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Self-management Strategies for Risk Reduction of Subclinical and Mild Stage of Breast Cancer–Related Lymphedema

A Longitudinal, Quasi-experimental Study

KEY WORDS

Breast cancer–related lymphedema
Breast neoplasms
Early intervention
Self-management
Symptom

Background: Early intervention with self-management strategies can potentially reduce the risk of progression of breast cancer–related lymphedema (BCRL). **Objective:** To determine if The-Optimal-Lymph-Flow (TOLF) program focused on self-management strategies applied to patients with a subclinical or mild stage of BCRL can improve lymphedema-related behaviors, symptom experience, and limb circumference changes. **Methods:** A total of 41 women with subclinical or mild lymphedema were enrolled in TOLF program. Lymphedema-related behaviors and lymphedema-related symptom experiences were measured by the Breast Cancer and Lymphedema Symptom Experience Index, and limb circumference changes were measured by sequential circumferential limb measurements at baseline and 1, 3, 6, and 12 months after the intervention. Generalized estimating equations were used to estimate the effects of the intervention on outcomes. **Results:** Generalized estimating equations revealed that lymphedema-related behaviors and the number and severity of lymphedema-related symptoms were significantly improved at 4 postintervention test points compared with baseline (all $P < .001$). Reduced lymphedema-related symptom distress in functional, social, emotional, and psychological and self-perception (all $P < .01$) also resulted. The

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This study was supported by Nursing Research Grant of Peking University Health Science Center (BMU20160517).

The authors have no conflicts of interest to disclose.

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Accepted for publication October 27, 2020.

DOI: 10.1097/NCC.0000000000000919

majority (77.5%) of patients maintained their preintervention lymphedema status; 17.5% of them reversed from mild lymphedema to subclinical lymphedema; 5.0% of them had lymphedema status progression. **Conclusion:** Positive outcomes in terms of lymphedema-related behaviors, relieving lymphedema-related symptom experience, and halting the progression of lymphedema status were documented following TOLF. **Implications for Practice:** Nurses could educate patients to incorporate the self-management strategies of TOLF program into daily life to help patients prevent or reverse subclinical or mild stage of BCRL.

Breast cancer–related lymphedema (BCRL) is one of the major postoperative complications suffered by breast cancer survivors.¹ It is defined as the abnormal accumulation of fluid in the interstitial space of the affected arm, breast, and chest wall.² Breast cancer treatments, especially axillary lymph node dissection (ALND) and radiotherapy, are blamed for the occurrence of BCRL for impairing the lymphatic system of the axilla.³ Additionally, inappropriate use of upper extremity and high body mass index (BMI) may contribute to the risk of developing BCRL.⁴ The incidence of BCRL varies widely between 2.5% and 42.9% in different studies, depending on the patient characteristics, definition, and measurements.^{3,5–8} Without timely and appropriate intervention, BCRL can be a progressive condition. A study that followed up 964 patients after ALND for 10 years, in which BCRL was defined by 200-mL difference between affected and unaffected limb volume, found that the cumulative incidence was 13.5% at 2 years of follow-up, 30.2% at 5 years, and 41.1% at 10 years.⁵ The incidence of BCRL increased significantly over the postoperative period.

Breast cancer–related lymphedema severity also increased over time. The International Society of Lymphology classified lymphedema as stages 0 to III.⁹ Stage 0 refers to a latent or subclinical condition where swelling is not evident, but subjective symptoms occur. Stage I represents an early and mild accumulation of protein-rich fluid in the arm, hand, trunk, or breast that can reverse with limb elevation or compression. It may present with pits, but the skin is typically soft with no dermal fibrosis. Stages II to III develop excess subcutaneous fat, fibrosis, and lymphatic elephantiasis, which are difficult to intervene. Specific diagnostic criteria were used to assess the severity of BCRL further, regarding the difference in limb volume,⁹ limb circumference,¹⁰ and L-Dex value.¹¹ With the progress of the BCRL stage, survivors might suffer from more symptoms,¹² which led to functional, psychological, and social morbidity and a severe negative impact on patients' quality of life.^{13,14} Preliminary research findings suggested that early diagnosis and intervention in the subclinical phase and mild stage might prevent the development of BCRL and minimize symptoms.^{1,15,16}

A variety of interventions, including manual lymph drainage,¹⁷ physical therapy,¹⁸ compressive garments,¹⁹ upper extremity exercise,²⁰ and yoga,²¹ have been applied to the subclinical and mild stage of BCRL. A randomized controlled study involving 45 breast cancer survivors demonstrated that light compression sleeves combined with physical activity applied early after

surgery might be a safe and efficient option to prevent postsurgical arm swelling and development of BCRL.¹⁹ In another prospective observational study, patients diagnosed with subclinical BCRL by bioimpedance spectroscopy received a series of interventions including short-term physical therapy, compression garments, and education, and the incidence of BCRL reduced from 36.4% to 4.4% over a 20-month follow-up.¹¹

As the irreversible and progressive nature of this complication, patients will lifelong struggle with BCRL.²² Interventions focusing on self-management held great promise for slowing the progression of BCRL.²³ The Optimal-Lymph-Flow (TOLF) program is a patient-centered nurse-led self-management program developed by Fu et al.^{24,25} It helps patients understand what BCRL is and how important to prevent it and empower patients to take safe actions. In 2014, 140 patients after breast cancer surgery were stratified into the ALND group ($n = 81$) and the sentinel lymph node biopsy group ($n = 59$) and received the preventive intervention of TOLF program. Findings showed that no patients in the sentinel lymph node biopsy and ALND group exceeded $\geq 10\%$ limb volume increase. TOLF program is effective in risk reduction of lymphedema.²⁴ However, there is a paucity of evidence to apply these self-management strategies to the subclinical and mild stage of BCRL. It is unclear if TOLF program targeting daily behaviors, proactive exercises, and optimal BMI can effectively reduce the risk or halt the progression of the subclinical and mild stage of BCRL.

To address this critical clinical need, we conducted a quasi-experimental study to evaluate the effectiveness of TOLF program in reducing the risk of the subclinical and mild stage of BCRL in Chinese breast cancer survivors over a 12-month intervention period. This study was guided by a conceptual framework called the Model of Self-care for Lymphedema Symptom Management.²⁵ In this model, physiological treatment factors, such as surgery and radiotherapy, which directly lead to BCRL symptoms, are difficult to be modified.^{5,7} However, compromised lymphatic drainage and BMI can be modified through self-care strategies to reduce the risk of BCRL.^{4,25,26} By targeting compromised lymphatic drainage, shoulder mobility exercises, muscle tightening–breathing, muscle tightening–pumping exercises, and large muscle exercises are provided by TOLF program to promote lymph flow and lessen lymphedema symptom burden and help reverse the mild BCRL and prevent further development of the subclinical BCRL.^{24,25} Meanwhile, general instructions are provided to encourage nutrition-balanced, portion-appropriate diet,

adequate hydration, and sleep to strive for maintaining optimal BMI and minimizing the risk of lymphedema.^{24,25}

■ Methods

Study Design

A longitudinal, quasi-experimental (single group), pre-post design with repeated measures was used to test the effect of TOLF program on the subclinical and mild stage of BCRL among Chinese breast cancer survivors.

Participants

We screened the medical records of breast cancer patients who had surgery from April 2017 to June 2018 at a large metropolitan tertiary hospital in northern China. The researcher contacted postoperative breast cancer patients by telephone and made an appointment to conduct limb circumference measurements during the next routine doctor appointment. The inclusion criteria for screening participants were as follows: (a) female, (b) aged 18 years or older, (c) initially diagnosed with unilateral breast cancer and finished surgery, and (d) completed ALND. The exclusion criteria for screening participants were as follows: (a) undergoing radiation and/or chemotherapy, (b) with tumor metastasis or recurrence, (c) other conditions that could lead to edema (eg, renal disease, malnutrition, or congestive heart failure), and (d) history of surgery or trauma on the affected axilla or arm.

Patients were screened again by the results of limb circumference measurements. Only patients with limb circumference difference of 1 to 3 cm (subclinical or mild stage of lymphedema) were invited to participate in this intervention study. Among 430 patients who received limb circumference measurements, 179 of them had a limb difference of 1 to 3 cm and were invited to participate in our study, and finally, 41 patients signed the written informed consent form and accepted intervention. Reasons provided by patients who did not enroll in the study included significant travel distance, stress from cancer treatment, or busy with work.

Interventions

The-Optimal-Lymph-Flow program is a patient-centered educational and behavioral program focused on daily self-management strategies, including basic knowledge about BCRL, exercises to promote lymph flow and drainage (muscle tightening–breathing, muscle tightening–pumping, and large muscle exercises), arm precautions to improve limb functional status, and instructions to optimize BMI.²⁵ Our research team has translated TOLF program handbook into Chinese after authorization. Table 1 presents the main self-management strategies of TOLF program.

After signing the written informed consent, the patient completed the self-report questionnaires, including demographic and clinical information, lymphedema-related behaviors, and the Breast Cancer and Lymphedema Symptom Experience Index. The researcher then carried out a 30-minute face-to-face individual education session with the patient, including self-management strategies in TOLF program handbook, demonstration, and feedback of

❁ **Table 1 • The-Optimal-Lymph-Flow Program**

	Strategies and Actions	Frequency and Situations
Basic knowledge about lymphedema	What is lymph system? What is breast cancer–related lymphedema? Why does lymphedema exist after breast cancer treatment? What time will the lymphedema exist? What are the common symptoms of lymphedema?	
Promoting lymph flow	Muscle tightening–breathing and Muscle tightening–pumping Large muscle exercises (walking, swimming, dancing, yoga, jogging, tai chi)	At least 3 times a day before meals or as much as the patient wants throughout the day Air travel: before take-off and after landing Sedentary lifestyle: at least every 4 h At least 15–30 min daily Air travel: get up and walk around every 1 h during flight Sedentary lifestyle: get up and walk at least every 1 h
Arm precautions	Skin care (keep skin clean and moist) Avoid skin damage Timely treatment of mild skin damage Avoid lifting heavy objects by affected limb Avoid repetitive and excessive activities Avoid high-temperature environment	Always
Instructions to optimize body mass index	Nutrition-balanced (ie, more vegetables and fruits, feeling 75% full for each meal) Stay hydrated Large muscle exercises (walking, swimming, dancing, yoga, jogging, tai chi) Get enough sleep	Each meal daily Drink 1500–1700 mL (6–8 glasses) water daily At least 15–30 min daily 3 times a week At least 7–8 h of sleep per night

muscle tightening–breathing and muscle tightening–pumping exercises. The-Optimal-Lymph-Flow program handbook was given to the patient after this session.

Another 4 face-to-face sessions were carried out at 1, 3, 6, and 12 months after the recruitment. During each session, the researcher checked the patient's lymphedema-related behaviors, collected the Breast Cancer and Lymphedema Symptom Experience Index questionnaires, and measured the patient's limb circumference. Based on the patient's condition, the researcher reviewed TOLF program with the patient to ensure that each component was done correctly. Besides, at least 15 telephone contacts were carried out during the intervention period (once a week in the first month and once a month during the following 11 months). During the telephone contacts, the researcher checked the adherence of self-management strategies and answered patients' questions about daily precautions.

Data Collection

DEMOGRAPHIC AND CLINICAL INFORMATION

We applied a self-designed questionnaire to collect demographic and clinical information regarding breast cancer and lymphedema. The demographic information included age, height, weight, education, marital status, and employment status. The clinical information included the dominant arm, surgical site, tumor staging, pathological type, type of surgery, neoadjuvant chemotherapy, chemotherapy, radiotherapy, and hormonal therapy. Patients completed this questionnaire at the recruitment, and the researcher would retrieve and check the information from electronic medical records.

LYMPHEDEMA-RELATED BEHAVIORS

This checklist was used to collect information on participants' lymphedema-related behaviors.²⁷ The checklist comprises 12 behaviors, including 5 protective behaviors (large muscle exercises, lifting affected limb, muscle tightening–breathing and muscle tightening–pumping exercises, skin care, progressive resistance training) and 7 risk behaviors (air travel, lift heavy objects with affected limb, trim cuticle around nails, carry a shoulder bag over the affected limb, take hot baths or saunas, hold a baby with the affected limb, smoking). Each item is rated on a Likert-type scale from 0 to 3 by frequency of the behavior. The protective behaviors use normal scoring method and ranged from 0 to 15, whereas the risk behaviors use reverse-scoring method and ranged from 0 to 21. The total score is the summation of all behaviors, ranging from 0 to 36. For the three scores, higher scores indicate better behaviors. This checklist was completed 5 times by patients during the whole intervention: at the recruitment and at the 4 face-to-face sessions.

THE BREAST CANCER AND LYMPHEDEMA SYMPTOM EXPERIENCE INDEX

This scale was used to collect information on participants' lymphedema-related symptom experience.²⁸ It is a self-report instrument consisting of 2 parts. Part I is used to assess the occurrence of lymphedema symptoms, comprising 24 items. By choosing either yes or no to indicate the presence or absence, each symptom can be considered as a categorical variable. Each item is also rated on a Likert-type scale from 0 to 4 by symptom

severity. The total score of symptom occurrence is the summation of all item scores ranging from 0 to 96. Higher scores indicate more severe symptom occurrence. Part II is used to assess the distress from the lymphedema symptoms, comprising 6 dimensions: functional, social, sleep, sexuality, emotional and psychological, and self-perception. The total score of symptom distress is the summation of all symptom distress item scores ranging from 0 to 128. Higher scores indicate more severe symptom distress. The total score of symptom experience is the summation of symptom occurrence score and symptom distress score, and higher scores indicate worse symptom experience. The English version was translated and tested in the Chinese population with the Cronbach's α ranging from .930 to .960 and the test-retest reliability ranging from 0.572 to 0.705.²⁹ This scale was also completed 5 times by patients during the whole intervention: at the recruitment and at the 4 face-to-face sessions.

LIMB CIRCUMFERENCE MEASUREMENTS

We used a well-established protocol for limb circumference measurements to measure both limbs: at hand proximal to the metacarpals, the wrist, and every 4 cm from the wrist to the axilla.² Circumference differences of 1 to 2 cm between limbs were defined as subclinical lymphedema, differences of 2 to 3 cm were defined as mild, differences of 3 to 5 cm were defined as moderate, and differences of more than 5 cm were defined as severe.^{10,30} Limb circumference measurements were performed with a flexible, nonelastic tape according to the protocol by a single researcher to avoid errors between the evaluators.

Ethical Aspects of the Study

The research project was approved by a biomedical ethics committee (IRB00001052-15073). All participants in this study provided informed written consent before being included.

Data Analysis

The analysis was performed with IBM SPSS Statistics for Windows, version 21.0 (IBM Corp, Armonk, New York). Frequency distributions and descriptive statistics were calculated to describe the demographic and clinical characteristics of the participants. Scores of lymphedema-related behaviors were presented as means with SD. Scores of lymphedema-related symptom experience and limb circumference differences were presented as medians with quartiles. Generalized estimating equations were used to estimate the effects of the intervention on lymphedema-related behaviors, lymphedema-related symptom experience, and limb circumference differences. α Level was set at $P < .05$ for all the statistical tests.

■ Results

Demographic and Clinical Characteristics

Among the 41 patients, 1 patient did not complete the 12-month follow-up. Forty-one patients were involved in the analysis. The demographic and clinical characteristics are shown in Table 2.

Table 2 • Demographic and Clinical Characteristics (n = 41)

Variables	n (%)	Variables	n (%)
Age, mean ± SD, y	58.0 ± 12.48	Pathological type	
Body mass index, mean ± SD, kg/m ²	25.17 ± 3.25	Noninfiltrative carcinoma	1 (2.4)
Education		Infiltrative nonspecific carcinoma	37 (90.2)
Primary school	3 (7.3)	Infiltrative specific carcinoma	1 (2.4)
Middle school	7 (17.1)	Data deficient	2 (4.9)
Senior high school/secondary school	13 (31.7)	Type of surgery	
Junior college	4 (9.8)	Breast conserving surgery	6 (14.6)
College degree or above	14 (34.1)	Partial mastectomy	1 (2.4)
Marital status		Total mastectomy	5 (12.2)
Married	40 (97.6)	Modified radical mastectomy	29 (70.7)
Single/divorced/separated	1 (2.4)	Neoadjuvant chemotherapy	
Employment status		No	34 (82.9)
Unemployed	11 (26.8)	Yes	7 (17.1)
Employed	30 (73.2)	Chemotherapy	
Surgery on dominant arm		No	5 (12.2)
No	17 (41.5)	Yes	36 (87.8)
Yes	24 (58.5)	Radiotherapy	
Surgical site		No	16 (39)
Left side	16 (39.0)	Yes	25 (61)
Right side	26 (63.4)	Hormonal therapy	
Staging (Union for International Cancer Control)		No	13 (31.7)
I	5 (12.2)	Yes	28 (68.3)
II	21 (51.2)	Lymphedema status	
III	13 (31.7)	Mild lymphedema	25 (61.0)
Data deficient	2 (4.9)	Subclinical lymphedema	16 (39.0)

Lymphedema-Related Behaviors

Generalized estimating equations were used to analyze the change of lymphedema-related behaviors among the 5 test points (Table 3 and Table 4). Table 3 presents the comparison results of scores of lymphedema-related risk behaviors, lymphedema-related protective behaviors, and lymphedema-related all behaviors at any 2 different test points. Not all the comparison results are significant, but there is a continuous improvement trend of behaviors in the first 3 months, which is well kept until the end of the follow-up.

Table 4 presents the β values of lymphedema-related risk behaviors, lymphedema-related protective behaviors, and lymphedema-related all behaviors at each follow-up point. The β values of lymphedema-related risk behaviors at each follow-up

point were .610 ($P < .001$), .707 ($P = .001$), .829 ($P < .001$), and .825 ($P < .001$), which indicated that lymphedema-related risk behavior score was significantly improved at 4 postintervention test points compared with baseline. The β values of lymphedema-related protective behaviors at each follow-up point were 4.366 ($P < .001$), 4.780 ($P < .001$), 4.707 ($P < .001$), and 4.626 ($P < .001$), which indicated that lymphedema-related protective behavior score was significantly improved at 4 postintervention test points compared with baseline. The β values of lymphedema-related all behaviors at each follow-up point were 4.976 ($P < .001$), 5.488 ($P < .001$), 5.537 ($P < .001$), and 5.456 ($P < .001$), which indicated that lymphedema-related all behavior score was significantly improved at 4 postintervention test points compared with baseline.

Table 3 • Scores of Lymphedema-Related Behaviors and Effect Test of Generalized Estimation Equation (Mean ± SD)

	Baseline (N ₁ = 41)	1-mo Follow-up (N ₂ = 41)	3-mo Follow-up (N ₃ = 41)	6-mo Follow-up (N ₄ = 41)	12-mo Follow-up (N ₅ = 40)	Wald χ^2	P
Lymphedema-related risk behaviors	19.85 ± 1.30 ^{a-d}	20.46 ± 0.67 ^{c,e}	20.56 ± 0.50 ^{c,e}	20.68 ± 0.47 ^{a,b,c}	20.68 ± 0.53 ^c	27.258	<.001
Lymphedema-related protective behaviors	3.46 ± 2.63 ^{a-d}	7.83 ± 2.14 ^{b,c}	8.24 ± 1.76 ^{a,c}	8.17 ± 1.66 ^c	8.13 ± 2.22 ^c	251.140	<.001
Lymphedema-related all behaviors	23.32 ± 2.83 ^{a-d}	28.29 ± 2.12 ^{b,c,e}	28.80 ± 1.69 ^{a,c}	28.85 ± 1.54 ^{a,c}	28.80 ± 2.16 ^c	216.958	<.001

^a $P < .05$ versus 1-month follow-up by ANOVA-GEE.

^b $P < .05$ versus 3-month follow-up by ANOVA-GEE.

^c $P < .05$ versus 6-month follow-up by ANOVA-GEE.

^d $P < .05$ versus 12-month follow-up by ANOVA-GEE.

^e $P < .05$ versus baseline by analysis of variance generalized estimation equation (ANOVA-GEE).

Table 4 • Parameter Estimation Results of Generalized Estimation Equation of Scores of Lymphedema-Related Behaviors

	N	Parameter	β	SE	95% CI		Wald χ^2	df	P
					Lower Limit	Upper Limit			
Lymphedema-related risk behaviors	41	Baseline	0 ^a						
	41	1 mo	0.610	0.1613	0.294	0.926	14.284	1	<.001
	41	3 mo	0.707	0.2188	0.278	1.136	10.449	1	.001
	41	6 mo	0.829	0.2151	0.408	1.251	14.858	1	<.001
	40	12 mo	0.825	0.2169	0.400	1.250	14.462	1	<.001
Lymphedema-related protective behaviors	41	Baseline	0 ^a						
	41	1 mo	4.366	0.3002	3.777	4.954	211.475	1	<.001
	41	3 mo	4.780	0.3133	4.166	5.395	232.790	1	<.001
	41	6 mo	4.707	0.3313	4.058	5.357	201.905	1	<.001
	40	12 mo	4.626	0.4153	3.812	5.440	124.066	1	<.001
Lymphedema-related all behaviors	41	Baseline	0 ^a						
	41	1 mo	4.976	0.3475	4.295	5.657	205.030	1	<.001
	41	3 mo	5.488	0.4024	4.699	6.277	185.955	1	<.001
	41	6 mo	5.537	0.4112	4.731	6.342	181.316	1	<.001
	40	12 mo	5.456	0.4801	4.515	6.397	129.157	1	<.001

^aNuisance parameter set as 0.

Lymphedema-Related Symptom Experience

Generalized estimating equations were used to analyze the change of lymphedema-related symptom experience among the 5 test points (Table 5 and Table 6). Table 5 presents the comparison results of the scores of lymphedema-related symptom experience, the numbers of lymphedema-related symptoms, the scores of lymphedema-related symptom occurrence, and the scores of lymphedema-related symptom distress at any 2 different test points. A continuous improvement trend showed up within 6 months and was well kept until the end of the intervention. Among the 6 dimensions of lymphedema-related symptom distress, there were statistically significant differences in the scores of functional, social, emotional, and psychological and self-perception among the 5 test points ($P < .05$), whereas no significant difference was found in sleep and sexuality among different test points ($P > .05$).

Table 6 presents the β values of lymphedema-related symptom experience, the numbers of lymphedema symptoms, lymphedema-related symptom occurrence, and lymphedema-related symptom distress at each follow-up point. The β values of lymphedema-related symptom experience at each follow-up point were -3.805 ($P < .001$), -4.951 ($P < .001$), -7.512 ($P < .001$), and -7.455 ($P < .001$), which indicated that lymphedema-related symptom experience score was significantly decreased at 4 postintervention test points compared with baseline. The β values of the number of lymphedema-related symptoms at each follow-up point were -0.610 ($P < .001$), -0.927 ($P < .001$), -1.488 ($P < .001$), and -1.662 ($P < .001$), which indicated that patients experienced fewer symptoms at 4 postintervention test points compared with baseline. The β values of lymphedema-related symptom occurrence at each follow-up point were -1.293 ($P < .001$), -1.756 ($P < .001$), -2.659 ($P < .001$), and -2.513 ($P < .001$), which indicated that the severity of symptoms was significantly decreased at 4 postintervention test points compared with baseline. The β values of lymphedema-related symptom distress at each follow-up point

were -2.512 ($P < .001$), -3.195 ($P < .001$), -4.854 ($P < .001$), and -4.925 ($P < .001$), which indicated that patients suffered from less symptom distress at 4 postintervention test points compared with baseline.

Limb Circumference Difference and Lymphedema Status

Generalized estimating equations were used to analyze limb circumference difference changes among the 5 test points (Table 7 and Table 8). The limb circumference difference was decreased at 1-month follow-up and then was well kept during the whole intervention period. The β values of limb circumference difference at each follow-up point were -0.205 ($P < .001$), -0.188 ($P < .001$), -0.176 ($P = .01$), and -0.155 ($P = .006$), which indicated that the limb circumference difference was significantly lower at 4 follow-ups compared with baseline.

Among 40 patients who finished the last follow-up, 31 (77.5%) of them maintained the lymphedema status the same as the baseline, 7 (17.5%) of them reversed the lymphedema status from mild lymphedema to subclinical lymphedema, and only 2 patients (5.0%) developed from subclinical lymphedema to mild lymphedema.

Discussion

Effect of TOLF on BCRL Behaviors

TOLF program can promote patients to avoid risky behaviors and take protective behaviors, so as to reduce the risk of BCRL. The changing trend of lymphedema-related behavior scores was positive in patients involved in TOLF program. In a qualitative study,²² focus group interviews were carried out to identify breast cancer survivors' experience of exercise adherence and found that

Table 5 • Scores of Lymphedema-Related Symptom Experience and Effect Test of Generalized Estimation Equation [M(Q₁, Q₃)]

	Baseline (N ₁ = 41)	1-mo Follow-up (N ₂ = 41)	3-mo Follow-up (N ₃ = 41)	6-mo Follow-up (N ₄ = 41)	12-mo Follow-up (N ₅ = 40)	Wald χ ²	P
Symptom experience	25.00 (13.00, 40.00) ^{a-d}	20.00 (11.50, 37.50) ^{c-e}	21.00 (9.50, 34.00) ^{c-e}	20.00 (10.00, 28.00) ^{a,b,c,e}	20.50 (10.00, 26.00) ^{a,c}	42.963	<.001
No. of symptoms	7.00 (5.50, 10.00) ^{a-d}	7.00 (5.00, 9.00) ^{c-e}	6.00 (4.50, 9.00) ^{c-e}	6.00 (4.00, 8.50) ^{a,b,c,e}	7.00 (4.00, 8.00) ^{a,b,c,e}	34.909	<.001
Symptom occurrence	11.00 (7.50, 14.00) ^{a-d}	10.00 (5.50, 12.50) ^{c-e}	9.00 (5.50, 12.00) ^{c-e}	10.00 (5.00, 11.00) ^{a,b,c,e}	9.50 (5.00, 11.75) ^{a,c}	24.784	<.001
Symptom distress	15.00 (7.00, 26.00) ^{a-d}	12.00 (5.50, 22.50) ^{c-e}	10.00 (4.00, 22.00) ^{c-e}	11.00 (4.50, 17.00) ^{a,b,c,e}	10.50 (4.25, 15.00) ^{a,c}	23.411	<.001
Functional	8.00 (3.00, 12.50) ^{a-d}	7.00 (3.00, 12.00) ^{c-e}	7.00 (2.50, 12.00) ^c	6.00 (2.50, 10.00) ^{a,c}	6.50 (2.25, 10.00) ^c	11.512	<.001
Social	1.00 (0.00, 2.00) ^{b-d}	1.00 (0.00, 2.00) ^{b-d}	0.00 (0.00, 1.50) ^{a-e}	0.00 (0.00, 1.00) ^{a,c}	0.00 (0.00, 1.00) ^{a,b,c,e}	22.168	<.001
Sleep	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	5.740	.219
Sexuality	0.00 (0.00, 1.00)	0.00 (0.00, 1.00)	0.00 (0.00, 1.00)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	1.171	.883
Emotional and psychological	3.00 (0.50, 6.00) ^{a-d}	2.00 (0.00, 5.00) ^c	2.00 (0.00, 6.00) ^c	1.00 (0.00, 5.50) ^e	1.00 (0.00, 4.00) ^e	15.657	.004
Self-perception	1.00 (0.00, 3.00) ^{a-d}	1.00 (0.00, 2.00) ^c	1.00 (0.00, 2.00) ^c	1.00 (0.00, 2.00) ^c	1.00 (0.00, 2.00) ^c	13.737	.008

^aP < .05 versus 1-month follow-up by ANOVA-GEE.

^bP < .05 versus 3-month follow-up by ANOVA-GEE.

^cP < .05 versus 6-month follow-up by ANOVA-GEE.

^dP < .05 versus 12-month follow-up by ANOVA-GEE.

^eP < .05 versus baseline by variance generalized estimation equation (ANOVA-GEE).

ambiguous and inadequate information was a barrier to exercise. Clear exercise information about how exercise should be done and how often it should be done is critical to breast cancer survivors at risk of lymphedema.^{13,31} TOLF program educated patients to avoid risk behaviors such as lifting heavy things and holding a baby with the affected limb because excessive use of the upper limb is considered as a risk factor for lymphedema as it may create extra lymph and stress the lymphatic system.³² In addition, TOLF program also encouraged patients to take protective behaviors such as muscle tightening–breathing and muscle tightening–pumping, large-muscle exercises, skin care, and healthy diet. Taking protective behaviors is equally important as avoiding risk behaviors to decrease the risk of BCRL.²⁵

Air travel was considered as a risk behavior in the lymphedema-related behavior checklist used in this study. It is controversial in studies about the relationship between air travel and lymphedema.^{7,33} Some researchers suggested that air travel was a risk for developing or aggravating swelling because of low cabin pressure and stationary state lacking exercise. However, a systematic review performed by Co and colleagues³³ in 2017, which included 12 studies and covered 2051 patients, demonstrated that air travel was not adversely associated with the development of lymphedema. Considering the uncertain relationship between air travel and lymphedema, we suggested patients wear compression sleeves during flight, take muscle tightening–breathing and muscle tightening–pumping before take-off and after landing, and get up and walk around every 1 hour during the flight.

Effect of TOLF on BCRL Symptom Experience

The goal of intervention is to prevent, relieve, or decrease both the number and severity of lymphedema symptoms, so as to achieve optimal limb volume and improve quality of life. In this study, decreasing trends of both the number and severity of symptoms were identified after the intervention. Improvement of patients' behaviors and release of symptom experience might complement each other.²⁵ Better behaviors can promote lymph flow, reduce limb volume, and relieve symptoms. Moreover, sustained behavior change is maintained if patients perceived the effectiveness of the intervention and perceived ease to integrate the strategies into daily life. Imamoglu et al³¹ applied an education program to patients with BCRL and evaluated the effectiveness. Thirty-eight patients were separated into 2 groups. The intervention group was educated about the causes and symptoms of lymphedema, skin care, daily life changes, exercises, and protective clothing and performed better in upper limb function after intervention.³¹ We also indicated that patients with the subclinical and mild stage of BCRL had an average of 7 symptoms. Fu and colleagues¹² study found the survivors at risk of BCRL reported an average of 5 symptoms and indicated survivors with BCRL suffered from more symptoms than at-risk survivors. Our study involved both subclinical lymphedema patients and mild lymphedema patients; thus, it is reasonable that our patients reported more symptoms than patients in Fu and colleagues¹² study.

The development of swelling, inflexibility, fatigue, pain, and other symptoms of BCRL will cause physical and psychological distress to the patient.^{22,34} Our study confirmed that the

Table 6 • Parameter Estimation Results of Generalized Estimation Equation of Scores of Lymphedema-Related Symptom Experience

	N	Parameter	β	SE	95% CI		Wald χ^2	df	P
					Lower Limit	Upper Limit			
Symptom experience	41	Baseline	0 ^a						
	41	1 mo	-3.805	0.6492	-0.5077	-2.533	34.352	1	<.001
	41	3 mo	-4.951	0.8692	-6.655	-3.248	32.451	1	<.001
	41	6 mo	-7.512	1.4272	-10.310	-4.715	27.704	1	<.001
	40	12 mo	-7.455	1.4899	-10.375	-4.535	25.040	1	<.001
No. of symptoms	41	Baseline	0 ^a						
	41	1 mo	-0.610	0.1417	-0.887	-0.332	18.515	1	<.001
	41	3 mo	-0.927	0.1963	-1.312	-0.542	22.291	1	<.001
	41	6 mo	-1.488	0.3145	-2.104	-0.871	22.383	1	<.001
	40	12 mo	-1.662	0.3272	-2.303	-1.021	25.802	1	<.001
Symptom occurrence	41	Baseline	0 ^a						
	41	1 mo	-1.293	0.2870	-1.855	-0.730	20.283	1	<.001
	41	3 mo	-1.756	0.4401	-2.619	-0.894	15.923	1	<.001
	41	6 mo	-2.659	0.5840	-3.803	-1.514	20.727	1	<.001
	40	12 mo	-2.513	0.6616	-3.828	-1.235	14.639	1	<.001
Symptom distress	41	Baseline	0 ^a						
	41	1 mo	-2.512	0.5574	-3.605	-1.420	20.314	1	<.001
	41	3 mo	-3.195	0.7503	-4.666	-1.724	18.132	1	<.001
	41	6 mo	-4.854	1.1302	-7.069	-2.639	18.444	1	<.001
	40	12 mo	-4.925	1.2967	-7.466	-2.384	14.426	1	<.001

^aNuisance parameter set as 0.

intervention of TOLF program reduced the number and severity of symptoms, as well as symptom distress at the same time. Among the 6 dimensions of symptom distress investigated in our study, functional, social, emotional, and psychological and self-perception were significantly improved. However, we did not find improvement in sleep and sexuality distress. One reason might be that patients recruited in this study were all at the sub-clinical or mild stage of BCRL so that symptoms-related sleep problem was not outstanding during the intervention period. Yoga seemed to be effective in the improvement of sleep issues,^{21,34} which could be considered as an intervention for BCRL patients bothered by sleep distress. Sexuality distress is influenced by multiple factors and needs comprehensive intervention. A qualitative study focused on sexual concerns of lymphedema extracted 4 interrelated factors determined the extent of lymphedema's sexual impact, including swelling severity and location, wearing a compression garment, body image concerns raised by lymphedema and breast cancer treatment, and sexual partner's acceptance and supportiveness.³⁵ Another research also demonstrated

that lymphedema symptoms, breast cancer treatment, and compression garments were issues hindering intimacy and bringing negative feelings about sexual relationships.³⁶

Effect of TOLF on Limb Circumference Difference and BCRL Status

Our study demonstrated the safety, feasibility, and acceptability of TOLF program. In this study, the intervention of TOLF program showed significant effectiveness in decreasing patients' limb circumference differences. Patients' limb circumference difference was significantly lower than baseline at any of the 4 follow-ups. In addition, 95% of patients maintained or improved their BCRL status according to limb circumference measurements at the 12-month follow-up. In line with this study, Fu et al²⁴ reported that 97% of 134 BCRL patients who received TOLF program intervention maintained and improved their preoperative limb volume at the study endpoint of 12 months after surgery. The

Table 7 • Limb Circumference Differences and Effect Test of Generalized Estimation Equation [$M(Q_1, Q_3)$]

	Baseline (N ₁ = 41)	1-mo Follow-up (N ₂ = 41)	3-mo Follow-up (N ₃ = 41)	6-mo Follow-up (N ₄ = 41)	12-mo Follow-up (N ₅ = 40)	Wald χ^2	P
Circumference difference	2.10 (1.60, 2.35) ^{a-d}	1.80 (1.50, 2.10) ^c	1.80 (1.35, 2.30) ^c	1.80 (1.50, 2.25) ^c	1.95 (1.50, 2.30) ^c	38.864	<.001

^aP < .01 versus 1-month follow-up by ANOVA-GEE;

^bP < .01 versus 3-month follow-up by ANOVA-GEE;

^cP < .01 versus 6-month follow-up by ANOVA-GEE;

^dP < .01 versus 12-month follow-up by ANOVA-GEE.

^eP < .01 versus baseline by variance generalized estimation equation (ANOVA-GEE).

**Table 8 • Parameter Estimation Results of Generalized Estimation Equation of Limb Circumference Difference**

	N	Parameter	β	SE	95% CI		Wald χ^2	df	P
					Lower Limit	Upper Limit			
Circumference difference	41	Baseline	0 ^a						
	41	1 mo	-0.205	0.0435	-0.290	-0.120	22.195	1	<.001
	41	3 mo	-0.188	0.0539	-0.293	-0.082	12.140	1	<.001
	41	6 mo	-0.176	0.0677	-0.308	-0.043	6.719	1	.010
	40	12 mo	-0.155	0.0560	-0.265	-0.045	7.666	1	.006

^aNuisance parameter set as 0.

present study indicated that 2 of 15 patients with subclinical lymphedema at baseline developed mild lymphedema 12 months after the intervention, with a progression rate of 13.3%. Soran and colleagues¹¹ study used bioimpedance spectroscopy to monitor lymphedema status and found that among 45 subclinical lymphedema patients who received the intervention, only 4.4% of them progressed to clinical lymphedema in an average of 21 months' follow-up. The different populations might be the reason for different results. All patients in our study have undergone ALND, which would significantly increase the risk of lymphedema.

Study Limitations

Our study was limited by the small sample size. This study required patients to accept 4 face-to-face follow-ups at a certain time during 12 months, which could be an extra burden for patients and hinder the willingness to participate. Another limitation was the sample nonhomogeneity. Patients in this study underwent different surgery types and adjuvant therapies, which were associated with the risk of BCRL. Lack of randomization might make it hard to completely attribute the effectiveness of the intervention because we could not ensure that patients were not acquiring knowledge from other sources. Despite the limitations, this study offers a clinical pathway to detect and intervene subclinical and mild stage of BCRL, and longitudinal information will provide us with the developing trajectory of BCRL after the intervention. Future research requires a more extensive study with a randomized controlled design to determine the long-term effectiveness of TOLF program. Also, more accurate diagnostic methods should be applied in BCRL research among Chinese survivors.

Conclusions

Self-management strategies in TOLF program were effective in managing subclinical and mild stages of BCRL to achieve beneficial effects on improving lymphedema-related protective behaviors, reducing the occurrence of risk behaviors, and alleviating lymphedema symptoms and symptom distress as well as optimizing limb circumference and lymphedema status. It could be beneficial to use TOLF program as clinical education materials to prevent or reverse the subclinical or mild BCRL.

ACKNOWLEDGMENT

The authors thank the breast surgery group of Peking University People's Hospital for permitting access to review the medical

records of breast cancer patients. They are also grateful to all those who participated in the study.

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