Original Article

Nighttime Compression Supports Improved Self-Management of Breast Cancer–Related Lymphedema: A Multicenter Randomized Controlled Trial

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BACKGROUND: Lymphedema is a prevalent long-term effect of breast cancer treatment associated with reduced quality of life. This study examined the efficacy of nighttime compression as a self-management strategy for women with chronic breast cancer–related lymphedema. **METHODS:** Th authors conducted a parallel 3-arm, multicenter, randomized trial. Women were recruited from 3 centers in Canada and randomized to group 1 (daytime compression garment alone [standard care]), group 2 (daytime compression garment plus nighttime compression bandaging), or group 3 (daytime compression garment plus the use of a nighttime compression system garment). The primary outcome was the change in excess arm volume from the baseline to 12 weeks. Participants from all groups used a nighttime compression system garment from weeks 13 to 24. **RESULTS:** One hundred twenty women were enrolled, 118 completed the randomized trial, and 114 completed the 24-week follow-up. The rates of adherence to nighttime compression were 95% ± 15% and 96% ± 11% in the compression bandaging and nighttime compression system groups, respectively. After the intervention, the addition of nighttime compression was found to be superior to standard care for both absolute milliliter reductions ($P = .006$) and percentage reductions ($P = .002$) in excess arm lymphedema volume. Significant within-group changes were seen for quality of life across all groups; however, no between-group differences were found ($P > .05$). **CONCLUSIONS:** The trial demonstrated a significant improvement in arm lymphedema volume from the addition of nighttime compression whether through the application of compression bandaging or through the use of a nighttime compression system garment. ***Cancer* 2022;128:587-596**. © *2021 American Cancer Society*.

LAY SUMMARY:

- Lymphedema is swelling that occurs in the arm on the side of the surgery for breast cancer.
- Lymphedema occurs in approximately 21% of women.
- Lymphedema tends to worsen over time and can result in recurrent infections in the arm, functional impairment, and pain.
- Currently, treatment consists of intensive treatments to reduce the swelling followed by regular use of a compression sleeve during the day.
- This study examined and found a benefit from the addition of nighttime compression (whether through self-applied compression bandaging or through the use of a nighttime compression system garment) to the use of a daytime compression sleeve.

KEYWORDS: breast cancer, compression therapy, lymphedema, physical therapy.

INTRODUCTION

Lymphedema, a significant swelling of the arm, chest wall, and breast on the surgical side, is one of the more frequent complications of breast cancer treatment. Data suggest that approximately 21% of women who undergo treatment for their cancer develop breast cancer–related lymphedema (BCRL).[1] The impact of BCRL on women is often profound: it can produce negative changes in self-image, increased anxiety, and poorer quality of life.[2,3] Over time, BCRL can create considerable disability with recurrent infections in the limb,[4] functional impairment, and pain, with each affecting the woman's work and career.[5] At present, there are no known curative surgical or pharmacological treatments for lymphedema.[6]

Conservative management of BCRL generally involves education, skin care, decongestive exercise, compression bandaging, and manual lymphatic drainage.[7] The initial reduction phase is followed by a maintenance phase of

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See editorial on pages 458-460, this issue.

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self-management typically involving continued skin care regimens, decongestive exercise, self-massage, and use of a daytime compression garment.[8] Applying compression at night is an option that is often presented to the survivor when the condition is advanced or when relapses in symptoms and/or arm lymphedema volume occur.[6] When nighttime compression is indicated, the survivor is taught how to apply compression bandaging (CB) to the arm. Reported barriers to the application of CB include the time burden of application (~20 minutes) and the difficulty in applying CB in a consistent and effective manner[9]; thus, adherence to this management option is low.[10] Nighttime compression system garments (NCSGs) emerged on the market as an alternative to CB. NCSGs are simple to use, quick to apply to the limb, and can be easily adjusted to provide the appropriate amount of pressure. Little is known about the effectiveness of nighttime compression whether through the application of CB or through the use of an NCSG.[11]

Objectives

The primary objectives of this randomized controlled trial (RCT) were to determine the efficacy of nighttime compression on arm lymphedema volume maintenance and quality-of-life outcomes in women with BCRL who were in the maintenance phase of treatment for lymphedema.

MATERIALS AND METHODS

Ethics approval was received from the Health Research Ethics Board of Alberta Cancer Committee and the University of British Columbia Ethics Board. The study was a parallel 3-arm, Canadian multicenter, randomized, fast-track trial (with delayed assignment to the experimental group for both comparison groups) and included the Cross Cancer Institute in Edmonton, the Tom Baker Cancer Centre in Calgary, and the University of British Columbia/Mount St. Joseph's Hospital in Vancouver.[12] The study's physical and occupational therapists had specialized training in lymphedema. Each site was visited twice by the lead research team before study initiation for the purposes of standardizing treatments and measurements. The detailed methods for the trial have been reported elsewhere.[12]

Participants

The following eligibility criteria were used to determine inclusion in the trial:

1. Woman with a diagnosis of BCRL in the ipsilateral arm.
2. A minimum increase of 200 mL or 10% in arm volume over the unaffected arm.[7]
3. Completion of all primary and adjuvant cancer treatments by a minimum of 1 month before randomization.
4. Being in the lymphedema maintenance phase and agreeable to not pursuing any other lymphedema treatments beyond the assigned intervention.
5. Having her own properly fitted compression sleeve for daytime maintenance and agreeing to wear her daytime sleeve as per standard care (SC) for a minimum of 12 hours per day.
6. Not using nighttime compression as a maintenance strategy before study entry.

The following were used as exclusion criteria:

1. Clinical or radiological evidence of active breast cancer, either local or metastatic.
2. History and clinical diagnosis of bilateral arm lymphedema.
3. Serious nonmalignant disease that would preclude daily treatment and follow-up.
4. Contraindications to compression therapy.
5. Other disorders that precluded obtaining informed consent or adherence to the protocol.
6. Inability to comply with the protocol, measurement, and follow-up schedule due to factors such as a vacation during the study period.

Women who enrolled in the study were stratified by accruing center (the Cross Cancer Institute, the Tom Baker Cancer Centre, or Mount St. Joseph's Hospital) and by lymphedema severity (ie, mild vs moderate lymphedema as per the classification criteria of the International Society of Lymphology[7]) and then were randomly assigned to 1 of 3 groups.

Group 1: SC—daytime use of compression sleeve alone (SC group)

Participants randomized to the SC group were provided with advice concerning appropriate skin care, regular exercise, and maintenance of a healthy body weight and were instructed to wear a daytime compression sleeve, with or without a gauntlet/glove (worn if there was swelling in the hand and fingers), providing a minimum of 30 mm Hg of pressure, for 12 hours per day each day of the week.[13-17] At week 12, participants in this arm of the trial were fitted for a NCSG and followed the protocol outlined in group 3 of the trial.

Group 2: SC plus nighttime multilayered compression bandaging (CB group)

Participants randomized to the nighttime CB group were instructed in the application of nighttime multilayered CB by the study's physical or occupational therapist. The multilayered CB involved the use of gauze for the hand and fingers as well as the application of a stockinette, a foam layer, and 3 to 4 Comprilan bandages to the limb. A multipurpose underpadding was used as an alternative for participants unable to tolerate the foam layer. Participants had a 2-week phase-in period, following which they were asked to wear the CB at night while sleeping for a minimum of 8 hours per night for a minimum of 5 nights per week for 4 weeks (weeks 3-6). From weeks 7 to 12, maintenance CB at least 3 times per week was introduced. After the 12-week RCT, participants in this arm of the trial were fitted for a NCSG and followed the protocol outlined for group 3 of the trial.

Group 3: SC plus NCSG (NCSG group)

Participants in this group were fitted for and instructed in the use of an inelastic NCSG[18] by the study's physical or occupational therapist. Participants had a 2-week phase-in period, following which they were asked to wear the NCSG at night while sleeping for a minimum of 8 hours per night for a minimum of 5 nights per week for 4 weeks (weeks 3-6). From weeks 7 to 12, maintenance NCSG at least 3 nights per week was introduced. After the 12-week assessment, participants in this group had the option to continue using their NCSG.

Baseline Data and End Points

The primary end point for the trial was arm lymphedema volume. Lymphedema was objectively measured with the Perometer (Pero-Systems, Wipputal, Germany). The Perometer is an optoelectric limb volumeter that uses infrared technology to quantify limb volume and determine interlimb differences.[19-21] Secondary end points included 1) quality of life measured with the condition-specific Lymphoedema Functioning, Disability, and Health Questionnaire (Lymph-ICF)[22]; 2) bioimpedance analysis (BIA) to assess the extracellular fluid status within the arm[23]; 3) sleep disturbance via the RAND Medical Outcomes Survey Sleep Survey[24]; and 4) self-efficacy of lymphedema management based on the 6-item Chronic Disease Self-Management scale.[25] Body height was recorded at the baseline, and body weight was recorded at the baseline and at each follow-up time point. Adherence to the assigned compression therapy regimen was recorded by participants (ie, days per week and hours per day) in a daily diary. Follow-up measurements occurred at weeks 6, 12 (end of the RCT portion), 18, and 24.

Adverse Events

Adverse events related to the application of compression, episodes of cellulitis, cancer recurrence, and other serious medical conditions were recorded.

Allocation Concealment and Method of Randomization

Participants were randomized in a 1:1:1 ratio to SC, CB, or NCSG by a secure central randomization service administered by the Clinical Trials Unit at the Cross Cancer Institute.

Blinding

Using the Perometer, BIA, and body weight, an independent assessor (blinded) performed the measurements of arm volume. The research coordinator administered the outcome measures for sleep disturbance, self-efficacy, and quality of life and collected the adherence diary at each visit. Study garments were purchased at cost from the participating industry partner through the grant funds. Participants remained in their randomized group to preserve the intent-to-treat principle.

Sample Size for the Randomized, Fast-Track Trial Phase

The sample size required per group to detect at least a minimal clinically important mean difference of 20% (SD, ±25%) in arm lymphedema volume in favor of either the SC+NCSG or SC+CB group versus SC alone was 36 participants. A total sample of 108 participants achieved a power of 86% for our primary outcome with a significance level of .05 via a 1-way analysis of variance (ANOVA) test. To detect at least a minimal clinically important difference on the Lymph-ICF quality-of-life scale of 15 points out of 100 (SD, ±22) between the 2 nighttime compression groups, this sample achieved a power of 80% with a significance level of .05 via a 2-sided Mann-Whitney test (under the assumption that the actual distribution was normal). To allow for an estimated 10% loss to follow-up and noncompliance/crossover of the SC group, an additional 12 patients were recruited for a total of 120 participants.

Statistical Analyses

Baseline medical and demographic characteristics, arm dominance with respect to the lymphedematous arm, and adverse events of the 3 groups were compared with a

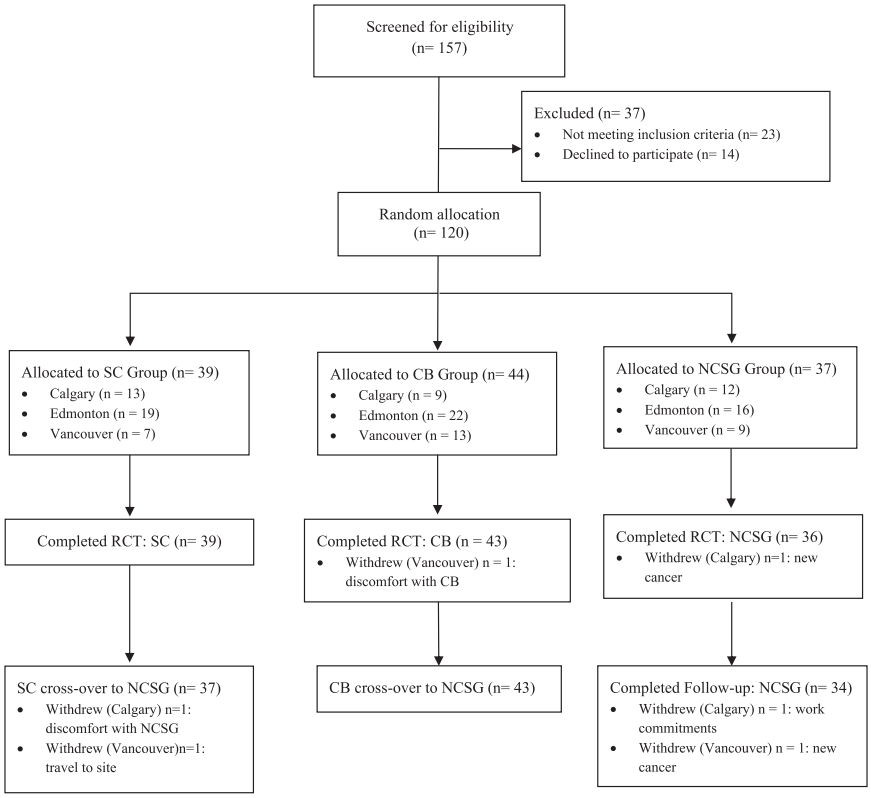

Figure 1. Consolidated Standards of Reporting Trials diagram of patient flow. CB indicates compression bandaging; NCSG, nighttime compression system garment; RCT, randomized controlled trial; SC, standard care.

1-way ANOVA for continuous data and with the Pearson χ^2 tests for categorical data. The primary analysis compared the groups with respect to the percentage excess lymphedema volume and quality of life at 12 weeks with a 1-way ANOVA on change scores. General linear models were used to adjust for center and lymphedema category (mild or moderate) and to evaluate the treatment effect in subgroups defined by the strata. Sleep quality, self-efficacy, and adherence-related outcomes were analyzed by repeated measures modeling and a 1-way ANOVA on change scores. Analyses of primary outcomes were performed at the end of the RCT with intent-to-treat analyses. Within-group analyses were conducted for primary and secondary outcomes from weeks 13 to 24.

RESULTS

Between November 2014 and August 2017, 157 women interested in taking part in the trial contacted the investigators (Fig. 1). Among the 120 participants who enrolled, 118 (98%) completed the 12-week intervention (primary end point), and 114 (95%) completed the 24-week follow-up. Participant characteristics are displayed in Table 1. We present an intent-to-treat analysis based on the entire accrued population, and we retained all outliers as reflecting the variability inherent in the BCRL population.[26]

Among participants, the reported adherence to daytime compression was 87% ± 17%, 81% ± 20%, and 73% ± 27% for the SC, CB, and NCSG groups, respectively. The rates of adherence to the application of nighttime compression were 95% ± 15% and 96% ± 11% in the CB and NCSG groups, respectively ($P = .718$). No major adverse events related to study participation occurred. During the 24-week study period, 14 minor adverse events were reported that were related to the application of nighttime compression (see the supporting information).

Primary End Point: Percentage Reduction in Excess Lymphedema Volume

The percentage excess lymphedema reduction was 1.5% ± 18%, 12.1% ± 16%, and 15.9% ± 22% in the SC, CB, and NCSG groups, respectively. The primary analysis showed a significantly larger percentage reduction from the application of nighttime compression

TABLE 1. Baseline Characteristics of the Study Participants

Characteristic	Overall (n = 120)	SC (n = 39)	CB (n = 44)	NCSG (n = 37)
Age, mean ± SD, y	61 ± 11	59 ± 11	62 ± 9	62 ± 12
Education, No. (%)				
High school or less	32 (26.5)	11 (28.2)	9 (20.5)	12 (32.4)
Some college	21 (17.5)	5 (12.8)	8 (18.2)	8 (21.6)
College degree or more	67 (56)	23 (59)	27 (61.4)	17 (45.9)
Ethnicity, No. (%)				
White	110 (91.7)	37 (94.9)	38 (86.4)	35 (94.6)
Asian	8 (6.6)	1 (2.6)	6 (13.6)	1 (2.7)
African American	1 (1)	—	—	1 (2.7)
Aboriginal	1 (1)	1 (2.6)	—	—
Time since surgery, median (range), mo	64 (4-351)	75 (8-351)	44 (4-266)	54 (6-348)
Cancer stage, No. (%)				
1	8 (7)	2 (5.1)	4 (9.1)	2 (5.4)
2	46 (38)	19 (48.7)	18 (40.9)	9 (24.3)
3	64 (53)	18 (46.2)	21 (47.7)	25 (67.6)
Missing	2 (2)	—	1 (2.3)	1 (2.7)
Surgical details				
Breast-conserving surgery, No. (%)	45 (37.5)	15 (38.5)	19 (43.2)	11 (29.7)
Mastectomy, No. (%)	75 (62.5)	24 (61.5)	25 (56.8)	26 (70.3)
Axillary lymph node dissection, No.	117	38	43	36
Sentinel lymph node biopsy, No.	3	1	1	1
Lymph nodes removed, mean ± SD, No.	14 ± 6.3	14 ± 6.0	13 ± 6.2	14 ± 6.8
Lymph nodes positive, mean ± SD, No.	4 ± 4.0	4 ± 4.6	3 ± 3.7	4 ± 3.9
Radiation therapy, No. (%)				
Breast only	22 (18.3)	6 (15.4)	11 (25)	5 (13.5)
Breast + lymph node regions	85 (70.8)	27 (69.2)	27 (51.4)	31 (83.8)
Locations not reported	1 (0.8)	—	1 (2.3)	—
No radiation therapy treatment	12 (10.0)	6 (15.3)	5 (11.3)	1 (2.7)
Chemotherapy, No. (%)				
Non–taxane-based regimen	12 (11.7)	6 (18.8)	4 (11.8)	2 (6.9)
Taxane-based regimen	74 (71.8)	24 (75)	25 (73.5)	25 (86.2)
Type not reported/unknown	19 (15.8)	3 (7.7)	11 (25.0)	5 (13.5)
No chemotherapy treatment	15 (12.5)	6 (15.3)	4 (9.0)	5 (13.5)
Lymphedema presentation				
Lymphedema duration, median (range), mo	34 (3-336)	48 (6-336)	25 (3-227)	30 (4-194)
Arm dominance: right, No. (%)	107 (89.2)	35 (89.7)	38 (86.4)	34 (91.9)
Affected side: right, No. (%)	59 (49.2)	19 (48.7)	22 (50)	18 (48.6)
Mild lymphedema, No. (%)	68 (56.7)	24 (61.5)	24 (54.5)	20 (54.1)
Moderate lymphedema, No. (%)	52 (43.3)	15 (38.5)	20 (45.5)	17 (45.9)
Lymphedema volume, mean ± SD, mL	564 ± 326	521 ± 348	588 ± 293	579 ± 343
Lymphedema % larger, mean ± SD	20.7 ± 11.1	19.4 ± 10.7	20.8 ± 9.5	22.0 ± 13.1
Body composition, mean ± SD				
Height (m)	1.62 ± 0.1	1.63 ± 0.1	1.62 ± 0.1	1.62 ± 0.1
Weight, kg	78.6 ± 16.0	78.1 ± 13.8	81.0 ± 18.0	76.3 ± 15.7
BMI, kg/m^2	29.8 ± 5.8	29.4 ± 5.2	30.6 ± 6.5	29.2 ± 5.7
Site, No. (%)				
Calgary	34 (28.3)	13 (33.3)	9 (20.5)	12 (32.4)
Edmonton	58 (48.7)	19 (48.7)	22 (50)	17 (45.9)
Vancouver	28 (17.9)	7 (17.9)	13 (29.5)	8 (21.6)

Abbreviations: CB, compression bandaging; NCSG, nighttime compression system garment; SC, standard care.

whether through NCSG ($P = .001$) or CB ($P = .01$) in comparison with SC (Table 2).

At the end of the RCT, the mean reduction in excess arm lymphedema was 11.6 ± 79, 62.9 ± 86, and 89.7 ± 134 mL in the SC, CB, and NCSG groups, respectively. Participants in the NCSG and CB groups were found to have a significantly larger reduction over the SC group ($P = .002$ and $P = .041$, respectively). As demonstrated in Figure 2, from the baseline to week 6, the excess lymphedema volume remained relatively stable

TABLE 2. Primary End Point: Percentage Reduction in Excess Lymphedema

Category	No.	% Reduction: T0 to T1		Adjusted Between-Group Mean Differences: T0 to T1, Mean (95% CI)		
		Group	Mean (SD)	NCSG vs SC	CB vs SC	NCSG vs CB
Overall	39	SC	1.5 (18)	14.9 (6 to 23); $P = .001$	10.8 (3 to 19); $P = .01$	4.1 (−4 to 12); $P = .33$
	43	CB	12.1 (16)[a]			
	36	NCSG	15.9 (22)[a]			

Abbreviations: CB, compression bandaging; NCSG, nighttime compression system garment; SC, standard care.
[a]Within-group improvement (adjusted for site, severity, and baseline value).

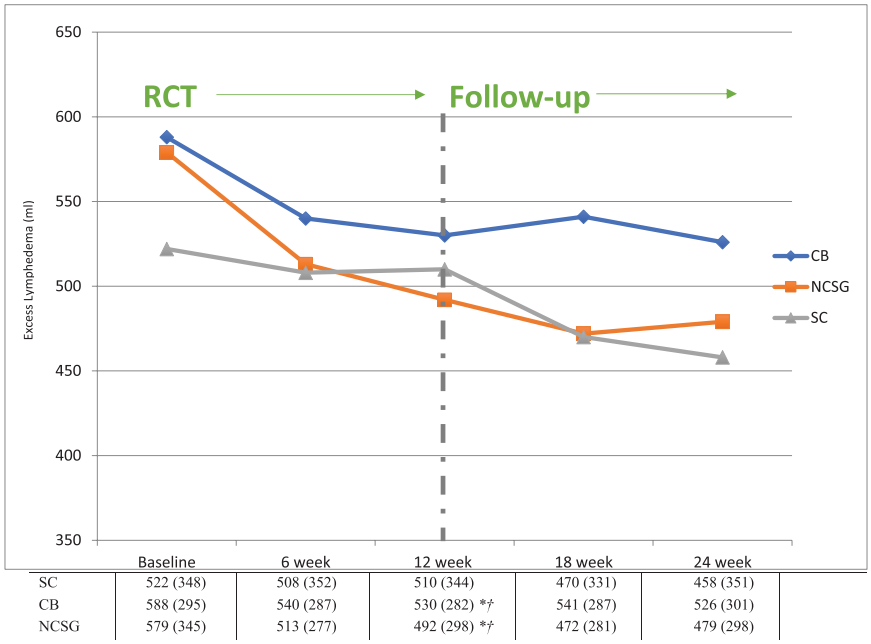

Figure 2. Change in excess lymphedema: baseline to 24 weeks in milliliters (with SDs in parentheses). *Within-group improvement $P < .05$ from the baseline to week 12. †Between-group difference $P < .05$ from the baseline to week 12 (adjusted for site, severity, and baseline value). CB indicates compression bandaging; NCSG, nighttime compression system garment; RCT, randomized controlled trial; SC, standard care.

in the SC group, whereas a reduction in lymphedema was seen in both the CB and NCSG groups, with a tapering in the reduction from weeks 7 to 12. In the follow-up period, the SC group demonstrated a similar reduction of excess volume with the use of an NCSG, whereas a plateau in the lymphedema volume was seen in the 2 original nighttime compression groups. No significant differences were found in lymphedema volume reduction between the groups at the 24-week follow-up ($P = .822$).

Changes in Quality of Life and Secondary Outcomes

Significant within-group changes were seen for quality of life across all groups as measured by the Lymph-ICF; however, no between-group differences were found. Improvements were also seen for the outcomes of self-efficacy, BIA, and sleep disturbance; however, no significant between-group differences were found. Body weight remained stable across groups throughout the RCT and the follow-up period (Table 3).

Exploratory Subgroup Analyses

In protocol-specified analyses of the stratification groups, no significant differences were found by randomized group for the strata of mild and moderate severity ($P = .655$) or among centers ($P = .234$). Prespecified subgroup analyses indicated a significant difference in favor of the addition of nighttime compression for those with mild lymphedema. By center, significant differences were found in favor of NCSG over SC in both Edmonton ($P = .043$) and Vancouver ($P = .013$), a significant benefit was found for CB over SC in Calgary ($P = .032$), and a significant benefit

TABLE 3. Quality of Life and Secondary Outcomes

Outcome	T0: Baseline (n = 120), Mean (SD)	T1: End of RCT (n = 118), Mean (SD)	T2: Follow-Up (n = 114), Mean (SD)	Mean Change: T0 to T1 (End of RCT) (n = 118), Mean (SD)	Mean Change: T1 to T2 (Follow-Up) (n = 114), Mean (SD)	Adjusted Between-Group Mean Difference: T0 to T1, Mean (95% CI)		
						NCSG vs SC	CB vs SC	NCSG vs CB
Lymph-ICF[a]								
SC	23.7 (18.6)	19.2 (17.7)	15.4 (14.4)	−4.5 (7.5)[b]	−4.1 (9.7)[b]	−0.3 (−4.8 to 4.2)	−0.5 (−4.9 to 3.8)	+0.2 (−4.2 to 4.6)
CB	25.2 (16.8)	21.2 (18.1)	17.5 (15.9)	−4.3 (13.1)[b]	−3.5 (8.3)[b]			
NCSG	26.0 (16.0)	21.2 (16.5)	18.2 (17.7)	−4.8 (8.8)[b]	−2.1 (7.6)			
Bioimpedance[a]								
SC	25.9 (19.0)	23.4 (19.5)	20.3 (17.4)	−2.8 (11.4)	−3.1 (8.8)[b]	−0.9 (−5.8 to 4.0)	+2.3 (−2.1 to 6.8)	−3.3 (−8.1 to 1.5)
CB	27.7 (18.2)	22.3 (14.6)	25.4 (17.6)	−5.3 (10.7)[b]	+3.0 (9.5)			
NCSG	29.9 (22.0)	26.3 (19.3)	23.0 (18.2)	−2.7 (13.5)	−3.2 (5.9)[b]			
Self-efficacy[c]								
SC	7.7 (2.1)	8.3 (1.7)	8.1 (1.6)	+0.5 (1.8)	−0.1 (1.9)	−0.5 (−1.1 to 0.1)	−0.2 (−0.8 to 0.4)	−0.3 (−0.9 to 0.3)
CB	7.5 (1.9)	8.0 (1.6)	8.2 (1.7)	+0.5 (1.6)	+0.2 (1.4)			
NCSG	7.4 (1.6)	7.6 (1.9)	8.1 (1.6)	+0.2 (1.1)	+0.5 (1.8)			
Sleep disturbance[a]								
SC	39.8 (23)	34.1 (21)	27.7 (20)	+5.7 (16.5)[b]	+6.8 (17)[b]	+2.6 (−4.7 to 9.9)	−3.7 (−10.6 to 3.3)	+6.3 (−1.0 to 13.4)
CB	38.0 (21)	36.1 (26)	29.7 (22)	+1.5 (16.5)	+6.4 (19)[b]			
NCSG	38.1 (22)	30.5 (18.7)	29.5 (20)	+7.9 (18.7)[b]	+1.1 (18)			
Weight[a]								
SC	78.2 (14)	78.3 (13)	77.4 (13)	+0.1 (1.7)	−0.3 (1.8)	−0.13 (−0.7 to 1.0)	−0.2 (−0.6 to 1.0)	−0.1 (−0.9 to 0.8)
CB	81.0 (18)	81.0 (18)	81.2 (18)	0 (1.7)	+0.3 (2.1)			
NCSG	76.3 (16)	76.2 (16)	74.6 (14)	−0.1 (2.1)	−0.4 (2.1)			

Abbreviations: CB, compression bandaging; Lymph-ICF, Lymphoedema Functioning, Disability, and Health Questionnaire; NCSG, nighttime compression system garment; RCT, randomized controlled trial; SC, standard care.

[a]Lower scores are better.

[b]Within-group improvement (adjusted for site, severity, and baseline value).

[c]Higher scores are better.

of NCSG over CB was found in Vancouver ($P = .027$). Exploratory analyses demonstrated a significantly larger benefit from NCSG versus SC for participants who had not received radiation therapy to local lymph node regions (see the supporting information).

DISCUSSION

This study is, to our knowledge, the first RCT to evaluate nighttime compression as a self-management strategy for BCRL.[12] Our findings support the benefit of nighttime compression in reducing arm lymphedema volume, and they are consistent with an observational study reporting a positive association between the application of nighttime compression and better control of lymphedema volume.[11] Furthermore, the benefits were consistent whether assessed as the absolute change (milliliters) or relative change (percentage) in excess lymphedema volume, with and without outliers, and with missing data imputed or not. Although statistically significant differences were not found between mild and moderate lymphedema or among centers, in agreement with findings from other lymphedema interventions, a better response to nighttime compression was observed in those with mild lymphedema.[27]

Lifelong self-management of BCRL is critical to prevent progression of the condition and exacerbations requiring costly and intensive reduction treatments.[28] Self-management regimens typically involve the prescription of multiple daily self-care practices, which carry significant associated patient burdens resulting in poor adherence.[9,10,29] Applying compression at night has been reported as a self-care practice among survivors with BCRL.[9,30] The benefit and high adherence seen in both CB and NCSG groups support nighttime compression as a strategy that can be added to a nightly routine and can provide a means to treat lymphedema while the survivor is sleeping.[8] Although the findings from the CB and NCSG interventions were similar, the intervention costs differ. The market cost of an NCSG is approximately US $450, whereas the yearly cost of compression bandages is approximately US $50 to $60, with underlayers of foam and stockinette (replaced every 6-12 weeks) priced at approximately US $10 to $20. Although the cost of an NCSG garment may be prohibitive for some women, its advantages include time efficiency and ease in application, which enable long-term adherence to self-management.

Quality of life and self-efficacy also improved across all groups over the trial period. The failure of nighttime compression to significantly improve lymphedema-specific quality of life and self-efficacy over SC may be, in part, due to minimal disturbance in quality of life and the high self-efficacy of lymphedema self-management reported at the baseline. Moreover, aspects related to the trial itself, such as the high adherence reported for daytime compression, the scheduled follow-ups every 6 weeks, the re-evaluation of arm measures, and the additional support of and interaction with lymphedema-trained physical/occupational therapists, may have positively influenced quality of life and self-efficacy outcomes among all participants.[31]

No significant between-group differences were found for outcomes related to BIA, and this was probably related to the inherent variability of BIA. Although BIA measurements were quick to conduct, discordance was noted between BIA and perometry measurements, and this is a finding reported in other studies.[32,33] BIA is a technology that uses resistance to electrical current as a means of comparing the composition of fluid compartments within the body; thus, it is recommended for use in the early stages of lymphedema when excess fluid is the primary cause of the increased arm volume.[34]

Although the findings overall did not differ statistically between mild and moderate lymphedema or among centers, exploratory subgroup analyses revealed differences worth noting. Consistent with findings from other lymphedema interventions, a better response to nighttime compression was observed in those with mild lymphedema.[27] We hypothesize that in those with moderate lymphedema, progression in terms of adipose tissue deposition and fibrosis may have resulted in a limb less responsive to compression.[35]

Subtle differences were also found across centers, which likely can be explained by site differences in clinical care. In Edmonton and Calgary, cancer-related lymphedema services are provided as part of the public health care system at no charge to patients, whereas in Vancouver, publicly funded services are limited, and patients access private providers for care. Vancouver participants appeared to benefit greatly from participation in the trial, especially if they were assigned to the CB or NCSG group. In Calgary, a significant difference was found in favor of CB over SC. At this site, women are taught self-bandaging as part of their usual care for BCRL; thus, many participants were familiar and proficient with the technique. In contrast, for the vast majority of participants in Edmonton and Vancouver, self-bandaging was a new skill to learn.

Our trial's strengths include the direct comparison of the application of CB and NCSGs, a large sample size, multicenter recruitment, the use of validated

measurements, high intervention adherence, and minimal loss to follow-up. Limitations include a primarily White population and high baseline quality of life and self-efficacy. The use of a randomized fast-track design precluded our ability to analyze trial findings by original group allocation at the 24-week follow-up; however, this design was used successfully to optimize the recruitment and retention of the SC and CB participants.

In summary, our trial demonstrates the benefit of nighttime compression as a self-management strategy for chronic BCRL. Given the benefits seen and the high adherence rates, we recommend early introduction of nighttime compression as a self-management strategy for BCRL.

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CONFLICT OF INTEREST DISCLOSURES

Lori Radke reports belonging to the editorial board for the Canadian Lymphedema Framework (unpaid). Marc Webster reports honoraria/consulting fees from Merck, Genomic Health, Roche, Novartis, Knights, and Lilly. Kristin L. Campbell reports consulting fees from Astellas. The other authors made no disclosures.

AUTHOR CONTRIBUTIONS

Margaret L. McNeely: Study concept and design. **Naomi D. Dolgoy:** Intervention. **Bolette Skjodt Rafn:** Recruitment and intervention. **Sunita Ghosh:** Study concept and design. **Paula A. Ospina:** Recruitment and intervention. **Mona M. Al Onazi:** Intervention. **Lori Radke:** Recruitment. **Mara Shular:** Study concept and design and intervention. **Urve Kuusk:** Study concept and design and recruitment. **Marc Webster:** Recruitment. **Kristin L. Campbell:** Study concept and design. **John R. Mackey:** Study concept and design and recruitment. All authors contributed to data acquisition, analysis, and interpretation and the preparation of the manuscript.

DATA AVAILABILITY

For the availability of data and materials, go to https://dataverse.library.ualberta.ca/privateurl.xhtml?token=816549e7-91b4-43b0-83db-811217ec043b.

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