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The Efficacy of Manual Therapy for Rotator Cuff Tendinopathy: A Systematic Review and Meta-analysis

STUDY DESIGN: Systematic review and meta-analysis.

OBJECTIVES: To evaluate the efficacy of manual therapy (MT) for patients with rotator cuff (RC) tendinopathy.

BACKGROUND: Rotator cuff tendinopathy is a highly prevalent musculoskeletal disorder, for which MT is a common intervention used by physical therapists. However, evidence regarding the efficacy of MT is inconclusive.

METHODS: A literature search using terms related to shoulder, RC tendinopathy, and MT was conducted in 4 databases to identify randomized controlled trials that compared MT to any other type of intervention to treat RC tendinopathy. Randomized controlled trials were assessed with the Cochrane risk-of-bias tool. Meta-analyses or qualitative syntheses of evidence were performed.

RESULTS: Twenty-one studies were included. The majority had a high risk of bias. Only 5 studies had a score of 69% or greater, indicating a moderate to low risk of bias. A small but statistically significant overall effect for pain reduction of MT compared with a placebo or in addition to another intervention was observed (n = 406), which may or may not be clinically important, given a mean difference of 1.1 (95% confidence interval: 0.6, 1.6) on a 10-cm visual analog scale. Adding MT to an exercise program (n = 226) significantly decreased pain (mean difference, 1.0; 95% confidence interval: 0.7, 1.4), as reported on a 10-cm visual analog scale, which may or may not be clinically important. Based on qualitative analyses, it is unclear whether MT used alone or added to an exercise program improves function.

CONCLUSION: For patients with RC tendinopathy, based on low- to moderate-quality evidence, MT may decrease pain; however, it is unclear whether it can improve function. More methodologically sound studies are needed to make definitive conclusions.

LEVEL OF EVIDENCE: Therapy, level 1a–.
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KEY WORDS: *mobilization, physical therapy, shoulder impingement syndrome, shoulder pain*

Shoulder pain is highly prevalent and among musculoskeletal disorders is the third most common reason for visiting a primary care physician.[16,33,46] As many as two thirds of people who have shoulder complaints receive a diagnosis of rotator cuff (RC) tendinopathy.[46] Rotator cuff tendinopathy often leads to decreased function,[34] lower health-related quality of life,[34] poor sleep quality,[47] and work absenteeism.[40]

Rotator cuff tendinopathy is a broad diagnosis, and mounting evidence suggests that diagnoses such as shoulder impingement syndrome, RC tendinitis/tendinosis, as well as subacromial bursitis may be considered as the same clinical entity.[19]

Conservative treatment of RC tendinopathy generally includes rest, nonsteroidal anti-inflammatory drugs, and rehabilitation interventions such as exercise.[19] High-level evidence supports exercise as an effective treatment.[20] In conjunction with exercise, physical therapists often add manual therapy (MT) interventions to address impairments potentially associated with RC tendinopathy.[50] Manual therapy interventions have been defined by the International Federation of Orthopaedic Manipulative Physical Therapists as skilled hand movements performed by a therapist.[26]

Systematic reviews on the efficacy of MT and exercises for the treatment of RC tendinopathy have recently been published[7,8] and concluded that there is a lack of evidence concerning the efficacy of MT when used alone and that evidence regarding the efficacy of the addition of MT to exercise for the treatment of RC

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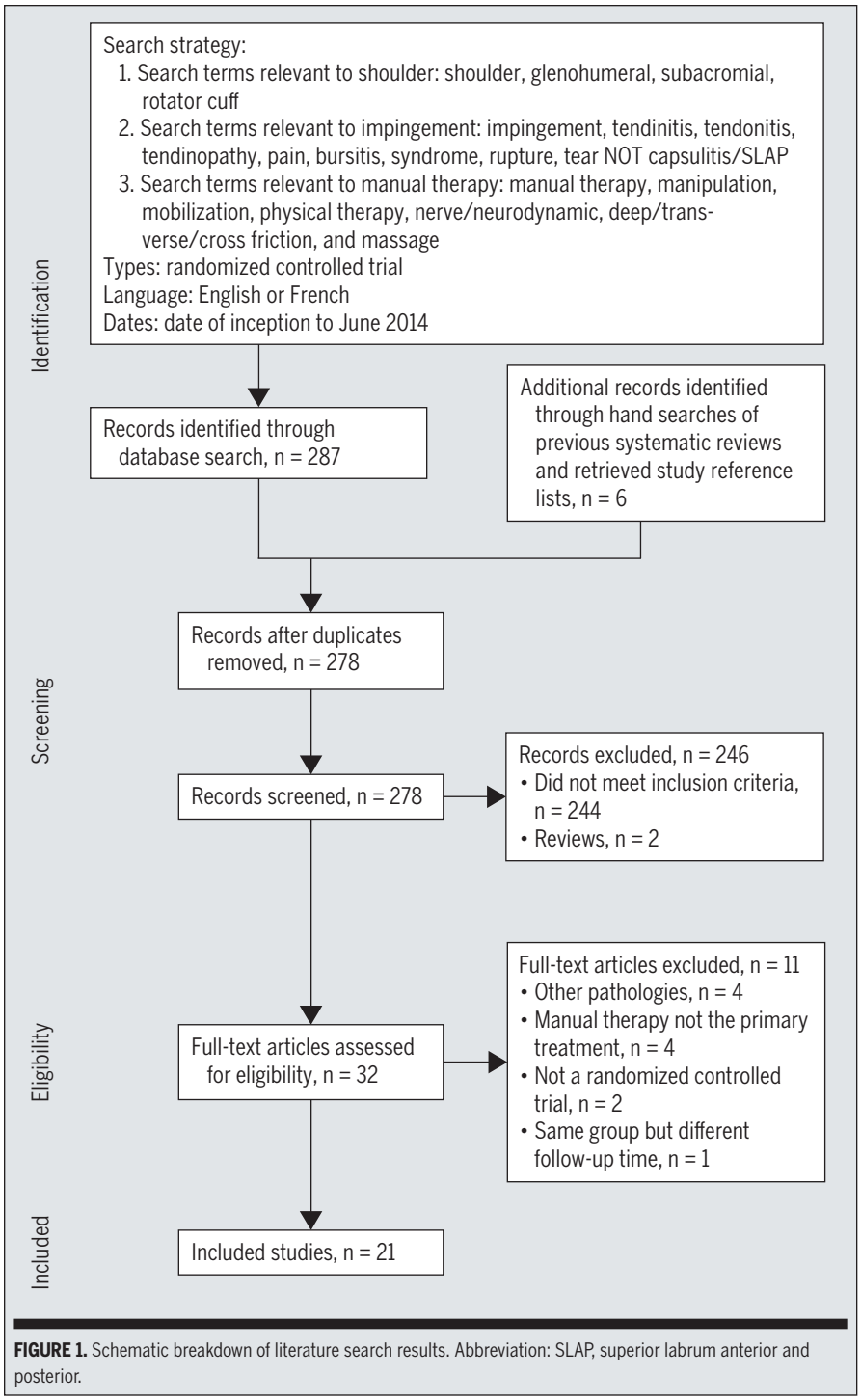

FIGURE 1. Schematic breakdown of literature search results. Abbreviation: SLAP, superior labrum anterior and posterior.

tendinopathy is inconclusive. However, these reviews only performed qualitative synthesis of the results, without pooling the results into meta-analyses. Moreover, many relevant clinical trials were excluded from these reviews,[1,3,5,10,12,37,44,48] and, since the publication of these reviews, new trials have been published.[22,28,52] Thus, the aim of this systematic review and meta-analysis was to perform an updated review of the evidence regarding the efficacy of MT, used either alone or in combination with other interventions, for the treatment of RC tendinopathy.

METHODS

Literature Search

An electronic bibliographical search was conducted in MEDLINE, Embase, PEDro, and CINAHL from their dates of inception to June 2014. A combination of Medical Subject Headings terms and text words was used to identify relevant articles. In addition, a hand search was performed of the reference lists of included articles and previously published reviews (**FIGURE 1**).

Study Selection

Two reviewers independently reviewed titles and abstracts to identify articles of interest. A consensus of the 2 reviewers was needed to include the studies in the literature review. A third reviewer was available for final determination if a consensus was not achieved by the pair of initial reviewers.

Articles were included if they met the following inclusion criteria: participants were diagnosed with RC tendinopathy/tendinitis, shoulder impingement syndrome, or subacromial bursitis; participants were adults; an MT intervention was compared with another type of treatment, including other MT interventions; the study design was a randomized controlled trial (RCT); and the article was published in English or French (**FIGURE 1**). Manual therapy interventions that were considered for inclusion had to be specific hands-on interventions.[26] Included interventions that met this definition were joint mobilizations, manipulations, specific soft tissue massage techniques, neurodynamic interventions, and mobilizations with movement (MWM) of the shoulder girdle or spine. All types of outcome measures were considered for inclusion. Studies that included participants who had shoulder pain without further diagnostic information were included for review if it was possible to determine that the majority of participants had RC

TABLE 1 Characteristics of the Included Studies for the Efficacy of MT Alone

Study	Participants	Interventions	Follow-up Period	Outcome Measure, Units	Main Results	Risk-of-Bias Score
Atkinson et al[1]	n = 60; 43 male, 17 female; mean age, 41.8 y Diagnosis: 3 of 4 positive tests: pain on palpation of the greater tuberosity or the anterior acromion, painful arc in abduction, empty can test	Group 1 (n = 30): MT (manipulation of the GH or AC joint) Group 2 (n = 30): placebo (detuned laser)	2 wk	NPRS (0-100 mm)	Pre-post difference within groups: group 1, 19.9 ± 13.9 (*P* = .000); group 2, 10.6 ± 14.7 (*P* = .002) Difference between groups: 9.3 ± 3.69, *P* = .0629	8/16
				ROM in flexion (deg)	Pre-post difference within groups: group 1, 14.5 ± 5.9 (*P* = .000); group 2, 11.2 ± 6.0 (*P* = .002) Difference between groups: 3.2 ± 1.5, *P*≥.05	
				ROM in abduction (deg)	Pre-post difference within groups: group 1, 18.4 ± 8.0 (*P* = .000); group 2, 7.1 ± 6.8 (*P* = .047) Difference between groups: 11.3 ± 1.9, *P*≥.05	
				Pain pressure threshold on the anterior shoulder (kg/cm^2)	Statistically significant difference between groups favoring group 1 (*P*<.001)	
Bansal and Padamkumar[3]	n = 40; 21 male, 19 female; mean ± SD age, 30.6 ± 5.4 y Diagnosis: pain on palpation of the greater tuberosity, painful resisted abduction, positive empty can test	Group 1 (n = 20): MT (supraspinatus transverse frictions) Group 2 (n = 20): ultrasound	10 d	Pain at rest (10-cm VAS)	Pre-post difference within groups: group 1, 4.4 (*P*<.001); group 2, 3.5 (*P*<.001) Difference between groups: 0.85, *P* = .014	6/16
				Active ROM in abduction (deg)	Pre-post difference within groups: group 1, 32.6 (*P*<.001); group 2, 25.9 (*P*<.001) Difference between groups: 6.7, *P* = .023	
McClatchie et al[35]	n = 21; 7 male, 14 female; mean ± SD age, 49.8 ± 9.8 y Diagnosis: painful arc in shoulder abduction No improvement following previous physical therapy treatments	Crossover trial Group 1 (n = 21): MT (lateral glides of C5, C6, and C7) Group 2 (n = 21): sham MT (hands on patient, no movement)	Same day	Pain on active abduction (10-cm VAS)	Pre-post difference within groups: group 1, 1.3 ± 1.1 (*P*<.001); group 2, 0.2 ± 0.6 (*P* = .078) Difference between groups: 1.1, *P* = .0002	10/16
				Total range of the painful arc for abduction (deg)	Pre-post difference within groups: group 1, 12.5 ± 15.6 (*P* = .002); group 2, 8.8 ± 12.7 (*P* = .005) No statistical test was performed between groups	

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tendinopathy. Studies were excluded if participants had RC full-thickness tear, calcific tendinopathy, or presented with a postsurgical condition.

Data Extraction

Data and results from the included studies were extracted using a standardized form that documented characteristics of the participants, diagnostic criteria, interventions, follow-up periods, outcome measures, and results (**TABLES 1** through **3**). When results were missing or not fully reported, efforts were made to contact the contributing authors to retrieve missing data.

Risk-of-Bias Appraisal Tool

The internal validity of the included studies was assessed with the Cochrane risk-of-bias tool.[23] This tool uses

TABLE 1 Characteristics of the Included Studies for the Efficacy of MT Alone (continued)

Study	Participants	Interventions	Follow-up Period	Outcome Measure, Units	Main Results	Risk-of-Bias Score
Munday et al[37]	n = 30; 16 male, 14 female; mean age, 22.5 y Diagnosis: 3 out of 5: pain on palpation of the greater tuberosity or the anterior acromion, painful arc in abduction, positive Neer impingement sign or Hawkins-Kennedy test	Group 1 (n = 15): MT (manipulation of the GH joint, AC joint, ribs, and scapula) Group 2 (n = 15): placebo (detuned ultrasound)	4 wk	Pain (10-cm VAS)	Pre-post difference within groups: group 1, 2.7 ± 2.4 (P<.05); group 2, 1.9 ± 2.3 (P<.05) Difference between groups: 0.80 ± 0.86, P = .019	10/16
				Pain pressure threshold on the anterior shoulder (kg/cm^2)	Pre-post difference within groups: group 1, 1.9 ± 2.1 (P<.05); group 2, 0.6 ± 2.6 (P<.05) Difference between groups: 1.3 ± 3.34, P = .014	
				Short-form McGill Pain Questionnaire	Pre-post difference within groups: group 1, 10.7 ± 22.1 (P<.05); group 2, 24.1 ± 16.6 (P<.05) Difference between groups: –13.4 ± 27.6, P<.005	
Surenkok et al[44]	n = 39; 17 male, 22 female; mean ± SD age, 54.3 ± 14.1 y Diagnosis: limited painful abduction in scapular plane Individual diagnoses: impingement, n = 22; tenosynovitis, n = 10; frozen shoulder, n = 7	Group 1 (n = 13): MT (scapular mobilization) Group 2 (n = 13): sham MT Group 3 (n = 13): no intervention	Immediately after treatment	Pain at rest and activity (100-mm VAS)	Pre-post difference within groups: group 1, 0.46 ± 9.2; group 2, 0.16 ± 13.0; group 3, 0.92 ± 8.76 No statistically significant differences between groups (P≥.05)	8/16
				CMS* (%)	Pre-post difference within groups: group 1, 2.2 ± 2.2; group 2, 0.31 ± 2.3; group 3, 3.8 ± 10.8 Statistically significant differences between groups postintervention favoring group 1 over groups 2 (1.92 ± 0.92) and 3 (6.1 ± 3.1) (P<.016)	
				ROM in active flexion (deg)	Pre-post difference within groups: group 1, 7.8 ± 6.3; group 2, 0.23 ± 6.6; group 3, 1.7 ± 8.5 Statistically significant differences between groups favoring group 1 over groups 2 (7.6 ± 2.5) and 3 (6.1 ± 2.9) (P<.016)	
				ROM in active abduction (deg)	Pre-post difference within groups: group 1, 5.6 ± 4.6; group 2, 0.52 ± 4.2; group 3, 1.8 ± 1.3 Statistically significant differences between groups favoring group 1 over groups 2 (5.1 ± 1.7) and 3 (3.8 ± 1.3) (P<.016)	
				Scapular upward rotation at rest (deg)	Statistically significant differences between groups favoring group 1 over groups 2 and 3 (P<.016)	

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TABLE 1 Characteristics of the Included Studies for the Efficacy of MT Alone (continued)

Study	Participants	Interventions	Follow-up Period	Outcome Measure, Units	Main Results	Risk-of-Bias Score
Teys et al[48]	n = 24 (11 male, 13 female); mean ± SD age, 46.1 ± 9.8 y Diagnosis: limited painful shoulder abduction	Crossover trial Group 1 (n = 24): MT (mobilization with movement) Group 2 (n = 24): sham MT (sham mobilization with movement) Group 3 (n = 24): no intervention	Immediately after treatment	Pressure pain threshold (kPa)	Pre-post difference within groups: group 1, 62.6 (95% CI: 33.6, 91.5); group 2, 25.9 (95% CI: 0.2, 51.6); group 3, 20.0 (95% CI: −1.5, 41.5) Difference between groups 1 and 2, 36.7 (95% CI: −0.01, 73.4); between groups 1 and 3, 42.6 (95% CI: 8.3, 76.8)	12/16
				Pain-free abduction in scapular plane (deg)	Pre-post difference within groups: group 1, 15.6 (95% CI: 10.1, 21.1); group 2, 3.9 (95% CI: −0.1, 7.9); group 3, 0.27 (95% CI: −0.24, 3.0) Difference between groups 1 and 2, 11.7 (95% CI: 5.3, 18.1); between groups 1 and 3, 15.3 (95% CI: 9.5, 21.1)	

Abbreviations: AC, acromioclavicular; CI, confidence interval; CMS, Constant-Murley score; GH, glenohumeral; MT, manual therapy; NPRS, numeric pain-rating scale; pre-post, preintervention to postintervention; ROM, range of motion; VAS, visual analog scale.
**A pain and function questionnaire that measures isometric abduction strength and active ROM in flexion and abduction and in internal and external rotation. Higher scores indicate a greater level of function.*

8 different domains (methodological items) to appraise 5 different biases (selection, performance, attrition, detection, reporting). The items are scored on a 3-point scale that assigns a risk of bias of 0 for high risk, 1 for unclear risk, and 2 for low risk, with a maximum possible score of 16 points for studies with the lowest risk of bias. Two reviewers independently assessed the risk of bias of each study and met to compare ratings. Disagreement was resolved by consensus. If no consensus was reached, a third reviewer made the final determination.

Data Analysis

A preconsensus intraclass correlation coefficient was calculated for total score on the Cochrane risk-of-bias tool, and interrater agreement was calculated for the 8 risk-of-bias domains using the kappa statistic. Statistical analyses were performed with IBM SPSS Statistics Version 21 (IBM Corporation, Armonk, NY).

Results from studies with similar comparators or outcome measures were pooled into meta-analyses. Only meta-analyses without a significant degree of heterogeneity (chi-square $P>.10$ and $I^2<60\%$) were retained for reporting.[24] When quantitative pooling was not performed, results were qualitatively synthesized. The primary analysis compared the overall efficacy of MT to a placebo or to another intervention. Secondary analyses included the comparisons of (1) MT alone to a placebo, (2) MT with an exercise program to an exercise program, (3) MT alone to another intervention, (4) MT combined with other types of interventions to a placebo or a multimodal intervention, and (5) different types of MT.

Mean differences or standardized mean differences with 95% confidence intervals (CIs) were calculated using Review Manager Version 5.2 (The Nordic Cochrane Centre, Copenhagen, Denmark).[23] Because the overall number of studies included in the meta-analyses was small and true effect sizes varied between studies, random-effects models were used. Alpha level was set at .05 to test for overall effect. Funnel plots were not generated because of the small number of trials included in each meta-analysis.[23]

RESULTS

From the 32 potentially relevant articles identified after title and abstract review, 21 studies met the eligibility criteria following full-text review (**FIGURE 1**).[1-6,10-12,22,27,28,35,37,42-44,48,52-54]

Risk-of-Bias Appraisal

The mean ± SD score on the Cochrane risk-of-bias tool across all studies was 52.7% ± 17.0%. Five studies[5,12,27,28,48] had a score of at least 69% (11/16), indicating a moderate to low risk of bias. The other 16 studies[1-4,6,10,11,22,35,37,42-44,52-54] scored less than 69%, indicating a high risk of bias. The agreement between reviewers on the overall risk-of-bias score was excellent, with an intraclass correlation coefficient of 0.93 (95% CI: 0.84, 0.97). Preconsensus interrater agreement for individual items of the Cochrane risk-of-bias tool ranged from fair to perfect (κ = 0.49-

TABLE 2 Characteristics of the Included Studies for the Efficacy of Adding an MT Intervention to Exercises or to a Multimodal Rehabilitation Program That Includes Exercise

Study	Participants	Interventions	Follow-up Period	Outcome Measure	Main Results	Risk-of-Bias Score
Bang and Deyle[2]	n = 50; 29 male, 21 female; mean ± SD age, 43.4 ± 9.1 y Diagnosis: positive Neer or Hawkins-Kennedy test and painful active abduction or painful resisted movement; abduction or internal or external rotation	Group 1 (n = 27): MT (mobilization and manipulation of the upper quarter) and supervised exercises Group 2 (n = 23): supervised exercises (flexibility and strengthening of the shoulder)	6-7 wk	Pain during activities (10-cm VAS)	Pre-post differences within groups: group 1, 4.1 ± 0.54; group 2, 2.0 ± 0.77 Difference between groups, 2.1 ± 0.19 (P = .0017)	8/16
				Isometric strength (abduction and internal and external rotation) (N)	Statistically significant difference between groups favoring group 1 (P<.001)	
			2 mo	Functional questionnaire (0-45)	Pre-post differences within groups: group 1, 9.8 ± 1.3; group 2, 4.7 ± 2.0 Difference between groups, 5.1 ± 0.9 (P = .0049)	
Barbosa et al[4]	n = 14; 5 male, 9 female; mean ± SD age, 46.1 ± 7.6 y Diagnosis: pain on palpation and at least 1 positive test: speed, Yergason, Jobe	Group 1 (n = 7): MT (GH mobilization) with ultrasound and exercises Group 2 (n = 7): ultrasound and eccentric exercises	4 wk	DASH* (%)	Pre-post differences within groups: group 1, 40.5 ± 13.6 (P<.001); group 2, 19.9 ± 11.9 (P<.001) Difference between groups, 20.6 ± 18.1 (P = .021)	6/16
				CMS† (%)	Pre-post differences within groups: group 1, 21.5 ± 11.6 (P<.001); group 2, 14.5 ± 10.0 (P<.001) Difference between groups, 7.0 ± 15.3 (P = .004)	
Bialoszewski and Zaborowski[6]	n = 30; 18 male, 12 female; mean age, 51.3 y Diagnosis: positive Jobe relocation test and painful arc in abduction	Group 1 (n = 15): MT (AP and roll-glide GH mobilization, mobilization with movement, deep transverse friction) and standard care Group 2 (n = 15): standard care (TENS, ultrasound, strengthening, and passive exercises)	Not reported	Pain on functional tests (10-cm VAS)	Pre-post differences within groups: group 1, 5.3 ± 2.9; group 2, 3.2 ± 1.3 Difference between groups, 2.1 ± 3.18 (P<.005)	6/16
				Active ROM in abduction (deg)	Pre-post differences within groups: group 1, 19.3 ± 12.9; group 2, 8.3 ± 5.2 Difference between groups, 11.0 ± 13.9 (P<.007)	

Table continues on page 336.

1.0).[31] Consensus was always achieved between the pair of initial reviewers.

None of the studies had a low risk of bias for all 8 methodological items. Due to the nature of the intervention, the blinding of participants was rarely possible and was achieved by only 6 of the studies.[5,12,27,37,48,52] Blinding of the provider was impossible due to the nature of the intervention. Blinding of assessors was adequately reported in 11 studies.[2,5,11,12,22,27,28,35,44,48,54] Risk of reporting bias was present in 17 of the 21 studies, because no protocol or trial registration number was provided (**FIGURES 2** and **3**).

Outcome Measures

Fourteen studies[1-3,5,6,10,11,27,28,35,37,42-44] used a visual analog scale (VAS) or a numeric pain-rating scale to measure a variety of pain-related outcomes. Nine trials[4,5,10,22,27,28,42,44,52] used validated functional outcome measures. Shoulder ac-

TABLE 2 Characteristics of the Included Studies for the Efficacy of Adding an MT Intervention to Exercises or to a Multimodal Rehabilitation Program That Includes Exercise (continued)

Study	Participants	Interventions	Follow-up Period	Outcome Measure	Main Results	Risk-of-Bias Score
Conroy and Hayes[11]	n = 14; 8 male, 6 female; mean ± SD age, 52.8 ± 19.3 y Diagnosis: pain on the superolateral shoulder and 1 of the following: decreased active ROM in flexion, painful subacromial compression test, or limited functional movement patterns in an elevated position	Group 1 (n = 7): MT (anterior, posterior, inferior mobilization or traction of the GH joint) and standard care Group 2 (n = 7): standard care (hot packs, active ROM, stretching and strengthening shoulder exercises, soft tissue mobilization, and patient education)	3 wk	Maximum pain intensity in the last 24 h (100-mm VAS)	Pre-post differences within groups: group 1, 37.0 ± 11.8 (P = .005); group 2, 2.2 ± 14.9 (P = .823) Difference between groups, 34.9 ± 7.0 (P = .008)	9/16
				Maximum pain intensity with subacromial compression test (100-mm VAS)	Pre-post differences within groups: group 1, 27.0 ± 10.5 (P = .003); group 2, 11.1 ± 15.0 (P = .842) Difference between groups, 15.9 ± 6.9 (P = .032)	
				Active ROM in abduction, flexion, abduction in scapular plane, internal and external rotation (deg)	No difference between groups (P≥.005)	
Kachingwe et al[27]	n = 33; 17 male, 16 female; mean age, 46.4 y Diagnosis: superolateral shoulder pain and 2 out of 4 positive tests: Neer, Hawkins-Kennedy, painful limitation of active shoulder elevation, pain or limitation with the functional movement patterns	Group 1 (n = 9): MT (posterior, anterior, inferior, or traction mobilizations of the GH joint) and supervised exercises Group 2 (n = 9): MT (mobilization with movement) and supervised exercises Group 3 (n = 8): supervised exercises (muscle strengthening, capsule stretching, postural correction) Group 4 (n = 7): unsupervised exercises, advice	6 wk	Change in maximum pain in the last 24 h (%)	Differences within groups: group 1, 4.4 ± 3.8 (P<.001); group 2, 5.5 ± 3.1 (P<.001); group 3, 2.0 ± 11.2 (P<.001); group 4, 1.1 ± 11.9 (P<.001) No differences between groups (P≥.05)	11/16
				Change in SPADI‡ (%)	Differences within groups: group 1, 56.7 ± 29.8 (P<.001); group 2, 55.5 ± 20.1 (P<.001); group 3, 61.6 ± 35.9 (P<.001); group 4, 34.2 ± 58.9 (P<.001) No differences between groups (P≥.05)	
				Change in active pain-free abduction in scapular plane (%)	Differences within groups: group 1, 2.5 ± 88.8 (P<.001); group 2, 66.5 ± 28.1 (P<.001); group 3, 19.8 ± 70.3 (P<.001); group 4, 29.8 ± 49.0 (P<.001) No differences between groups (P≥.05)	

Table continues on page 337.

TABLE 2 Characteristics of the Included Studies for the Efficacy of Adding an MT Intervention to Exercises or to a Multimodal Rehabilitation Program That Includes Exercise (continued)

Study	Participants	Interventions	Follow-up Period	Outcome Measure	Main Results	Risk-of-Bias Score
Kromer et al[28]	n = 90; 44 male, 46 female; mean ± SD age, 51.8 ± 11.2 y Diagnosis: 1 positive test: Neer, Hawkins-Kennedy, or painful arc; and pain on 1 resisted test: external rotation, internal rotation, abduction, or flexion	Group 1 (n = 46): MT (mobilization and manipulation of the shoulder girdle, upper thoracic and cervical spine) for 5 wk and individually adapted exercises Group 2 (n = 44): individually adapted exercises (shoulder and neck stretches, strengthening of the shoulder)	5 wk	Mean weekly pain score (11-point VNRS)	Pre-post differences within groups: group 1, 2.3 (95% CI: 1.7, 2.8); group 2, 1.6 (95% CI: 1.0, 2.3) Difference between groups, 0.6 (95% CI: −0.2, 1.5)	12/16
				SPADI‡ (%)	Pre-post differences within groups: group 1, 16.2 (95% CI: 10.8, 21.6); group 2, 14.4 (95% CI: 9.2, 19.6) Difference between groups, 1.8 (95% CI: −5.7, 9.2)	
				Patient global impression of change	Relative risk of slightly and much better overall change: 1.06 (95% CI: 0.93, 1.27)	
			12 wk	Mean weekly pain score (11-point VNRS)	Pre-post differences within groups: group 1, 0.6 (95% CI: 0.1, 1.0); group 2, 1.1 (95% CI: 0.5, 1.5) Difference between groups, −0.4 (95% CI: −1.1, 0.2)	
				SPADI‡ (%)	Pre-post differences within groups: group 1, 7.5 (95% CI: 3.7, 12.2); group 2, 7.0 (95% CI: 2.8, 11.2) Difference between groups, 0.4 (95% CI: −5.1, 6.0)	
Senbursa et al[42]	n = 30; proportion not reported; mean ± SD age, 48.8 ± 10.8 y Diagnosis: positive Neer impingement sign	Group 1 (n = 15): MT (GH and scapular mobilization, deep friction massage to supraspinatus tendon, radial nerve stretch, PNF) and exercises Group 2 (n = 15): exercises (stretching and strengthening of the shoulder)	4 wk	Global pain (at rest, at night, with movement) (10-cm VAS)	Pre-post differences within groups: group 1, 4.7 ± 0.83 (P<.05); group 2, 3.6 ± 0.58 (P<.05) Difference between groups, 1.1 ± 2.9 (P<.05)	5/16
				ROM (flexion, abduction, external rotation) (deg)	Pre-post differences within groups: group 1, statistically significant differences (P<.05); group 2, no statistically significant differences (P≥.05) Statistically significant difference between groups favoring group 1 (P<.05)	
			13 wk	Neer functional assessment questionnaire	Pre-post differences within groups: group 1, statistically significant differences (P<.05); group 2, no statistically significant differences (P≥.05) Statistically significant difference between groups favoring group 1 (P<.05)	

Table continues on page 338.

TABLE 2 Characteristics of the Included Studies for the Efficacy of Adding an MT Intervention to Exercises or to a Multimodal Rehabilitation Program That Includes Exercise (continued)

Study	Participants	Interventions	Follow-up Period	Outcome Measure	Main Results	Risk-of-Bias Score
Senbursa et al[43]	n = 77; proportion not reported; mean age, 48.8 y Diagnosis: positive Neer impingement sign or Hawkins-Kennedy test	Group 1 (n = 22): MT (GH and scapular mobilization, deep friction massage to supraspinatus tendon, radial nerve stretch, PNF) and supervised exercises Group 2 (n = 25): supervised exercises (stretching and strengthening) Group 3 (n = 30): home-based rehabilitation program (same exercises as supervised exercises)	4 and 12 wk	Global pain (at rest, at night, with movement) (10-cm VAS)	Statistically significant differences within all groups ($P<.05$) No statistically significant differences between groups ($P\geq.05$)	4/16
				MASES[§] (%)	At week 4: statistically significant differences within all groups ($P<.05$) Statistically significant differences between groups favoring group 1 over groups 2 and 3 ($P<.05$) At week 12: statistically significant differences within group 1 ($P<.05$); no statistically significant differences within groups 2 and 3 ($P<.05$) Statistically significant differences between groups favoring group 1 over groups 2 and 3 ($P<.05$)	
				ROM in flexion, abduction, external rotation (deg)	Statistically significant differences within all groups ($P<.05$) No statistically significant differences between groups ($P\geq.05$)	
				Isometric strength in flexion, abduction, internal and external rotation (5-point manual muscle testing)	Statistically significant differences within all groups ($P<.05$) No statistically significant differences between groups ($P\geq.05$)	

Abbreviations: AP, anteroposterior; CI, confidence interval; CMS, Constant-Murley score; DASH, Disabilities of the Arm, Shoulder and Hand questionnaire; GH, glenohumeral; MASES, Modified American Shoulder and Elbow Surgeons Standardized Shoulder Assessment Form; MT, manual therapy; PNF, proprioceptive neuromuscular facilitation; pre-post, preintervention to postintervention; ROM, range of motion; SPADI, Shoulder Pain and Disability Index; TENS, transcutaneous electrical nerve stimulation; VAS, visual analog scale; VNRS, visual numeric rating scale.

**Self-reported disability questionnaire. Higher scores indicate a greater level of disability.*

†A pain and function questionnaire that measures isometric abduction strength and active ROM in flexion and abduction and in internal and external rotation. Higher scores indicate a greater level of function.

‡Self-assessment of symptoms and function of the shoulder. Higher scores indicate a greater level of disability.

§Self-assessment of function and pain. Higher scores indicate a greater level of disability.

tive range of motion (ROM) in flexion or abduction was also commonly used as an outcome measure.[1,3,6,10-12,22,27,35,42-44,48] Seven studies did not report treatment effect estimates, only the conclusions of statistical testing or results in a graphical form.[1,2,6,10,11,43,53] Efforts made to contact the contributing authors to obtain additional results were all unsuccessful.

Primary Analyses

Overall Efficacy of MT Compared With a Placebo or in Addition to Another Intervention Thirteen RCTs assessed the effect of MT compared to a sham treatment or the effect of adding an MT intervention to another intervention, such as exercises, electrotherapy, or education.[1,2,4,6,11,27,28,35,37,42-44,48] Eleven RCTs[1,2,6,11,27,28,35,37,42-44] assessed treatment effect using pain as an outcome meas-

TABLE 3 Characteristics of the Included Studies for the Efficacy of MT Combined With Other Types of Interventions Compared With Multimodal Interventions

Study	Participants	Interventions	Follow-up Period	Outcome Measure	Main Results	Risk-of-Bias Score
Bennell et al[5]	n = 120; 64 male, 56 female; mean ± SD age, 60.1 ± 16.0 y Diagnosis: positive Neer impingement sign and pain on active external rotation or abduction	Group 1 (n = 59): MT and exercises (AP and inferior mobilization of the GH joint, PA mobilization of C5 to T1, soft tissue massage of the shoulder, posture correction with tape, stretching and strengthening of the shoulder) Group 2 (n = 61): placebo (sham ultrasound)	11 wk	Average pain on movement (11-point NPRS)	Pre-post differences within groups: group 1, 2.1 ± 2.6 (P<.001); group 2, 1.3 ± 2.2 (P<.001) Difference between groups, 0.7 (95% CI: −0.1, 1.5)	14/16
				SPADI* (%)	Pre-post differences within groups: group 1, 16.1 ± 17.7 (P<.001); group 2, 12.7 ± 16.3 (P<.001) Difference between groups, 3.6 (95% CI: −2.1, 9.4)	
				SF-36† (%)	Pre-post differences within groups: group 1, 11.7 ± 26.5 (P<.001); group 2, 6.1 ± 17.4 (P<.001) Difference between groups, 5.7 (95% CI: −2.1, 13.6)	
				Participant self-perceived overall change	Relative risk of much better overall change favoring group 1: 1.43 (95% CI: 0.87, 2.34)	
			22 wk	Average pain on movement (11-point NPRS)	Pre-post differences within groups: group 1, 2.6 ± 2.9 (P<.001); group 2, 1.6 ± 2.4 (P<.001) Difference between groups, 0.91 (95% CI: −0.03, 1.7)	
				SPADI* (%)	Pre-post differences within groups: group 1, 22.4 ± 22.0 (P<.001); group 2, 15.6 ± 17.8 (P<.001) Difference between groups, 7.1 (95% CI: 0.3, 13.9)	
				SF-36† (%)	Pre-post differences within groups: group 1, 10.8 ± 25.0 (P<.001); group 2, 4.7 ± 22.3 (P<.001) Difference between groups, 6.3 (95% CI: −2.0, 14.5)	
				Participant self-perceived overall change	Relative risk of much better overall change favoring group 1: 1.39 (95% CI: 0.94, 2.03)	

Table continues on page 340.

ure, and 5 trials used functional changes.[2,4,27,28,44] Ten[1,2,6,11,27,28,35,37,42,44] of the 11 RCTs (n = 406) provided results and were pooled to evaluate the efficacy of MT for pain relief. Pooled results demonstrated a significant effect in favor of the MT inter-

TABLE 3 Characteristics of the Included Studies for the Efficacy of MT Combined With Other Types of Interventions Compared With Multimodal Interventions (continued)

Study	Participants	Interventions	Follow-up Period	Outcome Measure	Main Results	Risk-of-Bias Score
Çitaker et al[10]	n = 40; proportion not reported; mean ± SD age, 54.1 ± 13.3 y Diagnosis: patient with prior diagnosis of RC tendinopathy made clinically and radiologically	Group 1 (n = 20): MT (mobilization) and standard care Group 2 (n = 20): PNF and standard care (hot packs and strengthening and pendulum exercises)	Not reported	Pain (at night and in the day, with and without motion) (10-cm VAS)	Statistically significant differences within both groups ($P<.005$) No statistically significant differences between groups ($P\geq.05$)	6/16
				ROM (flexion, abduction) (deg)	Statistically significant differences within both groups ($P<.001$) No statistically significant differences between groups ($P\geq.05$)	
				UCLA‡ (0-35)	Pre-post differences within groups: group 1, 16.6 ($P = .0001$); group 2, 14.1 ($P = .0001$) No statistically significant differences between groups ($P\geq.05$)	
Djordjevic et al[12]	n = 20; 7 male, 13 female; mean ± SD age, 53.0 ± 8.6 y Diagnosis: combination of positive impingement tests: Neer, Hawkins-Kennedy, speed, empty can	Group 1 (n = 10): MT (mobilization with movement) and Kinesio Taping Group 2 (n = 10): supervised exercise program (pain-free active ROM and strengthening of the shoulder)	10 d	Pain-free flexion (deg)	Pre-post differences within groups: group 1, 113.0 ± 11.1; group 2, 17.0 ± 8.3 Difference between groups, 96.0 ± 4.4 ($P = .000$)	11/16
				Pain-free abduction (deg)	Pre-post differences within groups: group 1, 117.0 ± 27.5; group 2, 14.5 ± 21.2 Difference between groups, 102.5 ± 34.8 ($P = .000$)	
Heredia-Rizo et al[22]	n = 22; 13 male, 9 female; mean ± SD age, 58 ± 10.8 y Diagnosis: at least 2 positive impingement tests out of 3: Neer, Jobe, Yergason	Group 1 (n = 11): MT (cervical, thoracic, and GH mobilization; soft tissue mobilization of the shoulder girdle) and electrotherapy Group 2 (n = 11): electrotherapy (laser, ultrasound, TENS) and exercises (passive, active, active assisted mobilization; PNF; proprioceptive exercises; pendular movement)	3 wk	DASH§ (%)	Pre-post differences within groups: group 1, 18.9 (95% CI: 10.9, 26.9; $P = .001$); group 2, 10.9 (95% CI: 0.04, 21.7; $P = .06$) Difference between groups, 8.07 ± 18.31 ($P = .184$)	10/16
				Active ROM in abduction (deg)	Pre-post differences within groups: group 1, 32.5 (95% CI: 16.6, 48.35); group 2, 10.9 (95% CI: 9.7, 28.0) Difference between groups, 21.6 ± 25.1 ($P = .120$)	

Table continues on page 341.

vention, either when used alone or when used in conjunction with another intervention (10-cm VAS mean difference, 1.2; 95% CI: 0.8, 1.6). This effect is small but could be considered clinically important (**FIGURE 4**).[45]

For the 5 RCTs (n = 206) using functional outcome measures, pooling of the results was attempted, but significant

TABLE 3 Characteristics of the Included Studies for the Efficacy of MT Combined With Other Types of Interventions Compared With Multimodal Interventions (continued)

Study	Participants	Interventions	Follow-up Period	Outcome Measure	Main Results	Risk-of-Bias Score
Winters et al[53,54]	n = 172; 76 male, 96 female; mean ± SD age, 49.3 ± 12.9 y Diagnosis: shoulder pain, limited shoulder ROM	Group 1 (n = 61): MT (mobilization and manipulation of the cervical spine, upper thoracic spine, upper ribs, AC joint, and GH joint) Group 2 (n = 64): classic physical therapy (exercises, massage, and physical-agent applications) Group 3 (n = 47): corticosteroid injections	11 wk	Shoulder pain questionnaire (0-28)	Statistically significant differences within all groups (P<.001) No statistical test was performed between groups	5/16
				Perception of being cured	Statistically significant differences within all groups (P<.001) No statistical test was performed between groups	
				Duration of complaints (wk)	Statistically significant differences between groups favoring group 3 over groups 1 and 2 (P<.001) Statistically significant difference between groups favoring group 1 over group 2 (P<.001)	
				Recurrence of complaints by week 11 (% of patients)	Group 1, 8.6%; group 2, 14.3%; group 3, 17.9% No statistical test was performed between groups	
	n = 130	Group 1, n = 44 Group 2, n = 48 Group 3, n = 38	2-3 y	Current or previous complaints	No statistically significant differences between groups (P≥.05)	
				Limitation in activities of daily living	No statistically significant differences between groups (P≥.05)	
				Perception of being cured	No statistically significant differences between groups (P≥.05)	

Table continues on page 342.

heterogeneity was present (chi-square P<.00001, I^2 = 93%). Therefore, the results from these trials are presented in the following sections, depending on the MT intervention under study and the comparators.[2,4,27,28,44]

Secondary Analyses

MT Alone Compared With a Placebo Four clinical trials assessed the efficacy of MT compared with a placebo to address pain.[1,35,37,44] Interventions consisted of shoulder girdle and cervical spine mobilization and manipulations. Results of these 4 trials (n = 175) were pooled into a meta-analysis and revealed a significant effect in favor of MT (10-cm VAS mean difference, 1.0; 95% CI: 0.6, 1.4) (**FIGURE 5**). The magnitude of the treatment effect is small but could be considered clinically important.[45]

Only 1 RCT (n = 39) measured function as an outcome measure. Significant differences were observed in the change on the Constant-Murley score (CMS) in favor of the MT group compared to no intervention (CMS mean ± SD difference, 6.1% ± 2.9%; P<.016) and to sham MT (CMS mean ± SD difference, 1.9% ± 0.92%; P<.016).[44]

Three trials (n = 123) assessed the efficacy of MT on active shoulder ROM, but results were not pooled into a meta-analysis because of high heterogeneity (chi-square P = .010, I^2 = 74%).[1,44,48] Results from the trial by Teys et al[48] revealed

TABLE 3 Characteristics of the Included Studies for the Efficacy of MT Combined With Other Types of Interventions Compared With Multimodal Interventions (continued)

Study	Participants	Interventions	Follow-up Period	Outcome Measure	Main Results	Risk-of-Bias Score
van Rensburg and Atkins[52]	n = 9; 6 male, 3 female; mean age, 57.6 y Diagnosis: 2 of 3 positive tests: Hawkins-Kennedy, Neer, painful arc test	Group 1 (n = 6): MT (manipulation of the thoracic spine plus regular MT at the shoulder girdle) and exercises Group 2 (n = 3): regular MT at the shoulder girdle and exercises (active or passive mobilization of GH joint and transverse frictions to the RC, strengthening of the RC and lower trapezius)	6 wk	DASH[§] (%)	Pre-post differences within groups: group 1, 22.4 ± 1.9; group 2, 21.4 ± 5.5 Difference between groups, 1.0 ± 5.8 No statistical test was performed within and between groups	7/16
				Active ROM in abduction (deg)	Pre-post differences within groups: group 1, 42.1 ± 12.2; group 2, 52.5 ± 13.0 Difference between groups, −9.3 ± 9.0 No statistical test was performed within and between groups	
				Active ROM in flexion (deg)	Pre-post differences within groups: group 1, 30.5 ± 7.4; group 2, 35.0 ± 12.2 Difference between groups, −4.5 ± 7.7 No statistical test was performed within and between groups	

Abbreviations: AC, acromioclavicular; AP, anteroposterior; CI, confidence interval; DASH, Disabilities of the Arm, Shoulder and Hand questionnaire; GH, glenohumeral; MT, manual therapy; NPRS, numeric pain-rating scale; PA, posteroanterior; PNF, proprioceptive neuromuscular facilitation; pre-post, preintervention to postintervention; RC, rotator cuff; ROM, range of motion; SF-36, Medical Outcomes Study 36-Item Short-Form Health Survey; SPADI, Shoulder Pain and Disability Index; TENS, transcutaneous electrical nerve stimulation; UCLA, University of California at Los Angeles shoulder score; VAS, visual analog scale.
**Self-assessment of symptoms and function of the shoulder. Higher scores indicate a greater level of disability.*
†Patient-reported survey of patient health. Higher scores indicate a greater level of function.
‡Assesses pain, function, active flexion, flexion strength, patient satisfaction. Higher scores indicate a greater level of function.
§Self-reported disability questionnaire. Higher scores indicate a greater level of disability.

that MT is effective in increasing pain-free abduction in the scapular plane immediately after the intervention (MWM) compared with sham MT (mean difference, 9.0°; 95% CI: 4.3°, 15.6°). Another trial observed a significant immediate increase in active shoulder flexion and abduction in the MT group (flexion mean ± SD difference, 7.6° ± 2.5° and abduction mean ± SD difference, 6.1° ± 2.9°; $P<.016$) compared with the sham MT group.[44] However, the third trial, by Atkinson et al,[1] reported no significant differences in ROM changes between the MT and the placebo groups at 2 weeks (flexion mean ± SD difference, 3.2° ± 1.5° and abduction mean ± SD difference, 11.3° ± 1.9°; $P\geq.05$).

Efficacy of Adding MT to an Exercise Program or to a Multimodal Rehabilitation Program With Exercises Seven trials observed the effects on pain of MT and exercises compared with exercises alone. Five trials[2,6,27,28,42] provided results that were pooled into a meta-analysis. The trial by Conroy and Hayes[11] was removed from these analyses because of its statistically significant heterogeneity (chi-square $P = .02$, $I^2 = 64\%$), and the results of the trial by Senbursa et al[43] were not pooled with the other studies because of missing data. For the remaining 5 studies (n = 226), a significant difference was observed for the addition of MT to exercises for overall pain reduction at 4 weeks (10-cm VAS mean difference, 1.0; 95% CI: 0.7, 1.4) (**FIGURE 6**). Although the treatment effect is small, it could be clinically important.[45]

The 2 trials that were not pooled reported conflicting results. Senbursa et al[43] reported no significant differences for MWM added to an exercise program for overall pain at 4 and 12 weeks (exact results not reported; $P\geq.05$). The RCT by

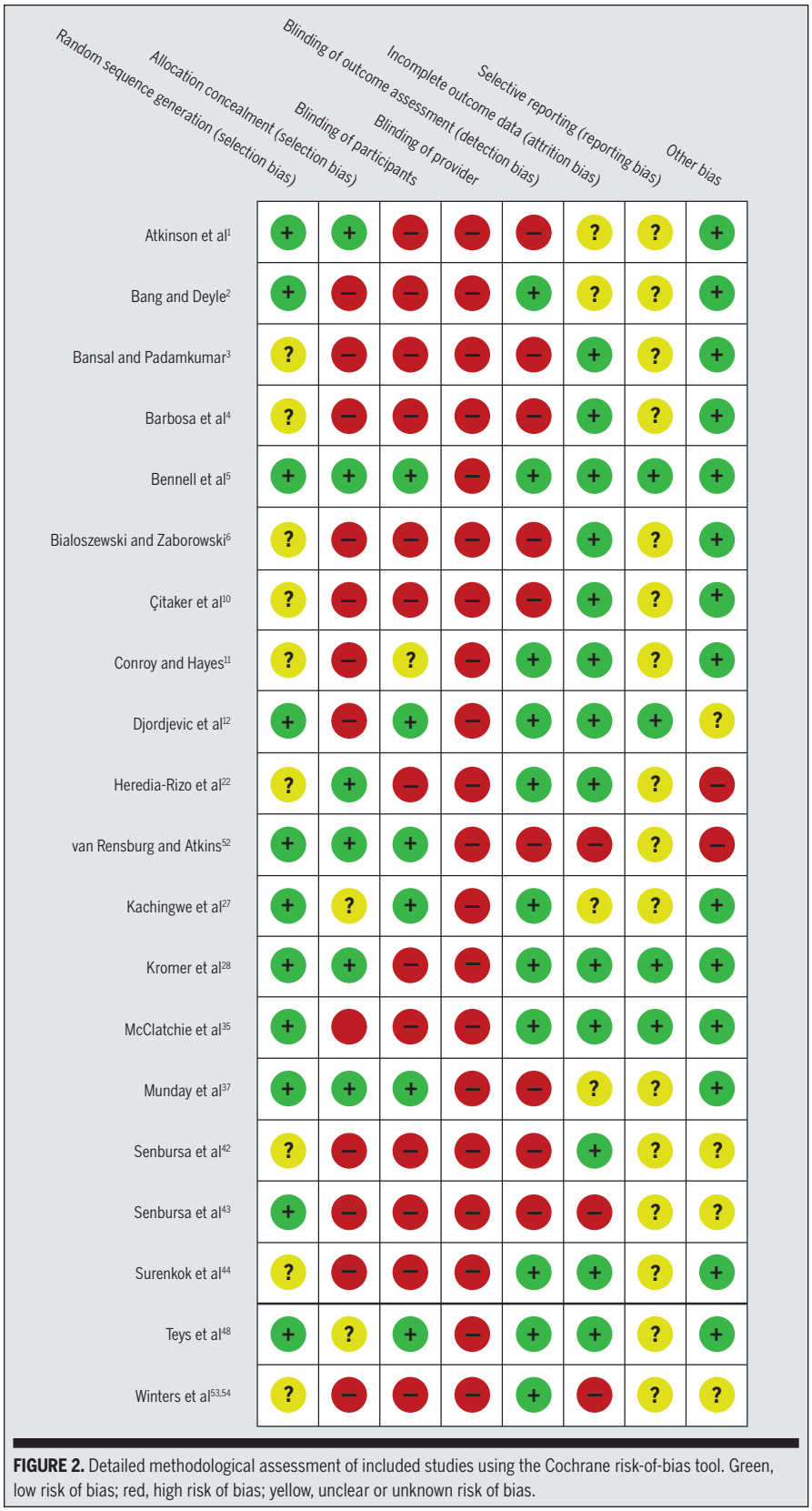


FIGURE 2. Detailed methodological assessment of included studies using the Cochrane risk-of-bias tool. Green, low risk of bias; red, high risk of bias; yellow, unclear or unknown risk of bias.

Conroy and Hayes[11] compared a standard rehabilitation intervention (hot pack, soft tissue mobilization, patient education, and stretching and strengthening exercises) with and without the addition of MT (glenohumeral joint mobilizations). The authors observed statistically and clinically important differences in maximum pain at 4 weeks (10-cm VAS mean difference, 3.2; $P = .008$; SD not reported) and in pain on the subacromial compression test (10-cm VAS mean difference, 2.2; $P = .032$; SD not reported) favoring the MT group.[45]

Six trials (n = 173) observed long-term functional outcomes of adding MT to an exercise program, but trials could not be pooled into a meta-analysis because of high heterogeneity (chi-square $P<.00001$, $I^2 = 95\%$). Four trials[2,4,42,43] concluded that there was a significant effect in favor of adding MT to an exercise program, and 2 trials[27,28] did not observe such benefits. In all trials, soft tissue and joint mobilizations of the shoulder girdle were added to an exercise program. The trials by Senbursa et al[42,43] observed a significant between-group difference at 12 weeks on the Neer functional score (exact results not reported; $P<.05$) and on the Modified American Shoulder and Elbow Surgeons Standardized Shoulder Assessment Form score at 4 and 12 weeks (exact results not reported; $P<.05$). In another trial,[2] the authors observed a significant difference at 2 months on a functional questionnaire (0-45) (mean ± SD difference, 2.1 ± 0.48; $P = .005$). Barbosa et al[4] also reported a significant and clinically important difference on the Disabilities of the Arm, Shoulder and Hand outcome measure (mean ± SD difference, 20.1% ± 18.1%; $P = .021$), and also a significant difference in the CMS scores (mean ± SD difference, 7.1% ± 15.4%; $P = .004$), between groups.[41] Finally, no significant differences between groups on the Shoulder Pain and Disability Index (SPADI) scores were observed after 6 weeks in the trial by Kachingwe et al[27] ($P \geq .05$) or in the trial by Kromer et al,[28] either at 5 weeks (SPADI mean differ-

TABLE 4 Summary of Evidence for the Efficacy of Manual Therapy

Treatment	Studies, n	Total Participants, n	Outcome Measures and Pooled Effect	Conclusions	Quality of Evidence
Overall effect of MT either alone or in conjunction with another intervention compared with placebo or another intervention	10	406	Pain (10-cm VAS) Pooled effect: 1.2 (95% CI: 0.8, 1.6), favoring MT	Significant effect that could be clinically important	Low to moderate
MT alone compared with a placebo	4	175	Pain (10-cm VAS) Pooled effect: 1.0 (95% CI: 0.6, 1.4), favoring MT	Significant effect that could be clinically important	Low
	1	39	Function	Unclear if MT has an effect on function	
	2	99	Strength and ROM	Contradictory results	
Adding an MT intervention to exercises or to a multimodal rehabilitation program with exercises	5	226	Pain (10-cm VAS) Pooled effect: 1.0 (95% CI: 0.7, 1.4), favoring MT added to exercises	Significant effect that could be clinically important	Low
	2	91	Pain (10-cm VAS)		
	6	287	Function	Unclear if MT has an effect on function	
	2	88	ROM pooled effect: −6.1° (95% CI: −20.6°, 8.4°)	MT does not improve ROM	
MT combined with other types of interventions compared with multimodal interventions	6	414	Pain, function, ROM	Contradictory results	Low

Abbreviations: CI, confidence interval; MT, manual therapy; ROM, range of motion; VAS, visual analog scale.

ence, 1.8%; 95% CI: −5.7%, 9.2%) or at 12 weeks (SPADI mean difference, 0.4%; 95% CI: −5.1%, 6.0%).

Four trials (n = 151) investigated changes in shoulder ROM when MT was added to an exercise program, but only data from 2 of the trials[6,11] were pooled, because the results of the other 2 trials[42,43] were incompletely reported. Pooled results demonstrated that there were no significant differences between groups when MT was added to an exercise program for overall ROM (mean difference, −6.1°; 95% CI: −20.6°, 8.4°) (**FIGURE 7**). The 2 remaining trials compared changes in ROM (flexion, abduction, external rotation) when manipulation and mobilization of the shoulder girdle and spine were added to an exercise program consisting of shoulder stretching and strengthening.[42,43] Although the first trial demonstrated a significant intergroup difference at 4 weeks in favor of the MT group (exact results not reported; $P<.05$), the second study did not report such a difference at 4 and 12 weeks (exact results not reported; $P\geq.05$).

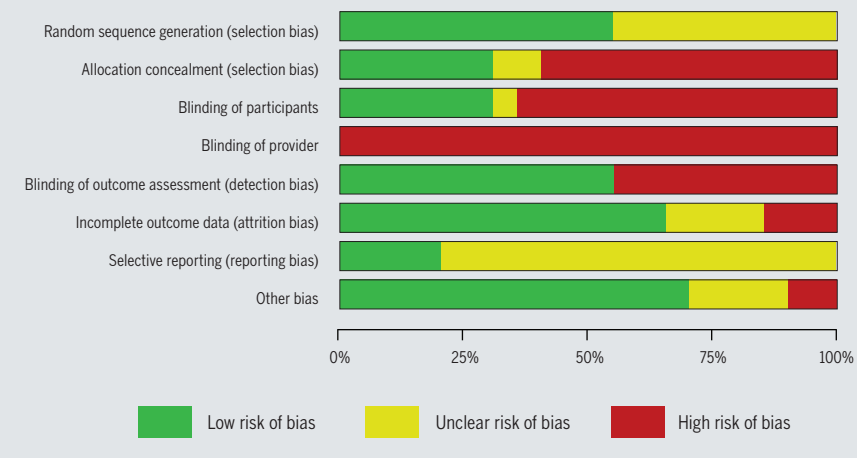
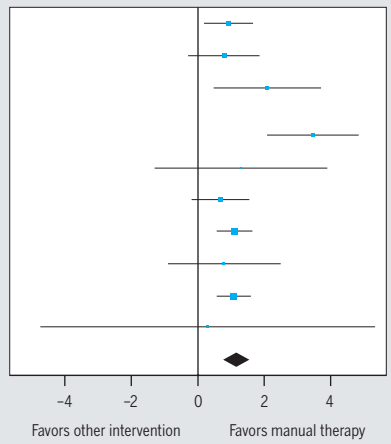


FIGURE 3. Risk-of-bias graph: review authors' judgments about each risk-of-bias item, presented as percentages across all included studies.

Efficacy of MT Alone Compared With Another Intervention Two studies compared MT (mobilizations and manipulations of the shoulder girdle) to corticosteroid injections and to standard care (exercises, massage, and physical-agent applications).[53,54] The mean duration of symptoms in the MT group was significantly longer than in the corticosteroid injection group (exact results not reported; $P<.001$), but significantly shorter compared with the standard

Manual Therapy Alone Versus Manual Therapy With Other Intervention: Pain*

Study	Manual Therapy Mean ± SD	Manual Therapy Total, n	Other Intervention Mean ± SD	Other Intervention Total, n	Weight	Mean Difference IV, Random (95% Confidence Interval)
Atkinson et al[1]	1.99 ± 1.39	30	1.06 ± 1.47	30	15.7%	0.93 (0.21, 1.65)
Bang and Deyle[2]	3.0 ± 1.7	27	2.2 ± 2.1	23	9.9%	0.80 (−0.27, 1.87)
Bialoszewski and Zaborowski[6]	5.3 ± 2.9	15	3.2 ± 1.3	15	5.3%	2.10 (0.49, 3.71)
Conroy and Hayes[11]	3.7 ± 1.1	7	0.22 ± 1.5	7	6.8%	3.48 (2.10, 4.86)
Kachingwe et al[27]	2.5 ± 0.61	9	1.2 ± 3.7	8	2.3%	1.30 (−1.29, 3.89)
Kromer et al[28]	2.3 ± 1.8	46	1.6 ± 2.3	44	13.1%	0.70 (−0.16, 1.56)
McClatchie et al[35]	1.3 ± 1.1	21	0.2 ± 0.6	21	20.3%	1.10 (0.56, 1.64)
Munday et al[37]	2.7 ± 2.4	15	1.9 ± 2.3	15	4.9%	0.80 (−0.88, 2.48)
Senbursa et al[42]	4.7 ± 0.83	15	3.6 ± 0.58	15	20.9%	1.10 (0.59, 1.61)
Surenkok et al[44]	0.46 ± 9.2	13	0.16 ± 1.3	30	0.6%	0.30 (−4.72, 5.32)
Total		198		208	100.0%	1.19 (0.78, 1.60)

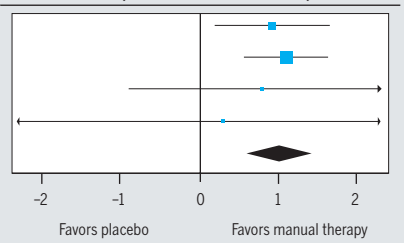


Abbreviation: IV, independent variable.
**Heterogeneity: $\tau^2 = 0.14$, $\chi^2 = 14.49$, $df = 9$ ($P = .11$), $I^2 = 38\%$. Test for overall effect: $Z = 5.73$ ($P<.00001$).*

FIGURE 4. Forest plot of pooled studies comparing manual therapy alone to manual therapy in conjunction with another intervention for change in pain. The squares are mean difference and the diamonds are pooled mean difference with 95% confidence interval.

Manual Therapy Versus Placebo: Pain*

Study	Manual Therapy Mean ± SD	Manual Therapy Total, n	Placebo Mean ± SD	Placebo Total, n	Weight	Mean Difference IV, Random (95% Confidence Interval)
Atkinson et al[1]	1.99 ± 1.39	30	1.06 ± 1.47	30	33.0%	0.93 (0.21, 1.65)
McClatchie et al[35]	1.3 ± 1.1	21	0.2 ± 0.6	21	60.2%	1.10 (0.56, 1.64)
Munday et al[37]	2.7 ± 2.4	15	1.9 ± 2.3	15	6.1%	0.80 (−0.88, 2.48)
Surenkok et al[44]	0.46 ± 9.2	13	0.16 ± 1.3	30	0.7%	0.30 (−4.72, 5.32)
Total		79		96	100.0%	1.02 (0.60, 1.44)



Abbreviation: IV, independent variable.
**Heterogeneity: $\tau^2 = 0.00$, $\chi^2 = 0.29$, $df = 3$ ($P = .96$), $I^2 = 0\%$. Test for overall effect: $Z = 4.81$ ($P<.00001$).*

FIGURE 5. Forest plot of pooled studies comparing manual therapy to placebo for change in pain. The squares are mean difference and the diamonds are pooled mean difference with 95% confidence interval.

care group (exact results not reported; $P<.001$).[54] At 2 to 3 years, there were no differences between groups in terms of symptoms, functional limitations, and perception of being cured.[53]

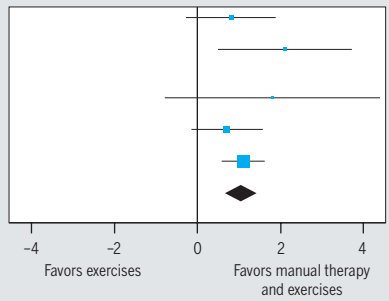
Another RCT compared supraspinatus deep friction massage to therapeutic ultrasound.[3] Results showed that while both groups improved at 10 days, the MT group had significantly lower pain at rest (10-cm VAS mean difference, 0.85; $P = .014$; SD not reported) and significantly greater active abduction ROM than the ultrasound group (mean difference, 6.7°; $P = .023$; SD not reported). However, those changes were not clinically important.

Efficacy of MT Combined With Other Types of Interventions Compared With a Placebo or a Multimodal Intervention Four trials (n = 202) assessed the efficacy of MT combined with other interventions compared with a different multimodal intervention for treating RC tendinopathy.[5,10,12,22] High heterogeneity between trials prevented the pooling of data for pain (chi-square $P = .06$, $I^2>72\%$) and function (chi-square $P = .02$, $I^2>76\%$); therefore, only a qualitative analysis was performed.

Bennell and colleagues[5] compared MT (soft tissue massage and mobilizations of the shoulder girdle and spine) in conjunction with an exercise program to a sham ultrasound intervention. These authors observed no significant differences at 11 weeks (10-cm VAS mean difference, 0.70; 95% CI: −0.10, 1.5) or at

Manual Therapy and Exercises Versus Exercises Alone: Pain*

Study	Manual Therapy and Exercises Mean ± SD	Total, n	Exercises Alone Mean ± SD	Total, n	Weight	Mean Difference IV, Random (95% Confidence Interval)
Bang and Deyle[2]	3 ± 1.7	27	2.2 ± 2.1	23	13.2%	0.80 (−0.27, 1.87)
Bialoszewski and Zaborowski[6]	5.3 ± 2.9	15	3.2 ± 1.3	15	5.9%	2.10 (0.49, 3.71)
Kachingwe et al[27]	3 ± 0.7	18	1.2 ± 3.7	8	2.3%	1.80 (−0.78, 4.38)
Kromer et al[28]	2.3 ± 1.8	46	1.6 ± 2.3	44	20.7%	0.70 (−0.16, 1.56)
Senbursa et al[42]	4.7 ± 0.83	15	3.6 ± 0.58	15	57.9%	1.10 (0.59, 1.61)
Total		121		105	100.0%	1.05 (0.66, 1.44)

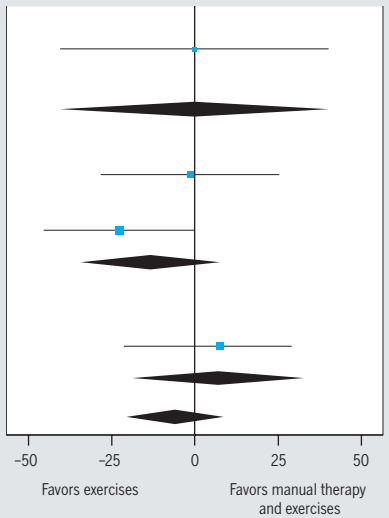


Abbreviation: IV, independent variable.
**Heterogeneity: $\tau^2 = 0.00$, $\chi^2 = 2.85$, $df = 4$ ($P = .58$), $I^2 = 0\%$. Test for overall effect: $Z = 5.29$ ($P<.00001$).*

FIGURE 6. Forest plot of pooled studies comparing manual therapy and exercises to exercises alone for change in pain. The squares are mean difference and the diamonds are pooled mean difference with 95% confidence interval.

Manual Therapy and Exercises Versus Exercises Alone: Shoulder Range of Motion

Subgroup/Study	Manual Therapy and Exercises Mean ± SD	Total, n	Exercises Alone Mean ± SD	Total, n	Weight	Mean Difference IV, Random (95% Confidence Interval)
Flexion*						
Bialoszewski and Zaborowski[6]	131.7 ± 73.3	15	131.8 ± 30.8	15	12.1%	−0.10 (−40.34, 40.14)
Subtotal		15		15	12.1%	−0.10 (−40.34, 40.14)
Abduction†						
Bialoszewski and Zaborowski[6]	120.2 ± 43.3	15	121.7 ± 30.2	15	25.5%	−1.50 (−28.22, 25.22)
Conroy and Hayes[11]	125.71 ± 26.21	7	148.57 ± 15.47	7	34.1%	−22.86 (−45.41, −0.31)
Subtotal		22		22	59.6%	−13.43 (−34.22, 7.36)
Abduction in the scapular plane‡						
Conroy and Hayes[11]	141.29 ± 19.54	7	133.86 ± 27.82	7	28.3%	7.43 (−17.75, 32.61)
Subtotal		7		7	28.3%	7.43 (−17.75, 32.61)
Tota§		44		44	100.0%	−6.08 (−20.56, 8.40)



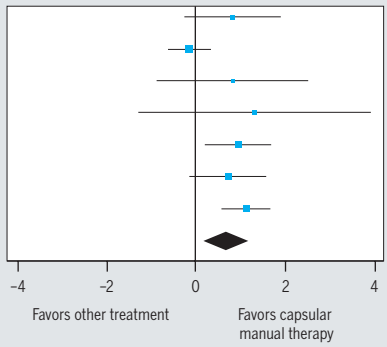
Abbreviation: IV, independent variable.
**Heterogeneity: Not applicable. Test for overall effect: $Z = 0.00$ ($P = 1.00$).*
†Heterogeneity: $\tau^2 = 69.06$, $\chi^2 = 1.43$, $df = 1$ ($P = .23$), $I^2 = 30\%$. Test for overall effect: $Z = 1.27$ ($P = .21$).
‡Heterogeneity: Not applicable. Test for overall effect: $Z = 0.58$ ($P = .56$).
§Heterogeneity: $\tau^2 = 27.95$, $\chi^2 = 3.43$, $df = 3$ ($P = .33$), $I^2 = 13\%$. Test for overall effect: $Z = 0.82$ ($P = .41$). Test for subgroup differences: $\chi^2 = 1.62$, $df = 2$ ($P = .45$), $I^2 = 0\%$.

FIGURE 7. Forest plot of pooled studies comparing manual therapy and exercises to exercises alone for change in shoulder range of motion. The squares are mean difference and the diamonds are pooled mean difference with 95% confidence interval.

22 weeks (10-cm VAS mean difference, 0.91; 95% CI: −0.03, 1.7) for pain with movement. Çitaker et al[10] also observed no significant changes in pain during movement when comparing shoulder mobilizations and standard care (hot pack and strengthening exercises) to proprioceptive neuromuscular facilitation and the same standard care program

Capsular Mobilization/Manipulation Versus Placebo or in Addition to Another Intervention: Pain*

Study	Capsular Mobilization or Manipulation Mean ± SD	Total, n	Other Treatment Mean ± SD	Total, n	Weight	Mean Difference IV, Random (95% Confidence Interval)
Bang and Deyle[2]	3 ± 1.7	27	2.2 ± 2.1	23	12.3%	0.80 (−0.27, 1.87)
Çitaker et al[10]	5.75 ± 0.76	20	5.9 ± 0.77	20	22.5%	−0.15 (−0.62, 0.32)
Munday et al[37]	2.7 ± 2.4	15	1.9 ± 2.3	15	6.7%	0.80 (−0.88, 2.48)
Kachingwe et al[27]	2.5 ± 0.61	9	1.2 ± 3.7	8	3.3%	1.30 (−1.29, 3.89)
Atkinson et al[1]	1.99 ± 1.39	30	1.06 ± 1.47	30	17.9%	0.93 (0.21, 1.65)
Kromer et al[28]	2.3 ± 1.8	46	1.6 ± 2.3	44	15.5%	0.70 (−0.16, 1.56)
McClatchie et al[35]	1.3 ± 1.1	21	0.2 ± 0.6	21	21.5%	1.10 (0.56, 1.64)
Total		168		161	100.0%	0.67 (0.17, 1.17)



Abbreviation: IV, independent variable.
**Heterogeneity: $\tau^2 = 0.22$, $\chi^2 = 14.20$, $df = 6$ ($P = .03$), $I^2 = 58\%$. Test for overall effect: $Z = 2.65$ ($P = .008$).*

FIGURE 8. Forest plot of pooled studies comparing joint (capsular) mobilization or manipulation to a placebo or in addition to another intervention for change in pain. The squares are mean difference and the diamonds are pooled mean difference with 95% confidence interval.

(10-cm VAS mean ± SD difference, −0.15 ± 4.8; $P \geq .05$).

In the trial by Bennell et al,[5] between-group differences in functional changes, as evaluated with the SPADI, were not significant at 11 weeks (mean difference, 3.6%; 95% CI: −2.1%, 9.4%) but were significant at 22 weeks in favor of the MT group (mean difference, 7.1%; 95% CI: 0.3%, 13.9%). Results from Çitaker et al[10] showed no significant differences in the University of California at Los Angeles shoulder score ($P \geq .05$). Heredia-Rizo et al[22] found no significant differences in function, as measured with the Disabilities of the Arm, Shoulder and Hand questionnaire (mean ± SD difference, 8.1% ± 18.3%; $P = .184$) at 3 weeks, when comparing MT (joint and soft tissue mobilizations of the shoulder girdle and spine) combined with electrotherapy to a group receiving electrotherapy and exercises.

Çitaker et al[10] and Heredia-Rizo et al[22] measured active ROM in abduction, and their results demonstrated no difference between both groups ($P \geq .05$ and $P = .12$, respectively). However, Djordjevic and colleagues[12] observed significant differences after 10 days in pain-free flexion and abduction that favored the MT intervention (MWM) combined with shoulder Kinesio Taping compared with a supervised exercise program ($P < .001$).

Effect of Different Types of MT A subgroup analysis of the efficacy of different types of MT for pain was also performed. Seven studies[1,2,10,27,28,35,37] in which interventions were only joint (capsular) mobilizations or manipulations (n = 329) compared with a placebo or in addition to another intervention were pooled into a meta-analysis. The resulting pooled effect showed a significant difference in favor of MT (10-cm VAS mean difference, 0.7; 95% CI: 0.2, 1.2), but this effect may not be clinically important (**FIGURE 8**).[45] Significant heterogeneity prevented us from pooling clinical trials using other types of MT interventions (chi-square $P < .10$, $I^2 > 60\%$).

Effect of Adding a Thoracic Manipulation to MT and Exercises One exploratory trial, not included in any of the current meta-analyses, that included only 9 participants assessed the efficacy of adding a thoracic spinal manipulation to active and passive glenohumeral joint mobilizations, transverse frictions to the RC tendons, and shoulder-strengthening exercises.[52] No statistical analyses were performed within and between groups, but the thoracic manipulation group tended to require fewer sessions to feel cured.

DISCUSSION

The aim of this systematic review was to assess the efficacy of MT for RC tendinopathy. Twenty-one RCTs were included, with risk of bias established as high to moderate.

Primary Findings

Based on our primary meta-analysis of 10 RCTs, there is low to moderate evidence that, overall, MT either alone or in conjunction with other modalities may be effective in reducing pain (**TABLE 4**). While pooled results demonstrate a statistically significant difference of 1.2 (95% CI: 0.8, 1.6) on a 10-cm scale, the point estimate is slightly below the previously reported minimal clinically important difference (MCID) of 1.4 cm.[45] However, this MCID is within the 95% CI, and therefore we cannot exclude the possibility that MT may have a clinically important therapeutic effect.[45] It is also important to highlight that this MCID has been defined for change occurring after 6 weeks of treatment, which does not reflect the exact time outcomes were

measured in the studies included in our meta-analysis.

Secondary Findings

Secondary analyses included research designs that specify the effects attributable to MT, which provide evidence of efficacy. Conclusions from those secondary analyses were consistent with those of our primary analysis and led to similar conclusions. Compared with a placebo, MT alone significantly reduces overall pain (**TABLE 4**). Similar to the results of the primary analysis, while the point estimate of the pooled treatment effect is slightly below the MCID, the MCID is within the limits of the 95% CI of the treatment effect.[45] Therefore, we cannot rule out the possibility that, although the treatment effect is small, it may be clinically important.

One study with moderate risk of bias concluded that MT significantly increases function, as measured with the CMS, compared with a placebo; however, the difference between the groups was small (mean ± SD, 2.0% ± 12%) and not considered clinically important.[44] Two trials assessed the effect of MT compared with a placebo for changes in shoulder ROM, with only 1 of the trials presenting a significant difference favoring MT, but, again, the differences were small (3°-7°); a third trial assessed pain-free shoulder ROM and found a significant difference favoring the MT group, which could be clinically important.[1,44,48] Therefore, it is unclear whether MT results in greater improvement in ROM when compared with a placebo, but it could be superior for improving pain-free ROM.

There is low evidence that adding MT to an exercise program can improve pain but may not lead to any additional improvement in function. Results from 7 trials[2,6,11,27,28,42,43] of low to moderate quality, of which 5 were pooled into a meta-analysis,[2,6,27,28,42] suggest a statistically significant decrease in pain that could be considered clinically important.[45] From a qualitative analysis of 6 low- to moderate-quality RCTs that assessed functional changes, a positive trend in functional improvement was observed. Results from 4 of the 6 RCTs reported a significant difference in favor of MT, but, again, for 3 of these RCTs the magnitude of the treatment effect was generally small, and it is unclear if the magnitude of change is clinically important. Because in these studies the results were only partially reported and the outcome measures of function were not formally validated, the strength of our recommendation is limited. Changes in shoulder ROM were assessed in 4 trials, and results from the pooled data of 2 RCTs, considered together with those of a third RCT, demonstrated no difference between groups; thus, adding MT to an exercise program does not seem to help further improve shoulder ROM.[6,11,42,43]

Six trials compared MT combined with other interventions to another multimodal intervention or to a placebo,[3,5,10,12,22,54] and the results from these studies generally suggest that adding MT to a multimodal intervention does not improve pain, function, or shoulder ROM. However, because of the heterogeneous nature of the studies, we are unable to make formal conclusions on this topic.

In our review, MT interventions were varied, and therefore it could be argued that the effect may differ depending on the technique used. A secondary analysis that included only clinical trials using joint (capsular) mobilizations and manipulations had slightly different results from those from our primary meta-analysis, suggesting that, while a statistically significant effect was observed, the effect may not be clinically important. Manual therapy interventions in the present review also varied in terms of intensity and duration. This is a factor that has the potential to affect the overall expected treatment effect, but we could not account for this factor in our analyses because the details of the MT interventions regarding intensity and duration were, in general, poorly described. Another factor that may limit the efficacy of MT is the clinical appropriateness of the techniques used. The use of MT may need to be tailored to the specific impairments observed in patients with RC tendinopathy. Two important subgroups of patients who may benefit the most from mobilization and manipulation techniques are patients who have posteroinferior capsular tightness of the glenohumeral joint and those who have decreased cervicothoracic extension. Several studies suggest that in these patients, shoulder kinematics are altered in a manner to promote RC tendinopathy.[14,17,18,21,38,50,51] In the included studies, the type of MT intervention was not based on the participants' impairments, which potentially limited the overall treatment effect observed. Future trials may want to take into account participants' impairments and tailor the MT intervention accordingly.

Our conclusions are somewhat different from those of the other published systematic reviews on the same topic.[7,8,13,15,29,36,49] The 2 most recent systematic reviews on this topic stated that there were inconclusive or conflicting results for the efficacy of MT used alone.[9,25] Our review, which included 5 additional clinical trials, concluded that MT alone or in conjunction with another intervention significantly decreases pain by a small but statistically significant amount, although it is unclear whether this pain reduction is clinically important. However, it is unclear whether MT used alone can improve function. Ho et al[25] specifically concluded that there is no clear evidence of an additional benefit when adding MT to another intervention, whereas we concluded that adding MT to an exercise program results in statistically significant pain decreases; however, these changes were small and may or may not be clinically significant. Until more methodologically sound studies are published on MT, widely accepted interventions such as exercises, which have been proven effective in treating RC tendinopathy, should be preferred.[20,30,32,39]

Strengths and Limitations of the Review

Strengths of this review are the use of 4 important databases, the use of the vali-

dated Cochrane risk-of-bias tool, and the strong interrater agreement in the evaluation of the risk of bias. We are able to make recommendations based on the efficacy of MT for RC tendinopathy, as shown by quantitative and qualitative analyses. Funnel plots were not generated, thus the risk of publication bias was not assessed, which limits the strength of our conclusions.

Unanswered Questions and Future Research

Before more definitive conclusions on the efficacy of MT used alone or combined with exercises can be made, RCTs with high methodological quality and larger sample sizes are required. To be more representative of current clinical practice, RCTs that compare specific MT interventions tailored to subgroups of patients defined by their impairments are also required. To facilitate data synthesis and meta-analyses, we also suggest that standardized and validated diagnostic tests and outcome measures be used in future trials.

CONCLUSION

Based on low- to moderate-level evidence, MT, either used alone or in conjunction with other interventions, significantly reduces pain in individuals with RC tendinopathy, and this effect may or may not be clinically important. Based on low-level evidence, an MT intervention added to an exercise program significantly reduces pain in individuals with RC tendinopathy, and this effect may or may not be clinically important. Based on low-level evidence, it is unclear whether MT can improve function in the treatment of RC tendinopathy. Future methodologically sound studies could possibly modify the present conclusions. ◉

KEY POINTS

FINDINGS: The overall effects of MT and the addition of MT to exercises significantly reduce pain in individuals with RC tendinopathy, and this effect may or may not be clinically important.

IMPLICATIONS: Clinicians should not rely solely on MT to treat RC tendinopathy. Randomized controlled trials that compare MT interventions for specific subgroups of patients with RC tendinopathy are required.

CAUTION: More methodologically sound studies are needed to further support the present conclusions.

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