Effects of Manual Lymphatic Drainage Techniques on Conditions Affecting the Musculoskeletal System: A Systematic Review

David Doubblestein, PT, PhD(ABD), OCS, CLT-LANA, Cert. MDT[1]
Sandy Sublett, PT, DPT, OCS, CLT[2]
Min Huang, PT, PhD, NCS[3]

[1]OrthoMichigan Therapy Services, Flint, MI
[2]Advanced Therapy Specialists, Cedar Rapids, IA
[3]University of Michigan – Flint, Flint, MI

ABSTRACT

Background: Manual lymphatic drainage techniques (MLdT) have received interest for their efficacy in orthopedic rehabilitation and sports medicine. Strength of the body of evidence for using MLdT on conditions affecting the musculoskeletal system is not established. **Purpose:** To determine whether MLdT in addition to conventional rehabilitation interventions on conditions affecting the musculoskeletal system can, decrease edema, and improve ROM, patient-reported outcomes, and health care use. **Methods:** Studies published between 2007 and 2018, with similar outcome measurements, were grouped for analysis. Strength of the body of evidence was determined by using the Cochrane GRADE guidelines, and the American College of Chest Physicians guidelines. **Findings:** There is moderate support for the use of MLdT for conditions affecting the musculoskeletal system as effective interventions to reduce pain, and improve patient-reported outcomes pertaining to functional activities and quality of life (QOL). Manual lymphatic drainage techniques are moderately effective treatment methods associated with lower health care use, edema reduction, and improving ROM. **Conclusions:** Moderate evidence was observed supporting the efficacy of MLdT in combination with conventional rehabilitation interventions for the treatment of conditions affecting the musculoskeletal system. Future research is needed to provide stronger evidence to support the use of MLdT for patients with conditions affecting the musculoskeletal system, and to determine which interventions concurrent with MLdT produce best outcomes.

INTRODUCTION

Inflammatory responses secondary to orthopedic disorders involve the lymphatic system with clinical presentations including non-infectious lymphangitis, lymphangiospasms, and lymphadenitis.[1] Subsequently, an altered cellular environment may lead to the proliferation of hyaluronan, fibrinogen, and irregular collagen that advance fibrosis and scar tissue.[2,3] Unmanaged edema promotes less favorable states of repaired tissue that is prone to subsequent injury, or is less functional than the uninjured tissue state.[2] Therapists in orthopedic practice are routinely required to select edema management interventions, which requires sound clinical reasoning.

Many modalities have been used within the rehabilitation field to address edema and pain resulting from orthopedic disorders, including but not limited to ice, elevation, compression, electrical stimulation, ultrasound, and massage.[4-10] The effectiveness of these modalities in reducing edema remains inconclusive. Additionally, their physiologic effect on the lymphatic system have not been fully explicated.[5,6,9,11] Manual lymphatic drainage techniques can decrease edema and are 1 of the 4 components of complete decongestive therapy, which is considered the "gold standard" treatment for lymphedema.[12-14] Manual lymphatic drainage techniques are gentle and rhythmic soft tissue techniques that stimulate the lymphatic structures without promoting erythema or inflammation[1,15,16] while supporting the absorption of excess fluid, protein, and waste products. The abolishment of an inflammatory reaction and associated edema is not expected from MLdT because this requires multifaceted treatment interventions. Although preliminary studies provide evidence to the effects of MLdT,[15-17] the mechanism for these effects are still under investigation. From a physiological perspective, the gentle pressure and stretching components of MLdT stimulate the intrinsic and extrinsic lymph pumps, which increases lymph velocity via the contraction of smooth muscles within the lymph collector vessel.[18] Manual lymphatic drainage techniques have demonstrated an effect on improving the contractility of the lymphatics as visualized by indocyanine green, near-infrared fluorescence imaging.[19]

In addition to edema reduction, MLdT are recognized for decreasing pain by stimulating a general parasympathetic response for the patient, resulting in general relaxation.[17,20,21] The absorption of nociceptive chemical stimulants, such as lactic acid, cytokines, and inflammatory mediators, from the interstitial environment as a result of MLdT may have an analgesic effect.[1,22,23] The rhythmic, intermittent, and gentle pressures of MLdT stimulate the large diameter, non-nociceptive nerve fibers and decrease pain.[24]

Manual lymphatic drainage techniques have received interest in orthopedic rehabilitation and sports medicine.[25,26] A 2009 systematic review concluded that manual lymphatic drainage techniques were effective when combined with conventional musculoskeletal therapies, in sports medicine and rehabilitation. The authors concluded that MLdT are particularly useful in reducing edema and enzyme serum levels associated with acute skeletal muscle cell damage.[26] Another review also confirmed the effectiveness of MLdT for patients with musculoskeletal edema in orthopedic injuries.[25] Although these previous reviews have provided some evidence of the benefits of MLdT pertaining to reducing musculoskeletal edema from acute orthopedic and sports-related injuries; the body of evidence on the effects of MLdT on range of motion (ROM), patient-reported outcomes pertaining to pain, functional activities and quality of life (QOL), and health care use have yet to be explored.

OBJECTIVES

The primary objective of this systematic review was to examine if the addition of MLdT to conventional rehabilitation interventions in people with conditions affecting the musculoskeletal system were effective in decreasing edema, and improving ROM and patient-reported outcomes. A secondary objective was to examine outcomes specifically related to edema, pain, ROM, functional outcomes, QOL, and health care use between interventions with and without MLdT.

SEARCH STRATEGY

This systematic review used the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) format.[27] An extensive literature probe was conducted from 09/07/17 through 04/07/18 using the following electronic databases: PEDro (via University of Sydney), CINAHL (via EBSCO), PubMed (via U.S. National Library of Medicine), Cochrane Library (via Wiley Online Library), Scopus (via Elsevier), Physical Therapy & Sports Medicine Collection (via GALE CENGAGE Learning), and Google Scholar. Key search terms included *lymph, lymphatic, mobilization, drainage, manual, orthopedic, musculoskeletal, edema, oedema, knee, foot, ankle, hip, back, neck, shoulder, elbow, wrist, and hand*. Filters included *[NOT] lymphedema, [NOT] cancer, human subjects, clinical trials, case reports, retracted publications, and controlled trials*. Examples of key word combinations are outlined in Appendix 1.

ELIGIBILITY CRITERIA

Screening of titles and abstracts were conducted by the principal investigator and co-investigator, using study selection-criterions, designed by the authors for guidance. Occasions in which there were discrepancies, a third reviewer also completed the screening for inclusion. Criteria for initial inclusion included those articles written in English, with a publication date range of 01/01/2007 through 05/15/2018. Due to a dearth of peer-reviewed journal articles on MLdT and conditions affecting the musculoskeletal system, the primary search included randomized trials, non-randomized controlled cohort studies, case-series, and case-control studies. The population of interest were human subjects aged 5 years or older with a confirmed condition affecting the neuromusculoskeletal system, not limited to a specific body region. The working definition for conditions affecting the musculoskeletal system was a result of searching for inclusionary terms under this broad heading.[28-31] Inclusionary terms for conditions affecting the musculoskeletal system are listed in Appendix 1. These broadly-based definitions, enabled searching for relevant literature to expand multiple methods of MLdT, as well as, multiple conditions that are commonly seen within orthopedic rehabilitation practices.

The intervention inclusion criteria included, manual interventions from frequently reported MLdT, including Vodder technique, manual lymph drainage, Chikly technique, lymph drainage therapy, Artzberger technique, manual edema mobilization (MEM), or Leduc technique.[32-36] Techniques that stimulated the lymphatics from a light touch, rhythmic, skin tractioning method, not directly associated with a specific tenet, were also included in the study selection. MLdT may have been used as a stand-alone treatment or concomitant with other modalities, other than those in the exclusion criteria.

Studies that were anecdotal, descriptive, expert opinions, or qualitative designs were excluded. Conditions, such as cancer, lymphedema, lympho-lipedema, and chronic venous insufficiency were excluded.

DATA EXTRACTION

Data extraction from the included studies was conducted independently by the principal investigator and the co-investigator, using a template adapted from the Cochrane Handbook for Systematic Reviews of Intervention – A.6.1 characteristics of included studies for systematic reviews.[37] Discrepancies were resolved with a third reviewer. The characteristics of interest included the authors, level of evidence, validity scale, participants, conditions affecting the musculoskeletal system, aims of the study, intervention group, control group, outcomes, key findings, and conclusions. The information on other conventional interventions were added to the characteristics template. The level of evidence was determined using the 2011 Oxford Centre for Evidence-based Medicine (OCEBM).[38] The PEDro scale, was used to determine the internal validity of the randomized controlled trial (RCT) studies.[39-41] The PEDro scale operational criteria are outlined in Appendix 2. The PEDro scores for each study were given individually by the authors, and discrepancies resolved by a third author. Upon scores finalization, studies were given a descriptive terminology quality rating, ranging from poor to excellent as previously developed by Foley et al.[42] The studies were grouped, based on similar outcomes data, for the synthesis of the body of evidence. The strength and quality of the body of evidence was determined by using the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) guidelines.[43-46] Using GRADE methodology levels of evidence (Appendix 3), outcomes from the studies were assessed based on their limitations, heterogeneity, directness, and publication bias. Using operational definitions and guidelines from the American College of Chest Physicians (ACCP)[46,47] the level of evidence was further evaluated. (Appendix 4).

RESULTS

The initial literature search resulted in retrieving 112 published articles. Duplicates were removed. Screening of the remaining 97 articles based on the title and abstract, resulted in the removal of 82 articles. A total of 15 articles met the inclusion criteria and were included for a full text review. A total of 5 articles[24,48-51] met eligibility criteria, and were included in the analyses (Figure 1). The kappa value for interrater agreement for manuscript selection was considered substantial[52] at 0.77.

Various tenets of MLdT were described in the literature, as well as various outcomes and their measures. All studies included in the analyses had RCT research design. Inadequate blinding of subjects, and of intervention therapists were noted in all the studies, as well as a lack of intention-to-treat analysis. Four out of 5 studies had a “good” rating of methodological quality (internal validity) according to the PEDro scale (Table 1), and categorical ratings.[42] The kappa value of 0.70 for interrater agreement for PEDro scores was considered substantial.[52] A low scoring RCT study[50] was included, as it offered information pertaining to the auxiliary intervention of compression.

Three of the included studies focused on the effects of MLdT in acute orthopedic disorders, specifically postoperative knee arthroplasty and transtibial amputation.[48,50,51] The study by Knygsand-Roenhoej and Maribo focused on subacute edema resulting from distal radius fracture.[49] The remaining study focused on the effect of MLdT in a chronic condition.[24] Homogeneous outcomes of the studies included edema, ROM, patient-reported outcomes on pain, function, and QOL, and health care use. A summary of the key findings is presented in Table 2, and a summary of qualitative assessments is shown in Table 3.

BENEFITS OF MLDT ON EDEMA

Various edema measurement methods were employed in the studies, including volumeter, bioimpedance, and circumferential measurements. Minimal clinically important difference (MCID) of edema measurements in breast cancer related lymphedema patients have been analyzed. In this population, MCID values for circumferential measurement range from 0.37 to 0.71 centimeter, and percent volume change range from 1.5%

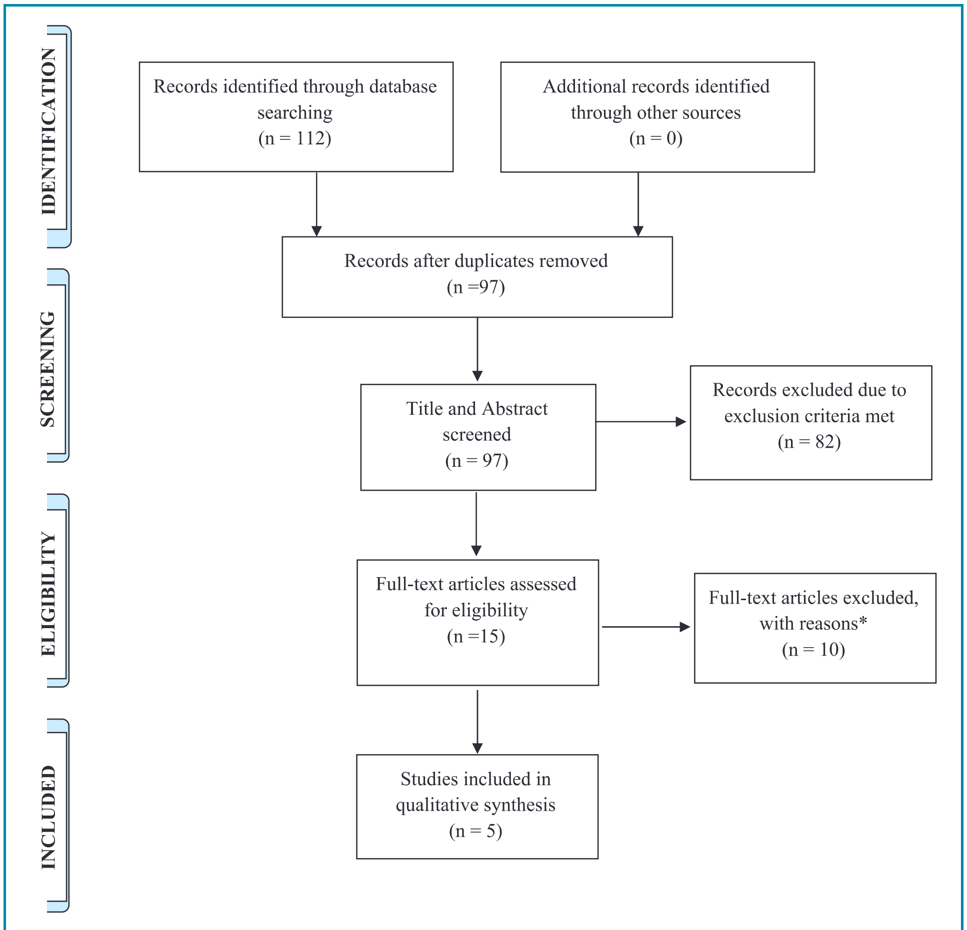

Figure 1. PRISMA flow diagram. *One study was a protocol with embedded MLdT text. One study was dismissed due to its case series design. Three studies focused on the physiological effects of MLdT not related to an orthopedic disorder. One study had English abstract but foreign manuscript. Two studies did not align with conditions affecting the mysculoskeletal system definition.

to 3.5%.[53] The MCID values have not been established for edema in conditions affecting the musculoskeletal system. Pichonnaz et al,[51] and Ebert et al,[48] reported a lack of significant changes in edema following MLdT. An increase in edema from the second to the seventh day during the MLdT treatment period has been reported.[51] Edema increased by 1.9% in the group receiving 30 minutes of MLdT in addition to conventional treatment, compared to 4.1% in the control group receiving 30 minutes of relaxation training in addition to conventional treatment.[51] Topuz et al found statistically significant reduction ($p < 0.05$) in circumferential measurements in patients who received complete decongestive physiotherapy (CDP).[50] In their study, multilayer short-stretch compression therapy was used in addition to MLdT.[50] In comparison with traditional edema management techniques (TEM) (ie, elevation, compression, and functional training), non-statistically significant reduction in edema following 3 ($p = 0.31$) and 6 weeks ($p = 0.31$) of MLdT was reported.[49] However, edema reduction was achieved with significantly fewer edema treatment sessions ($p = 0.03$) with MLdT (14.1 sessions) compared to TEM techniques (19.2 sessions).[49] In summary, studies providing MLdT alone or adding MLdT to a conventional treatment protocol have demonstrated effectiveness in reducing edema.

BENEFITS OF MLDT ON RANGE OF MOTION

Both MLdT and TEM improved active ROM ($p < 0.01$) for thumb opposition and fingertip to palm distance, but the difference between groups was not significant at 6 weeks ($p = 0.32$) and 9 weeks ($p = 0.23$) follow-up.[49] Studies of patients with TKA have demonstrated improvements in ROM following MLdT.[48,51] In the study by Ebert et al,[48] a significant increase in knee flexion active ROM was observed in the group receiving MLdT ($p = 0.031$) compared to controls who did not receive MLdT. Similarly, Pichonnaz et al found that knee flexion contracture was more than 2° less prevalent in the MLdT group compared to the control group at 3 months post TKA, although the difference between groups did not reach statistical significance ($p = 0.07$).[51] In summary, 3 out of 7 included studies measured ROM and all reported significant improvements in ROM with adding MLdT to the treatment.

BENEFITS OF MLDT ON PATIENT-REPORTED OUTCOMES

Pain

In the studies included for the review, pain was measured using a standard Visual Analog Scale (VAS), or a numeric pain scale.

Table 1. Characteristics of the 7 Included Studies

Author	Level of Evidence (OCEBM)	Experimental Design	Internal Validity Scale (PEDro)	Rating*
Knygsand-Roenhoej K, et al. (2011)	2	RCT	6/10	Good
Pichonnaz C, et al. (2011)	2	RCT	7/10	Good
Ebert D, et al. (2013)	2	RCT	7/10	Good
Ekici G, et al. (2009)	2	RCT	7/10	Good
Topuz S, et al. (2012)	2	RCT	4/10	Fair

Abbreviations: OCEBM, Oxford Centre of Evidence Based Medicine; RCT, Randomized Clinical Trial; PEDro, Physiotherapy Evidence Database
**Excellent = 9-10, Good = 6-8, Fair = 4-5, Poor = below 4*[40]

Table 2. Summary of Key Findings

Author	Participants	Intervention	Conventional Interventions
Knygsand-Roenhoej et al (2011)	29 patients, 72% Females with average age 64, 5-8 weeks after unilateral distal radius fracture, treated with plaster cast, internal or external fixation, and with a diagnosis of subacute edema.	n = 14; 3x/wk for 4 weeks and then 2x/wk for 2 weeks consisting of Modified MEM, HEP, low stretch bandage if needed, Isotoner glove daily.	Therapy for ROM and strengthening, HEP.
Pichonnaz et al (2016)	56 patients diagnosed status post TKA, 65% women with a mean age of 71.	n = 29; 5 thirty minutes sessions of MLD (Strossenreuther method) per working day from 2nd day to 7th day post operatively.	Postoperative hospital-based rehabilitation protocol = ROM, strengthening, CPM, gait training, and cryotherapy.
Ebert et al (2013)	43 patients/53 knees (72% males) with a mean age of 70 years, diagnosed status post TKA.	n = 24, 30 minutes of MLD and remedial postoperative orthopedic massage techniques, on postoperative days 2, 3, and 4.	Postoperative hospital-based rehabilitation protocol = ROM, strengthening, CPM, gait training, and cryotherapy.
Ekici et al (2009)	53 women with a mean age of 38 years, diagnosed with fibromyalgia.	n = 26 females; 5x/wk for 3 weeks consisting of 45 minutes of MLD therapy.	None
Topuz et al (2012)	11 patients, mean age 67 years, diagnosed postoperative transtibial amputee.	n = 5; Received CDP and diaphragmatic breathing.	Stretching, dynamic stump exercises, isometrics, and isotonics. The CDP was instructed to conduct diaphragmatic breathing.
Author	**Outcomes**	**Key Findings**	**Conclusions**
Knygsand-Roenhoej, et al (2011)	Measured at 1st, 3rd, 6th, 9th, and 26th week post inclusion. Edema, active ROM, pain, and ADL, number of treatment sessions.	n = 14; 3x/wk for 4 weeks and In the modified MEM group, improvement was observed in ADL after the 3 weeks measurement ($p = 0.03$). Fewer edema treatment sessions were needed ($p = 0.03$) in the modified MEM group.	Neither modified MEM treatment nor traditional edema treatment were superior to each other. Modified MEM resulted in fewer required sessions to decrease subacute edema compared to traditional methods.
Pichonnaz, et al (2016)	Measured at enrollment, 2nd day, 7th day, and 3 months postoperative TKA. Truncated Cone Volumetric measures via tape, bioimpedance, VAS, Knee Society Score, Osteoarthritis Index, Gait analysis, active and passive knee ROM.	Passive knee flexion contracture at the 3 months measurement was statistically significant for being lower and less frequent in the MLD group compared to the control group. Pain level decrease on the VAS immediately after the MLD treatment was statistically significant for 80% of the MLD sessions.	MLD applied in the short-term after TKA did not reduce swelling. MLD reduced pain after the treatment session and reduced the extent of knee flexion contracture and its frequency 3 months post operatively.
Ebert et al (2013)	Measured at enrollment, days 2, 3, 4 and 6 weeks post operatively. Active and passive knee ROM, Truncated Cone Volumetric measures via tape, VAS, and Knee Injury and Osteoarthritis Outcome Score.	Increased active knee flexion at day 4 post-surgery ($p = 0.014$, 95% CI, effect size =0.79,1.68-16.67) and at 6 weeks postoperatively ($p = 0.012$, 95% CI, effect size =0.87,2.32-16.78).	MLD applied in the short term after TKA improves active knee flexion up to 6 weeks postoperatively.
Ekici et al (2009)	Measured at baseline and at end of treatment (3 weeks). VAS, pain pressure threshold algometry, HRQoL, FIQ.	Improvements regarding pain intensity, pain pressure threshold, and HRQoL ($p < 0.05$). The MLD group improvements with the FIQ total score ($p = 0.010$). Subsets of the FIQ (morning tiredness FIQ-7 and anxiety FIQ-9) particularly demonstrated improvements ($p = 0.006$)	MLD Therapy was found to be more effective than Connective Tissue Massage according to subsets of the FIQ (morning tiredness and anxiety) and total FIQ scores.
Topuz et al (2012)	Circumferential measurements at 5 locations of the involved lower extremity, Days of hospital stay, and days to transition into permanent prosthesis.	The transition into permanent prosthesis was shorter in the CDP group ($p < 0.05$). Circumferential measurements were more obvious in the CDP group ($p < 0.05$).	CDP is effective in reducing post amputation stump edema in geriatric amputees. The reduction of edema was more obvious in the CDP group. CDP is effective in shortening the transitional period into permanent prostheses.

Abbreviations: CDP, complete decongestive physiotherapy; CPM, continuous passive motion; FIQ, Fibromyalgia Impact Questionnaire; HRQoL, health related quality of life; HEP, home exercise program; MEM, manual edema mobilization; MLD, manual lymph drainage; QOL, quality of life; ROM, range of motion; TKA, total knee arthroplasty; VAS, Visual Analog Scale

Table 3. Summary of Qualitative Assessments ◊

Outcomes	Subgroups	Author(s)	No. of Subjects	Risk of Bias
Edema	Circumferential measurements, Bioimpedance, Volumeter, Truncated Cone Volume	Ebert et al 2013; Knygsand-Roenhoej and Maribo 2011; Pichonnaz et al 2016	128	(-0)♦
Pain	Frequency, Visual Analog Scale, Numeric Scale	Ebert et al 2013; Ekici et al 2009; Knygsand-Roenhoej and Maribo 2011; Pichonnaz et al 2016	181	(-0)♦
Range of Motion	Active and/or Passive	Ebert et al 2013; Knygsand-Roenhoej and Maribo 2011; Pichonnaz et al 2016	128	(-0)♦
Quality of Life and Other Self-Reported Outcomes	Functional and Quality of Life Scales	Ebert et al 2013; Ekici et al 2009; Knygsand-Roenhoej and Maribo 2011; Pichonnaz et al 2016	181	(-0)♦
Healthcare Utilization	Decreased supplies, treatment time, or sessions	Topuz et al. 2012; Knygsand-Roenhoej and Maribo 2011	40	(-1)≡

◊ Due to limited number of events, small sample size, and studies with non-normal distribution, effect sizes were not pooled.
♦ No serious risk of bias. PEDro internal validity scale ranged 6-8, and a "good"[40] rating.
≡ Topuz et al used different compression strategies between groups, which may have influenced a type 1 error. PEDro internal validity scale is a 4/10.

Outcomes	Inconsistency	Indirectness	Publication Bias	Imprecision
Edema	(-1)♦♦	(- 0)♦♦♦	(- 0)♦♦♦♦	(- 0) ⊄
Pain	(-1)♦♦	(- 0)♦♦♦	(- 0)♦♦♦♦	(- 0)
Range of Motion	(-1)♦♦	(- 0)♦♦♦	(- 0)♦♦♦♦	(- 0)
QOL and Other Self-Reported Outcomes	(-1)♦♦	(- 0)♦♦♦	(- 0)♦♦♦♦	(- 0)
Healthcare Utilization	(-1)♦♦	(- 0)♦♦♦	(- 0)♦♦♦♦	(- 0) ⊄

◊ Due to studies with small sample sizes and studies with non-normal distribution, effect sizes were not pooled.
♦♦ Due to heterogeneity of studies and small populations resulted in inconsistent effect sizes.
♦♦♦ Conclusions of the studies directly applied to the PICO.
♦♦♦♦ Not observed and unlikely. No conflicts of interest reported.
⊄ Topuz, et al. (2012) had small number of events and moderate confidence intervals, but did not distract from the overall summary for imprecision.

Outcomes	Dose-Response Association	Residual Confounders	Large Effect	Quality of Evidence*	Quality of Evidence**
Edema	(+ 0)	(+ 0)	(+ 0) ≈	✪✪✪❍ Moderate	Moderate
Pain	(+ 0)	(+ 0)	(+ 0)	✪✪✪❍ Moderate	Moderate
Range of Motion	(+ 0)	(+ 0)	(+ 0)	✪✪✪❍ Moderate	Moderate
QOL and Other Self-Reported Outcomes	(+ 0)	(+ 0)	(+ 1) ⊕	✪✪✪✪ High	Moderate
Healthcare Utilization	(+ 0)	(+ 0)	(+ 0) ≈	✪✪❍❍ Low	Moderate

◊ Due to studies with small sample sizes and studies with non-normal distribution, effect sizes were not pooled.
≈ Topuz et al (2012) had large and/or very large effect sizes for outcomes.
⊕ Ekici et al (2009) contributed a large effect size.
*As analyzed using GRADE[41-44]; **As analyzed using American College of Chest Physicians[44-45]

Pain scales have been analyzed for MCID with various patient populations and disorders, and therefore should be considered context-specific, and interpreted appropriately to avoid any misguidance.[54] The MCID improvements in pain, represented on a 10 cm (100 mm) visual analog scale have also been noted to range widely from 8 mm to 40 mm.54 Diagnosis may also influence the MCID; noted when comparing TKA pain levels measuring a 22.6 mm MCID;[55] whereas, in systemic sclerosis MCID was represented by 32.02 mm.[56] In this review, comparing the effect on pain levels post-distal radius fracture, during rest and activity, both MLT and TEM techniques decreased pain levels, but showed no statistically significant overall mean differences between groups (rest = 0.40, p = 0.30; activity = 0.22, p = 0.42).[49] Similarly studies in patients post-TKA did not find differences between MLdT and TEM.[48,51] Pichonnaz et al[51] noted a significant decrease in pain immediately after the application of 4 out of 5 MLdT treatment sessions, but it was not statistically significant between groups 3 months postoperative at rest (9.0 mm, p = 0.52) and during gait activities (16.7 mm, p = 0.06), and the reduction in pain did not meet or exceed the MCID for pain levels.[55] Ekici et al[24] noted significant and progressive decreases in fibromyalgia pain levels with both MLdT and massage groups, but no significant difference in pain levels between groups at the end of 5 weeks of treatment was found (p = 0.06). The improvements in pain remained stable from the first treatment till the end of the study. In summary, 4 out of 5 studies measured pain levels and all reported effectiveness in reducing pain with providing MLdT alone or adding MLdT to a conventional treatment, however, not all improvements were statistically significant in comparison to controls.

Other Self-Reported Outcomes

Various self-reported outcome measurement tools on functional activities and QOL were used across the studies. Using an investigator designed questionnaire, Knygsand-Roenhoej and Maribo[49] found statistically significant improvements in activities of daily living that were seen after 3 weeks of MEM (p = 0.03) compared to TEM techniques, but the improvements plateaued at the sixth and ninth weeks follow-up. Tying shoelaces, eating with a knife and fork, peeling potatoes, and cutting a slice of bread were among the activities included in the questionnaire.[49] The study of patients post-TKA by Ebert et al[48] reported improvements in QOL as measured by the Knee Injury and Osteoarthritis Outcome Score questionnaire, with significant time effect (p < 0.001), but without significant group or interaction effects. In comparison, another study of patients post-KA observed that MLdT had no significant effect on self-reported knee function as measured by Knee Society Score questionnaire (p = 0.90), and the Western Ontario and McMaster Universities Osteoarthritis Index (p = 0.50).[51] Patients with fibromyalgia treated with MLdT demonstrated significant improvements in the total score of Fibromyalgia Impact Questionnaire (p = 0.01), and scores in areas of feeling more rested in the morning (p = 0.006), and less anxiety (p = 0.060), compared to those treated with connective tissue massage.[24] In summary, 4 out of 5 included studies reported on self-reported outcomes, in which 2 reported effectiveness in improving either functional activities or QOL, when providing MLdT alone or adding MLT to a conventional treatment. Not all improvements were statistically significant in comparison to controls.

Benefits of MLdT on Health Care Use

Two studies addressed the efficacy of MLdT from a framework of health care use. Health care use can be associated with appropriate or inappropriate treatment, frequent or infrequent visits, and of high or low cost. In comparison with TEM, significantly fewer sessions for edema treatment were required with MEM (p = 0.03), in order to decrease subacute arm/hand edema.[49] In geriatric patients post transtibial amputation, the application of complete decongestive therapy, consisting of MLdT and reusable, multilayer short-stretch compression bandages, resulted in a significantly shorter transition period to a permanent prostheses (p < 0.05); compared to single use, multi-application compression bandages.[50] In summary, a decrease in medication costs for migraine patients, a decrease in total number of visits for individuals with hand/arm edema, and a decrease in the cost of supplies for individuals using permanent prostheses have been reported. Therefore, MLdT may lower health care use in selected patient conditions.

DISCUSSION

Summary of Evidence

Moderate evidence supports the use of MLdT for decreasing edema in acute, subacute, and chronic healing phases of conditions affecting the musculoskeletal system. While studies pertaining to acute edema evidenced a lack of volume reduction with MLdT, one study[51] reported less increase in edema compared to the control group. Reduction in girth[50] suggested that acute edema may benefit from MLdT, when the addition of auxiliary multilayer short-stretch compression bandaging and exercises is incorporated. Compression was one key treatment that appeared to influence the outcomes of one study;[49] all subjects in the control group used compression by means of Coban® and Isotoner® gloves, whereas, the MEM intervention group used a "low-stretch bandage system if needed."[49]

Moderate evidence suggests the use of MLdT for improving ROM after TKA. This evidence seems to be antithetical with the lack of significant edema reduction noted in two studies.[48,51] One author[51] suggested that their improved ROM observations may be attributed to the slight decrease in edema, mechanical effects of MLdT during popliteal maneuvers, prevention of fibrosis through protein reabsorption, or simply through relaxation.

Moderate evidence promotes the use of MLdT for decreasing pain and improving outcomes pertaining to functional activities and QOL. While MLdT do not present with superiority in decreasing pain levels compared to other forms of manual therapy techniques, there seems to be preliminary evidence that these techniques may afford a quicker and more stable analgesic effect.[51] Similar to the effects on pain level outcomes, MLdT are not superior in improving self-reported functional or QOL outcomes compared to other treatment measures.

Moderate evidence supports the use of MLdT for improving health care use. Patient advocacy requires rehabilitation therapists to be responsible with the delivery of evidence-based practice. In these preliminary studies, MLdT promoted the use of less medication and supplies, and fewer treatment sessions.[49,50]

Limitations and Strengths

While the available body of literature pertaining to orthopedics and MLdT continues to build, there are limited high quality evidence studies encompassing the broad spectrum of conditions affecting the musculoskeletal system, which poses the inevitable random error of significant heterogeneity of included studies. The diversity of study populations, outcome measures, and study designs may lead the intended audience to question the applicability of the summary of the evidence provided. In addition, the low number of participants included in the studies render results that are not necessarily generalizable. However, the notable heterogeneity embodies the orthopedic practice of rehabilitation specialists, which establishes this systematic review true and applicable to orthopedic practice diversity. Another limitation that arises from a dearth of literature, is the uncertainty of gathering all related studies. Finally, there may have been studies with non-significant or inconclusive data, which have not been published, that would have influenced the overall results.

CONCLUSIONS

There was moderate support for using MLdT for conditions affecting the musculoskeletal system as effective interventions to reduce pain, and improve function and/or QOL. This review also affirms that MLdT are effective treatment methods associated with lower health care use. Pertaining to ROM improvement and edema reduction, the results of this study suggest that MLdT with auxiliary therapies may be effective, and certainly not ineffective or harmful. However, due to moderate methodological quality of the included studies, the evidence-based practice of MLdT should only proceed with clinical expertise and the patient values in perspective. While the studies represented in this review demonstrated heterogeneity, their differences are an appropriate generalizable outcome for orthopedic therapy practices. Since the first similar systematic review by Vairo et al[26] there has been an increase number of randomized clinical trials pertaining to MLdT. However, the need for further RCTs and cohort studies are warranted, to understand the attributes, benefits, and limitations of MLdT. Standardized measurements are imperative to these future studies, and researchers are advised to consider homogenous methodology with previous studies. In addition, research on MCID for edema pertaining to conditions affecting the musculoskeletal system would make significant clinical and comparative lymphedema research contributions. Future research is needed to provide stronger evidence to support the use of MLdT for patients with conditions affecting the musculoskeletal system, and provide evidence as to which auxiliary interventions concurrent with MLdT produce best outcomes.

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Appendix 1. Inclusionary Terms and Examples of Key Word Combinations

Inclusionary Terms

Conditions affecting the musculoskeletal system may consist of many conditions including, but not limited to, fractures, tendinitis, tendinosis, bursitis, sprains, strains, tears, degenerative conditions, post orthopedic surgical conditions, arthritis, bursitis, elbow pain and conditions, fibromyalgia, foot pain and conditions, fractures, hip pain and conditions, low back pain and conditions, hand pain and conditions, knee pain and conditions, neck pain and conditions, osteoporosis, shoulder pain and conditions, and soft tissue injuries.[28-31]

Key Search Terms and Strategy

System	Disorder	Treatment	Localization
Lymph	Edema	Lymph Drainage	Knee
Lymphatic	Oedema	Manual Lymph Drainage	Foot
Orthopedic		Manual Edema Mobilization	Ankle
Musculoskeletal			Hip
			Back
			Neck
			Shoulder
			Elbow
			Wrist
			Hand

PubMed Search Strategy Examples:
1. lymphatic AND drainage AND hand NOT lymphedema
2. lymphatic AND drainage AND knee NOT lymphedema
3. manual lymph drainage AND ankle NOT lymphedema
4. manual lymph drainage NOT lymphedema NOT cancer
5. lymphatic drainage AND orthopedic NOT cancer NOT lymphedema

Google Scholar Search Strategy Examples:
1. "manual lymph drainage" knee edema -lymphedema
2. "manual edema mobilization" hand edema -lymphedema
3. "manual lymph drainage" -cancer -lymphedema
4. "lymph drainage" "orthopedic" -cancer -lymphedema

Appendix 2. Operational Criteria of the PEDro Scale

1. Eligibility criteria were specified;
2. Random allocation of subjects into groups (in a crossover study, subjects were randomly allocated an order in which treatments were received);
3. Allocation was concealed;
4. Groups were similar at baseline regarding the most important prognostic indicators;
5. There was blinding of all subjects;
6. There was blinding of all therapists who administered the therapy;
7. There was blinding of all assessors who measured at least one key outcome;
8. Measures of at least one key outcome were obtained from > 85% of the subjects initial allocated to groups;
9. All subjects for whom outcome measures were available received the treatment or control condition as allocated or if not the case, then data for at least one key outcome was analyzed by "intention to treat"
10. The between-group statistical comparisons are reported for at least one key outcome; and
11. The study provides both point measures and measures of variability for at least one key outcome.

Appendix 3. Operational Definitions of GRADE's Four Levels of Evidence

1. High Level of Quality (✪✪✪✪): Authors are very confident that the true effect lied close to that of the estimate of the effect.

2. Moderate Level of Quality (✪✪✪❍): Authors are moderately confident in the effect: The true effect is likely to be close to the estimate of the effect but there is a possibility that it is substantially different.

3. Low Level of Quality (✪✪❍❍): Authors confidence in the effect estimate is limited. The true effect may be substantially different from the estimate of the effect.

4. Very Low Level of Quality (✪❍❍❍): Authors have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of the effect.

Five categories which may downgrade the quality of evidence:
1. Risk of Bias: -1 if serious, -2 if very serious
2. Inconsistency: -1 if serious, -2 if very serious
3. Indirectness: -1 if serious, -2 if very serious
4. Imprecision: -1 if serious, -2 if very serious
5. Publication Bias: -1 if likely, -2 if very likely

Three categories which may upgrade the quality of evidence:
1. Large Effect: +1 if large, +2 if very large
2. Dose Response: +1 if evidence of a gradient
3. All plausible residual confounding: +1 would reduce a demonstrated effect, or would suggest spurious effect if no effect was observed

Appendix 4. Operational Definitions of ACCP

1. High Level of Quality: Reports from RCTs without significant limitations or overriding evidence from observational studies.

2. Moderate Level of Quality: Reports from RCTs with consequential limitations (inconsistent results, methodological flows, indirect, or imprecise) or from observational studies with exceptionally strong evidence.

3. Low Level of Quality: Reports from observational studies or case series.

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