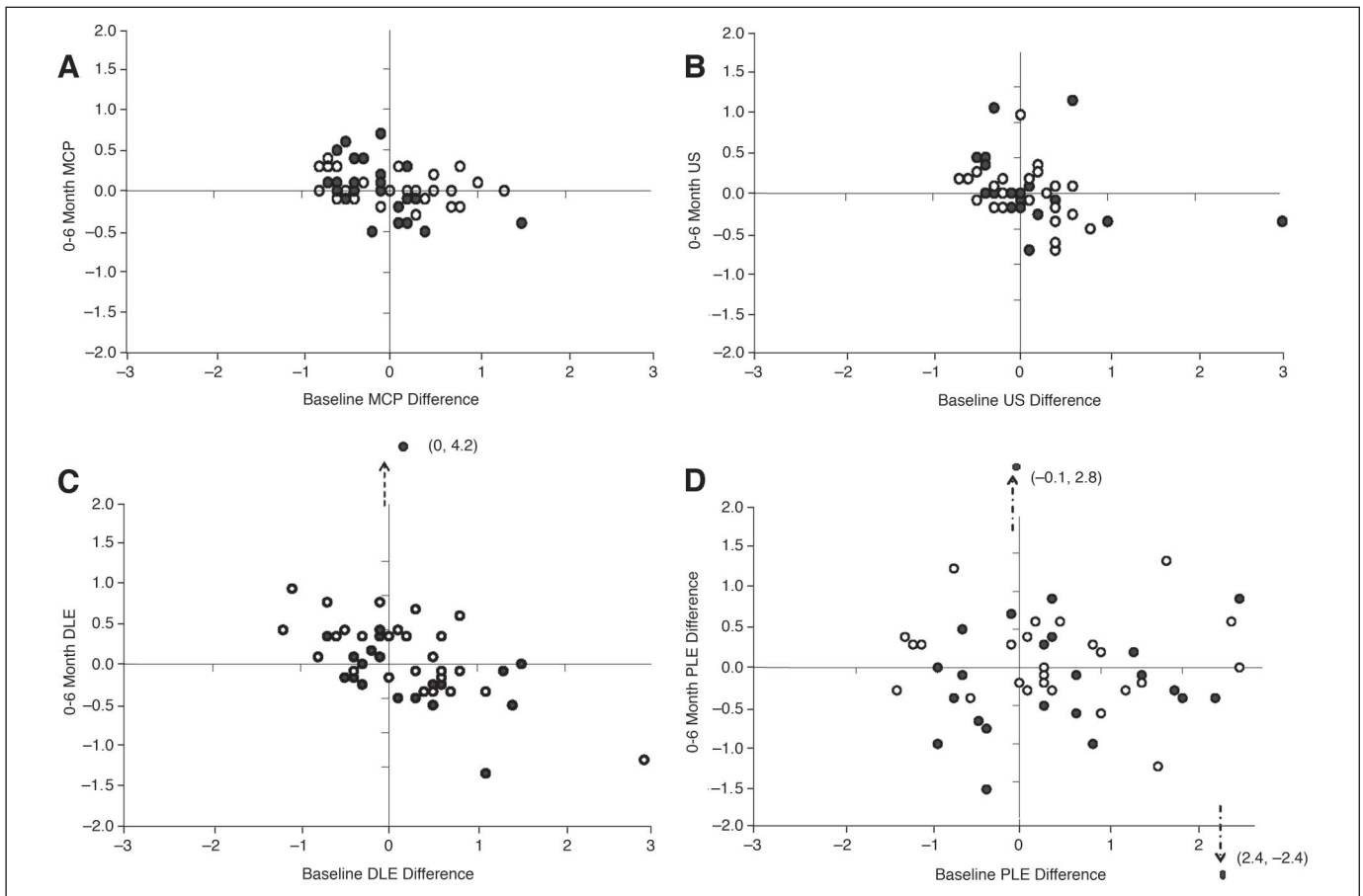
†Ipsilateral minus contralateral measures.

onset and study participation coincided by chance. There also remains the possibility that the intervention exacerbated an underlying condition—these four participants all described having symptoms and/or having seen a physician for possible lymphedema at baseline.

An intervention of slow and carefully controlled increase of physiological stress to the treated arm, through stretching, aerobic exercise, and weight training may be preferable to inactivity in breast cancer survivors. There are plausible biologic mechanisms through which exercise may help prevent lymphedema or may improve its symptoms. Exercise enhances lymph flow<sup>29-31</sup> and improves protein reabsorption.<sup>32</sup> Lymph flow increases<sup>33</sup> from the reduction in the intrathoracic pressure associated with inspiration, suggesting that increased pulmonary work associated with exercise may reduce swell-

ing.<sup>34</sup> Further, as upper extremity venous drainage is frequently compromised in lymphedema patients,<sup>35</sup> flexibility training may lessen soft tissue contracture, reducing blood and lymph obstruction.<sup>34</sup>

The results from WTBS are consistent with prior studies. A case-series report<sup>13</sup> and two pilot interventions<sup>14,15</sup> have examined associations between exercise and the onset or exacerbation of lymphedema symptoms in breast cancer survivors; none of these studies reported an increase in lymphedema symptoms from exercise. There have been 23 controlled physical activity interventions in breast cancer survivors during and after treatment.<sup>36</sup> Of these, 10 reported on adverse events in participants, and only one noted any effect of a physical activity intervention on lymphedema symptoms.<sup>37</sup> That study was a controlled trial in which the overall rates of adverse events were similar



**Fig 2.** Ipsilateral minus contralateral arm circumference measurement differences (see Methods) for the intervention and control group participants at baseline and from 0 to 6 months. (A) Metacarpophalangeal (MCP) joint, (B) ulnar styloid (US) process, (C) distal lateral epicondyle (DLE), (D) proximal lateral epicondyle (PLE). (●), control group; (○), intervention group.

between the intervention and control groups, but the rate of incident lymphedema was higher in the intervention group than the control group.<sup>37</sup> The authors noted two of the three participants who developed lymphedema had received axillary radiation. They further commented that it was unclear whether or not the onset of lymphedema was attributable to the intervention.

WTBS is the first exercise intervention to use the validated survey to examine change from an exercise intervention on lymphedema symptoms and adherence to lymphedema self-care outside of the intervention.<sup>27</sup> We observed greater change in lymphedema symptoms than circumference measures at 6 months; symptoms may provide a more complete or earlier representation of pathology than circumference change alone. To better interpret the onset of lymphedema or change in symptoms, future interventions should include extensive monitoring of lymphedema self-care activities and exposure to risk factors.

WTBS is the largest and longest randomized controlled trial to date to examine the effects of upper body exercise on lymphedema. Women were sedentary to moderately active at baseline; diet and physical activity outside of the study were monitored, allowing us to examine changes attributable to the intervention. There are limitations to this study. The lymphedema measures represent a secondary outcome of WTBS. We used circumference measures to be consistent with prior studies, however, we did not measure change in volume,

which is correlated with circumference measures but may be more sensitive to change.<sup>38</sup> Measurements at baseline and 6 months may not have adequately captured acute or transient changes in circumferences and/or symptoms that may result from exercise. Infection in participants was not monitored. Relatively few of the women randomly selected at baseline had lymphedema and the women selected were heterogeneous with respect to their cancer diagnoses and treatments. Final analyses excluded the subgroup of participants who had  $\leq$  four nodes dissected. Given that all breast cancer survivors are at risk for lymphedema and are instructed to avoid upper body physical activity, future studies should stratify or block the sample on participant breast cancer diagnosis, treatment, and lymphedema variables so that we may learn whether or not the findings are generalizable.

In summary, twice-a-week weight training over a period of 6 months did not increase incidence, arm-circumference measurement differences, or symptoms of lymphedema in breast cancer survivors compared with nonintervention controls. WTBS represents early research in the field of exercise and lymphedema. Additional work is needed to determine whether or not exercise leads to physiological change of lymphatic structure and/or function as well as timing between exposure to a risk factor and incidence of lymphedema.

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