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Association between Lymphedema Self-Care Adherence and Lymphedema Outcomes among Women with Breast Cancer-Related Lymphedema

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Abstract

Objective—To determine if adherence to self-care modalities for breast cancer-related lymphedema (BCRL) predicts BCRL outcomes among 128 breast cancer (BrCa) survivors who participated in the 12-month physical activity and lymphedema (PAL) trial.

Design—This was a prospective cohort study. Adherence to 10 BCRL self-care modalities, as recommended in the clinical practice guidelines for the management of BCRL was assessed by questionnaire at baseline. BCRL outcomes assessed at baseline and 12-months included volumetry, circumferences, bioimpedence spectroscopy, the Norman lymphedema survey, and clinician-defined lymphedema exacerbations requiring treatment. Generalized linear models were used to estimate the relationship between adherence to BCRL self-care modalities and the likelihood of experiencing a BCRL outcome.

Results—Adherence to BCRL self-care activities did not predict experiencing any BCRL outcomes at 12-months. Levels of adherence to BCRL self-care modalities did not predict a ≥5% decrease in interlimb volume (P_{trend}=0.79), ≥5% decrease in the sum of interlimb arm circumferences (P_{trend}=0.47), ≥10% decrease in bioimpedence spectroscopy (P_{trend}=0.83), ≥1 decrease in self-reported lymphedema symptoms (P_{trend}=0.91), or clinician-defined lymphedema exacerbation requiring treatment (P_{trend}=0.84).

Conclusions—Our findings suggest levels of BCRL self-care adherence do not predict BCRL outcomes among BrCa survivors with stable lymphedema who were followed for 12-months.

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Keywords

compliance; physiotherapy; clinical guidelines; measurement

INTRODUCTION

Breast cancer-related lymphedema (BCRL) is a complication of breast cancer (BrCa) treatment that affects 6-70% of BrCa survivors.[1, 2] BCRL is an incurable, lifelong condition characterized by accumulation of protein-rich fluid that manifests as swelling of the upper limb, and causes discomfort, altered physical function, and impaired quality of life.[2, 3]

The chronic, cyclic clinical sequence of BCRL forces BrCa survivors to allocate a considerable amount of time to manage BCRL.[4] Among 39 BrCa survivors in a cross-sectional survey, 66% reported spending ≥150 min·wk^{-1} on BCRL self-care activities.[5] In this same survey, women reported a number of barriers and burdens to BCRL self-care including lack of time and convenience, high cost, lack of results, and aggravation.[5] Corroborating these findings, among 141 BrCa survivors, 41% reported BCRL self-care adherence <50% of levels prescribed by their lymphedema clinicians.[6] Weight-lifting exercise has emerged as an efficacious modality to improve BCRL outcomes among BrCa survivors. This addition of weight-lifting to the armamentarium of BCRL prevention and management has challenged prior beliefs that weight-lifting was detrimental to BCRL outcomes.[7] The rapidly increasing number of modalities available for BCRL management has prompted the need to empirically review the evidence relating to BCRL management. Two recent reviews that included more than 3,200 BrCa survivors,[8, 9] and the advisory committee for Centers for Medicare and Medicaid Services,[10] concluded that despite widespread use, the depth, breadth, and quality of literature supporting BCRL management is scant, and subsequent studies should focus on strengthening the evidence to provide efficacious modalities to BrCa survivors to manage BCRL.

This study sought to deepen the understanding of the relationship between BCRL self-care adherence and BCRL outcomes by exploring the hypothesis that adherence to BCRL self-care activities predicts BCRL outcomes among BrCa survivors who entered 12-months of follow-up with stable lymphedema. We hypothesized that higher levels of BCRL self-care adherence would predict a reduction in the likelihood of experiencing a BCRL outcome, relative to low levels of BCRL self-care adherence.

METHODS

Participants

Participants were enrolled in the physical activity and lymphedema (PAL) trial, a randomized controlled trial to examine the safety of progressive weight-lifting among women with BCRL. The Social Cognitive Theory formed the theoretical basis for the PAL intervention.[11] A detailed account of the PAL study has been published elsewhere.[11] In short, participants were randomized to either a progressive weight-lifting intervention or no exercise. Eligibility criteria included: 1) female BrCa survivor 1–15 years post-diagnosis; 2)

free from cancer at study entry; 3) ≥1 lymph node removed; and 4) no medical conditions or contraindicated medications that would prohibit participation in an exercise program. Additional criteria included: 5) body mass index ≤50kg/m^2; 6) no plans for surgery during the intervention period; 7) no history of bilateral lymph node dissection; 8) no weight-lifting in the previous year; and 9) stable body weight and not attempting to lose weight.

A participant was considered to have BCRL at study entry if she had one or more of the following: 1) ≥10% interlimb discrepancy in total arm volume; or 2) meeting any of the Common Toxicity Criteria Adverse Event version 3.0 for BCRL (swelling, obscuration, or pitting);[12] or 3) prior clinical diagnosis of BCRL that was confirmed by study measurements or by a clinician. In the event that a participant reported having BCRL that was not evident at study entry, she was required to provide written documentation of a previous diagnosis of BCRL from her lymphedema therapist. All study participants were required to have stable BCRL at study entry, defined as absence of all of the following in the three-months prior to enrolling in the study: 1) receiving complete decongestive therapy; or 2) self-reporting a ≥10% change in arm volume or circumference that lasted ≥1 week; or 3) having a BCRL-related infection that required the use of antibiotics; or 4) experiencing a change in activities of daily living as a result of a BCRL exacerbation. This study was approved by the Institutional Review Board of the University of Pennsylvania. Participants provided written informed consent and written clearance from their physicians.

BCRL Outcome Variables

Measurements were obtained for all study participants at baseline and 12-months by blinded measurement staff. The five BCRL outcomes for this exploratory analysis were: 1) volumetry;[13, 14] 2) arm circumferences;[14] 3) bioimpedence spectroscopy;[15, 16] 4) the Norman lymphedema survey;[17] and lymphedema exacerbation requiring treatment.[11, 12]

Volumetric measures were obtained by submerging the arm and hand in water and using the displaced water volume to determine limb volume. If the volume of the treated side was 10% greater than that of the untreated side, the participant was deemed to have clinically evident BCRL. Volumerty is correlated with circumference measures (r=0.90; P<0.0001),[13] and is reliably measured (intra-class correlation: 0.99).[14] Circumference measures were taken at the metacarpal, wrist, and every four centimeters along the arm until the axillary fold. We used arm circumferences to calculate two outcomes: 1) the sum of arm circumferences,[18] and 2) arm volume using the truncated cone method.[19] If the sum (or volume) of the arm circumferences for the treated side was 10% greater than the sum of the arm circumferences for the untreated side, the participant was considered to have clinically evident BCRL. In the PAL cohort, water displacement volumetry was strongly correlated with arm volume circumferences calculated using the truncated cone method; r=0.960; P<0.0001. Consequentially, the statistical analysis of circumference-calculated arm volume was similar to that of water displacement volumetry (data not shown). Bioimpedence spectroscopy was used to measure the impedance of extracellular fluid of each arm. The impedance of the treated and untreated arms was compared. If the ratio of measurements exceeded normative values, BCRL was deemed to be clinically evident.[18] Bioimpedence spectroscopy is correlated with deuterium-isotope dilution (r=0.986; P<0.001), the gold-

standard method to quantify total body water.[16] Participants were asked to complete the Norman lymphedema survey, which evaluated the frequency and severity of 14 BCRL-related symptoms.[17] The Norman lymphedema survey correctly classifies 84-88% of women with therapist-diagnosed lymphedema, and has high agreement across therapists (κ=0.80).[17] After randomization into the study, participants were evaluated for a possible BCRL exacerbation that required treatment if they reported a change in symptoms that lasted ≥1 week or measurements indicated an increase of ≥5% in interlimb discrepancy, accompanied by an increase of ≥5% in affected arm, as compared to the previous measurement time point. Exacerbations were diagnosed by the evaluating lymphedema therapist, based on clinical evaluation of tissue tone, texture, and color, as well as swelling and symptom changes in accordance with the Common Toxicity Criteria Adverse Event version 3.0 for BCRL.[12]

BCRL Self-Care Adherence Questionnaire

Study investigators with training in physical medicine and rehabilitation, BCRL self-care and clinical treatment, and survey design developed a questionnaire that assessed utilization and adherence to 10 BCRL self-care modalities,[6] as recommended in the 2001 clinical practice guidelines for the treatment and care of BCRL.[4] After receiving feedback from other investigators in the area of BCRL, this questionnaire was implemented in the PAL trial. Modalities in the questionnaire included: physical therapy exercise, pneumatic compression pump, medication (i.e., benzopyrones), lymphedema bandaging, arm elevation, self-administered lymphatic drainage, therapist-administered lymphatic drainage, compression garment, skin care, taping, or other modalities not listed. In 2009 the clinical practice guidelines for the care of BCRL were revised, given evidence supporting the association of benzopyrones with liver toxicity.[20]

BCRL self-care adherence was defined as the proportion of the current frequency of use relative to the prescribed frequency of use.[6] If a participant responded yes to having been prescribed one or more of the self-care modalities, she was further questioned about her adherence to each self-care modality.[6] A multiple-choice response was provided for adherence to each BCRL self-care modality with four possible responses: 1) <25% of the time; 2) 25-49% of the time; 3) 50-74% of the time; 4) 75-100% of the time, as recommended by their lymphedema therapist. We generated a composite adherence score for each participant based on the BCRL self-care modalities reported at study entry, using the adherence categories described above (<25, 25-49, 50-74, or 75-100%). Average adherence equally weighted each BCRL self-care modality prescribed to a participant. This weighting approach implies equal importance of adherence across all prescribed BCRL self-care modalities (i.e., that one modality is not more important to adhere to than another). We elected to use an equal weighting approach given the paucity of data to support the proportional importance of individual BCRL self-care modalities in relation to one-another.[4, 21] We have previously reported that over the 12-month study the total number of BCRL self-care modalities did not change, and the composite adherence to BCRL self-care modalities did not change.[6] Therefore, this analysis utilized baseline BCRL self-care adherence (other analysis methods did not change the results presented herein; data not shown).

Demographic and Clinical Variables

Demographic characteristics, cancer treatment, and medication history were obtained by self-report. Cancer staging was taken from state cancer registries, surgical pathology reports, or self-report. The number of lymph nodes removed was obtained from surgical pathology reports. Body mass index was calculated using objectively-measured height and weight. These variables were collected at baseline.

Statistical Analysis

Descriptive statistics for BCRL outcome variables include counts and percentages for binary variables, and means and standard deviations, or medians and interquartile ranges for continuous variables. Generalized linear models were used to estimate risk ratios for categorical variables. *P* values from the test for trend (P_{trend}) were calculated using BCRL self-care adherence as a continuous variable in the regression models. BCRL outcomes (i.e., volumetry, circumference measures, etc.) were also examined as continuous variables in a multivariable-adjusted sensitivity analysis. Hand dominance may influence measurement and diagnostic precision of lymphedema outcomes,[22] therefore we adjusted for dominance in our statistical analysis. In post-hoc power calculations, we had ≥80% statistical power to detect a significant test for trend for the continuous variable outcomes. The nature of this study was exploratory rather than confirmatory with respect to statistical hypothesis testing. Stata v.12/SE was used for all statistical analysis.

RESULTS

Participant Characteristics

The PAL trial recruited 141 women with BRCL to assess the effects of a slowly progressive weight-lifting program on lymphedema outcomes. Two women were excluded from this analysis because of a second primary or recurrent cancer. Eleven women were excluded from this analysis because they reported being prescribed no BCRL self-care modalities and thus provided no information on BCRL self-care adherence. The 128 participants included in this analysis were aged 37–80 at baseline and had a variety of educational, racial, and occupational backgrounds (Table 1). Time since breast cancer diagnosis ranged from 14–183 months, and the number of lymph nodes removed ranged from 1–38. Time since lymphedema diagnosis ranged from 1–183 months. Baseline BCRL outcome measures are presented in Table 2.

Lymphedema self-care adherence and lymphedema outcomes

Use of individual BCRL self-care modalities has been reported elsewhere in detail.[6] In short, the most commonly used BCRL self-care modalities included compression garments (79%), bandaging (68%), exercise (58%), elevation (42%), therapist-administered lymphatic drainage (46%), self-administered lymphatic drainage (39%), and skin care (33%). The least commonly used BCRL self-care modalities included pneumatic compression pumps (12%), taping (8%), and medications (5%). Adherence to individual BCRL self-care modalities has been reported elsewhere in detail.[6] Collectively, BCRL self-care adherence among the 128 women prescribed ≥1 lymphedema self-care modality was as follows: 16 (13%) reported an

average of <25% adherence, 36 (28%) reported an average of 25–49% adherence, 40 (31%) reported an average of 50–74% adherence and 36 (28%) reported an average of 75–100% adherence.

Using generalized linear regression models, higher levels of adherence to BCRL self-care activities did not predict BCRL outcomes (Table 3). When BCRL outcomes were examined as continuous variables in a multivariable-adjusted sensitivity analysis (adjusted for factors listed in Table 1 in addition to hand dominance and randomized group assignment), adherence to BCRL self-care activities did not predict changes in volumetry (<25% compared to ≥75% adherence: β=0.09; P_{trend}=0.741), sum of arm circumferences (<25% compared to ≥75% adherence: β=−0.63; P_{trend}=0.693), bioimpedence spectroscopy (<25% compared to ≥75% adherence: β=4.04; P_{trend}=0.753), or lymphedema symptoms (<25% compared to ≥75% adherence: β=−0.14; P_{trend}=0.306). Lymphedema exacerbation was a binary variable, and subsequently was not included in our continuous variable sensitivity analyses.

DISCUSSION

The major finding of our study is that levels of BCRL self-care adherence did not predict BCRL outcomes over 12-months. Adherence to BCRL self-care activities has been noted as an impediment to the long-term success of BCRL treatment.[4] In our sample, among BrCa survivors with stable lymphedema, we were unable to identify an association between adherence to BCRL self-care modalities and a variety of BCRL outcomes over 12-months.

While this analysis begins to shed light on the efficacy of BCRL self-care, there are several important limitations that influence the interpretation of our exploratory findings. The first limitation is that this was a secondary analysis of the PAL trial. The PAL trial had a variety of inclusion and exclusion criteria regarding BCRL,[11] such as stability of BCRL prior to entering the study. Further, the time since BCRL diagnosis varied from 1 to 183 months, and time since last lymphedema treatment varied from 3 to 120 months at study entry. Therefore, BrCa survivors for whom BCRL frequently fluctuated or required intensive therapy were not included in the PAL trial. Despite this criterion, 16 participants (12%) experienced a ≥5% increase in interlimb arm volume difference, 28 participants (22%) experienced a ≥5% decrease in interlimb arm volume difference, and 28 participants (22%) required complete decongestive therapy during the 12 month intervention.[7] The PAL study was a yearlong weight-lifting exercise trial. Women who did not have sufficient time to participate or did not have interest in enrolling in an exercise study were also excluded. Therefore, the generalizability of our findings are limited to BrCa survivors similar to those in the PAL trial. The analysis of our questionnaire was not weighted, such that all BCRL self-care modalities were given equal importance. We elected to use this non-weighted approach on the basis that if a combination of BCRL self-care modalities were recommended to a specific participant, then the adherence to all of the self-care modalities in that combination were equally important, as part of a comprehensive BCRL self-care program. There is no data to inform how weights would be assigned to each self-care modality and the relative impact that weighting of BCRL self-care modalities has on lymphedema outcomes. There exists the possibility of recall bias because of the self-report

nature of our questionnaire. Participants may have forgotten that their lymphedema clinician prescribed certain BCRL self-care modalities which may result in underreporting. Furthermore, participants may have also forgotten the frequency in which their lymphedema clinician recommended certain BCRL self-care activities be undertaken. All participants were required to attend a one-hour educational lecture entitled the 'Lymphedema Education Session' that was based on material from the National Lymphedema Network (NLN). This education session was taught by the PAL principal investigator (Schmitz) to ensure that all participants had a comparable understanding of lymphedema self-care methods while in the PAL trial. However, we did not collect information that allowed us to quantify the level of BCRL self-care education or skill in completing the prescribed BCRL self-care activities. Therefore, our null findings may reflect poor or inappropriate use of the prescribed modalities as a result of insufficient patient education, rather than poor subject adherence to the BCRL self-care modalities.

Additional limitations to our exploratory analysis include the limited number of observed outcomes. The small sample size of outcomes precluded the examination of adherence to individual BCRL modalities and BCRL outcomes. The small sample size also precluded the exploration of specific demographic and clinical subgroups. When we conducted sensitivity analyses treating the outcome variables (i.e., volumetry, circumference measures, etc.) as continuous measures in multivariable-adjusted regression models, our results were similar to one-another. Adjustment for randomized group assignment did not influence our study findings. Our prior report demonstrated that randomized group did not influence BCRL self-care practices over the 12-month study.[6]

The ability for those with BCRL to adequately adhere to BCRL self-care has been a concern for over a decade.[21] A prior study determined that non-compliance with BCRL bandaging and compression garment use were risk-factors for increased arm volume one-year after receiving complete decongestive therapy.[23] Poor BCRL self-care compliance to phase II decongestive activities after receiving phase I complete decongestive therapy has resulted in failure rates of 38%, 53%, and 65% at 1, 2, and 4 years, respectively.[24] Restricting our analyses to only include phase II complete decongestive activities, our conclusions did not change. Nonetheless, these data suggest new strategies and methods to maintain arm health are needed among BrCa survivors with BCRL.[25]

The PAL trial demonstrated twice weekly weight-lifting reduced the need for clinician-defined BCRL treatment by 53% ($p=0.04$).[7] Participants in the PAL trial were required to wear a well-fitting, study-provided compression garment during all weight-lifting activities. The physiologic underpinning of the PAL trial was that slowly progressive weight-lifting improves flow of lymphatic fluid.[7] Indeed, there is evidence that exercise improves flow of lymphatic fluid by changes in sympathetic outflow, muscular constriction, diaphragmatic movement with physical exertion and increased breathing, and possibly lymphangiogenesis and recruitment of dormant lymphatic vessels.[26] A prior study examined isometric handgrip exercise among breast cancer survivors who were not wearing compression sleeves concluded lymphatic flow did not improve 5-6 hours after exercise.[27] It has been hypothesized that isotonic weight-lifting exercise coupled with a well-fitting compression garment may be effective in moving lymphatic fluid out of the arm, whereas weight-lifting

without adequate compression may be insufficient.[26] In the PAL trial, participants completed twice-weekly weight-lifting. It is plausible that twice-weekly weight-lifting is sufficient to improve lymphedema outcomes despite non-optimal adherence to other BCRL self-care modalities.[6] This evidence may suggest that twice-weekly weight-lifting coupled with a compression garment may be superior to daily self-care activities alone to improve BCRL outcomes. However, this hypothesis would need to be tested in a randomized controlled trial to provide definitive evidence.

A majority of BrCa survivors (66%) spend ≥150 min·wk^{-1} engaging in BCRL self-care activities.[5] Interestingly, weight-lifting, such as that prescribed in the PAL trial, requires a similar amount of time (120–180 min·wk^{-1}), but is performed twice-weekly, rather than daily.[7, 11] The twice-weekly schedule of weight-lifting might serve to reduce burden among those with BCRL, and to help improve long-term compliance. In the PAL trial, the average adherence to supervised weight-lifting was 92% in months 1–6, and to unsupervised weight-lifting was 78% in months 6–12; these levels of adherence exceed those for individual BCRL self-care activities.[5-7] In addition to reducing the likelihood for lymphedema treatment, and reducing self-reported BCRL symptom severity, weight-lifting improves muscular strength and body composition,[7] bone health,[28] and quality-of-life,[29] among BrCa survivors. Thus, weight-lifting may be a time-efficient multidimensional intervention to promote the health and longevity of BrCa survivors with BCRL.[25]

In our study, increasing levels of BCRL self-care adherence are did not predict BCRL outcomes among BrCa survivors with stable BCRL over one-year. These findings will need to be replicated in a separate cohort of BrCa survivors. Our current hypothesis is that weight-lifting with a well-fitting compression garment may serve as an efficacious modality to manage BCRL, while providing a multitude of other known health benefits to those with BrCa, compared to BCRL self-care alone. However, this hypothesis needs to be examined in a randomized controlled trial. Such a trial would provide definitive evidence of the efficacy of BCRL self-care versus weight-lifting.

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Table 1

Demographic and clinical characteristics of study participants (n=128)

Characteristic	Value[a]
Age – yr	57.2±9.7
Education – no. (%)	
High school or less	26 (20%)
Some college	46 (36%)
College degree or more	56 (44%)
Self-reported race – no. (%)	
White	74 (58%)
Black	49 (38%)
Other	5 (4%)
Occupation – no. (%)	
Professional	45 (35%)
Clerical or service	20 (15%)
Homemaker, student, or unemployed	11 (9%)
Other or unknown	10 (8%)
Retired	42 (33%)
Body mass index – kg/m^2	30.5±6.4
Months since cancer diagnosis	83.3±46.3
Cancer stage – no. (%)	
1	53 (41%)
2	1 (1%)
3	38 (30%)
Data not available	36 (28%)
No. of nodes removed	15.6±8.2
Chemotherapy – no. (%)	103 (80%)
Radiation – no. (%)	104 (81%)
Current receipt of drugs – no. (%)	
Tamoxifen	16 (13%)
Aromatase inhibitor	1 (1%)
Months since lymphedema diagnosis	60.6±44.8
Months since last lymphedema treatment	36.2±36.2
Common Toxicity Criteria Lymphedema grade – no. (%)	
0	9 (7%)
1	26 (20%)
2	54 (42%)
3	39 (31%)

[a] Continuous variables are mean ± standard deviation. Categorical variables are n (%). Percentages may not sum to 100% due to rounding error.

Table 2

Baseline lymphedema outcome variables (n=128)

Outcome lymphedema variable	Value[a]
Volumetry	
Volumetric interlimb % difference	16.91±15.19
Absolute interlimb difference (mL)	428.05±418.92
Clinical Diagnosis	
Lymphedema exacerbation	0 (0%) (all stable)
Circumferences	
Circumferential interlimb % difference[b]	7.31±8.03
Absolute interlimb difference (cm)[b]	23.87±26.69
Circumferential interlimb % difference[c]	14.66±15.22
Absolute interlimb difference (cm^3)[c]	363.23±414.64
Bioimpedence	
Bioimpedence spectroscopy interlimb ratio	1.07±0.22
Norman lymphedema survey [b]	
No lymphedema (No symptoms)	10 (8%)
Mild lymphedema (1–3 symptoms)	56 (44%)
Moderate+ lymphedema (≥4 symptoms)	62 (48%)
Number of symptoms	5.56±2.82
Severity of symptoms	2.00±0.70

[a] Continuous variables are mean ± standard deviation. Categorical variables are n (%).

[b] Data were reported by patients regarding 14 symptoms: rings too tight, watch too tight, bracelets too tight, clothing too tight, puffiness, knuckles not visible, veins not visible, skin feels leathery, arm feels tired, pain, pitting, swelling after exercise, difficulty writing, or other. The mean severity is for all 14 symptoms, with the possible severity score for each ranging from 0 (no symptom) to 4 (very severe). [b] Calculated using the sum of arm circumferences.

[c] Calculated using the truncated cone formula for arm circumferences.

Table 3

Adherence to lymphedema management modalities prescribed at baseline and lymphedema outcomes at 12 months

Lymphedema outcome variable	N (%)	Adherence	Risk Ratio (95% CI)	P_{trend}
Volumetry				
≥5% increase	1 (7%)	<25%	1 — Referent	0.63
	4 (27%)	25–49%	1.77 (0.22–14.67)	
	6 (40%)	50–74%	2.46 (0.33–18.84)	
	4 (27%)	75–100%	1.78 (0.22–14.67)	
≥5% decrease	4 (16%)	<25%	1 — Referent	0.79
	6 (24%)	25–49%	0.53 (0.19–1.49)	
	9 (36%)	50–74%	0.66 (0.25–1.70)	
	6 (24%)	75–100%	0.71 (0.28–1.83)	
Clinical Diagnosis				
Lymphedema exacerbation	1 (4%)	<25%	1 — Referent	0.84
	11 (39%)	25–49%	5.50 (0.78–38.94)	
	9 (32%)	50–74%	3.79 (0.52–27.50)	
	7 (25%)	75–100%	3.29 (0.44–24.57)	
Sum of Arm Circumferences				
≥5% increase	1 (20%)	<25%	1 — Referent	0.91
	1 (20%)	25–49%	0.50 (0.03–7.49)	
	1 (20%)	50–74%	0.42 (0.03–6.33)	
	2 (40%)	75–100%	0.94 (0.09–9.63)	
≥5% decrease	1 (33%)	<25%	1 — Referent	
	1 (33%)	25–49%	0.50 (0.03–7.48)	0.47
	0 (0%)	50–74%	—	
	1 (33%)	75–100%	0.47 (0.03–7.05)	
Bioimpedence				
≥10% increase	2 (7%)	<25%	1 — Referent	0.58
	11 (33%)	25–49%	3.67 (0.93–14.40)	
	11 (33%)	50–74%	2.84 (0.71–11.29)	
	9 (27%)	75–100%	2.48 (0.61–10.12)	
≥10% decrease	3 (17%)	<25%	1 — Referent	0.83
	4 (22%)	25–49%	0.88 (0.23–3.45)	
	5 (28%)	50–74%	0.86 (0.23–3.15)	
	5 (33 %)	75–100%	1.10 (0.32–3.83)	
Norman lymphedema survey [a]				

Lymphedema outcome variable	N (%)	Adherence	Risk Ratio (95% CI)	P_{trend}
≥1 increase in symptoms	2 (20%)	<25%	1 — Referent	0.15
	4 (40%)	25–49%	1.00 (0.20–4.89)	
	3 (30%)	50–74%	0.65 (0.12–3.52)	
	1 (10%)	75–100%	0.24 (0.02–2.41)	
≥1 decrease in symptoms	3 (12%)	<25%	1 — Referent	0.91
	7 (27%)	25–49%	1.17 (0.35–3.92)	
	9 (35%)	50–74%	1.30 (0.40–4.17)	
	7 (27%)	75–100%	1.10 (0.32–3.70)	

[a]Datawere reported by patients regarding 14 symptoms: rings too tight, watch too tight, bracelets too tight, clothing too tight, puffiness, knuckles not visible, veins not visible, skin feels leathery, arm feels tired, pain, pitting, swelling after exercise, difficulty writing, or other. The change in severity of symptoms is the mean of the changes in severity for all 14 symptoms, with the possible severity score for each ranging from 0 (no symptom) to 4 (very severe).