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ORIGINAL RESEARCH

Randomized Trial Assessing Prospective Surveillance and Exercise for Preventing Breast Cancer-Related Lymphedema in High-Risk Patients

Karol Ramírez-Parada, PT, MSc, MBA,[a,b] Cesar Sánchez, MD,[b,c] Irene Cantarero-Villanueva, PT, MSc, PhD,[d,e,f] Álvaro Reyes, PT, MSc, PhD,[g] Mauricio P. Pinto, PhD,[h] M. Loreto Bravo, PhD,[h] Denise Montt-Blanchard, MSc,[b,i] Francisco Acevedo, MD,[b,c] Benjamín Walbaum, MD,[c,j,k] Margarita Alfaro-Barra, PT,[l] Margarita Barra-Navarro, PT,[a] Scarlet Muñoz-Flores, PT,[a] Constanza Pinto,[m] Sabrina Muñiz, RN,[c] Felipe Contreras-Briceño, PT, MSc, PhD,[a,n] Tomás Merino, MD,[c] Gina Merino, MSc[o]

From the [a]Departamento de Kinesiología, Escuela Ciencias de la Salud, Facultad de Medicina, Pontificia Universidad Católica de Chile, Santiago, Chile; [b]Centro para la prevención y el control del cáncer, CECAN, Santiago, Chile; [c]Department of Hematology-Oncology, Faculty of Medicine, Pontificia Universidad Católica de Chile, Santiago, Chile; [d]Department of Physical Therapy, Faculty of Health Sciences, University of Granada, Granada, Spain; [e]Instituto de Investigación Biosanitaria (ibs.GRANADA), Granada, Spain; [f]Sport and Health Joint University Institute (iMUDS), Granada, Spain; [g]Exercise and Rehabilitation Sciences Laboratory, School of Physical Therapy, Faculty of Rehabilitation Sciences, Universidad Andres Bello, Santiago, Chile; [h]Support team for Oncological Research and Medicine (STORM), Santiago, Chile; [i]School of Design, Faculty of Architecture, Design and Urban Studies. Pontificia Universidad Católica de Chile, Santiago, Chile; [j]Translational Genomics and Targeted Therapies in Solid Tumors Group, August Pi I Sunyer Biomedical Research Institute, Barcelona, Spain; [k]Department of Medical Oncology, Hospital Clinic of Barcelona, Barcelona, Spain; [l]Clínica Universidad de los Andes, Servicio de Kinesiología, Santiago, Chile; [m]Unidad de patología mamaria, Complejo Asistencial Dr. Sótero del Río, Santiago, Chile; [n]Laboratory of Exercise Physiology, Department of Physical Therapy, School of Health Sciences, Faculty of Medicine, Pontificia Universidad Católica de Chile, Santiago, Chile; and [o]Departamento Agencia Nacional de Prevención y Control del Cáncer, Subsecretaria de Salud Pública, Ministerio de Salud de Chile, Santiago, Chile.

Abstract

Objective: To evaluate if combining a prospective surveillance model (PSM) with a supervised multimodal exercise program prevents breast cancer-related lymphedema (BCRL) and its effect on the functional capacity and quality of life (QoL) of high-risk breast cancer (BC) patients undergoing treatment.

Design: Two-arm parallel superiority randomized controlled trial.

Setting: Outpatient physical therapy service in a public hospital.

Participants: 116 adult women (N=116; age ≥18y) diagnosed with stage I-III BC were enrolled. Inclusion criteria included recent surgery and indication for adjuvant chemotherapy. Exclusion criteria were significant arm volume difference, previous cancer, exercise contraindications, and extreme body mass index values.

Interventions: Participants were randomized into experimental (n=61) or control groups (n=55) in a 1:1 ratio. The experimental group received PSM with a supervised multimodal exercise program for 12 weeks. The control group received PSM alone.

Main Outcome Measures: Arm volume, grip strength, 6-minute walk test, and QoL were blindly assessed at baseline, 3, 6, and 9 months.

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Results: The combination of PSM with a supervised multimodal exercise program significantly reduced arm volume and body weight and improved grip strength, functional capacity, and the QoL of patients.
Conclusions: Combining PSM and physical exercise reduces arm volume, prevents BCRL, and improves physical performance and QoL in high-risk patients. The combination of PSM and STRONG-B was superior to PSM alone, validating the study's superiority design.
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Breast cancer-related lymphedema (BCRL) is a chronic condition affecting approximately 21.9% of patients with breast cancer (BC).[1,2] Characterized by increased arm volume, pain, heaviness, and tightness, BCRL can significantly affect quality of life (QoL).[2-4] Risk factors include high body mass index (BMI), axillary lymph node dissection,[1,2,5-7] axillary web syndrome (AWS),[8,9] and adjuvant therapies.[1,6] A recent systematic review found that co-occurrence of extensive axillary lymph node dissection, a BMI ≥23.0 kg/m^2, and postoperative chemotherapy was associated with a significantly increased (+44.4%) BCRL risk.[10]

The current criterion standard for managing BCRL is complete decongestive therapy, which, despite its effectiveness, can be costly and logistically challenging.[11,12] In response, Stout et al[13] introduced a prospective surveillance model (PSM) focusing on early detection and intervention to mitigate the onset and severity of BCRL. This model includes surveillance for common physical impairments, providing education to reduce risk or prevent side effects, facilitating early identification of physical impairments, introducing rehabilitation and exercise interventions when necessary, and promoting physical activity and weight management behaviors throughout the trajectory of disease treatment and survivorship.[13] By integrating these components, the PSM offers a comprehensive strategy for addressing BCRL, emphasizing early intervention and patient empowerment among high-risk patients.[14] However, the incorporation of PSM into health care practice remains limited.[15-17]

Although PSM shows promise in reducing the incidence and severity of BCRL, it has not been reported to improve functional capacity or QoL,[14,18] emphasizing the importance of complementary interventions that can enhance physical function and QoL for patients at risk of BCRL.

Physical exercise, especially resistance training, is a safe and potentially protective strategy for patients at high-risk of developing BCRL.[19] Indeed, resistance exercises not only enhance arm functionality and muscle strength but also improve the QoL of patients.[20-22] Adopting more active lifestyles, increasing overall physical activity levels, and aiming for higher daily step counts can further augment the benefits of structured resistance exercise programs.[23,24] This synergistic combination transforms the exercise regimen into a multimodal approach,[20] thereby optimizing the therapeutic potential for high-risk patients. However, the heterogeneity of the reported outcomes among studies highlights the need for further research to optimize exercise and health education strategies that align with the principles of PSM.[7,14,22]

Our aim was to evaluate the effect of a rehabilitation program that combines a PSM with a supervised multimodal exercise program on BCRL in high-risk BC patients undergoing adjuvant chemotherapy.

List of abbreviations:

AWS	**axillary web syndrome**
BC	**breast cancer**
BCRL	**breast cancer-related lymphedema**
BMI	**body mass index**
EORTC-QLQ	**European Organization for Research and Treatment of Cancer-Quality of Life Questionnaire**
PSM	**prospective surveillance model**
STRONG-B	**Supervised resistance TRaining amONG women at risk of breast cancer-related lymphedema**
QoL	**quality of life**

Methods

Study design

The Supervised resistance TRaining amONG women at risk of breast cancer-related lymphedema (STRONG-B) trial was a single-center, 2-arm, parallel superiority randomized controlled trial comparing a PSM with a supervised multimodal exercise program versus PSM alone on BCRL onset (primary aim) and functional capacity and QoL (secondary aims) in high-risk patients undergoing chemotherapy[25] (fig 1). All participants were informed orally and verbally of the purpose, protocol, and procedures before informed consent was obtained. This study was conducted in accordance with the Declaration of Helsinki and approved by 2 Ethics Committees. The trial is registered at ClinicalTrials.gov (identifier: NCT04821609).

Patient eligibility

Eligible participants for the study were adult (aged ≥18y) women newly diagnosed with stage I-III BC at a high-risk of developing BCRL. Eligibility criteria included patients that underwent (1) total or partial mastectomy with axillary node dissection; (2) sentinel node biopsy with positive AWS; (3) sentinel node biopsy along with a BMI ≥30.0 kg/m^2; (4) indication of adjuvant chemotherapy. Conversely, patients with (1) >200 mL of difference in volume between arms; (2) previous cancer diagnosis; (3) medical contraindication for exercise; (4) self-reported physical activity equivalent to 150 min/wk of moderate exercise, or 75 min/wk of vigorous exercise and resistance training strength exercises ≥2 d/wk[20]; and (5) BMI <18.5 kg/m^2 (indicative of malnutrition) or >40 kg/m^2 (indicative of high cardiovascular risk) were excluded.

Recruitment

Participants were recruited from January 2022 to October 2023 from a public hospital. After confirming the chemotherapy prescription and obtaining oncologist approval, potential participants were screened. Eligible and interested individuals were then asked to provide informed consent.

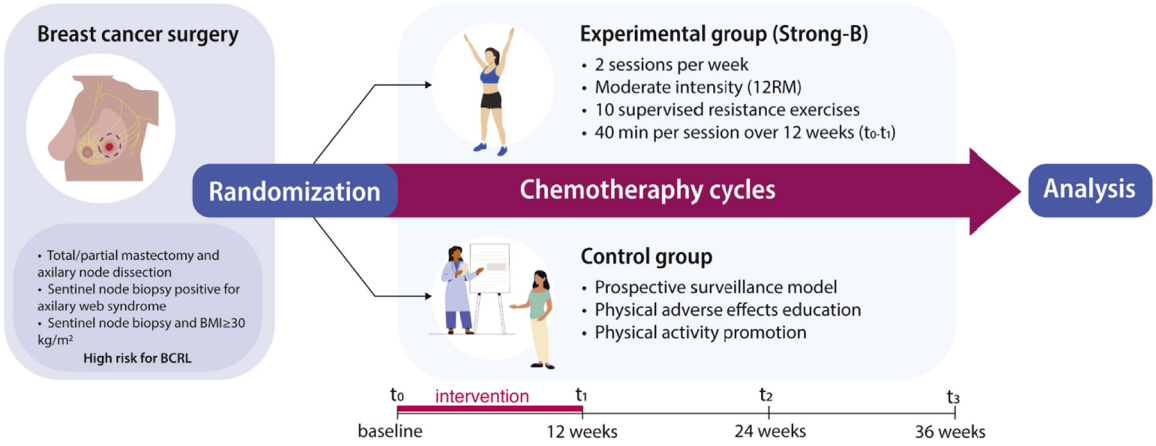

Fig 1 Study design. BCRL, breast cancer-related lymphedema; BMI, body mass index; RM, repetitium maximum.

Randomization

After completing the baseline assessment, participants were randomly assigned to the experimental or control groups in a 1:1 ratio using the software Sealed Envelope. This software generates unique codes for each patient that correspond to their assigned group. The codes were printed and placed in sealed, opaque envelopes. A blinded external researcher performed the randomization.

Outcomes

Outcomes were assessed at baseline (t_0; before chemotherapy) and at 12 (t_1; postintervention), 24 (t_2), and 36 weeks (t_3). Arm volume (primary outcome) was assessed using a Perometer (NT 1000). Volume was expressed in milliliters (mL). A volume difference of ≥200 mL between arms was indicative of BCRL.[26] Grip strength was assessed using a Hydraulic Hand Dynamometer (Jamar). Patients squeezed the dynamometer as hard as they could, 3 times, with 1-minute rest intervals. Results were reported in kilograms (kg). A change of 5.0-6.5 kg indicated a significant difference in grip strength.[27] Functional capacity was evaluated using the 6-minute walk test (6MWT).[28] Results were expressed in meters (m). A change of 54 m indicated a significant difference.[29] QoL was assessed using the European Organization for Research and Treatment of Cancer-Quality of Life Questionnaire Core 30 v.3.0 (EORTC QLQ-C30) with the Breast Cancer-Specific Quality of Life Questionnaire BR23 (EORTC QLQ-BR23).[30] These questionnaires have been previously validated in Spanish and in the Chilean population.[30,31] Functional assessments were blindly performed by researchers.

The safety of the intervention was assessed weekly by tracking and monitoring adverse events according to the National Cancer Institute Common Terminology Criteria for Adverse Events version 5.0. Adherence was calculated as the percentage of scheduled sessions that participants completed.

Experimental (STRONG-B) and control groups

The intervention (STRONG-B) combined PSM principles (physical assessment, physical activity promotion, and health

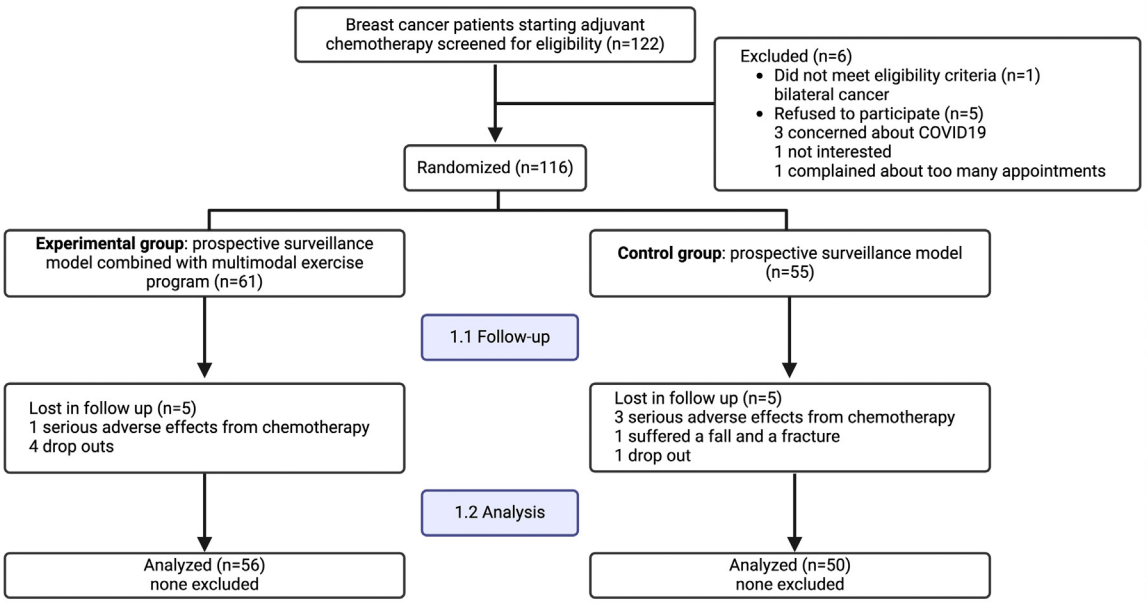

Fig 2 Flowchart of patients in the study (CONSORT flowchart).

Table 1 Patient characteristics in both groups at baseline

Variable (Units)	Total (n=116)	STRONG-B (n=61)	Control (n=55)	*P*
Age (y)				
Median (range)	55 (30-70)	54 (30-70)	57 (32-70)	.385
Mean ± SD	54.08±9.51	53.3±9.41	54.9±9.64	
Weight (kg)				
Median (range)	74 (45-108)	72 (45-105)	78 (45-108)	.140
Mean ± SD	74.79±13.54	73±13.7	76.7±13.2	
Height (m)				
Median (range)	1.58 (1.40-1.76)	1.57 (1.45-1.76)	1.58 (1.40-1.70)	.555
Mean ± SD	1.58±0.06	1.58±0.06	1.57±0.05	
BMI (kg/m^2)				
Median (range)	29.8 (18.5-39.7)	28.9 (18.5-39.7)	31.2 (20.0-39.7)	.064
Mean ± SD	30.03±5.15	29.2±5.07	31.0±5.12	
Median with AWS (range)	27.17 (18.49-39.11)	27.00 (18.49-39.11)	27.34 (20-36.68)	.917
Mean with AWS ± SD	27.20±4.03	27.15±4.22	27.27±3.89	
Median without AWS (range)	32.65 (20.31-39.72)	30.35 (20.31-39.66)	34.21 (22.66-39.72)	.014
Mean without AWS ± SD	32.32±4.82	30.92±5.14	33.82±4.01	
Surgery side, n (%)				
Right	69 (59.5)	35 (57.4)	34 (61.8)	.766
Left	47 (40.5)	26 (42.6)	21 (38.2)	
Righthanded; n (%)	98 (84.5)	49 (80.3)	49 (89.1)	.296
Type of surgery, n (%)				
Total mastectomy	54 (46.6)	29 (47.5)	25 (45.5)	.969
Partial mastectomy	62 (53.4)	32 (52.5)	30 (54.5)	
Removed lymph nodes, (n)				
Median (range)	6 (1-33)	5 (1-27)	6 (1-33)	.849
Mean ± SD	8.57±7.44	8.44±7.33	8.71±7.63	
+ AWS, n (%)	52 (44.8)	28 (45.9)	24 (43.6)	.954
Volume difference (mL)				
Median (range)	43.5 (−158 to 182)	44 (−158 to 167)	36 (−44 to 182)	0.974
Mean ± SD	48.60±47.56	48.7±52.1	48.4±42.5	
Dynamometry (kg), median (range)				
Surgery side	15 (8-28)	15 (8-28)	15 (8-28)	0.848
Contralateral side	19 (10-33)	20 (10-33)	18 (10-32)	
Dynamometry (kg), mean ± SD				
Surgery side	15.67±4.81	15.8±4.77	15.6±4.89	.481
Contralateral side	19.20±4.98	19.5±5.19	18.9±4.75	
6MWT (m)				
Median (range)	413 (45-589)	417 (80-589)	406 (45-578)	.196
Mean ± SD	397.79±107.15	410±102	384±112	
Type of chemotherapy, n (%)				
ACT	88 (76.52)	46 (75.4)	42 (77.8)	.622
CMF	14 (12.18)	8 (13.1)	6 (11.1)	
TC	13 (11.30)	7 (11.5)	6 (11.1)	

Data are expressed as median and interquartile range and/or mean and SD. Abbreviations: ACT, adriamycin, cyclophosphamide and taxane; CMF, cyclophosphamide, methotrexate and fluorouracil; IQR, interquartile range; TC, taxane and cyclophosphamide.

education, delivered individually on a monthly basis) with a supervised 12-week multimodal exercise program. Exercise sessions were conducted in groups and included 10 moderate-to-high intensity resistance exercises for the upper and lower limbs, adjusted per individual capability and progressively intensified based on tolerance.[25] The workload of resistance exercise was progressively increased by 5%-10% for participants who completed 3 consecutive sessions with the prescribed volume and intensity. For more detailed information, please refer to the protocol.[25]

The control group received a PSM alone, based on physical assessment, physical activity promotion, and health education, delivered individually on a monthly basis, as established in prior protocols.[25,32]

We promoted and tracked daily steps using smart bracelets in both groups during intervention and follow-up.[33] Participants were encouraged to wear the bracelets 24 h/d. Data were collected weekly and included if participants wore the bracelets for ≥12 h/d during ≥5 d/wk consecutively. Missing data points were addressed by averaging step counts from surrounding days.

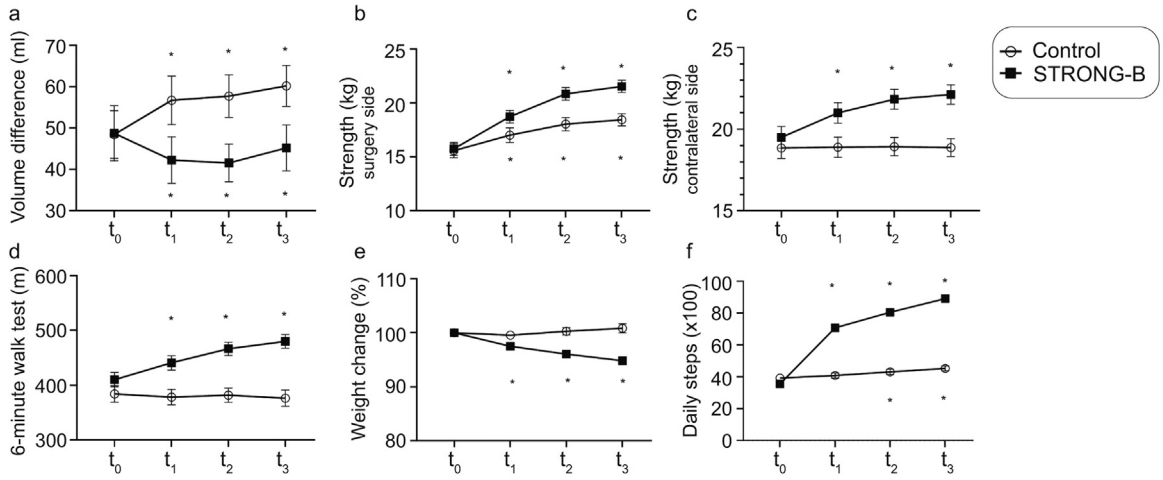

Fig 3 Effects of STRONG-B on: (a) arm volume, (b) and (c) grip strength, (d) physical performance (6MWT, 6-minute walk test), and (e) percentage of body weight change, and (f) daily steps. *P<.05 versus baseline.

Physical therapy referrals

Patients who experienced AWS or restricted range of arm motion were referred to physiotherapy, and this information was tracked and registered.

Statistical considerations and statistical analyses

Arm volume was the primary outcome. Statistical power was set at 0.9 and the alpha level at 0.05. We estimated a sample size of at least 36 participants per group (n=72 total) and 10% dropout. Therefore, the final sample size was 40 per group (n=80 total). Continuous variables are presented as mean (SD) or median (range) while categorical variables are expressed as percentages. Normal distribution was tested using the Shapiro−Wilk test. Differences in continuous demographic and physiological variables between groups (at baseline) were compared using 2-sample independent t tests, while differences in categorical variables were assessed using the chi-square test. For nonnormally distributed continuous variables, the Mann−Whitney U test was used to compare changes from baseline (t_0) to 9 months (t_3; 36 wk) between groups. The effectiveness of the intervention was evaluated using a linear mixed model, incorporating an unstructured correlation matrix to adjust for intraindividual correlations over time. The model included arm volume, grip strength, 6MWT, and body weight as response variables. Explanatory variables in the model were the group factor (STRONG-B or control), time factor (assessments at 0, 3, 6, and 9 mo; called t_0. t_1, t_2, and t_3), and their interaction. In our model, *"group"* was treated as a fixed effect, whereas *"time"* was considered a random effect. Additional covariates included BMI and the presence of AWS, to adjust for potential confounding factors. All statistical tests were 2-tailed, and significance was set at P<.05. Statistical analyses were performed in STATA[a] version 15.1 and R[b] version 4.3.2.

Intention-to-treat

Data were summarized and reported according to the Consolidated Standards of Reporting Trials guidelines for randomized controlled trials.[34] All analyses were conducted according to an intention-to-treat,[35] for which participants were required to complete at least 18 sessions of training (75% of total sessions).

Results

Patient enrollment and characteristics

A total of 122 BC patients were initially screened. Subsequently, 116 eligible patients were enrolled in the study and were randomly assigned to the intervention STRONG-B (n=61) or control (n=55) groups (fig 2). Table 1 shows that BMI levels in the subset of patients without AWS were significantly lower in STRONG-B versus control (P=.014), while other clinical and sociodemographic characteristics at baseline did not show statistically significant differences between groups.

Arm volume, grip strength, functional capacity, body weight, and daily steps

Our primary outcome was arm volume differences. The AWS/BMI adjusted linear mixed model revealed a significant increase in arm volume in the control group from baseline to t_1-t_3. In contrast, the STRONG-B group displayed a significant reduction in arm volume versus the control group from baseline to t_1-t_3 (fig 3a; table 2). The presence of AWS had a significant effect in increasing arm volume in both groups, while BMI did not show a significant association with arm volume (table 2).

Grip strength in the surgery side significantly increased in the control group from baseline to t_1-t_3. Similarly, grip strength in the STRONG-B group was significantly higher from baseline to t_1-t_3 (fig 3b). AWS and BMI did not show a significant association with grip strength for either group (see table 2). On the nonsurgical side, grip strength in the control group did not change significantly over time (t_0-t_3). In contrast, grip strength in the nonsurgical side in the STRONG-B group was significantly higher versus control from baseline to t_1-t_3 (fig 3c). Again, AWS and BMI did not show a significant association with grip strength in the STRONG-B or control group (see table 2). Regarding the 6MWT, the control group showed no significant differences from baseline to t_1-t_3, whereas participants in the STRONG-B group displayed a significant increase in functional capacity versus control from baseline to t_1-t_3 (fig 3d). Neither AWS nor BMI had significant associations with 6MWT (see table 2). Notably, STRONG-B participants showed a significant reduction in body

Table 2 Results of the linear mixed model analysis on arm volume, grip strength, and physical performance adjusted by AWS and BMI

	Volume Difference (mL)		Strength (Surgery Side, kg)		Strength (Contralateral Side, kg)		6MWT (m)	
Predictors	Estimates (95% CI)	*P*	Estimates (95% CI)	*P*	Estimates (95% CI)	*P*	Estimates (95% CI)	*P*
(Intercept)	0.87 (−50.80 to 52.54)	.974	14.93 (8.69-21.17)	<.001*	19.05 (12.71-25.39)	<.001*	507.18 (368.33-646.03)	<.001*
group: STRONG-B	1.42 (−13.63 to 16.47)	.852	0.23 (−1.50 to 1.96)	.793	0.65 (−1.10 to 2.40)	.465	19.37 (−19.39 to 58.12)	.324
Time t_1	8.40 (0.36-16.45)	.041*	1.46 (0.79-2.14)	<.001*	−0.10 (−0.76 to 0.56)	.775	−8.22 (−24.22 to 7.78)	.313
Time t_2	9.77 (1.67-17.87)	.018*	2.50 (1.82-3.18)	<.001*	−0.09 (−0.75 to 0.58)	.802	−3.09 (−19.21 to 13.02)	.706
Time t_3	12.23 (4.13-20.33)	.003*	2.90 (2.22-3.58)	<.001*	−0.15 (−0.81 to 0.52)	.668	−8.55 (−24.67 to 7.56)	.297
AWS: yes	33.57 (18.09-49.05)	<.001*	0.03 (−0.16 to 0.21)	.772	−0.00 (−0.19 to 0.18)	.961	−3.84 (−7.94 to 0.27)	.067
BMI	1.06 (−0.46 to 2.59)	.170	−0.42 (−2.30 to 1.45)	.656	−0.12 (−2.02 to 1.79)	.903	−9.78 (−51.44 to 31.88)	.643
group: STRONG-B; t_1	−13.15 (−24.14 to −2.16)	.019*	1.47 (0.55-2.40)	.002*	1.62 (0.71-2.52)	<.001*	38.14 (16.28 to 60.00)	.001*
group: STRONG-B; t_2	−13.36 (−24.49 to −2.23)	.019*	2.45 (1.51-3.38)	<.001*	2.40 (1.49-3.32)	<.001*	54.12 (31.98 to 76.27)	<.001*
group: STRONG-B; t_3	−12.20 (−23.33 to −1.06)	.032*	2.74 (1.81-3.68)	<.001*	2.75 (1.83-3.66)	<.001*	73.12 (50.98 to 95.26)	<.001*

$Time_0$ and control group were used as base level for coefficient comparisons.
* Indicates statistical significance.

weight (fig 3e) and a significant increase in daily steps (fig 3f) from baseline to t_1 and t_3.

QoL measures

Next, we sought to determine the effect of STRONG-B on the QoL of participants using specific questionnaires (EORTC QLQ-C30 and EORTC QLQ-BR23). Figure 4 and supplemental table S1 (available online only at http://www.archives-pmr.org/) show significant increases in global QoL (fig 4a) and functional scales, including physical, role, emotional, and social functioning at 36 weeks (t_3). Notably, increases were observed in both the control and STRONG-B groups, except for cognitive functioning, which showed a significant reduction in both groups (fig 4b). Among symptom scales, the STRONG-B group had significantly reduced insomnia and pain scores (fig 4c, d) at 36 weeks (t_3). Interestingly, no changes in insomnia were observed in the control group. In addition, although pain was significantly reduced in the control group, pain reduction in the STRONG-B group was significantly higher than that in the control group. We then analyzed the effects on functional and symptom scales of the EORTC QLQ-BR23 (see supplementary table S1). Among symptom scales, both control and STRONG-B were associated with significantly increased systemic therapy side effects but reduced arm symptoms over time (fig 4e, f).

Physical therapy referrals

Patients that required physical therapy because of AWS or those with restricted range of arm motion were identified between t_0 and t_1. No additional referrals occurred after this period. The experimental group included 28 patients with AWS and 13 with restricted arm motion, while the control group had 24 patients with AWS and 12 with restricted arm motion. On average, these patients underwent 3 60-minute physical therapy sessions.

Safety and adherence

No adverse events were reported during the study, indicating a high level of safety for both the STRONG-B and control groups. Participants showed high adherence to the monthly PSM sessions, with 96% of the STRONG-B group and 97% of the control group attending all 3 sessions. This level of engagement highlights the participants' dedication to the PSM program. Additionally, STRONG-B participants completed at least 18 of the 24 sessions included in the program (77%).

Discussion

BCRL affects >20% of BC patients posttreatments.[1,2] Despite its high prevalence, there are no definitive clinical guidelines for its management. Our study demonstrated that the combination of a PSM and a supervised exercise program (STRONG-B) effectively reduces arm volume and prevents BCRL in high-risk patients. Furthermore, this strategy also improves physical performance and QoL of participants. To our knowledge, this is the first report to show the effects of combining PSM with supervised exercise on arm volume and BCRL. Importantly, these findings could serve as a basis for the development of more effective strategies for the prevention and clinical management of BCRL.[36]

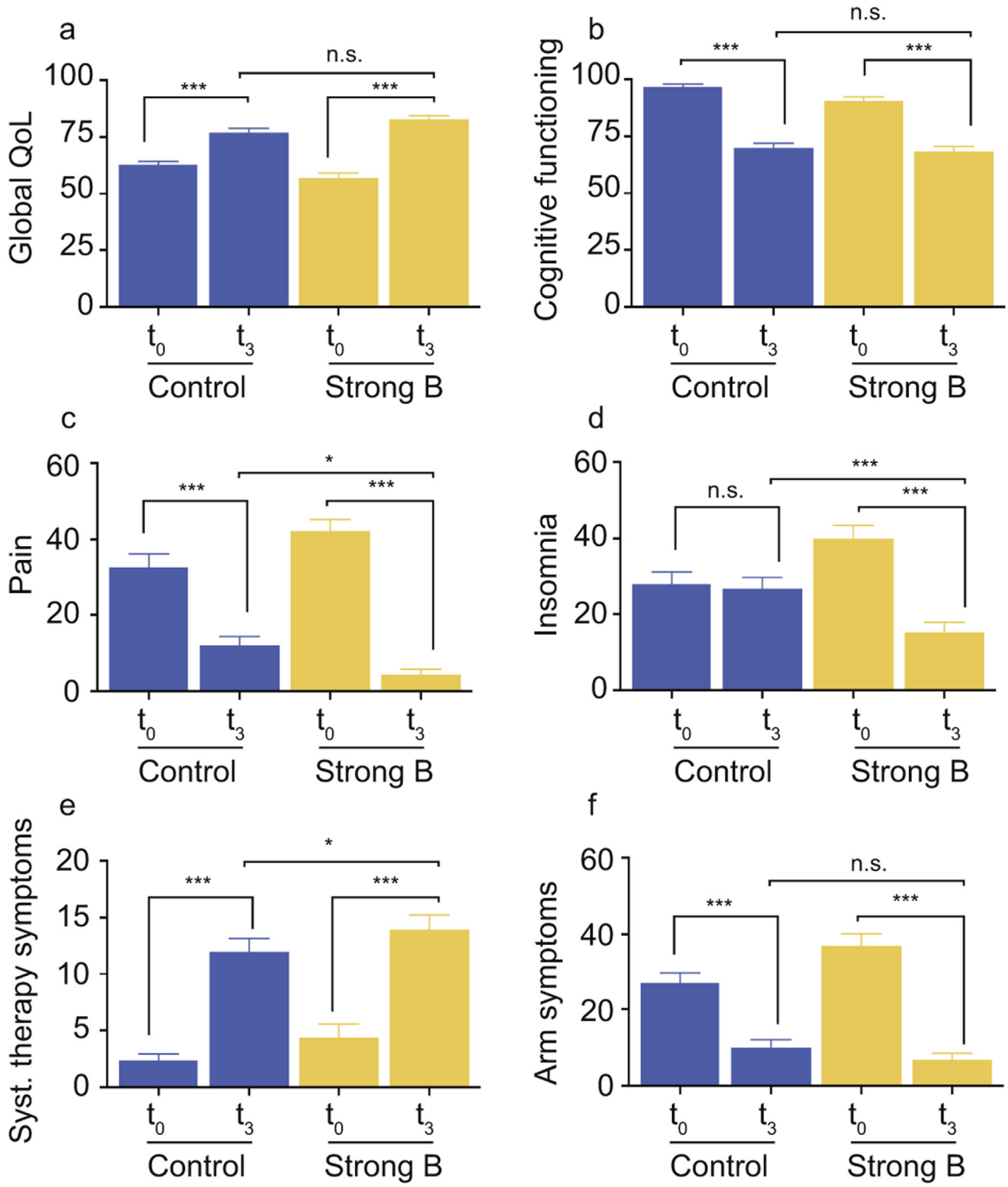

Fig 4 Effects of STRONG-B on selected QoL dimensions. (a) Global QoL (b) Cognitive functioning (c) Pain (symptoms scale) (d) Insomnia (symptom scale) (e) systemic therapy symptoms (f) Arm symptoms. n.s., not significant; QoL, quality of life; Syst., systemic. *P<.05, ***P<.001.

In addition to arm volume reduction, we demonstrated significant improvements in upper limb muscular strength, particularly in grip strength, in both arms. Grip strength is a critical indicator of overall muscle strength and physical function, essential for daily activities and independence. Improved grip strength is associated with enhanced QoL in BC patients, enabling them to perform tasks more efficiently and with less discomfort.[37-40] The significant effect on grip strength exceeded the clinical threshold of 5.0-6.5 kg,[27] suggesting that the combination of PSM with a multimodal exercise program has a major effect on the functional capacity of patients. These findings have important implications for clinical practice and support the incorporation of multimodal exercise programs into the routine care of patients.

Our intervention also significantly improved patient performance in the 6MWT. This is in line with previous studies[41,42] that demonstrated improvements in the physical function of BC patients after early interventions (within 3 mo of surgery) consisting of supervised exercises. The observed change of ≥54 m is considered clinically significant[29] and reinforces the practical implications for patients undergoing chemotherapy.

The precise mechanisms by which exercise reduces or prevents BCRL are not fully elucidated because of the heterogeneity of

studies. However, resistance training has been consistently shown to reduce inflammation and stimulate lymphatic circulation, which may explain the reduction in arm volume.[40] Our findings also show that a multimodal exercise program based on resistance exercise and promoting daily steps reduces body weight in BC patients. Obesity is a risk factor for BCRL[43] and a prevalent disorder in the Chilean population,[44] including BC patients.[45]

Despite the significant improvements in global QoL and in most functional scales (see supplementary table S1), both groups suffered cognitive impairment and a reduction of arm symptoms, likely because of adjuvant chemotherapy. The postchemotherapy decline in cognitive functioning of BC patients has been previously reported by others.[46] Cancer-related cognitive impairment affects 15%-75% of cancer patients[47] and may involve impairments in perception, attention, language, reasoning, thinking, and memory. Studies speculate that cognitive difficulties are linked to increased fatigue and insomnia caused by chemotherapy-related neurotoxicity and inflammation.[48] Notably, STRONG-B significantly decreased insomnia, while control levels remained unaffected (fig 4d). Previous studies report improved sleep and an anti-inflammatory effect of resistance training in sarcopenic patients[49] and in overweight/obese BC patients.[50] Although STRONG-B was also associated with a decrease in fatigue over time, these differences did not reach statistical significance (P=.141).

The analgesic benefit of physical exercise is widely recognized in both healthy individuals and cancer patients/survivors.[51] Accordingly, we found a significant decrease in the STRONG-B group in the pain symptom scale of the EORTC-QLQC30. Although this was also observed in the control group, pain scores were significantly lower in STRONG-B. We speculate that decreased pain could explain, at least in part, the better physical performance (6MWT) observed in the STRONG-B group. As expected during adjuvant chemotherapeutic treatments, our assessment of symptom scales from the EORTC QLQ-BR23 revealed a significant increase in systemic therapy side effects symptoms in both the control and STRONG-B groups. Intriguingly, systemic therapy side effect symptoms were significantly higher in STRONG-B participants. Although we could attribute this to the higher baseline scores of systemic therapy side effect symptoms in the STRONG-B group, a definitive explanation for this phenomenon is unclear and warrants further investigation.

Importantly, our study demonstrated high levels of safety and adherence, with no adverse events reported and significant participant engagement. The STRONG-B group exhibited high adherence to the exercise program, attending 77% of the scheduled sessions, and both groups showed high attendance rates to the monthly PSM sessions. This engagement underscores the potential for successful integration of such interventions into routine clinical care. However, maintaining compliance with exercise programs can be challenging for BC patients, particularly those undergoing chemotherapy. Fatigue, pain, and other side effects can significantly affect a patient's mood, affecting their ability, motivation, and adherence to exercise programs. In response to these challenges, patient-tailored programs, remote monitoring, motivational support, and integration with routine care can help maintain engagement and adherence, despite the challenges posed by cancer treatments.

Study limitations

Our study has certain limitations. First, it was performed at a single-center; therefore, our findings should be interpreted with caution. Future studies should incorporate more centers to increase the applicability of our exercise program. Second, this was a 2-arm parallel superiority randomized controlled trial with potential inherent bias such as differences in the care provided to the experimental and control groups, which can potentially lead to increased interaction and attention from health care providers. Third, the exercise program was limited to 12 weeks, which may not account for long-term effects or consequences on patients. Fourth, although we initially projected a total of 80 participants (n=40 for each group), our study was developed during the COVID-19 pandemic, and therefore we overestimated the percentage of patient dropout, which explains the uneven excess of participants in both groups (n=56 and n=50 for the experimental and control groups, respectively). Additionally, we did not assess medical outcomes, such as chemotherapy response or associated adverse events, which could be a valuable area for future research.

Conclusions

Our findings demonstrate that integrating PSM with structured exercise not only reduces arm volume and prevents BCRL but also significantly improves physical performance and QoL in high-risk patients. Importantly, the combination of PSM and STRONG-B was found to be superior to PSM alone, thereby validating the superiority design of the study. This supports the incorporation of the STRONG-B program into standard care for BC patients, with the potential to enhance clinical outcomes and QoL. As such, this study sets the stage for further research to explore the long-term benefits and broader applicability of this promising intervention.

Suppliers

a. Stata, version 15.1; StataCorp.
b. R, version 4.3.2; R Software Foundation.

Keywords

Breast neoplasm; Exercise, Lymphedema, Physical performance; Rehabilitation; Risk factors

Corresponding author

Karol Ramírez-Parada, PT, MSc, MBA, Departamento de Kinesiología, Escuela Ciencias de la Salud, Facultad de Medicina, Pontificia Universidad Católica de Chile, Benito Rebolledo 1988-2054, Macul, Región Metropolitana, Santiago, Chile. *E-mail address:* kramirezp@uc.cl.

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