Scientific Research Publishing

Advances in Breast Cancer Research, 2022, 11, 120-127
https://www.scirp.org/journal/abcr
ISSN Online: 2168-1597
ISSN Print: 2168-1589

Efficacy of Manual Lymphatic Drainage for Breast Cancer-Related Lymphedema*

Na Li[1#], Qi Wu[2#], Feng Liu[1], Liping Zhang[1], Lijuan Zhang[1], Qiaoling Zhong[1], Huizhen Zhang[1‡]

[1]Department of Nursing, Sun Yat-sen University Cancer Center, Guangzhou, China
[2]Yancheng Kindergarten Teachers College, Yancheng, China
Email: lina@sysucc.org.cn, zswqdwb@163.com, liufeng@sysucc.org.cn, zhanglp@sysucc.org.cn, zhongql@sysucc.org.cn, zhanglj@sysucc.org.cn, [†]zhanghz@sysucc.org.cn

How to cite this paper: Li, N., Wu, Q., Liu, F., Zhang, L.P., Zhang, L.J., Zhong, Q.L. and Zhang, H.Z. (2022) Efficacy of Manual Lymphatic Drainage for Breast Cancer-Related Lymphedema. *Advances in Breast Cancer Research*, **11**, 120-127.
https://doi.org/10.4236/abcr.2022.112010

Received: March 2, 2022
Accepted: April 15, 2022
Published: April 18, 2022

Copyright © 2022 by author(s) and Scientific Research Publishing Inc.
This work is licensed under the Creative Commons Attribution International License (CC BY 4.0).
http://creativecommons.org/licenses/by/4.0/

Open Access

Abstract

Purpose: The effect of manual lymphatic drainage in patients with breast cancer is controversial. The purpose of this study is to evaluate the role of manual lymphatic drainage (MLD) in breast cancer-related lymphedema treatment. **Methods:** The electronic databases of EMBASE, PubMed, Web of Science, and The Cochrane Library were searched to find English articles on MLD which were published before January 2020. After two evaluators selected the studies and independently evaluated literature quality, meta-analysis was carried out with RevMan 5.3 software. The outcome index of lymphedema treatment changed in edema volume. **Results:** The study included six RCTs of 364 patients and the meta-analysis showed no significant difference in the effect of MLD for BCRL compared with other treatments (mean difference, 3.76; 95% confidence interval, −35.09 to 42.62; Z, 0.19; $p = 0.850$). **Conclusion:** MLD can relieve the body tissue, rapidly improve local condition, and enhance complete decongestive therapy (CDT) efficacy. MLD can prevent BCRL and improve the symptoms of stage I lymphedema. It should be widely applied to prevent BCRL from entering an irreversible state.

Keywords

Manual Lymphatic Drainage, Meta-Analysis, Breast Cancer Lymphedema

1. Introduction

Breast cancer is the most common cancer and the leading cause of cancer death among women worldwide [1]. Cancer statistics from 2019 show that nearly 30% of newly diagnosed cancers in women are breast cancer [2]. Surgery is still the

*The work should be attributed by Sun Yat-sen University Cancer Center, Guangzhou, China.
[#]The first two authors contributed equally to this article.
[†]Corresponding author.

main treatment for breast cancer, but this causes anatomical injury that can lead to a variety of complications. Breast cancer-related lymphedema (BCRL) is one of the most serious complications after breast cancer surgery [3]. Decreased lymphatic transport capacity and/or increased lymphatic load of the affected limb after surgery, result in fluid accumulation outside the soft tissue cells and eventually swelling [4]. Approximately 12% to 30% of patients develop BCRL within 1 - 3 years after operation with symptoms such as heavy limb, numbness, pain, and swelling [5]. BCRL also restricts movement, damages self-image, increases financial burden, and reduces the quality of life of millions of breast cancer survivors.

In recent years, the research on the treatment of BCRL is increasing day by day. The gold standard for the treatment of lymphedema is complete decongestive therapy (CDT). This comprehensive approach includes manual lymphatic drainage (MLD), compression therapy, exercise, and skin care. MLD is an expensive, labor-intensive, specialized massage technique that helps stimulate excessive fluid flow by imitating the pumping action of lymphatic vessels to open lymphatic pathways and enhancing the drainage of affected limbs. Some clinical trials and systematic reviews have explored the efficacy of MLD [6] [7], but the results are controversial. In this study, the data of all randomized controlled trials (RCTs) were systematically reviewed and meta-analyzed to assess the effect of MLD in the treatment of BCRL to provide a reliable basis for clinical decision making.

2. Methods

2.1. Search Strategies

Searches were performed in the EMBASE, PubMed, Web of Science, and The Cochrane Library databases from their establishments to January 2020 using the following search terms: "manual lymph drainage," "MLD," "breast cancer," "breast neoplasm," "lymphoedema," "lymphedema." The Institutional Review Board of the SYSUCC approved the study (Approval no. GYX2020-002).

2.2. Inclusion Criteria

1) Type of study: RCT published in English. 2) Participants: female breast cancer patients over 18 years old who have received surgical treatment. 3) Intervention: the control group received routine nursing including health education, functional exercise, bandage pressure, resistance exercise, deep diaphragmatic breathing, skin care and physiotherapy, while the experimental group also received manual lymphatic drainage during routine nursing. 4) Outcome index: decreased arm swelling volume (or circumference) of BCRL patients, with a greater reduction indicating a better curative effect.

2.3. Data Extraction

All researchers received complete systematic review training. Literature retrieval was performed independently by two researchers. Primary selection was conducted by reading titles and abstracts, and then by reading the full text to ex-

clude the studies that do not meet the inclusion criteria. The data were extracted according to the pre-designed table, including the author, year of publication, operation type, sample size, follow-up time, and outcome index. Comparing the decisions recorded by the two reviewers, and any different opinions were evaluated and resolved by a third reviewer.

2.4. Quality Assessment of Selected Studies

The study uses The Cochrane Handbook for Systematic Reviews of Interventions to evaluate the quality of the literature, including random sequence generation, allocation hiding, implementation bias, measurement bias, follow-up bias, report bias, and other biases. The evaluator answered a specific question for each item; the answer "yes" indicated low risk bias, and "no" indicated high risk bias. If there was a lack of relevant details or items were not relevant to the study, it was listed as "unclear," indicating that the risk bias is unknowable. To avoid subjective bias, the journal names, publication years, and author lists were hidden before quality evaluation. The process was carried out independently by two researchers, and disagreements were discussed by both parties or decided by arbitration with a third researcher.

2.5. Statistical Analysis

The study used Review Manager Software (RevMan 5.3) for meta-analysis. The two classification variables of the main outcome indicators were Relative risk (RR) and 95% confidence intervals (95% CIs), and mean difference (MD) and 95% CI were used as indicators for continuous variables to analysis statistics. Statistical heterogeneity was analyzed by the means of chi-squared statistic and heterogeneity index (I^2). Studies with good homogeneity ($p > 0.100$) were analyzed with a fixed effect model. If there was statistical heterogeneity ($p < 0.100$), the sources of heterogeneity were analyzed first, and sensitivity or subgroup analyses were carried out if necessary. If there is no significant clinical heterogeneity among the studies, the random effect model can be used for combined analysis. If the heterogeneity is too large to determine the source, descriptive analysis was performed.

3. Results

3.1. Literature Selection

508 articles were retrieved from the databases. 18 related articles were detected by reading titles and abstracts followed by weight removal and re-selection. After reading the full text and excluding unqualified literatures, we finally included six articles [8]-[13]. 364 patients were divided into MLD group (n = 192) and control group (n = 172). **Figure 1** shows the literature screening process.

3.2. The Characteristics of Included Studies

All six articles were published from 2000 to 2018 with sample sizes ranging from

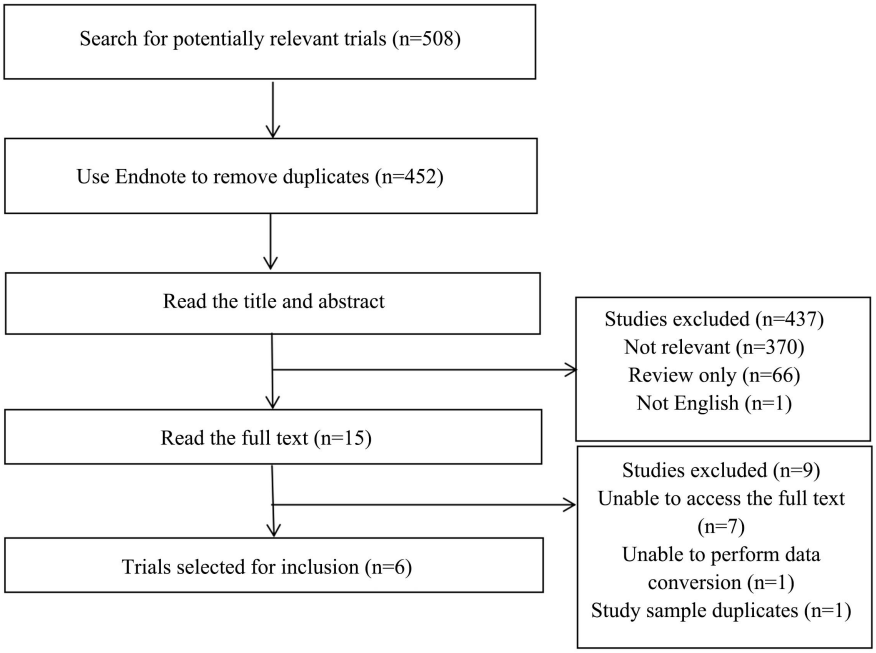

Figure 1. Flow chart describing literature extraction process.

41 to 95. All patients underwent unilateral breast cancer surgery, and patients who received MLD treatment were in BCRL stages II and III. All studies used decrease in arm volume (or circumference) as the outcome index. **Table 1** shows the basic characteristics of each study.

3.3. The Quality of Included Studies

All six articles mentioned randomization, but only two [9] [11] explicitly describe the use of computers to generate random sequences. The remaining four studies did not include the details of randomization. Two studies explicitly mentioned the concealment of distribution, and four studies implemented a single-blind design. All six studies mentioned loss during follow-up (**Table 2**).

3.4. Outcomes

Volume Reduction

Six articles of RCT reported the effect of MLD on limb swelling in patients with BCRL. The 364 patients with BCRL were divided into MLDMLD group (n = 192) and control group (n = 172). There was moderate heterogeneity among the studies ($p = 0.850$, $I^2 = 58.0\%$), so we used the random effect model. The results showed no significant difference in the reduction of arm swelling between the two groups (MD, 3.76; 95% CI, −35.09 to 42.62; Z, 0.19; $p = 0.850$) (**Figure 2**).

4. Discussion

BCRL can restrict patient activity, damage self-image, increase financial burden, and may also be associated with infection (e.g., cellulitis and lymphangitis). Although BCRL is not life threatening, it can cause great suffering among breast

Table 1. Characteristics of included studies (n = 6).

Study	Patients (C/I)	Inclusion criteria	Intervention		Treatment time	Follow-up time	Outcomes/ assessments
			Control group	Intervention group			
Williams *et al.* (2002) [13]	30/29	Lymphedema ≥ 3 months after surgery, ≥10% volume difference between arms	Simple lymphatic drainage (SLD)	MLD	12 weeks	12 weeks	Lymphedema volume; trunk swelling; dermis thickness; quality of life; symptoms/ altered sensations
McNeely *et al.* (2004) [11]	21/24	150 ml Volume difference between arms	Multi-layered compression bandaging	MLD + multi-layered compression bandaging	6 months	60 months	Lymphedema volume
Gradalski *et al.* (2015) [10]	26/25	≥20% difference between limb volumes	Bandaging + physical exercises + deep diaphragmatic breathing	Bandaging + physical exercises + deep diaphragmatic breathing + MLD	26 weeks	12 months	Lymphedema volume
Tambour *et al.* (2018) [12]	35/38	Patients after breast cancer surgery; 20 mm circumference difference between arms, ll-lll stage	CDT+ MLD	CDT without MLD	4 weeks	7 months	Volume reduction in arm lymphoedema
Andersen *et al.* (2000) [8]	21/20	4 months after surgery; 20 mm circumference or 200 ml volume difference between arms	Standard therapy	Standard therapy + MLD	2 weeks	1, 3, 6, 9, 12 months	Volume reduction in arm with lymphoedema
Dayes *et al.* (2013) [9]	39/56	≥10% Volume difference between arms	Elastic compression garments	Elastic compression garments + MLD	4 weeks	6, 12, 24, 52 weeks	Volume reduction in arm with lymphoedema; quality of life; arm function assessed

Note. MLD = manual lymphatic drainage; C = control group; I = intervention group.

Table 2. Quality assessment of included studies (n = 6).

Study	Allocation generation	Allocated concealment	Implementation bias	Measurement bias	Follow-up bias	Report bias	Other bias
Williams *et al.* (2002)	Unclear	Unclear	Unclear	Unclear	High	High	High
McNeely *et al.* (2004)	Computer-generated	High	Assessor blinded	High	High	High	High
Gradalski *et al.* (2015)	Unclear	Unclear	Assessor blinded	High	High	High	High
Tambour *et al.* (2018)	Unclear	Unclear	Assessor blinded	High	High	High	High
Andersen *et al.* (2000)	Unclear	Unclear	Unclear	High	High	High	High
Dayes *et al.* (2013)	Computer-generated	High	Assessor blinded	High	High	High	High

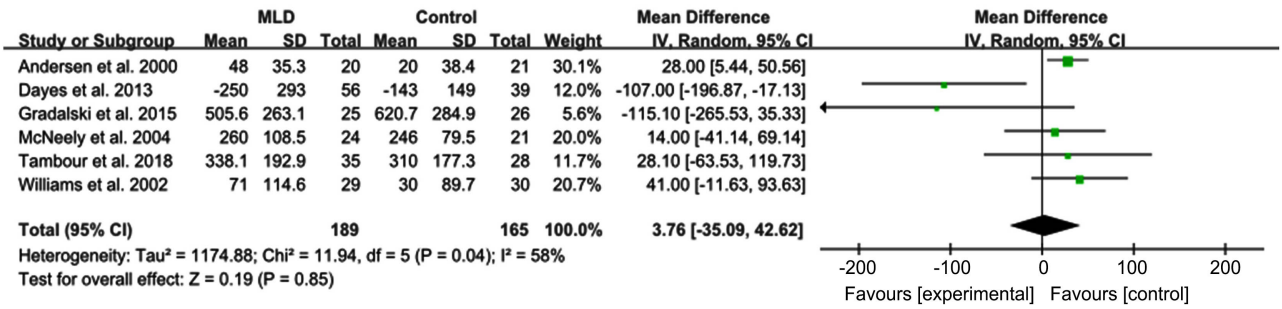

Figure 2. Volume reduction. MLD = manual lymphatic drainage.

cancer survivors, including physical and psychological effects. MLD was invented by the French physiotherapist Estrid Vodder in 1932. This mild massage technique moves through the skin in the direction of lymphatic reflux, increasing the reabsorption function of lymphatic vessels and lymph nodes and promoting venous and lymphatic reflux. The aim of MLD is to promote lymphoid formation and drive and redirect lymph stagnated by lymphatic vascular injury into a healthy lymphatic pathway [14]. Eisenhart and colleagues reported that MLD treatment for patients with ankle sprain can relieve pain in swollen limbs [15]. Breast cancer patients with BCRL also have a good acceptance of MLD, because they believe it can improve the quality of life and reduce fatigue [16]. In addition, MLD can enhance the effects of CDT, which is a recognized treatment standard for acquired lymphedema [17]. As an important part of CDT and an expensive, labor-intensive technology, the individual effect of MLD has also attracted much attention.

Lymphedema has four internationally recognized stages [18]. MLD can improve and relieve stage 0 (subclinical; lymphatic transport system is damaged without edema) and stage I lymphedema. If patients only receive MLD but not the full CDT protocol, patients with stage I will progress to stage II. The reason is that pressure therapy is an indispensable adjuvant therapy and the most basic treatment for lymphedema [14]. When breast cancer lymphedema is stage II or III, proteins in the lymphatic system can induce tissue fibrosis, resulting in the gradual decrease of lymphatic elasticity. MLD only temporarily disperses the lymph, which re-accumulates when MLD is stopped. This is also consistent with the results of this meta-analysis. Compared with routine nursing measures, MLD showed no obvious advantage in the treatment of stage II and III BCRL.

Our meta-analysis is limited by the quality of included literature. Firstly, some RCTs assessed small sample sizes. Secondly, some trials had a short intervention time and long follow-up time, which may explain why some groups reported an insignificant therapeutic effect of MLD on BCRL. One study [8] only intervened for 2 weeks and followed patients for 12 months. Two studies [9] [12] applied interventions for 4 weeks and followed patients for 7 and 13 months, respectively. In addition, some studies were not included in this meta because the original text could not be found.

5. Conclusion

The long-term effect of MLD is not significant for patients with severe BCRL. However, MLD can relieve the tissue of the body, rapidly improve the local condition, and enhance the efficacy of CDT. Therefore, we do not recommend omitting MLD as an important component of CDT. We should widely apply MLD to decrease BCRL severity. Due to the influence of the rigor and number of included studies, high-quality, multicenter RCTs are still needed.

Acknowledgments

This study was supported by Nursing Research Project of Guangdong Nursing Association (No. gdhlxueh2019zx029), Medical Scientific Research Foundation of Guangdong Province of China (No. 201611216437706, No. A2020267).

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] Torre, L.A., Islami, F., Siegel, R.L., Ward, E.M. and Jemal, A. (2017) Global Cancer in Women: Burden and Trends. *Cancer Epidemiology, Biomarkers & Prevention*, **26**, 444-457. https://doi.org/10.1158/1055-9965.EPI-16-0858

[2] DeSantis, C.E., Ma, J.M., Gaudet, M.M., Newman, L.A., Miller, K.D., Sauer, A.G., *et al.* (2019) Breast Cancer Statistics, 2019. *CA*: *A Cancer Journal for Clinicians*, **69**, 438-451. https://doi.org/10.3322/caac.21583

[3] Salonen, P., Rantanen, A., Kellokumpu-Lehtinen, P.L., Huhtala, H. and Kaunonen, M. (2014) The Quality of Life and Social Support in Significant Others of Patients with Breast Cancer—A Longitudinal Study. *European Journal of Cancer Care*, **23**, 274-283. https://doi.org/10.1111/ecc.12153

[4] Lasinski, B.B., Thrift, K.M., Squire, D., Austin, M.K., Smith, K.M., Wanchai, A., *et al.* (2012) A Systematic Review of the Evidence for Complete Decongestive Therapy in the Treatment of Lymphedema from 2004 to 2011. *PM&R*, **4**, 580-601. https://doi.org/10.1016/j.pmrj.2012.05.003

[5] Asdourian, M.S., Swaroop, M.N., Sayegh, H.E., Brunelle, C.L., Mina, A.I., Zheng, H., *et al.* (2017) Association between Precautionary Behaviors and Breast Cancer-Related Lymphedema in Patients Undergoing Bilateral Surgery. *Journal of Clinical Oncology*, **35**, 3934-3941. https://doi.org/10.1200/JCO.2017.73.7494

[6] Huang, T.W., Tseng, S.H., Lin, C.C., Bai, C.H., Chen, C.S., Hung, C.S., *et al.* (2013) Effects of Manual Lymphatic Drainage on Breast Cancer-Related Lymphedema: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. *World Journal of Surgical Oncology*, **11**, Article No. 15. https://doi.org/10.1186/1477-7819-11-15

[7] Shao, Y. and Zhong, D.S. (2017) Manual Lymphatic Drainage for Breast Cancer-Related Lymphoedema. *European Journal of Cancer Care*, **26**, e12517. https://doi.org/10.1111/ecc.12517

[8] Andersen, L., Hojris, I., Erlandsen, M. and Andersen, J. (2000) Treatment of Breast-Cancer-Related Lymphedema with or without Manual Lymphatic Drai-

nage—A Randomized Study. *Acta Oncologica*, **39**, 399-405. https://doi.org/10.1080/028418600750013186

[9] Dayes, I.S., Whelan, T.J., Julian, J.A., Parpia, S., Pritchard, K.I., D'Souza, D.P., *et al.* (2013) Randomized Trial of Decongestive Lymphatic Therapy for the Treatment of Lymphedema in Women with Breast Cancer. *Journal of Clinical Oncology*, **31**, 3758-3763. https://doi.org/10.1200/JCO.2012.45.7192

[10] Gradalski, T., Ochalek, K. and Kurpiewska, J. (2015) 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. *Journal of Pain and Symptom Management*, **50**, 750-757. https://doi.org/10.1016/j.jpainsymman.2015.06.017

[11] McNeely, M.L., Magee, D.J., Lees, A.W., Bagnall, K.M., Haykowsky, M. and Hanson, J. (2004) The Addition of Manual Lymph Drainage to Compression Therapy for Breast Cancer Related Lymphedema: A Randomized Controlled Trial. *Breast Cancer Research and Treatment*, **86**, 95-106. https://doi.org/10.1023/B:BREA.0000032978.67677.9f

[12] Tambour, M., Holt, M., Speyer, A., Christensen, R. and Gram, B. (2018) Manual Lymphatic Drainage Adds No Further Volume Reduction to Complete Decongestive Therapy on Breast Cancer-Related Lymphoedema: A Multicentre, Randomised, Single-Blind Trial. *British Journal of Cancer*, **119**, 1215-1222. https://doi.org/10.1038/s41416-018-0306-4

[13] Williams, A.F., Vadgama, A., Franks, P.J. and Mortimer, P.S. (2002) A Randomized Controlled Crossover Study of Manual Lymphatic Drainage Therapy in Women with Breast Cancer-Related Lymphoedema. *European Journal of Cancer Care*, **11**, 254-261. https://doi.org/10.1046/j.1365-2354.2002.00312.x

[14] Leduc, O., Leduc, A., Bourgeois, P. and Belgrado, J.P. (1998) The Physical Treatment of Upper Limb Edema. *Cancer*, **83**, 2835-2839. https://doi.org/10.1002/(SICI)1097-0142(19981215)83:12B+<2835::AID-CNCR36>3.0.CO;2-V

[15] Eisenhart, A.W., Gaeta, T.J. and Yens, D.P. (2003) Osteopathic Manipulative Treatment in the Emergency Department for Patients with Acute Ankle Injuries. *The Journal of the American Osteopathic Association*, **103**, 417-421.

[16] Odebiyi, D.O., Aborowa, A.T., Sokunbi, O.G., Aweto, H.A. and Ajekigbe, A.T. (2014) Effects of Exercise and Oedema Massage on Fatigue Level and Quality of Life of Female Breast Cancer Patients. *European Journal of Physiotherapy*, **16**, 238-245. https://doi.org/10.3109/21679169.2014.959048

[17] McLaughlin, S.A., DeSnyder, S.M., Klimberg, S., Alatriste, M., Boccardo, F., Smith, M.L., *et al.* (2017) Considerations for Clinicians in the Diagnosis, Prevention, and Treatment of Breast Cancer-Related Lymphedema, Recommendations from an Expert Panel: Part 2: Preventive and Therapeutic Options. *Annals of Surgical Oncology*, **24**, 2827-2835. https://doi.org/10.1245/s10434-017-5964-6

[18] Smile, T.D., Tendulkar, R., Schwarz, G., Arthur, D., Grobmyer, S., Valente, S., *et al.* (2018) A Review of Treatment for Breast Cancer-Related Lymphedema: Paradigms for Clinical Practice. *American Journal of Clinical Oncology*, **41**, 178-190. https://doi.org/10.1097/COC.0000000000000355