

Effect of manual lymphatic drainage combined with targeted rehabilitation therapies on the recovery of upper limb function in patients with modified radical mastectomy: A randomized controlled trial

Qian Xiong¹, Feng Luo¹, Jing Zhan¹, Jia Qiao², Yi Duan¹, Jie Huang¹, Rong Li¹, Hong Liu¹, Pengjuan Jin¹

¹Department of Breast Surgery, The First Affiliated Hospital of Chongqing Medical University, Chongqing, China

²Sun Yat-Sen University, Guangdong, China

Received: June 14, 2022 Accepted: October 14, 2022 Published online: December 08, 2022

ABSTRACT

Objectives: This study aimed to evaluate the effect of manual lymphatic drainage (MLD) combined with targeted rehabilitation therapies on the recovery of upper limb function in patients with breast cancer after modified radical mastectomy.

Patients and methods: In the randomized controlled study conducted between October 2019 and June 2020, 104 eligible breast cancer patients who underwent modified radical mastectomy were randomly divided into two groups. The routine functional exercise group (Group RF) received regular functional exercise guidance. In addition, the MLD combined with targeted rehabilitation therapies group (Group MLDT) received MLD, targeted rehabilitation therapies, and regular functional exercise guidance. The primary endpoints were shoulder range of motion, arm circumference and the incidence of axillary web syndrome (AWS). The secondary endpoints included the duration of axillary drainage, the duration of chest wall drainage, and complications.

Results: One hundred participants (mean age: 51.9±8.0 years; range, 28 to 72 years) were included in the final analysis as four patients could not complete the study. A significant improvement in shoulder range of motion was observed in Group MLDT compared to Group RF ($p<0.05$). Additionally, in Group MLDT, the duration of chest wall drainage was reduced ($p=0.037$). The frequency of AWS in Group RF was twice that in Group MLDT ($p=0.061$), but there was no significant difference in arm circumference ($p>0.05$) or the duration of axillary drainage ($p=0.519$). Regarding complications, there was one case of necrosis in the MLDT group and four cases in the RF group, including wound infection and seroma.

Conclusion: Manual lymphatic drainage combined with targeted rehabilitation therapies is an effective strategy to improve shoulder function, shorten the duration of chest wall drainage, reduce complications, and partly lower the incidence of AWS.

Keywords: Axillary web syndrome, breast cancer-related lymphedema, breast cancer, shoulder range of motion.

The incidence and mortality of breast cancer cause it to rank among the top female malignancies,^[1] and surgery is the main treatment. Upper limb dysfunction is a common postoperative complication in patients treated with modified radical mastectomy, with sequelae including shoulder joint dysfunction, breast cancer-related lymphedema (BCRL), and axillary web syndrome (AWS), for which the incidence

rate varies from 2.5 to 86% in previous studies.^[2-6] The presence of complications has negative impacts on breast cancer survivors, such as restricted arm movement when dressing, abnormal appearance, difficulty lifting objects, and painful discomfort.^[7] In addition, without timely intervention or treatment, these complications may gradually develop into chronic conditions.^[8]

Corresponding author: Feng Luo, MD. Department of Breast Surgery, the First Affiliated Hospital of Chongqing Medical University, No: 1 Youyi Road, Yuzhong District, Chongqing 400042, China. e-mail: luofeng201413@163.com

Cite this article as:

Xiong Q, Luo F, Zhan J, Qiao J, Duan Y, Huang J, et al. Effect of manual lymphatic drainage combined with targeted rehabilitation therapies on the recovery of upper limb function in patients with modified radical mastectomy: A randomized controlled trial. Turk J Phys Med Rehab 2023;69(2):161-170. doi: 10.5606/tftrd.2023.11221.

©2023 All right reserved by the Turkish Society of Physical Medicine and Rehabilitation

This is an open access article under the terms of the Creative Commons Attribution-NonCommercial License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited and is not used for commercial purposes (<http://creativecommons.org/licenses/by-nc/4.0/>).



Exercise such as aerobic exercise and stretching are common ways to prevent and improve upper extremity dysfunction in breast cancer patients,^[9,10] but they neglect the local changes in the shoulder joint after surgery and the individualized rehabilitation needs of patients. McNeely et al.^[1] noted that physical therapy was more beneficial to the patient's functional status of the shoulder joint and did not increase the risk of lymphedema in the affected limb. Common physiotherapy treatments include manual lymphatic drainage (MLD) and manual therapy.

Manual lymphatic drainage is directly performed on the skin surface with a certain pressure to pump the lymph flow, create new lymph pathways, and soften fibrotic tissue.^[11,12] Some studies support the early application of MLD because inflammation secondary to surgical injury makes lymphatic drainage difficult, increasing limb volume and protein stagnation, and reinforces factors that may produce lymphatic vessel overload, contributing to complications such as AWS and subclinical edema.^[13-16] Torres Lacomba et al.^[15] found that early use of rehabilitation techniques such as MLD reduced the incidence of lymphedema by as much as three times. Patients who develop lymphedema in the mid-to-distant postoperative period are usually treated with MLD in combination with other modalities, such as compression bandages, skin care, and functional exercise, but this approach is more effective for mild to moderate lymphedema.^[12] Such findings indicate that MLD should be used prophylactically rather than symptomatically.

Moreover, MLD combined with other therapies has a synergistic effect.^[12,17] Manual lymphatic drainage combined with manual therapy yielded additional benefits for decreasing arm volume and pain for breast cancer with AWS.^[18] Manual therapy covers numerous elements, including soft tissue mobilization and joint mobilization. By acting directly on tissues, manual therapy can directly detect the different conditions of each patient and perform targeted measures as needed. Studies have shown that manual therapy optimizes superficial and deep tissue function to release tight tissue, promote blood flow, and decrease pain.^[19-22] However, few studies have examined the effect of combined MLD and manual therapy in the early postoperative period.

Despite the effectiveness of rehabilitation techniques, they are unavailable for the majority of breast cancer patients due to the huge shortage of rehabilitation doctors. In China, postoperative breast cancer rehabilitation is usually conducted by nurses

for health education. The intervention of rehabilitation led by rehabilitation doctors usually occurs when the patient has symptoms of upper limb dysfunction or when the symptoms are severe, and the effect of rehabilitation is usually slow and minimal.

Based on the actual situation, our study fully mobilized existing resources; that is, rehabilitation doctors and nurses cooperated to provide patients with MLD combined with targeted rehabilitation therapies to achieve the satisfaction of commonality and individuality associated with breast cancer recovery.

PATIENTS AND METHODS

In the randomized controlled study, the interventions were administered over three months, and five evaluations were carried out: one on the first day before the surgery and the others at follow-ups occurring on the fifth day, one month, two months, and three months after surgery. Participants were recruited from the inpatient clinic of the Department of Breast Surgery, The First Affiliated Hospital of Chongqing Medical University between October 2019 and June 2020. The inclusion criteria were as follows: (i) diagnosis of unilateral breast cancer and (ii) treatment with modified radical mastectomy. The exclusion criteria were as follows: (i) a history of shoulder joint dysfunction, (ii) a history of upper-limb lymphatic system disease, (iii) a history of axillary surgery, and (iv) cognitive dysfunction, breast cancer metastasis, recurrence, or death during this period. Randomization was carried out utilizing a random number table. Patients were randomly divided into two groups: the routine functional exercise group (Group RF) and the MLD combined with targeted rehabilitation therapies group (Group MLDT). The evaluator was blinded to the grouping.

Patients were separated into two groups, one receiving functional exercise instruction by nurses and the other receiving MLD in conjunction with targeted rehabilitation therapies by rehabilitation doctors and nurses on this basis. Rehabilitators and nurses examined the patients' functional state before each rehabilitation treatment and altered the rehabilitation procedures as needed. Figure 1 illustrates this process. The rehabilitation doctors and nurses had more than five years of clinical experience, relevant qualifications, and unified training.

Functional exercise guidance

The nurses instructed patients regarding the functional exercises, starting after the first

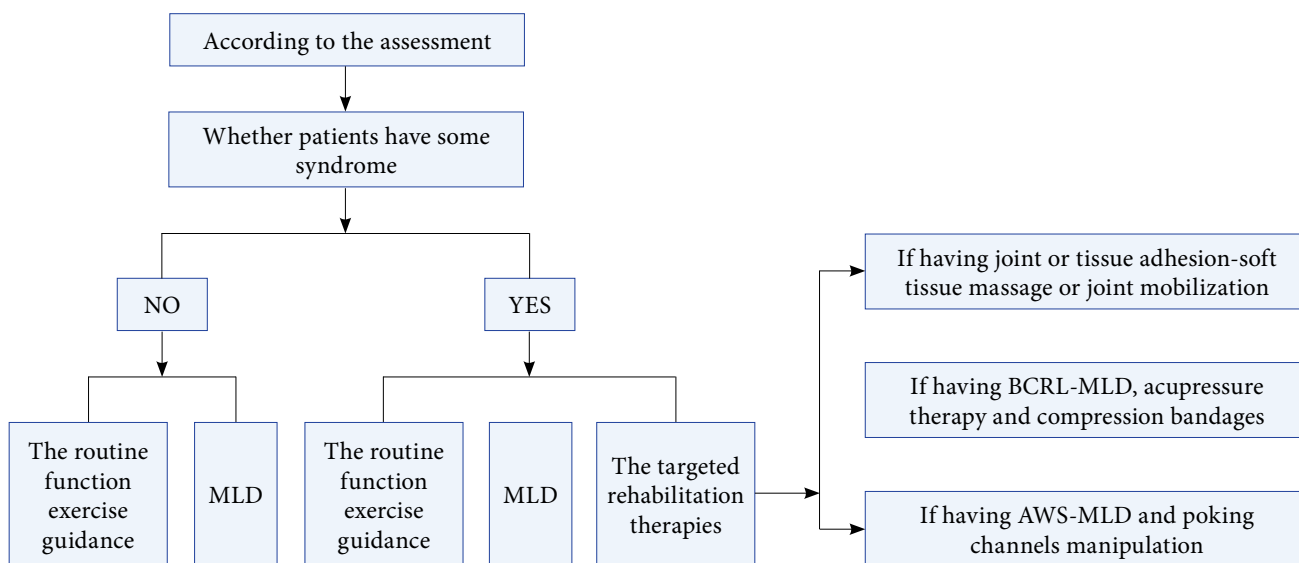


Figure 1. Flow diagram of the group MLDT.

BCRL: Breast cancer-related lymphedema; MLD: Manual lymphatic drainage; MLDT: Manual lymphatic drainage therapies.

postoperative day when vital signs were stable (Table 1). Patients needed to exercise three to four times per day for 20-30 min. When the patients were discharged, the nurses ensured that they had mastered the functional exercise content shown in Table 1 and informed them regarding the identification of and precautions against complications.

Manual lymphatic drainage

Before the manipulation of MLD, rehabilitation doctors or nurses led patients to perform active and passive activities of the affected limb in bed or the standing position starting on the first day after the operation to arouse the body. Manual lymphatic drainage was applied with light pressure in the following order: central area (neck, superficial and

deep abdomen) lymph nodes, adjacent drainage areas (axillary, groin area), anastomotic areas (chest, back) lymph nodes, and edema areas.^[18] The duration of MLD was 20-25 min, and the frequency was one to two times a day.

Targeted rehabilitation therapies

Based on the assessment, the rehabilitation doctors formulated targeted measures for patients with rehabilitation problems. If a patient was found to have tissue or joint adhesions, soft tissue massage or joint mobilization was given until the patient's symptoms were relieved. The rehabilitation doctor first pressed on the patient's tissues or shoulder joint adhesions to feel the tension and then applied different pressures to the tissues or slid the shoulder joint surface until

TABLE 1 Exercise content of Group RF	
Time	Content
Vital signs stabilized on the 1 day after surgery	Finger extension, fisting, wrist bending
1~3 days after surgery	Some upper limb isometric contraction training such as elbow flexion, arm extension, and a small range of shoulder joints
4~7 days after surgery	Use affected limb to wash their face, comb their hair, touch the contralateral shoulder and ipsilateral ear with the affected side's hands
7 days after the operation	With the shoulder as the center, front and back swing the arm
10 days after the operation	Patients were guided to raise the affected limb to perform finger climbing activities

RF: Routine functional.

the tissue or joint tension was felt to a soft end-feel. The frequency was one to two times a day, 10-15 min each time.

Patients who had symptoms of lymphedema or developed lymphedema were treated with MLD, acupressure therapy, and compression bandages. The frequency of MLD was increased to two times a day, 20-25 min each time. Acupressure therapy acts on acupoints, such as Quchi, Shousanli, and Hegu, by pressing and kneading to promote blood circulation and reduce edema. Each point is massaged for 1-2 min. In addition, compression bandages are an important measure in the treatment of BCRL. The rehabilitation doctor instructed the patient to wear the compression bandages in a spiral direction from the palm upwards, with the next layer covering 50% of the width of the previous one. The patient was informed of the importance, necessity, and precautions of the compression bandage and that it should be worn for as long as possible.

When patients had AWS, MLD and Poking channel manipulation were used. The frequency of MLD was increased to two times a day, 20-25 min each time. In detail, Poking channel manipulation involved placing the finger end of the thumb perpendicular to the cording and then moving it back and forth. This therapy was administered one to two times a day for 10-15 min. It is worth mentioning that if a patient had fever, active bleeding, deep vein thrombosis, or an acute infection, rehabilitation treatment was suspended.

Main outcome assessment

Shoulder joint function was assessed in degrees using a simple measuring instrument. The patients assumed a standing or sitting position for measurement of their degree of flexion, extension, abduction, internal rotation, and external rotation range of motion (ROM).

A measuring tape was used to measure the patients' upper limb arm circumferences at the ulnar styloid and 10, 20, 30, and 40 cm above the ulnar styloid, comparing the circumference of the affected side with that of the unaffected side. If the maximum difference for any one point was more than 2 cm, it was diagnosed as BCRL. The degree of BCRL was divided into three grades: <3 cm indicated mild edema, 3-5 cm indicated moderate edema, and >5 cm indicated severe edema.^[23]

Axillary web syndrome was assessed by rehabilitation doctors through a physical

examination. To avoid obstructing the visual field of the physical examination, the patients needed to abduct the affected limb as much as possible to expose the armpit and arm. This made it easier for the rehabilitation doctor to see and palpate the cording in the patient's armpit, inner arm, forearm, and wrist. If the rehabilitation doctor found one cord in those locations, the patient was diagnosed with AWS.

Minor outcome assessment

During the three-month follow-up, nurses observed and recorded the extubation time, wound healing, wound infection, and seroma of patients. Once the patients experienced complications, rehabilitation doctors and nurses could intervene in a timely manner.

Statistical analysis

Data were analyzed using IBM SPSS version 24.0 software (IBM Corp., Armonk, NY, USA). A sample size of 50 patients in each group was determined to be necessary to detect the difference with a case ratio of 1:1, considering a difference of 30% in BCRL,^[18] a statistical power of 0.8, an α level of 0.05, and the possible loss to follow-up of 20%. Quantitative data are presented as the mean \pm standard deviation (SD), and qualitative data are presented as frequencies or percentages. The patient's baseline data were analyzed by the t-test, Fisher test, chi-square test, or Wilcoxon test for comparisons between the two groups. The differences in shoulder ROM and arm circumference of both upper limbs were analyzed by repeated measures analysis of variance from three aspects: time effect, group effect, and effect of the interaction between time and group. As these data did not satisfy the Mauchly spherical hypothesis test, Greenhouse-Geisser correction was adopted. The incidence of AWS was tested by the chi-square test. A p value of <0.05 indicated that there was a significant difference between the two groups.

RESULTS

One patient in Group MLDT and two patients in Group RF did not complete the study because of failed postoperative evaluations. A total of one patient in Group MLDT who refused to receive the treatment was also excluded, as presented in Figure 2. Ultimately, 50 patients in Group MLDT and 50 patients in Group RF were included for a total of 100 female participants (Group MLDT mean age: 50.4 \pm 8.8 years; range, 28 to 72 years; Group RF mean age: 53.5 \pm 7.0 years; range 39 to 67 years).

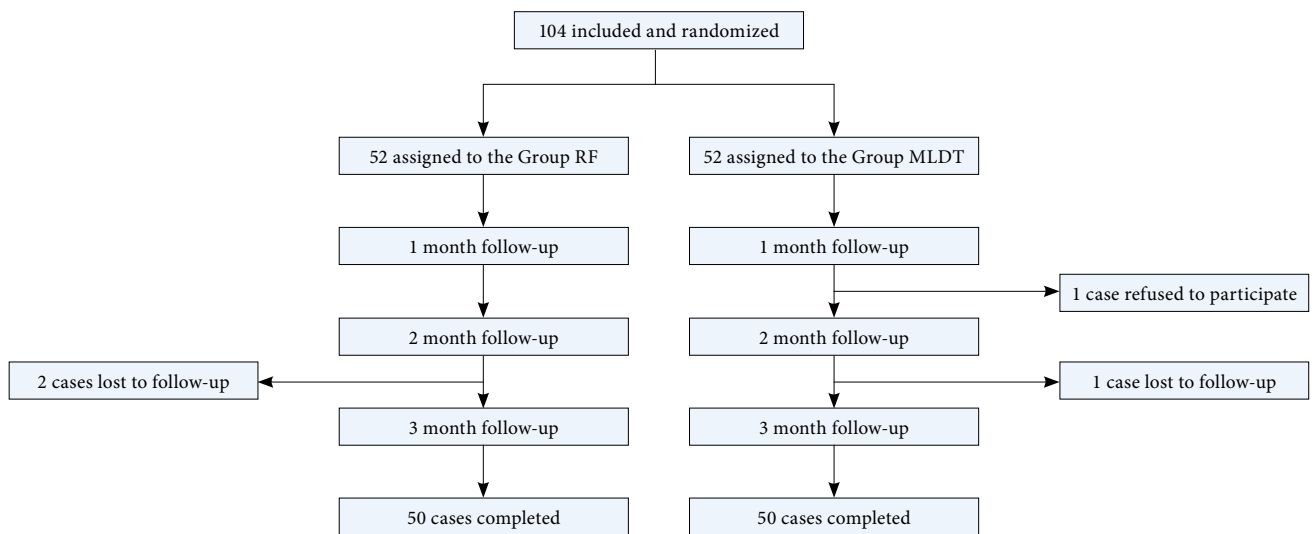


Figure 2. Flow diagram of the study.

MLDT: Manual lymphatic drainage therapies; RF: Routine functional.

TABLE 2 Comparison of baseline data between two groups							
Characteristics	Group MLDT			Group RF			<i>p</i>
	n	%	Mean±SD	n	%	Mean±SD	
Age (year)			50.4±8.8			53.5±7.0	0.056
Body mass index (kg/m ²)			24.1±3.0			23.5±3.6	0.410
Staging of disease							0.744
I	1	2		2	4		
II	46	92		45	90		
III	3	6		3	6		
Chemotherapy regime							0.567
TEC/TAC	23	46		18	36		
EC-T/AC-T	22	44		25	50		
Other	5	10		7	14		
Chemotherapy treatment course							0.839
<8	21	42		20	40		
≥8	29	58		30	60		
Axillary clearance							0.086
Yes	43	86		36	72		
No	7	14		14	28		
Lymph node cleaning range							0.059
Low group lymph nodes	4	8		7	14		
Low and median group lymph nodes	28	56		15	30		
Low, median and high group lymph nodes	11	22		14	28		
No lymph nodes	7	14		14	28		
Shoulder ROM							
Flexion			175.8±7.5			173.2±6.3	0.064
Extension			59.8±1.4			59.4±2.4	0.357
Abduction			175.4±7.7			173.2±6.7	0.130
Internal rotation			88.9±2.9			87.8±4.1	0.123
External rotation			89.5±2.1			88.8±3.7	0.248
Ulnar styloid			-0.1±0.3			-0.1±0.4	0.808
Arm circumference							
Above the ulnar styloid 10 cm			-0.1±0.6			-0.1±0.7	0.975
Above the ulnar styloid 20 cm			0.1±0.7			-0.1±0.7	0.190
Above the ulnar styloid 30 cm			0.1±0.7			-0.0±0.9	0.618
Above the ulnar styloid 40 cm			-0.1±0.7			-0.1±1.0	0.937

MLDT: Manual lymphatic drainage therapies; RF: Routine functional; SD: Standard deviation; TEC: Taxus epirubicin cyclophosphamide; TAC: Taxus anthracycline cyclophosphamide; EC-T: Epirubicin cyclophosphamide-taxus; AC-T: Anthracycline cyclophosphamide-taxus; ROM: Range of motion.

TABLE 3
Changes of shoulder ROM over time and between groups

Variables	1 day before surgery	5 days after surgery	1 month after surgery	2 months after surgery	3 months after surgery	Time effect	Group effect	Interaction effect between time and group
	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD	<i>p</i>	<i>p</i>	<i>p</i>
Flexion								
Group MLDT	175.8±7.5	93.2±22.5	118.9±25.9	136.3±24.2	149.2±23.5	<0.001	<0.001	<0.001
Group RF	173.2±6.3	89.9±19.2	100.5±18.6	123.0±18.9	134.1±17.4			
Extension								
Group MLDT	59.8±1.4	40.1±8.2	50.0±10.0	53.4±10.1	55.4±8.7	<0.001	0.034	0.010
Group RF	59.4±2.4	39.3±8.8	46.3±7.9	48.7±9.5	51.0±8.7			
Abduction								
Group MLDT	175.4±7.7	91.7±23.1	114.5±31.4	134.7±27.6	147.8±25.0	0.001	<0.001	0.019
Group RF	173.2±6.7	88.2±15.9	100.3±18.3	121.0±22.3	133.6±18.4			
Internal rotation								
Group MLDT	88.9±2.9	32.0±6.3	46.1±9.5	59.6±7.0	70.0±6.9	<0.001	<0.001	<0.001
Group RF	87.8±4.1	30.1±4.2	37.2±6.4	50.1±8.5	62.0±9.0			
External rotation								
Group MLDT	89.5±2.1	34.1±8.1	50.1±10.6	62.0±9.7	76.4±10.9	<0.001	<0.001	<0.001
Group RF	88.8±3.7	31.3±7.5	39.7±7.7	51.7±9.1	64.4±10.5			

ROM: Range of motion; SD: Standard deviation; MLDT: Manual lymphatic drainage therapies; RF: Routine functional.

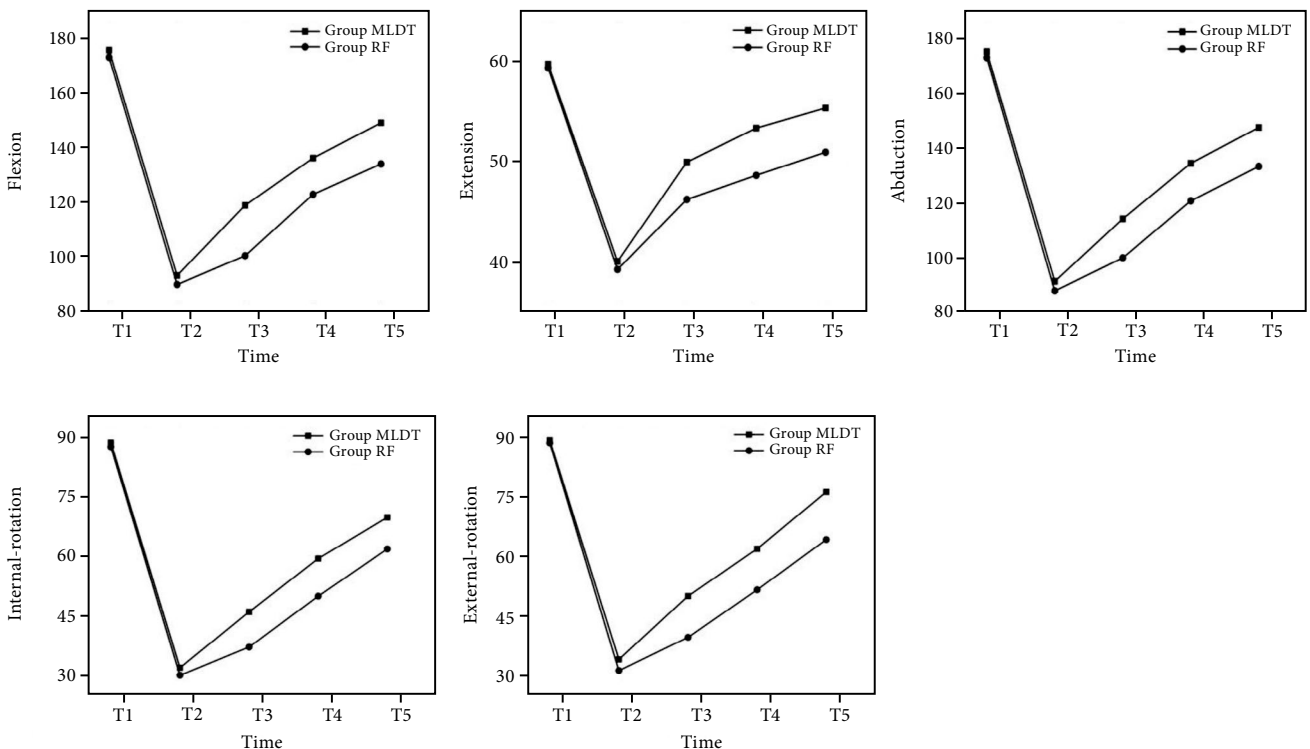


Figure 3. Changes in the shoulder joint ROM between two groups. T1: 1 day before surgery; T2: 5 days after surgery; T3: 1 month after surgery; T4: 2 months after surgery; T5: 3 month after surgery.

MLDT: Manual lymphatic drainage therapies; RF: Routine functional; ROM: Range of motion.

TABLE 4
Changes of arm circumference difference over time and between groups

Variables	1 day before surgery	5 days after surgery	1 month after surgery	2 months after surgery	3 months after surgery	Time effect	Group effect	Interaction effect between time and group
	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD	<i>p</i>	<i>p</i>	<i>p</i>
a								
Group MLDT	-0.1±0.3	0.0±0.4	0.1±0.4	0.1±0.4	0.1±0.3	<0.001	0.600	0.883
Group RF	-0.1±0.4	0.0±0.4	0.1±0.3	0.1±0.4	0.1±0.4			
b								
Group MLDT	-0.1±0.6	0.1±0.8	0.1±0.8	0.2±0.8	0.2±0.8	0.015	0.991	0.975
Group RF	-0.1±0.7	0.1±0.9	0.1±0.7	0.2±0.9	0.2±0.8			
c								
Group MLDT	0.1±0.7	0.3±0.8	0.2±0.7	0.3±0.7	0.4±0.7	0.005	0.129	0.642
Group RF	-0.1±0.7	0.1±0.9	0.1±0.8	0.2±0.7	0.2±0.8			
d								
Group MLDT	0.1±1	0.3±0.8	0.4±0.9	0.5±0.8	0.5±0.8	0.002	0.248	0.535
Group RF	-0.0±0.9	0.2±0.9	0.3±0.9	0.3±0.9	0.2±0.8			
e								
Group MLDT	-0.1±0.7	0.1±0.7	0.3±0.9	0.3±0.8	0.5±0.8	<0.001	0.354	0.253
Group RF	-0.1±1.0	-0.0±1.0	0.0±1.0	0.3±1.1	0.2±1.0			

SD: Standard deviation; MLDT: Manual lymphatic drainage therapies; RF: Routine functional; a: The difference of arm circumference on the ulnar styloid; b: The difference of the arm circumference 10 cm above the ulnar styloid; c: The difference of the arm circumference 20 cm above the ulnar styloid; d: The difference of the arm circumference 30 cm above the ulnar styloid; e: The difference of the arm circumference 40 cm above the ulnar styloid.

Age, body mass index, staging of disease, chemotherapy regimen, chemotherapy treatment course, axillary clearance, lymph node cleaning range, preoperative shoulder ROM, and arm circumference data for participants at baseline indicated similar characteristics between the two groups (Table 2).

The affected side of Group MLDT had a more significant improvement in shoulder ROM compared to Group RF ($p<0.05$). The effect including time effect, group effect, and the interaction effect between time effect and group effect indicated a significant difference (all $p<0.05$). This showed that the recovery of shoulder ROM was better over time, particularly in the MLDT group within three months of surgery (Table 3, Figure 3).

Arm circumference presented a significant time effect between two groups, suggesting that the risk of BCRL occurrence increased over time ($p<0.05$, shown in Table 4). Group MLDT did not present any statistically significant differences in the group effect or the interaction effect between the time effect and group effect from Group RF (all $p>0.05$).

A total of five cases of BCRL occurred in this study, including two in Group MLDT and three in Group RF. The symptoms of two mild BCRL patients in Group MLDT were relieved after receiving MLD, acupuncture therapy, and compression bandages. After the end of the study, one patient with mild lymphedema and one patient with moderate lymphedema in the RF group improved after receiving the above treatments. Only one patient with moderate lymphedema remained on treatment due to poor compliance.

The frequency of AWS in Group RF was 16 (32%), which was twice that in Group MLDT ($p=0.061$), indicating that MLD combined with targeted rehabilitation therapies had some positive effect in preventing AWS.

Treatment in Group MLDT was associated with a significantly decreased duration of chest wall drainage (6.00 vs. 9.50 day, $Z=-2.09$, $p=0.037$). There was no significant difference in the duration of axillary drainage between the two groups (29 vs. 30 day, $Z=-0.65$, $p=0.519$). Five complications were noticed in both groups during the three-month follow-up. There was one case of wound necrosis in Group MLDT and

two wound infections and two cases of seroma in Group RF.

DISCUSSION

From presurgery to three months of follow-up, MLD combined with targeted rehabilitation therapies helped improve shoulder mobility, shortened the duration of chest wall drainage, reduced complications, and actively prevented AWS. Thus, we could conclude that MLD combined with targeted rehabilitation therapies favors the recovery of the affected limb.

Group MLDT showed a significant increase in the shoulder ROM compared to the Group RF during three months of follow-up. Our study supported previous investigations reporting that rehabilitation therapies led to a remarkable improvement in shoulder function.^[12,18,24,25] Belmonte et al.^[26] pointed out that the changes in muscle functional status in breast cancer patients were the root cause of the patients' lack of strength in the affected limb. This showed the importance of focusing on changes in shoulder muscle groups. Shoulder muscle groups included the shoulder rotator, abductor, or serratus anterior muscle and latissimus dorsi. Changes in each muscle group profoundly affect the patient's upper extremity functional status. These rehabilitation techniques, which were lightly performed on the affected arm, not only prevented muscular shortening and tightening,^[1,27] restored muscle functional status, and promoted joint mobility^[28] but also improved blood circulation,^[29] aiming at restoring the optimal physiological condition of the upper limb.

Our study reported that the risk of BCRL increased over time. Norman et al.^[30] found that the incidence of BCRL at one, two, three, and four years after surgery was 26%, 31%, 36%, and 40%, respectively. Ribeiro Pereira et al.^[4] indicated in a 10-year follow-up study that the incidence of BCRL was 13.5% within two years, 30.2% within five years, and 41.1% within 10 years. The above study well illustrated that the incidence of BCRL increases with time. This may be because BCRL is influenced by various factors, such as the type of axillary surgery, radiotherapy, chemotherapy, body mass index, subclinical edema, and cellulitis.^[31,32] However, this study suggested that MLD combined with targeted rehabilitation therapies made no significant difference in patients with BCRL in the early postoperative period, which was in line with the study of Andersen et al.^[33] There may be several reasons for these results. First, we followed

up for only three months after surgery, but the peak of lymphedema occurrence was 18 months after surgery,^[16] so it is possible that long-term follow-up would reveal more about the effect of this method on lymphedema. Second, in this study, a tape measure was employed to monitor patients for BCRL, and this approach could have overlooked microscopic changes in the patient's affected arm.

When comparing both groups, we found that the frequency of AWS in Group MLDT was lower than that in Group RF, but the difference was not significant. The pathobiology of AWS is not clear, but most studies have suggested that AWS development is associated with superficial lymphatic thrombosis.^[34,35] Based on this, studies used MLD for AWS, usually in combination with other therapies. Liu et al.^[36] found that MLD combined with vacuum sealing drainage shortened the duration of disappearance and tightness of cording. Cho et al.^[18] conducted a four-week intervention in 41 breast cancer patients with AWS and found no significant difference in the incidence of AWS between patients who received physical therapy and MLD and those who received physical therapy only (28.5% vs. 35%, $p=0.658$). More clinical trials are needed to further examine the effect of MLD on AWS. In this study, MLD and Poking channel manipulation composed the treatment for AWS. There were eight (16%) AWS in Group MLDT and 16 (32%) AWS in Group RF. Related studies have shown that the incidence of AWS is 36-86%,^[6-9] which is lower than that reported in the literature and may be related to the postoperative implementation of rehabilitation therapies and the short follow-up period.

In this study, Group MLDT had one case of wound necrosis, and Group RF had two cases of wound infection and two cases of effusion. Through skin grafting, local fluid drainage, dressing changes, and antibiotic infusion, these complications were ultimately resolved. Studies have reported that the incidence of wound infection after breast cancer surgery is 12.9%,^[4,37] and the incidence of postoperative seroma can reach 30.8-62.6%.^[37,38] In this study, the incidence of postoperative wound infection and fluid effusion was lower than that of related studies, which indicated the safety of MLD combined with targeted rehabilitation therapies.

This is a new attempt at postoperative rehabilitation after modified radical mastectomy for breast cancer in China, from nurse-led rehabilitation to doctor-led early postoperative recovery of patients. We did pay attention to the changes in shoulder joint

tissue and muscles of each patient, monitored patient rehabilitation effects and problems, and provided targeted and professional rehabilitation guidance, aiming at meeting rehabilitation needs and promoting early recovery for each patient.

There also are some limitations. First, this study was restricted to a single center. Therefore, a multicenter follow-up study needs to be performed to validate the effect of this method in the long term. Second, there was only a three-month follow-up period after surgery, which failed to reflect the effect of MLD combined with targeted rehabilitation therapies in the long term.

In conclusion, MLD combined with targeted rehabilitation therapies provides targeted rehabilitation techniques that have no remarkable effect on early BCRL. However, there are more favorable changes in shoulder joint function and AWS without severe complications or extension of the extubation time.

Ethics Committee Approval: The study protocol was approved by the First Affiliated Hospital of Chongqing Medical University Ethics Committee (date: 16.10.2019, no: 2019-346). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Patient Consent for Publication: A written informed consent was obtained from each patient.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions: Idea, design, data collection, analysis, writing of manuscript, references and literature review: Qi.X.; Data collection and processing: J.Z., J.Q., Y.D., J.H., R.L., H.L., P.J.; Idea, design, control/Supervision and critical review: F.L.

Conflict of Interest: The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

Funding: The authors received no financial support for the research and/or authorship of this article.

REFERENCES

- McNeely ML, Campbell K, Ospina M, Rowe BH, Dabbs K, Klassen TP, et al. Exercise interventions for upper-limb dysfunction due to breast cancer treatment. *Cochrane Database Syst Rev* 2010;(6):CD005211. doi: 10.1002/14651858.CD005211.pub2.
- Dahl AA, Nesvold IL, Reinertsen KV, Fosså SD. Arm/shoulder problems and insomnia symptoms in breast cancer survivors: Cross-sectional, controlled and longitudinal observations. *Sleep Med* 2011;12:584-90. doi: 10.1016/j.sleep.2011.01.011.
- Devoogdt N, Van Kampen M, Christiaens MR, Troosters T, Piot W, Beets N, et al. Short- and long-term recovery of upper limb function after axillary lymph node dissection. *Eur J Cancer Care (Engl)* 2011;20:77-86. doi: 10.1111/j.1365-2354.2009.01141.x.
- Ribeiro Pereira ACP, Koifman RJ, Bergmann A. Incidence and risk factors of lymphedema after breast cancer treatment: 10 years of follow-up. *Breast* 2017;36:67-73. doi: 10.1016/j.breast.2017.09.006.
- Zou L, Liu FH, Shen PP, Hu Y, Liu XQ, Xu YY, et al. The incidence and risk factors of related lymphedema for breast cancer survivors post-operation: A 2-year follow-up prospective cohort study. *Breast Cancer* 2018;25:309-14. doi: 10.1007/s12282-018-0830-3.
- Huang HC, Liu HH, Yin LY, Yeh CH, Tu CW, Yang CS. The upper-limb volumetric changes in breast cancer survivors with axillary web syndrome. *Eur J Cancer Care (Engl)* 2017;26. doi: 10.1111/ecc.12637.
- Furlan C, Matheus CN, Jales RM, Derchain S, Sarian LO. Vascular alterations in axillary and brachial vessels in patients with axillary web syndrome after breast cancer surgery. *Lymphat Res Biol* 2018;16:287-93. doi: 10.1089/lrb.2017.0037.
- Koehler LA, Hunter DW, Blaes AH, Haddad TC. Function, shoulder motion, pain, and lymphedema in breast cancer with and without axillary web syndrome: An 18-month follow-up. *Phys Ther* 2018;98:518-27. doi: 10.1093/ptj/pty010.
- Wilson DJ. Exercise for the patient after breast cancer surgery. *Semin Oncol Nurs* 2017;33:98-105. doi: 10.1016/j.soncn.2016.11.010.
- Aydin M, Kose E, Odabas I, Meric Bingul B, Demirci D, Aydin Z. The effect of exercise on life quality and depression levels of breast cancer patients. *Asian Pac J Cancer Prev* 2021;22:725-32. doi: 10.31557/APJCP.2021.22.3.725.
- Gradalski T, Ochalek K, Kurpiewska J. Complex decongestive lymphatic therapy with or without Vodder II manual lymph drainage in more severe chronic postmastectomy upper limb lymphedema: A randomized noninferiority prospective study. *J Pain Symptom Manage* 2015;50:750-7. doi: 10.1016/j.jpainsymman.2015.06.017.
- Ezzo J, Manheimer E, McNeely ML, Howell DM, Weiss R, Johansson KI, et al. Manual lymphatic drainage for lymphedema following breast cancer treatment. *Cochrane Database Syst Rev* 2015;(5):CD003475. doi: 10.1002/14651858.CD003475.pub2.
- Devoogdt N, Christiaens MR, Geraerts I, Truijten S, Smeets A, Leunen K, et al. Effect of manual lymph drainage in addition to guidelines and exercise therapy on arm lymphoedema related to breast cancer: Randomised controlled trial. *BMJ* 2011;343:d5326. doi: 10.1136/bmj.d5326.
- Sarri AJ, Moriguchi SM, Dias R, Peres SV, DA Silva ET, Koga KH, et al. Physiotherapeutic stimulation: Early prevention of lymphedema following axillary lymph node dissection for breast cancer treatment. *Exp Ther Med* 2010;1:147-52. doi: 10.3892/etm_00000024.

15. Torres Lacomba M, Yuste Sánchez MJ, Zapico Goñi A, Prieto Merino D, Mayoral del Moral O, Cerezo Téllez E, et al. Effectiveness of early physiotherapy to prevent lymphoedema after surgery for breast cancer: Randomised, single blinded, clinical trial. *BMJ* 2010;340:b5396. doi: 10.1136/bmj.b5396.
16. de Oliveira MM, de Rezende LF, do Amaral MT, Pinto e Silva MP, Morais SS, Gurgel MS. Manual lymphatic drainage versus exercise in the early postoperative period for breast cancer. *Physiother Theory Pract* 2014;30:384-9. doi: 10.3109/09593985.2013.876695.
17. Ha KJ, Lee SY, Lee H, Choi SJ. Synergistic effects of proprioceptive neuromuscular facilitation and manual lymphatic drainage in patients with mastectomy-related lymphedema. *Front Physiol* 2017;8:959. doi: 10.3389/fphys.2017.00959.
18. Cho Y, Do J, Jung S, Kwon O, Jeon JY. Effects of a physical therapy program combined with manual lymphatic drainage on shoulder function, quality of life, lymphedema incidence, and pain in breast cancer patients with axillary web syndrome following axillary dissection. *Support Care Cancer* 2016;24:2047-57. doi: 10.1007/s00520-015-3005-1.
19. Listing M, Reissshauer A, Krohn M, Voigt B, Tjahono G, Becker J, et al. Massage therapy reduces physical discomfort and improves mood disturbances in women with breast cancer. *Psychooncology* 2009;18:1290-9. doi: 10.1002/pon.1508.
20. Nijs J, Van Houdenhove B. From acute musculoskeletal pain to chronic widespread pain and fibromyalgia: Application of pain neurophysiology in manual therapy practice. *Man Ther* 2009;14:3-12. doi: 10.1016/j.math.2008.03.001.
21. Pinheiro da Silva F, Moreira GM, Zomkowski K, Amaral de Noronha M, Flores Sperandio F. Manual therapy as treatment for chronic musculoskeletal pain in female breast cancer survivors: A systematic review and meta-analysis. *J Manipulative Physiol Ther* 2019;42:503-13. doi: 10.1016/j.jmpt.2018.12.007.
22. Wisotzky E, Hanrahan N, Lione TP, Maltser S. Deconstructing postmastectomy syndrome: Implications for physiatric management. *Phys Med Rehabil Clin N Am* 2017;28:153-69. doi: 10.1016/j.pmr.2016.09.003.
23. American Physical Therapy Association. Guide to physical therapist practice. Second edition. American Physical Therapy Association. *Phys Ther* 2001;81:9-746.
24. Massingill J, Jorgensen C, Dolata J, Sehgal AR. Myofascial massage for chronic pain and decreased upper extremity mobility after breast cancer surgery. *Int J Ther Massage Bodywork* 2018;11:4-9.
25. Serra-Añó P, Inglés M, Bou-Catalá C, Iraola-Lliso A, Espi-López GV. Effectiveness of myofascial release after breast cancer surgery in women undergoing conservative surgery and radiotherapy: A randomized controlled trial. *Support Care Cancer* 2019;27:2633-41. doi: 10.1007/s00520-018-4544-z.
26. Belmonte R, Messaggi-Sartor M, Ferrer M, Pont A, Escalada F. Prospective study of shoulder strength, shoulder range of motion, and lymphedema in breast cancer patients from pre-surgery to 5 years after ALND or SLNB. *Support Care Cancer* 2018;26:3277-87. doi: 10.1007/s00520-018-4186-1.
27. Ebaugh D, Spinelli B, Schmitz KH. Shoulder impairments and their association with symptomatic rotator cuff disease in breast cancer survivors. *Med Hypotheses* 2011;77:481-7. doi: 10.1016/j.mehy.2011.06.015.
28. Stubblefield MD, Keole N. Upper body pain and functional disorders in patients with breast cancer. *PM R* 2014;6:170-83. doi: 10.1016/j.pmrj.2013.08.605.
29. Goats GC. Massage--the scientific basis of an ancient art: Part 2. Physiological and therapeutic effects. *Br J Sports Med* 1994;28:153-6. doi: 10.1136/bjism.28.3.153.
30. Norman SA, Localio AR, Potashnik SL, Simoes Torpey HA, Kallan MJ, Weber AL, et al. Lymphedema in breast cancer survivors: Incidence, degree, time course, treatment, and symptoms. *J Clin Oncol* 2009;27:390-7. doi: 10.1200/JCO.2008.17.9291.
31. Gillespie TC, Sayegh HE, Brunelle CL, Daniell KM, Taghian AG. Breast cancer-related lymphedema: Risk factors, precautionary measures, and treatments. *Gland Surg* 2018;7:379-403. doi: 10.21037/gs.2017.11.04.
32. McLaughlin SA, Brunelle CL, Taghian A. Breast cancer-related lymphedema: Risk factors, screening, management, and the Impact of locoregional treatment. *J Clin Oncol* 2020;38:2341-50. doi: 10.1200/JCO.19.02896.
33. Andersen L, Højris I, Erlandsen M, Andersen J. Treatment of breast-cancer-related lymphedema with or without manual lymphatic drainage--a randomized study. *Acta Oncol* 2000;39:399-405. doi: 10.1080/028418600750013186.
34. Rashtak S, Gamble GL, Gibson LE, Pittelkow MR. From furuncle to axillary web syndrome: Shedding light on histopathology and pathogenesis. *Dermatology* 2012;224:110-4. doi: 10.1159/000337210.
35. Johansson K, Chong H, Ciornei CD, Brorson H, Mortimer PS. Axillary web syndrome: Evidence for lymphatic origin with thrombosis. *Lymphat Res Biol* 2020;18:329-32. doi: 10.1089/lrb.2019.0074.
36. Liu, J, Chen, D, Yin, X. Effect of manual lymphatic drainage combined with vacuum sealing drainage on axillary web syndrome caused by breast cancer surgery. *Int Wound J* 2022;1-8. doi:10.1111/iwj.13862
37. Macedo FO, Bergmann A, Koifman RJ, Torres DM, Costa RM, Silva IF. Axillary surgery in breast cancer: Acute postoperative complications in a hospital cohort of women of Rio de Janeiro, Brazil. *Mastology* 2018;28:80-6. doi:10.29289/2594539420180000377.
38. Teodózio CGC, Marchito LO, Fabro EAN, Macedo FO, de Aguiar SS, Thuler LCS, et al. Shoulder amplitude movement does not influence postoperative wound complications after breast cancer surgery: A randomized clinical trial. *Breast Cancer Res Treat* 2020;184:97-105. doi: 10.1007/s10549-020-05826-9.