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ORIGINAL ARTICLE – BREAST ONCOLOGY

Effects of Progressive Upper Limb Exercises and Muscle Relaxation Training on Upper Limb Function and Health-Related Quality of Life Following Surgery in Women with Breast Cancer: A Clinical Randomized Controlled Trial

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ABSTRACT

Objective. The aim of this study was to examine the effects of progressive upper limb exercises and muscle relaxation training (PULE-MRT) on upper limb function and health-related quality of life (HRQoL) following surgery in Chinese mainland women with breast cancer (BC).

Methods. Overall, 102 patients following surgery (i.e. mastectomy or breast-conserving surgery, with sentinel lymph node biopsy or axillary lymph node dissection) were randomly allocated to the intervention ($n = 51$) or control ($n = 51$) groups. The former received PULE-MRT plus routine nursing care, whereas the latter received only routine nursing care for 6 months. Upper limb function and HRQoL were measured at baseline and 1, 3, and 6 months using Constant–Murley scores (CMS) and Functional Assessment of Cancer Therapy-Breast version 4.0 (FACT-Bv4.0), respectively.

Results. All patients in the intervention group completed the exercises and training, with 100% compliance and no adverse events. The intervention group had significantly higher total CMS and FACT-Bv4.0 scores at 1-, 3-, and 6-month follow-up than the control group. The significant effects in total CMS comparisons were group ($F = 25.30$, $p < 0.001$), time ($F = 18.02$, $p < 0.001$), and group-by-time interaction ($F = 9.95$, $p < 0.001$), and, in FACT-Bv4.0, total score comparisons were group ($F = 15.87$, $p < 0.001$), time ($F = 17.92$, $p < 0.001$), and group-by-time interaction ($F = 7.88$, $p < 0.001$). Similar results were observed for the scale scores of CMS and FACT-Bv4.0.

Conclusions. PULE-MRT had positive effects on improving upper limb function and HRQoL following surgery in women with BC and could be used as an optional rehabilitation management strategy in post-surgery BC patient populations.

Trial Registration ChiCTR-IOR-16008253 (Chictr.org.cn; 9 April 2016).

Since surgery remains the main modality for breast cancer (BC), many patients inevitably experience debilitating effects caused by surgery,[1,2] especially restricted surgical side upper limb function and health-related quality of life (HRQoL) impairments following mastectomy and axillary lymph node dissection (ALND).[3] Thus, post-surgery rehabilitation, especially restricted upper limb function recovery, is still a critical health problem in this patient population.

Many effective exercise programs have been used in BC care, including physical activity,[4–8] aerobic exercise,[9] resistance training,[10,11] yoga,[12] Qigong/Tai Chi Easy,[13] and combined interventions;[14–16] however, they are not focused on surgical side upper limb function, and only two studies reported upper limb mobility as an intervention outcome.[4,11] Although some studies have focused on exercises targeting upper limb function,[17,18] they neither targeted progressive daily exercises of the surgical side fingers and shoulder since the first day after surgery nor considered HRQoL as the outcome. Thus, the effects of progressive

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upper limb exercises on surgical side upper limb function and HRQoL following surgery still lack sufficient supporting evidence.

Except for the combination use with therapeutic walking or guided imagery and deep diaphragmatic breathing,[15,16] progressive muscle relaxation training has also been used in BC patients to relieve negative psychological states (ego, anxiety, and depression)[19] and chemotherapy-induced side effects (e.g. nausea and vomiting).[20] The positive effects might be beneficial for women with BC who pay more attention to physical exercises under a relatively comfortable status. However, the comprehensive effects of progressive upper limb exercises with muscle relaxation training in improving upper limb function and HRQoL are still unknown.

The purpose of this study was to examine the effects of progressive upper limb exercises and muscle relaxation training (PULE-MRT) on upper limb function and HRQoL following surgery in Chinese mainland women with BC. The primary hypothesis was that the intervention group would achieve better HRQoL than the control group at 6 months. The secondary hypotheses were that patients receiving the intervention would have improved HRQoL at 1 and 3 months, and improved upper limb function at 1, 3, and 6 months. The findings of this study will provide evidence for expanding the comprehensive use of PULE-MRT in improving physical health and rehabilitation in the early post-surgery stage in women with BC.

METHODS

Design

This was a clinical randomized controlled trial.

Participants

Participants were hospitalized women with BC in the breast surgical department of a general hospital in Xi'an, China. Subjects who were recruited by convenience sampling met the following criteria: newly diagnosed BC (stages I–III), age 18 years or older, preparing to undergo surgery (including mastectomy, breast-conserving surgery, and breast reconstructive surgery, with sentinel lymph node biopsy [SLNB] or ALND), can speak Chinese, and provided written informed consent. Patients with other malignant tumors, mastitis, active or other severe potential infection (screened by physical examination), or psychiatric or cognitive disorders (screened by a blinded psychiatrist according to the *Diagnostic and Statistical Manual of Mental Disorders, 5th edition*) were excluded. All patients received a self-controlled analgesia pump following surgery. All procedures were performed in accordance with the ethical standards of the Institutional Research Committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The study protocol received ethical approval from the Ethics Committee of our center.

Sample Size and Randomization

Sample size was estimated based on the expected change in Functional Assessment of Cancer Therapy-Breast version 4.0 (FACT-Bv4.0) and Constant–Murley total scores,[21,22] with a larger sample size being considered as the sample size of the study. At least 92 patients (46 in each group) were required to detect the between-group difference, with a power of 80% at the 5% level of statistical significance. These patients were randomly allocated to two groups using a randomization code generated by SPSS version 23.0 (IBM Corporation, Armonk, NY, USA). Patient enrollment and allocation were performed by KZ, JL, and XL.

Procedures

Intervention Group The intervention group received PULE-MRT (Table 1) based on routine nursing care. PULE-MRT was conducted by well-trained nursing staff (experts in directing PULE-MRT) before surgery in individual (one-to-one) or group (one-to-more) format until the patients could perform the exercises and training freely and easily without discomfort. This was considered to be beneficial for achieving better intervention effects. If the patients had difficulties in performing the exercises and training following surgery, the nursing staff would help and encourage the patient via one-to-one supervision (in hospital) or home visiting (discharged from hospital) until the patients could do the exercises and training independently. To avoid interference with routine nursing care delivery, the nursing staff implemented PULE-MRT during the visiting time (i.e. 3:00–5:00 pm) of the hospital, which allowed the nurses to have enough time to instruct the patients in performing the exercises and training stepwise.

Due to individual and environmental differences, we only recorded the parameters of 'duration per session' and 'sessions per day', as shown in Table 1, which were helpful for quantifying how patients performed the training and exercises in terms of duration and frequency. It was also beneficial for the patients themselves to be able to determine the most suitable time and frequency of exercises and training to achieve the best rehabilitation outcomes.

In this study, the intervention group attended and completed the exercises and training. The nursing staff

TABLE 1 Progressive upper limb exercises and muscle relaxation training following surgery

Progressive upper limb exercises					Progressive muscle relaxation training	
Start time	Part	Methods	Duration per session	Sessions per day	Training	Duration/frequency
Days 1–2	Fingers and wrist	Fingers: flexion and extension; fist movement Wrist: internal flexion, abduction, rotation	10 min	3–6	Contracting and relaxing movements of the following 16 muscle groups: Right hand and forearm → right biceps → left hand and forearm → left biceps → upper section of the cheeks and nose → lower section of the cheeks and nose → neck and throat → chest → shoulders and upper part of back → abdominal region and stomach → right thigh → right calf → right foot → left thigh → left calf → left foot	30 min per session Twice per day (according to the patients' condition and time arrangement) From the first day to 6 months after surgery, continuously
Days 3–4	Elbow	Flexion and extension	15 min (including 5-min exercises on days 1–2)	3–6		
Days 5–6	Shoulder[a]	Adduction: fingers touch the opposite shoulder and ipsilateral ear Internal rotation: the back of the hand touches the lateral thigh and buttocks	20 min (including 5-min exercises on days 1–4)	3–7		
Days 7–10	Shoulder	Upward: the degrees between the upper arm and trunk should $\leq 90°$ Adduction: fingers touch the opposite ear Internal rotation: the back of the hand touches the lumbosacral portion and waist	20 min (including 10-min exercises on days 1–6)	3–7		
Day 11	Upper limb	Upward: the degrees between the upper arm and trunk should $> 90°$ Internal rotation: the back of the hand touches the level of the 12th thoracic vertebrae	25 min (including 10-min exercises on days 1–10)	3–6		
Day 12	Upper limb	Fingers: climbing wall movement Internal rotation: the back of the hand touches the level of 12th thoracic vertebrae	30 min (including 15-min exercises on days 1–11)	3–6		
Days 13–14	Upper limb	Surgical side hand: do up one's hair; touch the opposite ear over the top of the head Internal rotation: the back of the hand touches the level of the inferior angle of the scapula	30 min (including 15-min exercises on days 1–12)	3–6		
Day 15 to 6 months	From wrist to shoulder	Comprehensive exercises of days 1–14: fingers→wrist→elbow→shoulder→upper limb	30 min	3–6		

The above exercises were conducted under the supervision of well-trained nursing staff. For those patients without abnormal condition and complications after surgery, the exercises were performed in a step-by-step modality. If the patients had complications or abnormal conditions after surgery (e.g. severe flap necrosis, subcutaneous fluid, drainage fluid > 50 mL on the first week after surgery), the duration, frequency, and shoulder range of motion would be decreased accordingly. The patients were allowed to maintain their normal activity on the non-surgical side upper limb and other parts of the body

[a]Shoulder movement could be started earlier or later once permitted

conducted individual (one-to-one) supervision once per day in the evening (7:00–9:00 pm) in the hospital and via a home visit once per week after the patients were discharged from the hospital.

Control Group The routine nursing care delivered to the control group included surgery district nursing, drainage tube nursing, routine health education and physical exercises, vital sign monitoring, and post-surgery complication observation. Once the patients were discharged from the hospital, follow-up assessments were conducted by blinded data collectors via a home visit.

To avoid between-group contamination, the intervention and control groups were organized in two independent separate areas of the breast surgical department. There was no overlap in nursing personnel between the areas.

Masking

All recruited patients with BC, as well as data collectors, were blinded to the group allocation information. The control group was not provided any intervention information during the study period to avoid bias.

Measures

Constant–Murley Score The Constant–Murley score (CMS) is a multicomponent scoring system with four subscales: pain (15 points), activities of daily living (ADL; 20 points), range of motion (ROM; 40 points), and strength (25 points). The total score ranged from 0 to 100, with a higher score indicating higher quality of function.[23] The Chinese CMS was used in this study (Cronbach α, 0.80).

FACT-Bv4.0 The Chinese FACT-Bv4.0 includes breast-cancer-specific subscales for additional concerns (BCS) and a general cancer subscale (FACT-G) comprising physical well-being (PWB), social/family well-being (SWB), emotional well-being (EWB), and functional well-being (FWB).[24] The FACT-Bv4.0 has 36 items, with each item being rated on a 5-point Likert scale (from 0 to 4). The FACT-Bv4.0 total score (0–144) is the sum of the FACT-G and BCS scores, with a higher score representing better HRQoL.[25] The Cronbach α of the FACT-Bv4.0 in the study was 0.75.

Data Collection

Data were collected from May 2017 to July 2018 by well-trained blinded data collectors. Sociodemographic and FACT-Bv4.0 score baseline data were collected on the day when the patient was admitted to the hospital. The baseline measurement of the scales of pain, ADL, and strength of CMS were performed on the first day after surgery; however, owing to the prescribed shoulder immobilization immediately after surgery, the ROM scale was measured once the shoulder exercises were permitted via a protractor specific to shoulder joint. The FACT-Bv4.0 and CMS follow-up data were collected at 1, 3, and 6 months after surgery.

Data Analyses

All data analyses were performed using SPSS version 23.0 (IBM Corporation) and on an intention-to-treat basis. The primary endpoint was the FACT-Bv4.0 score change at 6 months, while the secondary endpoints were FACT-Bv4.0 score changes at 1 and 3 months and CMS changes at 1, 3, and 6 months. A linear mixed-effect model with repeated measurements was used to analyze the score changes in FACT-Bv4.0 and CMS. In the model, the FACT-Bv4.0 or CMS baseline measurement was considered as a covariate. Group, time, and group-by-time interaction were considered as fixed effects, and the patient was considered as a random effect. The missing data caused by loss to follow-up across the study were assumed to be missing at random in the model analysis. The estimated within- and between-group differences with their 95% confidence intervals (CIs) are reported. A two-sided p value < 0.05 was considered statistically significant, and a difference of more than 2 standard deviations was considered to be clinically relevant.

RESULTS

All intervention group patients completed the exercises and training, with no adverse events and a compliance of 100%. Electronic supplementary Fig. 1 shows the enrollment flowchart. Table 2 shows the patient sociodemographic and clinical characteristics, which were similar between the two groups ($p > 0.05$). The CMS and FACT-Bv4.0 scores at baseline regarding the two groups were shown in Tables 3 and 4, respectively. There were no significant between-group differences of the baseline CMS and FACT-Bv4.0 scores ($p > 0.05$).

The total CMS revealed significant improvement for the intervention group in terms of group ($F = 25.30$, $p < 0.001$), time ($F = 18.02$, $p < 0.001$), and group-by-time interaction ($F = 9.95$, $p < 0.001$) effects (Table 3, electronic supplementary Fig. 2e). Similar effects were found in the other four subscales (Table 3, electronic supplementary Fig. 2a–d).

TABLE 2 Sociodemographics and clinical characteristics of patients (n = 102)

	Total	Intervention group (n = 51)	Control group (n = 51)	Statistics	p value
Sociodemographics					
Age, years	49.70 ± 9.32	49.94 ± 8.88	49.40 ± 9.88	t = 0.31	0.76
Education level					
Primary and below	18 (17.6)	11 (21.6)	7 (13.7)	χ^2 = 0.60	0.74
Secondary	68 (66.7)	32 (62.7)	36 (70.6)		
Tertiary	16 (15.7)	8 (15.7)	8 (15.7)		
Marital status					
Married	88 (86.3)	45 (88.2)	43 (84.3)	χ^2 = 1.79	0.63
Other marital status	14 (13.7)	6 (11.8)	8 (15.7)		
Employment status					
Employed	67 (50.7)	36 (70.6)	31 (60.8)	χ^2 = 1.84	0.40
Unemployed	35 (34.3)	15 (28.3)	20 (39.2)		
Average monthly income over the past year (Chinese Yuan)					
< 1000	23 (22.5)	10 (19.6)	13 (25.5)	χ^2 = 2.31	0.18
1000–3000	47 (46.1)	27 (52.9)	20 (39.2)		
> 3000	32 (31.4)	14 (27.5)	18 (35.3)		
Chronic disease					
Yes	24 (23.5)	10 (19.6)	14 (27.5)	χ^2 = 1.68	0.50
No	78 (76.5)	41 (80.4)	37 (72.5)		
Clinical characteristics					
Breast cancer stages					
I	32 (31.4)	18 (35.3)	14 (27.5)	χ^2 = 3.04	0.55
II	56 (54.9)	27 (52.9)	29 (56.9)		
III	14 (13.7)	6 (11.8)	8 (15.7)		
Surgery type					
Mastectomy + SLNB	49 (48.0)	24 (47.1)	25 (49.0)	χ^2 = 1.23	0.58
Mastectomy + ALND	32 (31.4)	15 (29.4)	17 (33.3)		
BCS + SLNB	16 (15.7)	10 (19.6)	6 (11.8)		
BCS + ALND	5 (4.9)	2 (3.9)	3 (5.9)		
Chemotherapy					
Yes	84 (82.4)	41 (80.4)	43 (84.3)	χ^2 = 1.87	0.37
No	18 (17.6)	10 (19.6)	8 (15.7)		

Data are expressed as mean ± standard deviation or n (%)

Chronic disease was defined as other non-breast carcinoma disease with long-term illness history (i.e. > 6 months). Patients answered this item by responding 'yes' or 'no'

BCS breast-conserving surgery, *SLNB* sentinel lymph node biopsy, *ALND* axillary lymph node dissection

The intervention group patients also showed significant improvement in FACT-Bv4.0 total scores in terms of group (F = 15.87, $p < 0.001$), time (F = 17.92, $p < 0.001$), and group-by-time interaction (F = 7.88, $p < 0.001$) effects (Table 4, electronic supplementary Fig. 3f). Similar effects were observed in the other five subscales (Table 4, electronic supplementary Fig. 3a–e).

DISCUSSION

The clinical randomized controlled trial of PULE-MRT following surgery for women with BC showed a significant improvement in terms of the CMS and FACT-Bv4.0 scores, demonstrating that PULE-MRT is an effective strategy for early rehabilitation.

TABLE 3 Changes in the CMS scores from baseline: linear mixed-model analysis within- and between-group comparison

Constant–Murley scores	Baseline	1 month after surgery		3 months after surgery		6 months after surgery	
		Score	Change from baseline (95% CI)	Score	Change from baseline (95% CI)	Score	Change from baseline (95% CI)
Pain[a]							
Intervention group	8.01 ± 2.98	11.89 ± 1.32	3.88 (− 0.63, 8.40)	13.66 ± 2.15	5.65 (0.54, 10.76)	14.82 ± 1.86	6.81 (1.89, 11.73)
Control group	8.32 ± 2.11	8.97 ± 1.60	0.65 (− 3.02, 4.32)	9.52 ± 1.87	1.20 (− 2.72, 5.12)	11.23 ± 1.71	2.91 (− 0.88, 6.70)
MD (95% CI)	− 0.31 (− 5.37, 4.75)	2.92 (0.05, 5.79)		4.14 (0.19, 8.09)		3.59 (0.09, 7.09)	
ADL[b]							
Intervention group	6.98 ± 1.56	11.67 ± 1.95	4.69 (1.23, 8.15)	16.52 ± 2.51	9.54 (5.46, 13.61)	19.02 ± 2.07	12.04 (8.47, 15.61)
Control group	6.23 ± 1.60	7.19 ± 1.87	0.96 (− 2.45, 4.37)	11.01 ± 2.17	4.78 (1.07, 8.49)	14.69 ± 2.18	8.46 (4.75, 12.17)
MD (95% CI)	0.75 (− 2.35, 3.85)	4.48 (0.74, 8.22)		5.51 (0.90, 10.12)		4.33 (0.16, 8.50)	
ROM[c]							
Intervention group	15.11 ± 2.10	26.90 ± 2.19	11.79 (7.58, 16.00)	32.51±2.77	17.40 (12.60, 22.20)	38.86±2.41	23.75 (19.34, 28.16)
Control group	14.84 ± 2.89	19.02 ± 2.47	4.18 (− 1.09, 9.45)	27.22 ± 2.13	12.38 (7.37, 17.39)	31.58 ± 2.32	16.74 (11.57, 21.91)
MD (95% CI)	0.27 (− 4.68, 5.22)	7.88 (3.30, 12.46)		5.29 (0.43, 10.15)		7.28 (2.64, 11.92)	
Strength[d]							
Intervention group	10.63 ± 2.18	16.58 ± 2.77	5.95 (1.06, 10.84)	20.22 ± 2.53	9.59 (4.97, 14.21)	24.53 ± 2.29	13.90 (9.52, 18.28)
Control group	10.12 ± 2.45	12.57 ± 2.14	2.45 (− 2.06, 6.96)	15.29 ± 2.47	5.17 (0.35, 9.99)	19.89 ± 2.08	9.77 (5.29, 14.25)
MD (95% CI)	0.51 (− 4.04, 5.06)	4.03 (2,89, 5.17)		4.93 (0.03, 9.83)		4.64 (0.35, 8.93)	
CMS[e]							
Intervention group	42.71 ± 8.87	68.01 ± 8.15	25.30 (8.61, 41.99)	86.42 ± 8.49	43.71 (26.69, 60.73)	90.67 ± 8.17	47.96 (31.21, 64.71)
Control group	41.98 ± 8.19	50.69 ± 8.86	8.71 (− 8.01, 25.43)	66.49 ± 8.75	24.51 (7.92, 41.10)	70.51 ± 8.25	28.53 (12.42, 44.64)
MD (95% CI)	0.19 (− 16.54, 16.92)	17.32 (0.64, 34.00)		19.93 (3.04, 36.82)		20.16 (4.07, 36.25)	

Sample size of the intervention group: $n = 51$ (baseline), $n = 51$ (1 month post-surgery), $n = 49$ (3 months post-surgery), $n = 46$ (6 months post-surgery)

Sample size of the control group: $n = 51$ (baseline), $n = 51$ (1 month post-surgery), $n = 47$ (3 months post-surgery), $n = 45$ (6 months post-surgery)

A linear mixed model was used for the analysis of changes within groups and comparisons between groups of the CMS, with baseline measurement of the CMS total and four subscale scores as covariates: group, time, and group-by-time interaction as fixed effects, and patient as the random effect

MD mean difference, *CMS* Constant-Murley scores, *CI* confidence interval, *ADL* activities of daily living, *ROM* range of motion

[a]Pain model: (group) $F = 10.13$, $p < 0.001$; (time) $F = 25.30$, $p < 0.001$; (group-by-time interaction) $F = 3.46$, $p = 0.02$

[b]ADL model: (group) $F = 20.89$, $p < 0.001$; (time) $F = 15.61$, $p < 0.001$; (group-by-time interaction) $F = 5.40$, $p = 0.001$

[c]ROM model: (group) $F = 41.22$, $p < 0.001$; (time) $F = 53.61$, $p < 0.001$; (group-by-time interaction) $F = 8.40$, $p < 0.001$

[d]Strength model: (group) $F = 16.54$, $p < 0.001$; (time) $F = 28.10$, $p < 0.001$; (group-by-time interaction) $F = 10.12$, $p < 0.001$

[e]CMS model: (group) $F = 25.30$, $p < 0.001$; (time) $F = 18.02$, $p < 0.001$; (group-by-time interaction) $F = 9.95$, $p < 0.001$

TABLE 4 Changes in the FACT-Bv4.0 scores from baseline: linear mixed-model analysis within- and between-group comparison

	Baseline	1 month after surgery		3 months after surgery		6 months after surgery	
		Score	Change from baseline (95% CI)	Score	Change from baseline (95% CI)	Score	Change from baseline (95% CI)
PWB[a]							
Intervention	20.18 ± 2.30	19.87 ± 3.44	− 0.31 (− 6.05, 5.43)	24.87 ± 2.10	4.69 (0.37, 9.01)	25.70 ± 2.66	5.52 (0.66, 10.38)
Control	20.80 ± 2.15	18.12 ± 3.23	− 2.68 (− 8.06, 2.70)	19.32 ± 2.17	− 1.48 (− 5.71, 2.75)	20.85 ± 2.04	0.05 (− 4.06, 4.16)
MD (95% CI)	− 0.62 (− 4.98, 3.74)	1.75 (− 4.79, 8.29)		4.55 (0.37, 8.73)		4.85 (0.20, 9.50)	
SWB[b]							
Intervention	20.23 ± 2.61	21.98 ± 2.12	1.75 (− 2.91, 6.41)	25.08 ± 2.20	4.85 (0.11, 9.59)	25.73 ± 2.45	5.50 (0.53, 10.47)
Control	20.58 ± 2.02	17.30 ± 2.34	− 3.28 (− 7.56, 1.00)	19.02 ± 2.76	− 1.56 (− 6.27, 3.15)	20.07 ± 3.01	− 0.51 (− 5.47, 4.45)
MD (95% CI)	− 0.35 (− 4.92, 4.22)	4.68 (0.30, 9.06)		6.06 (1.18, 10.94)		5.66 (0.29, 11.03)	
EWB[c]							
Intervention	14.59 ± 2.24	19.94 ± 2.02	5.35 (1.17, 9.53)	22.07 ± 2.30	7.48 (3.03, 11.93)	23.35 ± 2.67	8.76 (3.95, 13.57)
Control	14.36 ± 2.31	15.87 ± 2.10	1.51 (− 2.82, 5.84)	17.63 ± 2.17	3.27 (− 1.13, 7.67)	18.40 ± 2.24	4.04 (− 0.42, 8.50)
MD (95% CI)	0.23 (− 4.23, 4.69)	4.07 (0.03, 8.10)		4.44 (0.05, 8.23)		4.95 (0.12, 9.78)	
FWB[d]							
Intervention	20.01 ± 2.05	19.93 ± 2.44	− 0.08 (− 4.50, 4.34)	22.98 ± 2.25	2.97 (− 1.24, 7.18)	24.56 ± 2.70	4.55 (− 0.12, 9.22)
Control	19.85 ± 2.52	14.27 ± 2.89	− 5.58 (− 10.89, − 0.27)	15.90 ± 2.88	− 3.95 (− 9.24, 1.34)	16.87 ± 2.92	− 2.98 (− 8.30, 2.34)
MD (95% CI)	0.16 (− 4.34, 4.66)	5.66 (0.42, 10.90)		7.08 (2.03, 12.13)		7.69 (2.18, 13.19)	
BCS subscales[e]							
Intervention	30.42 ± 2.22	27.65 ± 2.51	− 2.77 (− 7.41, 1.87)	29.86 ± 2.14	− 0.56 (− 4.84, 3.72)	33.62 ± 2.57	3.20 (− 1.49, 7.89)
Control	29.95 ± 2.30	24.43 ± 2.57	− 5.52 (− 10.30, − 0.74)	25.02 ± 2.28	− 4.93 (− 9.42, − 0.44)	25.13 ± 2.06	− 4.82 (− 9.11, − 0.53)
MD (95% CI)	0.47 (− 3.96, 4.90)	3.22 (− 1.76, 8.20)		4.84 (0.51, 9.17)		8.49 (3.92, 13.06)	
Total score[f]							
Intervention	110.41 ± 8.30	109.60 ± 8.11	− 0.81 (− 16.89, 15.27)	114.99 ± 8.52	4.58 (− 11.90, 21.06)	128.50 ± 8.16	18.09 (1.95, 25.23)
Control	111.25 ± 8.12	93.02 ± 8.65	− 18.23 (− 34.67, − 1.78)	98.13 ± 8.61	− 13.12 (− 29.50, 3.26)	101.30 ± 8.45	− 9.95 (− 26.17, 6.27)

TABLE 4 continued

	Baseline	1 month after surgery		3 months after surgery		6 months after surgery	
	Score	Score	Change from baseline (95% CI)	Score	Change from baseline (95% CI)	Score	Change from baseline (95% CI)
MD (95% CI)	− 0.84 (− 16.93, 15.25)	16.58 (0.15, 33.01)		16.86 (0.07, 33.65)		27.20 (10.92, 43.48)	

Sample size of the intervention group: $n = 51$ (baseline), $n = 51$ (1 month post-surgery), $n = 49$ (3 months post-surgery), $n = 46$ (6 months post-surgery)

Sample size of the control group: $n = 51$ (baseline), $n = 51$ (1 month post-surgery), $n = 47$ (3 months post-surgery), $n = 45$ (6 months post-surgery)

A linear mixed model was used for the analysis of changes within groups and comparisons between groups of the FACT-Bv4.0 scores, with baseline measurement of the FACT-Bv4.0 total and five subscales scores as covariates: group, time, and group-by-time interaction as fixed effects, and patient as the random effect

MD mean difference, *CI* confidence interval, *PWB* physical well-being, *SWB* social/family well-being, *EWB* emotional well-being, *FWB* functional well-being, *BCS* breast-cancer-specific subscales for additional concerns

[a]PWB model: (group) $F = 5.31$, $p = 0.001$; (time) $F = 6.58$, $p < 0.001$; (group-by-time interaction) $F = 6.46$, $p < 0.001$

[b]SWB model: (group) $F = 4.99$, $p = 0.003$; (time) $F = 4.03$, $p = 0.005$; (group-by-time interaction) $F = 5.78$, $p < 0.001$

[c]EWB model: (group) $F = 10.54$, $p < 0.001$; (time) $F = 3.65$, $p = 0.01$; (group-by-time interaction) $F = 8.80$, $p < 0.001$

[d]FWB model: (group) $F = 25.36$, $p < 0.001$; (time) $F = 3.01$, $p = 0.04$; (group-by-time interaction) $F = 3.12$, $p = 0.02$

[e]BCS model: (group) $F = 18.85$, $p < 0.001$; (time) $F = 9.66$, $p < 0.001$; (group-by-time interaction) $F = 9.60$, $p < 0.001$

[f]Total score model: (group) $F = 15.87$, $p < 0.001$; (time) $F = 17.92$, $p < 0.001$; (group-by-time interaction) $F = 7.88$, $p < 0.001$

Throughout the intervention period, the CMS and FACT-Bv4.0 scores showed an increasing trend from baseline to the follow-up tests in both groups, indicating that although the upper limb function and HRQoL could independently recover after surgery, PULE-MRT provided greater positive effects on upper limb function rehabilitation and health status for the patients. This finding is supported by the evidence that the CMS and FACT-Bv4.0 differences in the intervention group were all larger than those in the control group at the 1-, 3-, and 6-month follow-ups, demonstrating better upper limb function and HRQoL in the intervention group.

It should be noted that FACT-Bv4.0 in PWB, SWB (in the control group), FWB, BCS, and total scores had decreasing trends from baseline to 1 month following surgery, demonstrating that the patients had poor HRQoL in the early post-surgery stage. Although the between-group comparisons in EWB, FWB, BCS, and total scores had statistical significance, more efforts should be made to improve patients' health in these domains in the early rehabilitation stage following surgery.

Based on the between-group comparisons, the CMS and FACT-Bv4.0 score differences in the intervention group were all significantly higher than those in the control group at each point of the three follow-ups, indicating that women in the intervention group had better upper limb function and HRQoL than those in the control group during the post-surgery rehabilitation process. This finding is consistent with the positive intervention effects of related studies in BC,[5,11,15–18] and supports the hypotheses that PULE-MRT could improve upper limb function and HRQoL following surgery in women with BC, at 1, 3, and 6 months.

According to the findings of this study, the positive effects observed in the intervention group were probably due to a couple of reasons. First, the intervention group had more significant pain relief at the 6-month follow-up, which would largely reduce the chance of experiencing pain-induced negative psychological states (e.g. anxiety and depression), fatigue, sleep disturbance, and upper limb function disability. Second, better ADL, ROM, and muscle strength (surgical side upper limb) following the intervention might have been beneficial for the patients to more easily accomplish their self-care and daily activities, which is a positive predictor for post-surgery physical, psychological, and social function recovery. Therefore, our findings suggest that better upper limb function recovery might be helpful for HRQoL improvement during the rehabilitation process in post-surgery BC patient populations.[19]

This study had some limitations. First, both CMS (pain and ADL scales) and FACT-Bv4.0 were self-reported, which might be influenced by personal attitudes and

misrepresentation. Second, the focus group method for collecting individual experience on PULE-MRT was not used in this study. Third, the external validity and applicability of the findings to other centers may be limited as it was performed in a single center. Further study using the focus group method and objective outcome measurements conducted in a multicenter format should be considered.

CONCLUSIONS

Both upper limb function and HRQoL can be significantly improved under PULE-MRT. Significant improvement in upper limb function is beneficial for achieving better HRQoL. PULE-MRT can be used comprehensively following surgery in women with BC.

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COMPLIANCE WITH ETHICAL STANDARDS

DISCLOSURE The authors declare that they have no conflicts of interest.

ETHICAL STANDARDS All procedures were performed in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The study protocol received ethical approval from the Biomedical Ethics Committee of Xi'an Jiaotong University Health Science Center (reference 2015-170).

INFORMED CONSENT Written informed consent was obtained from all patients included in the study, prior to data collection.

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