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REVIEW

Manipulative Treatment of Myofascial Pain Syndrome: A Network Meta-Analysis Based on Randomized Controlled Trials

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Objective: Myofascial pain syndrome (MPS) is a common condition. Manual therapy is preferred over other invasive treatments due to its noninvasiveness and safety, but evidence for its effectiveness is lacking. We here conducted a comprehensive search of randomized controlled trial studies related to manipulative therapy for MPS and conducted a network meta-analysis to provide a basis for clinical applications and experimental studies.

Methods: Reports on randomized controlled trials of noninvasive therapy for MPS deposited in the China National Knowledge Infrastructure database, Chinese Science Citation Database(CSCD), Chinese Citation Database(CCD), Chinese Biomedical Database, PubMed, Embase, Cochrane Library, and Web of Science from their respective inception dates until November 10, 2024, were retrieved. A network meta-analysis was performed using Rv4.2.0 software.

Results: Fourteen studies involving 588 patients overall were included. The interventions included pain point compression, massage, and ischemic compression. Visual analogue scale scores were reported in 12 studies and the pressure pain threshold was reported in five studies. The outcomes demonstrated that manipulation had a notable effect, although not statistically significant, as compared with conventional treatment and placebo. Overall, the effect of pain-point compression was favorable. The results were stable, with no significant publication bias.

Conclusion: Manipulation was an effective treatment for MPS, but the effects were not statistically significant, based on the findings of this study. Owing to issues such as uneven methodological quality and the small sample size of the included studies, further high-quality multicenter, large-sample, randomized double-blind controlled trials are required to verify the reliability of this conclusion.

Keywords: comparative effectiveness research, musculoskeletal manipulations, myofascial pain syndromes, network meta-analysis, systematic review

Myofascial pain syndrome (MPS) is a common disorder affecting the shoulder, neck, and lumbar regions.[1] It is an acute/chronic non-specific neuromuscular dysfunction that mainly manifests as muscle pain, muscle loss, and decreased muscle activity, among other symptoms.[2] The lifetime prevalence rate of MPS in the general population is as high as 85%.[3] MPS accounts for approximately 30–85% of skeletal muscle disorder cases. Modern lifestyle characteristics, such as increased working hours, reduced exercise, abnormal posture, and prolonged sitting, are considered high-risk factors for MPS.[4] MPS has also become a significant barrier restricting work attendance and quality of life, imposing a considerable economic burden on patients and their families.

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At present, the main treatment modalities for MPS include manual acupuncture and drug injection therapies, which have favorable effects. Nevertheless, some patients are reluctant to undergo these treatments, and the treatments also have certain risks. If not performed carefully, infections, needle-related fainting, visceral injuries, broken needles, and other adverse consequences may occur.[5]

Owing to the noninvasive nature and safety of manual therapy, it may be preferred over other invasive treatment approaches. Manipulative therapies, such as point compression, massage, and other therapeutic techniques, are simple and effective treatments that can be performed by therapists and are widely used in physical therapy for MPS. However, clinical research evidence regarding the manipulative treatment of MPS has been insufficient to date. The quality of evidence in some such studies has not been high, and few systematic reviews on the application of manual treatment of MPS are available.

Therefore, to explore the clinical evidence for the manipulative treatment of MPS further, we sought to synthesize the available data from evidence-based medicine. We conducted a comprehensive literature search for randomized controlled trials related to the manipulative treatment of MPS and performed a network meta-analysis to provide a reference basis for clinical applications and experimental studies related to manipulative treatment.

Methods

Study Registration
This study has been registered with PROSPERO: https://www.crd.york.ac.uk/PROSPERO/view/CRD42024616488

Eligibility Criteria
Studies were included based on the PICOS principles. In terms of population, we included studies on patients with MPS, without restriction on sex, age, race, and nationality. As interventions, we included studies that used manipulative treatment, including massage, chiropractic care, osteopathic manipulation, mobilization, myofascial release, tuina, shiatsu, and point compression. For comparison, the included studies used conventional treatments, including the spray-and-stretch technique, thermomagnetic therapy, heat therapy, ultrasound therapy, and placebo. As outcomes, we used the visual analogue scale (VAS) score for pain.[6] The VAS scale is commonly used for pain assessment. It indicates pain through a 10-cm straight line, where 0 represents "no pain at all" and 10 represents "extreme pain." The patients were asked to mark on the line how much pain they felt before and after treatment with a higher score indicating more intense pain. Not only does it work for a variety of pain types and patient groups, but it also has a high level of accuracy, allowing it to reflect the experience of patients more accurately. The pressure-pain threshold (PPT) was also used as an outcome.[7] The higher the pain threshold, the lower is the patient's sensitivity to painful stimuli. In terms of study design, we limited the included studies to randomized controlled trials.

Exclusion Criteria
We excluded studies for which the required outcome indicators were not included in the literature or where the data on the outcome indicators were incomplete, or if serious defects were present in the research trial design. We also excluded animal experiments, reviews, case reports, conference papers, and control groups that received active recovery or other treatments that affected the recovery process.

Data Sources and Search Strategy
Reports on randomized controlled trials of tuina therapy for DOMS that were deposited in the China National Knowledge Infrastructure database, Chinese Science Citation Database, Chinese Citation Database(CCD), Chinese Biomedical Database, PubMed, Embase, Cochrane Library, and Web of Science from their inception dates through November 25, 2024 were identified. The languages in which we are conducting the search are limited to English and Chinese.The search strategy is presented in the Appendix (Supplementary Table 1 Retrieval strategy (PubMed)).

Study Selection

Two researchers independently searched and screened the literature and extracted data. First, the literature was screened based on the title and abstract. For reports that were identified as potentially eligible, the full text was read to verify eligibility for inclusion in the meta-analysis. In cases of disagreement, a third researcher adjudicated.

Data Extraction

Two researchers designed data extraction tables according to the information required and used these to extract the relevant data independently. The extracted data included the following. First, basic information included the first author, publication date, publication country, treatment modality, treatment time, and outcome index. Second, demographic characteristic of the patients included the: sample size, age, sex. Third, methodological information included the randomization method, assignment hiding scheme, blinding method, etc. When the information extracted by the two researchers was inconsistent, consensus was reached by discussion.

Risk-of-Bias in Studies

Two researchers used the Cochrane randomized Controlled Trial Bias Risk Assessment tool[8] to assess the risk-of-bias. The assessment tool included the following seven items: generation of random sequences, assignment hiding, blinding of participants and intervention providers, blinding of outcome evaluators, incomplete outcome data, selective outcome reporting, and other sources of bias, each of which assessed the outcome as having low, high, or unclear risk-of-bias.

Synthesis Methods

A Bayesian random-effects model was used to compare the effects between interventions and the effectiveness of various interventions. The Markov chain Monte Carlo method was used for modeling; four Markov chains were run simultaneously, with 20000 annealing times. Modeling was completed after 50000 simulation iterations. The Deviation Information Standard (DIC) was used to compare the model fit and global consistency, and the node-splitting method was used to analyze local consistency if a closed-loop network was present. In addition, the interventions were ranked based on surface under the cumulative ranking (SUCRA), and league tables were generated to compare the differences in effects across the interventions. Subgroup and sensitivity analyses were also performed. When the number of studies included in the outcome measure was ≥10, a funnel plot was used for intuitive interpretation of publication bias. The analysis was completed using Stata15 (Stata Corp., College Station, TX, USA) and R v.4.2.2 (https://www.r-project.org/).

Results

Study Selection

The literature search identified 983 studies. EndNoteX9.1 (https://researchsoftware.com/endnote-x91-for-windows-and-mac) was used to process the literature. A total of 496 duplicate articles were excluded. Additionally, 463 articles were excluded after reading the title and abstract, and 10 articles were excluded after reading the full text. Finally, 14 randomized controlled trials were included in analysis. Figure 1 shows a flowchart of the screening process.

Study Characteristics

This review included 14 studies,[9–21] with 588 patients overall: 295 patients in the experimental group, and 293 patients in the control group. The authors were from China, the Netherlands, Turkey, Iran, and Saudi Arabia. The interventions included pain-point compression, massage, and ischemic compression. The VAS score for pain was reported in 12 studies and the PPT was reported in five studies. Table 1 presents basic information on the included studies.

Risk-of-Bias in Studies

Regarding randomization methods, 11 studies[9,10,12,14–17,19–21] used a computer-based random number generator. One study[18] used an incorrect method of randomization, and two studies[11,13] made no mention of randomization. Two studies[15,16] used envelopes to conceal assignment. In terms of blinding, seven studies[9,10,12,14,16,19,21] used single blinding,
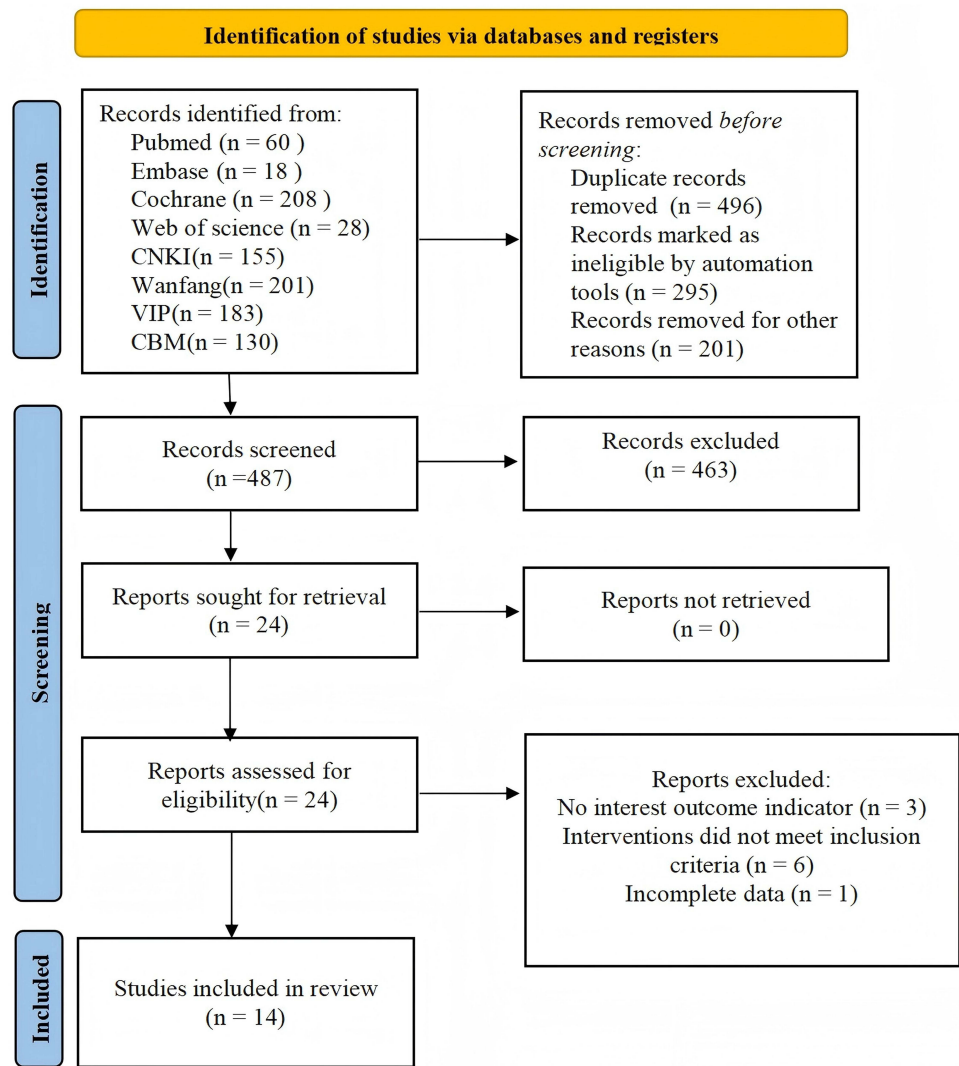
Figure 1 Literature screening process.

while two studies[15,17] used double blinding. In some studies, patients withdrew from the study; however, the sample sizes were small. No selective reporting or other publication biases were observed in any study. Figures 2 and 3 shows the results of the risk-of-bias analysis for the included studies.

Table 1 Basic Information of the Included Studies

First Author	Country of Origin	Year of Publication	Method of Intervention (Including Dose)	Number of Cases	Sex (Male/ Female)	Age (Years)	Course of Treatment	Outcome Indicators
Carel Bron[9]	Netherlands	2011	Pain-point compression, Placebo	34/31	13/21, 8/23	42.8 (11.7; 38.7–46.9)/ 45.0 (13.2; 40.2–49.9)	12 w	VAS
Weichang Huang[10]	China	2013	Pain-point compression, massage	30/30	17/13/14	41.57 ± 9.265/ 42.07–10.957	3 w	VAS
Nesrin Yagci[11]	Türkiye	2013	Massage, spray-and-stretch technique	20/20	7/13, 7/13	30.7 ± 6/31.0–5	-	VAS

(Continued)

Table 1 (Continued).

First Author	Country of Origin	Year of Publication	Method of Intervention (Including Dose)	Number of Cases	Sex (Male/ Female)	Age (Years)	Course of Treatment	Outcome Indicators
Zhixin Zheng[12]	China	2015	Pain-point compression, Thermomagnetic therapy	34/33	14/20/18	39.74 ± 9.22/ 42.48–10.47	2 w	VAS
Yuan-Chi Chan[13]	China	2015	Massage, Heat therapy	32/31	-	31.2 ± 9.4/ 34.7–11.6		VAS
Minhee Kim[14]	South Korea	2016	Pain-point compression, Ultrasonic therapy	22/23	3/19, 2/21	67.7 ± 5.65/ 71.15–5.06	4 w	VAS, PPT
Shabnam Behrangrad[15]	Iran	2017	Ischemic compression, Lumbar looseness	15/15	3/12, 3/12	24.3 ± 1.9/ 24.3–1.9	12 w	PPT
Mehdi Jafar i[16]	Iran	2017	Pain-point compression, Placebo	9/10	-	38.66 ± 13.20/ 35.70 ± 1.86	1 w	VAS, PPT
Albert F. Moraska[17]	Aurora	2017	Pain-point compression, Placebo	20/21	1/19, 2/19	31.2 ± 11.3/ 34.3–10.7	6 w	PPT
Luo Gang[18]	China	2017	Ischemic compression, Electromagnetic therapy	54/54	34/20, 35/19	52.4 ± 3.6/ 49.7–4.1	2 w	VAS
Richa Kashyap[19]	Saudi Arabia	2018	Pain-point compression, Muscle energy technology	15/15	-	21.27 ± 3.86/ 22.07–4.11	2 w	VAS, PPT
Xinjian Li[20]	China	2020	Ischemic compression, Placebo	10/10	-	22.37 ± 1.64/ 22.10–1.11	2 w	VAS
Xiao Hou[21]	China	2023	Pain-point compression, Conventional treatment	63/63	-	29.0 ± 4.8/ 29.3 ± 5.0	2 w	VAS
Bingxin Zheng[22,]	China	2024	Pain-point compression, Electrical stimulation therapy	103/103	-	29.11 ± 6.85/ 28.64–6.97	4 w	VAS

Notes: Conventional treatments: spray-and-stretch technique, thermomagnetic therapy, heat therapy, ultrasonic therapy, lumbar looseness, electromagnetic therapy, muscle energy technology, and electrical stimulation therapy.

Meta Analysis
VAS Score

Twelve studies using three techniques (pain-point compression, massage, and ischemic compression) reported the VAS score for pain. Closed loops are shown in the graph. The inconsistency test results showed that, at $P > 0.05$, the surface network was consistent, and the consistency model was used for analysis (see Figure 4). Heterogeneity test results showed an I^2 value of 11%, indicating little heterogeneity. The effect of manipulative treatment was good as compared to that of conventional treatment and placebo, but the difference in the VAS score for pain was not statistically significant (Figures 5, 6, Appendix (Supplementary Table 2 League table(VAS))). The treatments with the top-three SUCRA values were Pain-point compression (0.73), ischemic compression (0.69), and massage (0.28) (Table 2).
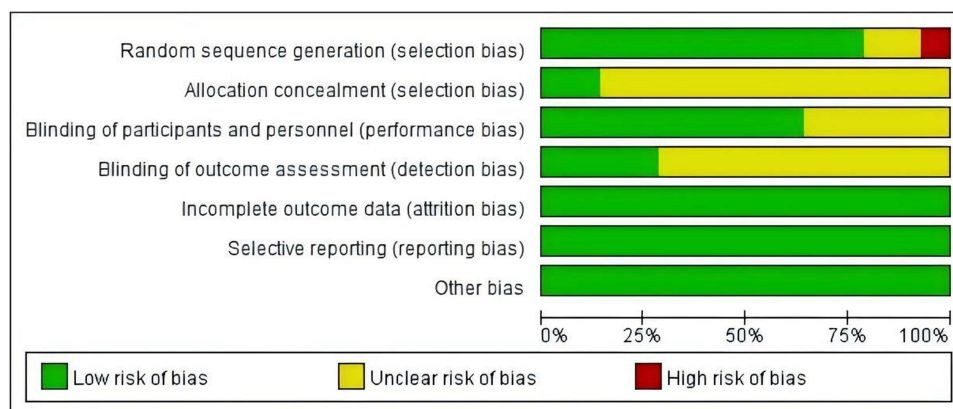

Figure 2 Risk-of-bias graph.
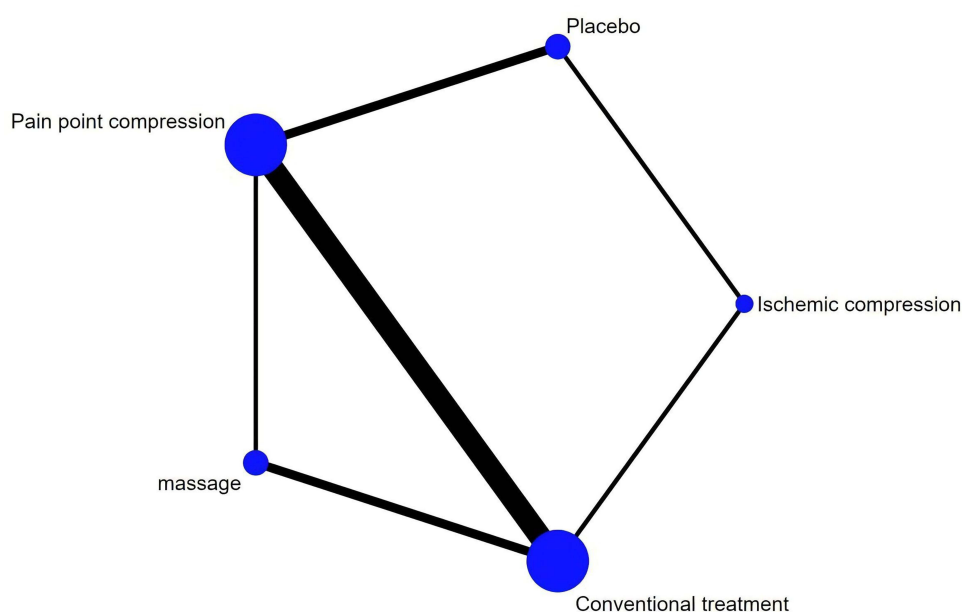
Figure 3 Risk-of-bias summary.

Figure 4 Mesh correlation graph (visual analogue scale score for pain) among different techniques.
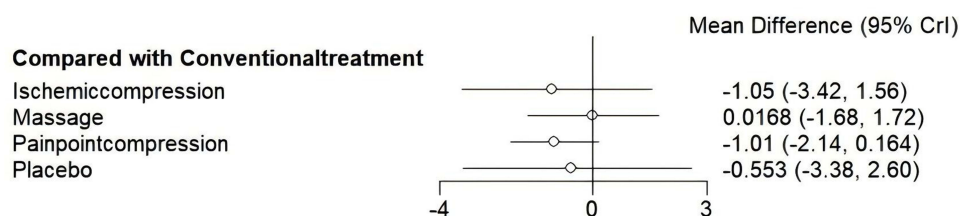

Figure 5 Forest plot of the effectiveness of different techniques compared to conventional treatment (visual analogue scale score for pain).
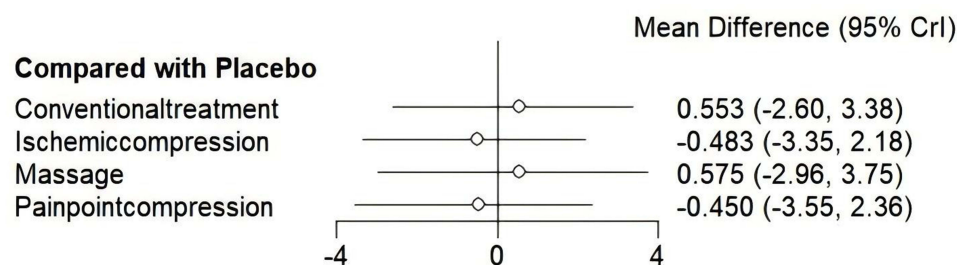

Figure 6 Forest plot of the effectiveness of different techniques compared with placebo (visual analogue scale score for pain).

PPT

Five studies, including two techniques (pain-point compression and ischemic compression) reported on the PPT. The absence of closed loops was analyzed using a conformance model (Figure 7). The heterogeneity test results showed an I^2 value of 3%, indicating little heterogeneity. The effect of manipulation treatment on the PPT was good as compared to that of conventional treatment and placebo, but the results were not statistically significant (Figures 8, 9, Appendix (Supplementary Table 3 League table(PPT))). The top-three SUCRA values were obtained for ischemic compression (0.65), conventional treatment (0.61), and pain-point compression (0.60) (Table 2).

Table 2 SUCRA Scores Obtained for Outcome Indicators in the Included Studies

	VAS		PPT	
	SUCRA	No	SUCRA	No
Pain-point compression	0.73	1	0.60	3
Massage	0.28	4		
Ischemic compression	0.69	2	0.65	1
Conventional treatment	0.26	5	0.61	2
Placebo	0.51	3	0.12	4

Abbreviations: VAS, visual analogue scale; PPT, pain-pressure threshold.

Publication Bias Analysis

The Egger test of results obtained at 24 h, 48 h, and 72 h showed a small possibility of publication bias ($P = 0.07$).

Discussion

We conducted a network meta-analysis to assess the effectiveness of different manipulations for MPS treatment. Fourteen studies encompassing three manipulation therapies (pain-point compression, massage, and ischemic compression) were included. The VAS and PPT were used to evaluate the degree of objective pain perception. These two approaches are the most significant means of evaluating the efficacy of addressing pain symptoms in patients with MPS. The results indicated that
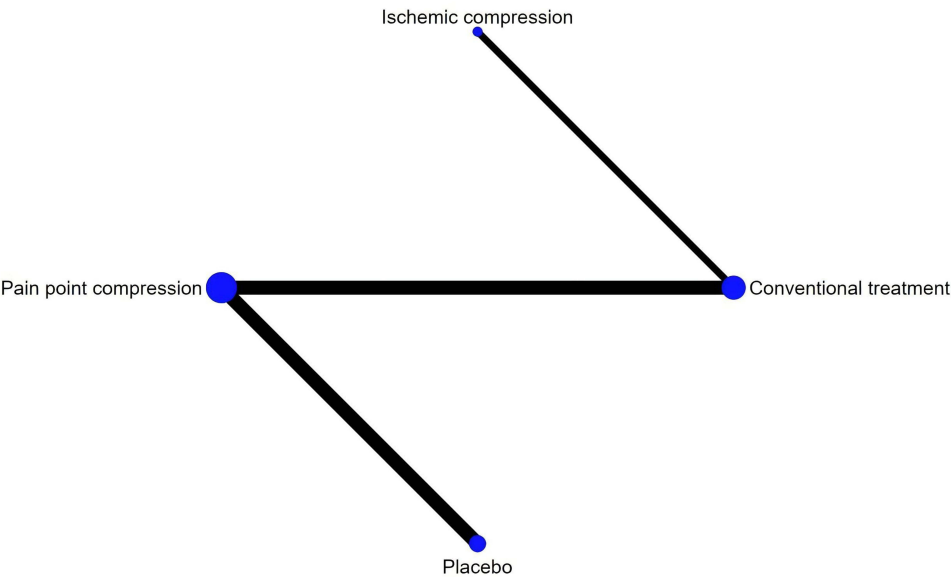
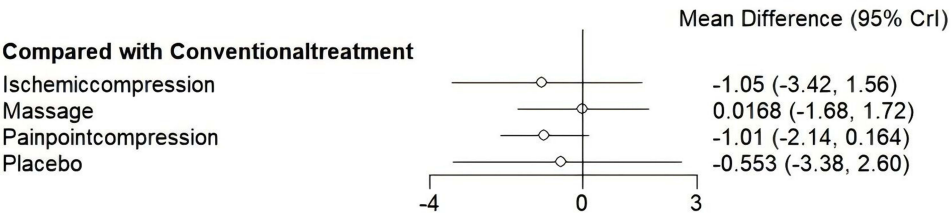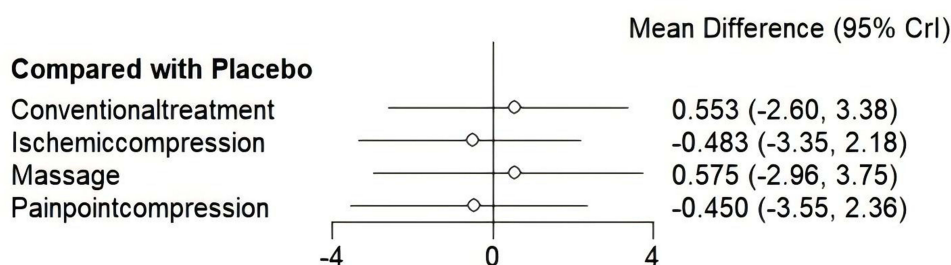**Figure 7** Network association diagram of different techniques (pain-pressure threshold).

Figure 8 Forest graph of the effectiveness of different techniques compared to conventional treatments (pain-pressure threshold).

Mean Difference (95% CrI)

Compared with Placebo

	Mean Difference (95% CrI)
Conventionaltreatment	0.553 (−2.60, 3.38)
Ischemiccompression	−0.483 (−3.35, 2.18)
Massage	0.575 (−2.96, 3.75)
Painpointcompression	−0.450 (−3.55, 2.36)

Figures 9 Forest plot of the effectiveness of different techniques compared with placebo (pain-pressure threshold).

manipulation had an effect, although it was not statistically significant as compared to conventional treatment or placebo. Overall, the effect of pain-point compression was favorable. The results were stable, with no significant publication bias.

Regarding the possible pathological mechanism of MPS, TPC can reduce the degree of contracture and ameliorate the local energy crisis by elongating the contracted muscle segment in the myofascial trigger point (MTrP) region.[23] TPC can alleviate pain symptoms by activating the pain gate control system[24] and descending pain inhibition system.[25] When compression is complete, the rapid influx of blood supplies oxygen and carries away pain-causing substances, reducing the stimulation of nociceptors, and interrupting the abnormal endplate release of excessive acetylcholine. Moraska et al[26] provided crucial evidence that TPC improved the local energy crisis in MPS in a 2013 study, in which two subjects were implanted with a set of microdialysis probes at a MTrP site in the trapezius muscle, which recorded biochemical changes in the MTrP before and after TPC treatment. They found that the local blood flow and local glucose concentration in the MTrP increased significantly after TPC treatment, signifying that the affected local muscle segments obtained sufficient energy supply to restore the normal metabolic state. In addition, TPC treatment restored the elasticity and malleability of the local muscles involved in the MTrP. In 2018, Kisilewicz et al[27] utilized the MyotonPRO muscle elasticity test instrument to analyze the efficacy of TPC for the treatment of patients with MPS and superior trapezius bundles. They discovered that the overall stiffness of the trapezius muscle was significantly reduced in patients after treatment, supporting the view that TPC alleviates local muscle spasms.

Although we found no statistically significant difference with manipulation therapy, this did not imply that the results were clinically insignificant. Some studies[28–30] suggested that pain-point compression therapy can significantly ameliorate the symptoms of MPS. The reasons for the nonsignificant results in our analysis may include the following: First, the form and standards of techniques were not standardized. For example, although ischemic compression at the MTrP is mechanically designed to relieve contracted soft tissue and promote fluid flow (including tissue fluid and blood) through pressure, the specific surgical methods used differ. International researchers have emphasized precise pressure at the trigger point, and the treatment is mainly through continuous pressure, whereas Chinese researchers treat the trigger point from the perspective of traditional Chinese meridians, and the application of force is not limited to the trigger point. The specific manipulations included shiatsu, finger kneading, and plucking. Second, the intensity parameters of the manipulations were not uniform. Some studies consider the subjective perception of the therapist as the basis for treatment, maintaining pressure when the nodules are touched, and applying pressure when the nodules are softened,[31] while others take the pain of the patient as the basis, maintaining pressure when the patient's main complaint reaches the maximum pain threshold, and exerting pressure when the pain decreases significantly, repeatedly.[32] Chao et al[33] combined patients' pain complaints with therapists' subjective perceptions in their own research. Although the above studies have demonstrated certain therapeutic effects, no literature on specific operational norms are available; thus, effective comparisons between different types of techniques in terms of efficacy cannot be made. Second, it may be related to the rigor of the study itself (including the inclusion of subjects, whether a blinding method was used, specific treatment methods, and measurement of indicators) and sample size. Therefore, the quality and sample size of the relevant literature need to be evaluated. We searched the Chinese clinical trial registration platform and found that many ongoing clinical studies on using manual therapy for MPS (for example, ChiCTR2300075495, ChiCTR2000030881, and ChiCTR2200058541), indicating that MPS using manual therapy holds great research value.

No previous network meta-analysis of MPS treated with different manipulations to provide evidence for clinical use has been published to date. However, this study had some limitations. Only 14 articles were included, which is a relatively small number. The outcome indicators included in each study differed, and the scale types used were difficult to standardize. Only the relatively common VAS scores and PPT measurement values could be selected for meta-analysis, whereas other parameters were difficult to include in a pooled analysis. The literature included in this study had different degrees of risk-of-bias. Moreover, this study only included Chinese and English literature, and thus a more comprehensive search and screening of existing studies could not be conducted. The results of this study were not limited by statistical significance. This is due to a number of reasons, which we have analyzed. In the future, we will further pay attention to the research updates in related fields, timely incorporate the latest research data, and update our results.

Conclusion

Based on the findings of this study, manipulation therapy was an effective treatment for MPS, but not statistically significantly different from conventional therapy or placebo, owing to issues such as inconsistent methodological quality and the small sample size of the included studies. Further high-quality multicenter, large-sample, randomized double-blind controlled trials are required in future to verify the reliability of this conclusion.

Abbreviations

MPS, myofascial pain syndrome; MTrP, myofascial trigger point; PPT, pain-pressure threshold; TPC, trigger point compression; VAS, visual analogue scale.

Data Sharing Statement

Data are available from the corresponding author (Lirong Zeng) upon request.

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Disclosure

The authors declare no conflicts of interest regarding the publication of this paper. The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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