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Scientific/Clinical Article

Do joint mobilizations assist in the recovery of lateral elbow tendinopathy? A systematic review and meta-analysis

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ABSTRACT

Study Design: Systematic review.
Introduction: No consensus exists as to which are the most effective methods to treat the symptoms associated with lateral elbow tendinopathy (LET). Research has suggested that joint mobilizations may assist in the recovery of patients with LET.
Purpose of the Study: To determine if joint mobilizations are effective in improving pain, grip strength, and disability in adults with LET.
Methods: Searches in 3 databases were performed to identify relevant clinical trials. Reviewers independently extracted data and assessed the methodological quality. Summary measures of quantitative data were extracted or calculated where possible. Appropriate data were pooled for meta-analysis using a random-effects model.
Results: A total of 20 studies met the inclusion criteria; 7 were included in the meta-analysis. Studies were broadly classified into 3 groups: mobilization with movement (MWM), Mill's manipulation, and regional mobilization techniques. Pooled data across all time periods demonstrated a mean effect size of 0.43 (95% confidence interval [CI]: 0.15-0.71) for MWM on improving pain rating, and 0.31 (95% CI: 0.11-0.51) for MWM on improving grip strength, 0.47 (95% CI: 0.11-0.82) for Mill's manipulation on improving pain rating. A mean effect size of −0.01 (95% CI: −0.27 to −0.26) shows Mill's manipulation did not improve pain free grip strength. Functional outcomes varied considerably among studies. Pain, grip strength, and functional outcomes were improved with regional mobilizations.
Conclusion: There is compelling evidence that joint mobilizations have a positive effect on both pain and/or functional grip scores across all time frames compared to control groups in the management of LET.

Introduction

Lateral elbow tendinopathy (LET) is described as a degenerative tendon pathology, characterized by a proliferation of fibroblasts, vascular hyperplasia, and immature collagen fibers.[1] Disagreement exists as to the role of inflammation in LET.[2] However, it is important to recognize the complex pain mechanisms that can be associated with this tissue pathology.[3] Although this is a common condition, especially in athletes and manual workers, its etiology remains poorly understood and is likely multifactorial. A recent systematic review reports the incidence and prevalence of LET as high as 7% and 12.2%, respectively, depending on activity and occupational risk factors present in workers.[4] The prevalence in tennis players has been reported to be even higher, 14%.[5] Yet, the annual incidence of LET in the general population is estimated to be 3%,[6] which is much lower compared to workers or athletes who are exposed to repetitive mechanical stresses.[7] In addition, middle-aged adults between the ages of 45-54 years tend to have the highest incidence of the condition.[8]

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Functional limitations and participation restrictions associated with LET can result in considerable economic costs for those affected, especially when LET becomes chronic.[9,10] Many individuals with severe elbow pain are not able to function optimally, although the precise impact of LET on society is not known. The National Institute for Occupational Safety and Health reports that individuals with LET have a higher rate of sick leave than individuals with other upper extremity disorders.[11] Functional limitations and participation restrictions and the resulting economic impacts are further compounded by high recurrence rates.[3,12,13]

Most health care practitioners, as well as patients, prefer initial conservative management of the condition. Recent high-level evidence suggests that conservative therapy management is a consistently more cost-effective intervention for LET than a single cortisone injection or a combination of therapy and cortisone injection.[14] Previous systematic reviews[15-19] recommend conservative interventions in general but often cannot definitively recommend specific interventions. While a great variety of conservative therapeutic interventions are available, collectively, the authors of these reviews provide some suggestion that joint mobilizations may be effective in alleviating impairments and loss of function related to LET.

A major limitation of the aforementioned systematic reviews is that most of the reviews on LET focus on multiple conservative interventions which often do not allow the opportunity to make definitive quantitative conclusions about a specific intervention. For example, in 2005, Bisset et al[18] were able to pool data of 2 studies[20,21] examining the effect of mobilization with movement (MWM) on pain-free grip strength and pressure pain threshold. The authors found a positive initial effect in favor of elbow joint mobilizations, but the conclusions were limited due to the small sample of studies included.[18] More recently, Olaussen et al[15] investigated treatments relating to physical therapy management of LET compared to cortisone injections. The authors were able to pool data from 2 studies[3,22] related to joint mobilization. However, they only included articles that used cortisone injection as a comparison, which limited the scope of the review.[15]

More specific to joint mobilizations, Hoogvliet et al[16] conducted a systematic review on exercise and joint mobilizations in the management of both medial and lateral epicondylitis. The authors found more compelling evidence to support resisted exercises and moderate evidence to support the analgesic effect of cervical/thoracic mobilizations in conjunction with other therapies when treating LET. There was limited evidence regarding the effectiveness of local joint mobilizations, but the inclusion criteria limited the scope of that review.

The effectiveness of joint mobilizations on patients with LET are often considered in systematic reviews, but their effectiveness has not been considered comprehensively. In addition, since the most recent systematic reviews on conservative interventions for LET, the authors of have noted that additional individual studies have since been published examining the effect of joint mobilization on LET symptoms.[23-25] Therefore, there is a current need for a comprehensive, systematic review of the current literature related to the specific effects of joint mobilizations on symptoms related to LET as well as to further quantitatively analyze and pool data, if possible. A current, quantitative report may provide a more transparent guide for clinicians treating patients with LET. Therefore, the purpose of this systematic review was to determine if joint mobilizations are effective in improving pain, grip strength, and disability in adults with LET.

Methodology

Eligibility criteria

We included control trial studies of adults aged 18 years and older clinically diagnosed with LET, that were written in English, and that scored 5 points or greater on the 11 point Physiotherapy Evidence Database (PEDro) quality assessment scale.[26] We defined joint mobilizations as an intervention to LET that includes either joint mobilizations or joint manipulations to the local region (elbow) or to a distant but related site (cervical spine, thoracic spine, or wrist) provided by one or more health care disciplines including physical therapists, occupational therapists, or chiropractors for the purpose of treating pain, strength deficits, and functional impairments related to LET. Studies on joint mobilization of the spine, shoulder, or lower extremity were excluded if they did not pertain to LET. We also excluded studies where the effectiveness of a manual therapy technique could not be isolated. For example, if manual therapy was included in all groups, that article was excluded. We also excluded case studies, case series, systematic reviews, and clinical practice guidelines from this review.

Information sources and search strategy

A comprehensive English language literature search was performed using the following computerized databases: CINAHL, PubMed, and PEDro up to June 2017. The search strategy was developed initially through the PubMed database using MESH headings and key words and was adapted for the other databases. The full electronic search strategy for PubMed is provided as an example: (((((tendinitis OR tendonitis OR tendinopathy OR tendinosis OR peritendinitis OR enthesopathy) AND elbow AND (mobiliz* OR manipula* OR musculoskeletal manipula*))) OR (Lateral Epicondyl* AND manipulation)) OR (Lateral Epicondyl* AND manual therapy)) OR (("Tennis Elbow"[Mesh]) AND "Musculoskeletal Manipulations"[Mesh]). The only limit applied was for English language articles. Additionally, hand searches were performed from reference lists of reviewed articles and previous systematic reviews.

Study selection

All titles and abstracts were reviewed by 2 reviewers (A.M.L. and J.M.D.) for relevance to the therapeutic management of LET utilizing joint mobilization as an intervention. Full-text articles were obtained for all abstracts that appeared to fulfill inclusion criteria for in-depth review, quality appraisal, and final decision.

Data extraction and analysis

A standardized set of data was extracted for the selected studies. Data collected included study design, sample characteristics, inclusion/exclusion criteria, setting of recruitment, mobilization technique, comparative or control condition(s) studied, and their parameters, treatment frequency, outcome measures, and effects of interventions at short-, mid-, and long-term follow-up. Follow-up time frames were divided into short- ($\leq$3 months or 12 weeks), intermediate- ($>$3 months to $\geq$ 6 months), and long-term ($>$6 months) periods for the purposes of this review, given that studies often varied on the specific duration for follow up. Outcomes related to the purpose of this review, including pain, grip strength, and disability, were of primary interest. Data related to the internal and external validity of each selected study were also retrieved based on the PEDro criteria for quality assessment purposes.

Summary measures of quantitative data including measures of central tendency and variability, standardized mean differences (SMDs), or mean differences (MDs) were extracted or calculated where possible. The summary data were considered to be statistically significant if the 95% confidence interval (CI) did not include 0. These data were interpreted within the context of the study as to a positive or negative sign associated with the SMD or MD to appropriately determine which intervention was favored in any given analysis. According to convention by Cohen,[27] a large effect was considered to be $\geq$ to 0.80, a moderate effect was >0.20 to <0.80, and a small effect was $\leq$0.20.

The majority of data in the individual studies were reported as means and standard deviations (SDs). One study[3] reported data in median and interquartile range and had to be converted into mean and SD to enable pooling of data. Wan et al[28] provide an overview of the details of this conversion technique. The freely available add-in, MetaEasy, was used to calculate effect sizes and heterogeneity within Excel.[29] MetaEasy has been validated and is available for download from this URL (http://www.statanalysis.co.uk/). Forest plots were developed with R.[30] Where data were pooled for meta-analysis, a random-effects model was employed, and the significance of the model was reported. Heterogeneity was reported with Cochran's Q and I^2 values where low, moderate, and high heterogeneity values corresponded with 25%, 50%, and 75%, respectively.[31]

Quality assessment

Independent reviewer pairs appraised eligible studies for methodological quality using the 11-item PEDro rating scale which has previously demonstrated good interrater reliability[26,32] and has demonstrated strong convergent validity with the Cochrane Risk of Bias Tool summary score 0.83 (95% CI: 0.76-0.88).[32] Each criterion was rated as "met" if that item was clearly outlined in the article text or as "not met" if the criterion was clearly not filled or if it was not clearly described in the manuscript. Published operational definitions of the PEDro criteria were used for scoring.[26] All "met" criteria were given a score of 1 point, and all "not met" criteria were given a score of 0. A total score of the methodological quality of each article was derived by a sum of all criteria scores (0-11); the maximum score of 11 indicated the highest quality. Any discrepancies were resolved by an independent reviewer (J.M.D.) not involved in the original article quality assessments. The Oxford Centre for Evidence-Based Medicine[33] differentiates levels of evidence based on the quality of the trial. Previous authors have classified the methodological quality of studies based on the PEDro scale; scores of 9-10 on the PEDro scale were considered to be of "excellent" quality and scores between 5 and 8 were considered to be of "fair" to "good" quality.[34,35] We, therefore, further classified the studies selected for this review as being "1b" higher level of evidence if the PEDro score was between 9 and 10 and as being "2b" evidence of lower quality if the PEDro score was between 5 and 8. Low-quality evidence rated below 5 was excluded from this review.

Reporting

The systematic review was organized and reported based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement.[36]

Results

Study selection

A total of 20 studies met the inclusion criteria for this review. A total of 257 articles were initially identified for potential inclusion, and a total of 225 were excluded based on the initial title and abstract reviews. On detailed review of the 32 full-text articles obtained, 12 were excluded[37-48] for various reasons outlined in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram (Fig. 1).[36]

Risk of bias in selected studies

Assessing risk of bias in individual studies can help prevent overestimating/underestimating the treatment effects.[49] Flaws in the included studies affect the validity of the systematic review itself. All selected studies were rated for quality using the PEDro scale (Tables 1-3). In the current review, most studies included randomization of assignment except for 2 studies.[50,51] Seven studies[3,13,20,22,24,52,53] used concealed allocation. Baseline comparisons of at least 1 key outcome measure to establish homogenous groups prior to the studied intervention were performed in all but 4 studies.[21,23,53,54] There were between-group analyses of at least 1 outcome measure in all the included studies. Point estimates and variability estimates were provided in all studies except for 2.[25,55] No study was able to satisfy blinding of the therapists administering the manual therapy techniques due to the nature of the intervention. Seven of the included studies were classified as level "1b" high-quality randomized controlled trials (RCTs), and 13 were classified as lower quality "2b" evidence (Tables 4-6).

Study characteristics

Search results revealed a variety of joint mobilization or manipulative techniques that were used both locally at the elbow and at distant joints related to the elbow. For this review, we broadly classified these techniques into 3 groups, MWM, Mill's manipulation, and regional mobilization techniques. Details of the studies are provided in Tables 4-6. Considerable variability was also noted in treatments used in conjunction with the mobilization techniques in the experimental groups. Seven of the comparison groups included what one could consider being true controls.[3,20-22,24,56,57] The comparison groups in the other studies only received a different type of

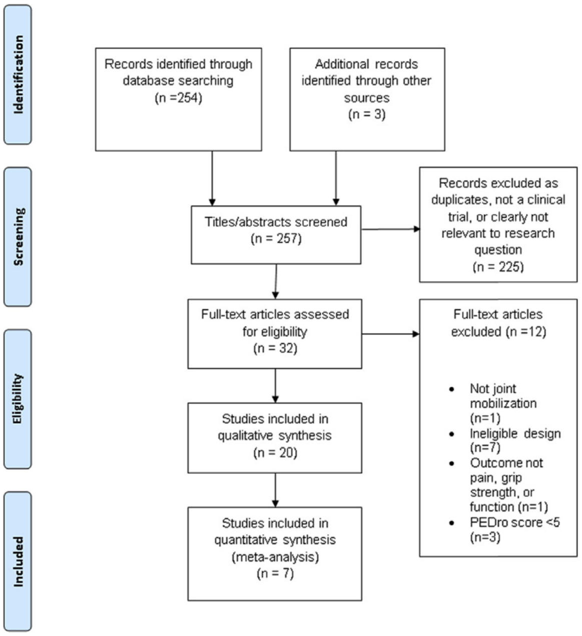

Fig. 1. PRISMA flow diagram summarizing study selection process. PEDro = Physiotherapy Evidence Database.

Table 1
Quality assessment scores of mobilization with movement studies using the PEDro scale

Primary author and year	1	2	3	4	5	6	7	8	9	10	11	Total
Vicenzino et al, 2001	x	x			x		x	x	x	x	x	8
Kochar et al, 2002	x	x		x				0	0	x	x	5
Paungmali et al, 2003	x	x	x	x	x		x	x	x	x	x	10
Bisset et al, 2007	x	x	x	x	x		x	x	x	x	x	10
Amro et al, 2010	x			x				x		x	x	5
Kim et al, 2012	x	x	x							x	x	5
Coombes et al, 2013	x	x	x	x			x	x	x	x	x	9
Afzal et al, 2016	x	x						x		x	x	5

PEDro = Physiotherapy Evidence Database.
See Appendix A for PEDro quality assessment questions 1-11.

Table 3
Quality assessment scores of regional mobilization studies using the PEDro scale

Primary author and year	1	2	3	4	5	6	7	8	9	10	11	Total
Vicenzio et al, 1996	x	x		x	x		x	x	x	x	x	9
Struijs et al, 2003	x	x	x	x			x	x	x	x	x	9
Cleland et al, 2005	x	x	x	x				x	x	x	x	8
Hsu et al, 2006	x	x		x				x	x	x	x	7
Fernandez-Carnero, et al 2008	x	x		x			x			x	x	6
Fernandez-Carnero, et al 2011	x	x						x	x	x	x	6
Joshi et al, 2013	x			x				x	x	x		5

PEDro = Physiotherapy Evidence Database.
See Appendix A for PEDro quality assessment questions 1-11.

active treatment rather than being exposed to a placebo or "wait-and-see" condition. A variety of outcome measures that assessed pain, grip strength, and/or function were reported in the selected studies. When pooling results, we chose the most common measures used between studies including pain at rest measured using the Visual Analog Scale (VAS) and pain free or maximum grip strength. The self-reported functional outcome tools used to assess disability varied among the studies.

None of the investigations that qualified for this review limited participation to any specific industrial or sports group. None of the studies limited inclusion of participants based on a specific diagnostic classification system with the exception of inclusion based on a minimum duration of symptoms or unilateral distribution of symptoms. Only 4 studies clearly designated an upper limit of symptom duration for any of the participants for inclusion.[24,25,53,55] No study described limiting inclusion to only first time vs recurrent episodes of LET. Some studies required subjects to have unilateral symptoms,[3,20,22,24,50,58] and the others did not specify distribution of symptoms.[23,55] One study included participants with bilateral symptoms, however, only examined the more affected arm.[13]

Exclusion of individuals based on concomitant conditions was listed in most studies; however, only 5 studies[3,21,52,59,60] explicitly described this screening process as a physical examination compared to self-report, 4 of which examined regional mobilizations. All investigations included both male and female genders with the distribution varied between studies. The age range of the participants in studies included was from 37 to 50 years.

MWM synthesis of evidence

The MWM technique, as described by Vicenzino et al,[21] consists of a lateral-glide MWM technique where the therapist glides the proximal forearm laterally and sustains it while the distal end of the humerus is fixed by the other hand. This is performed while the client performs the pain-free gripping action for 6 repetitions with a 15-second rest period between the repetitions. A total of 8 studies examined the effectiveness of MWM. The study characteristics are outlined in Table 4. Quality assessment ratings ranged from 5 to 10 on the PEDro scale, with the average rating equal to 7 out of a possible 11. The included studies represented a total sample of 551 participants.

Two studies[20,21] looked at this intervention in isolation. The remaining studies examined MWM in the context of a multimodal treatment administration including identical interventions used in a comparison group (without the mobilizations). Active treatment groups included a variety of interventions including multimodal physical therapy treatment (exercise, taping), US, or cortisone injections. Two studies included patients from a medical[53] or physical therapy[61] clinic, the remainder recruited patients from the general population in the region. One study[21] included individuals both from the general population and from a single physical therapy clinic.

Two studies required subjects to have had symptoms greater than 6-week duration.[3,22] One study limited the duration of symptoms to no more than 3 months,[53] and 1 study included individuals with subacute symptoms but did not operationally define the time frame.[51] Otherwise, none described an upper limit of symptom duration for any of the participants for inclusion. Duration of symptoms of participants for the included studies related to MWM ranged from 15 days to 36 months.

Effects of MWM on pain

Of the 8 studies examined for MWM, only 4 studies[3,22,51,53] qualified for VAS data extraction and pooled effect size computation (see Appendix B for an explanation of studies excluded from meta-analysis). Of these studies, one had a placebo condition[22] and another had a "wait-and-see" control condition[3] used in this comparison. The individual studies and their effect sizes for the VAS time periods are shown in the forest plot Figures 2A-2C. Pooled data (random-effects model, $P < .05$) demonstrated a mean effect size of 0.43 (95% CI: 0.15-0.71) across all time periods, which shows a moderate positive effect of MWM on improving VAS pain rating. Heterogeneity was not significant as Cochrane's Q was 3.02 ($P = .22$) and considered to be low with the $I^2 = 33.7\%$.[31] See Figure 3 for a funnel plot of the pooled VAS data.

Both Afzal et al[23] and Kochar et al[61] reported a significant decrease in pain scores in the MWM groups compared with the active treatment groups at a significance level of $P < .05$. The immediate effects of MWM compared to a placebo on PPT was measured in 2 studies[20,21]; however, no significant immediate increases in PPT were reported in either as a response to MWM.

Effects of MWM on grip strength

Pain-free grip associated with MWM had 2 studies[22,51] suitable for data extraction that included Amro et al[51] and Bisset et al.[22] The individual study effect sizes for the grip strength short-term time period are shown in the forest plot Figure 4. Only one paper[22] examined grip strength beyond 3 months, which occurred at 26 and 52 weeks. Pooled data (random-effects model, $P < .05$) demonstrated a mean effect size of 0.31 (95% CI: 0.11-0.51) across all time periods, which shows a moderate positive effect of MWM

Table 2
Quality assessment scores of Mill's manipulation studies using the PEDro scale

Primary author and year	1	2	3	4	5	6	7	8	9	10	11	Total
Verhaar et al, 1995	x	x	x	x				x		x	x	7
Stasinopoulos, 2005	x			x	x		x	x	x	x	x	8
Nagrale et al, 2009	x	x		x	x		x	x	x	x	x	9
Viswas et al, 2012	x	x		x	x		x	x	x	x		8
Olaussen et al, 2015	x	x	x	x	x	x	x	x	x	x	x	11

PEDro = Physiotherapy Evidence Database.
See Appendix A for PEDro quality assessment questions 1-11.

Table 4
Mobilization with movement study characteristics

Author (year)	Level of evidence	Sample characteristics	Interventions and dosages	Outcome measures	Results
Afzal et al (2016)	2b	Consecutive patients ($n = 30$) referred to PT with a diagnosis of LE. Age range 20-50 y.	Experimental: MWM (10 reps holding for 6 s over 12 sessions) plus ultrasound (3 MHz, 1.5w/cm squared) Control: ultrasound only Both groups received 12 visits over 4 wk	PRTEE Outcomes measured at visits 3, 6, 9, and 12.	Combination of MWM with ultrasound was more effective in relieving pain and function compared to ultrasound alone. Statistical method is not reported
Coombes et al (2013)	1b	165 patients with signs and symptoms of unilateral LE, 6-wk duration or longer. Mean age: 50 y	Group 1:Cortisone injection (triamcinolone) Group 2: Cortisone injection plus MWM and exercise Group 3: Placebo injection Group 4: Placebo injection plus MWM and exercise Physiotherapy: 8, 30-min sessions over 8 wk	Global rating of improvement; 1-year recurrence rate; pain on VAS, PRTEE; health-related quality of life; and outcomes measured at 4, 8, 12, 26, and 52 wk	The groups receiving corticosteroid injection vs placebo injection resulted in worse clinical outcomes at 1 y. There were no differences between the corticosteroid group vs physical therapy in conjunction with the corticosteroid
Kim et al (2012)	2b	10 subjects diagnosed with LE by an orthopedic physician. Symptom duration was no longer than 3 mo. Mean age: 49 y	Subjects were randomized in 2 groups. Both groups received various passive modalities and deep friction massage. The experimental group received MWM (2 sets of 10), and the control received a sham MWM. Both groups received treatment 5 sessions at 48-h intervals	PRTEE Outcomes measured at visit 5	Significant and clinically meaningful improvements were found in the group receiving MWM for both pain and function
Amro et al (2010)	2b	$N = 34$ patients diagnosed with subacute LE. Mean age experimental group 38; control 37	Experimental group received a combination of traditional treatment (thermal treatment, massage, and US, strengthening and stretching exercises) and MWM (36 reps) with taping techniques. Control group Received the traditional treatment only. Both groups were seen 3× per wk × 4 wk.	PRTEE, VAS, maximum grip strength, subjective reports of effectiveness of treatment (yes/no) Outcomes measured immediately after 1 session	Both traditional and the experimental groups experienced a significant reduction in pain intensity as well as improved daily function and grip strength. The addition of MWM to traditional treatment is more effective in improving daily function and pain.
Bissett et al (2006)	1b	198 patients with unilateral, chronic lateral epicondylalgia. Duration of symptoms less than 9 mo.	Group 1: MWM with exercise Group 2: Corticosteroid Group 3: Wait and see	Global improvement, grip force, and assessor's rating of outcomes were measured at baseline, six wk, and 52 wk	Corticosteroid injection group showed significantly better effects at 6 wk but with high recurrence rates thereafter (47/65 of successes subsequently regressed) and significantly poorer outcomes in the long term compared with physiotherapy. Physiotherapy was superior to wait and see in the short term; no difference was seen at 52 wk, when most participants in both groups reported a successful outcome. Participants who had physiotherapy sought less additional treatment, such as nonsteroidal anti-inflammatory drugs, than did participants who had wait and see or injections.
Paungmali et al (2003)	1b	24 patients with unilateral, chronic lateral epicondylalgia <9 mo. Mean age: 48.5 y; SD: 7.2.	Group 1: A lateral glide MWM treatment technique for the elbow. Group 2: Firm manual contact Group 3l: No manual contact	Pain-free grip strength, pressure pain threshold, thermal pain threshold, sympathetic nervous system activity (by measuring changes in heart rate, blood pressure, and cutaneous sudomotor and vasomotor function). Outcomes were measured before, during, and after-application.	Significant increase in PFGS 37.0% during application and 47.5% after application compared with the placebo and control conditions (group 2 and 3). There was no mean percentage increase in PPT following MWM compared with the placebo and control conditions. No change in thermal pain threshold. The mean increase in HR was 4.1% and 3.5% and 3.1% for systolic and diastolic BP. There was no change in placebo or control groups Skin temperature, cutaneous blood flux, and skin conductance were activated with MWM and not in the placebo and control condition

Table 4 (*continued*)

Author (year)	Level of evidence	Sample characteristics	Interventions and dosages	Outcome measures	Results
Kochar et al (2002)	2b	66 patients with LET	Group 1: US plus MWM treatment technique for the elbow. Group 2: US only Both groups completed 10 sessions within 3 wk, and both groups performed a prescribed exercise program for the final 9 wk Group 3 was not randomized and received no treatment.	Maximum isometric grip strength, pain intensity on VAS, a weight test (elbow extended, forearm pronated, and wrist neutral) and a patient assessment score were measured at baseline, once per wk for 3 wk, and at 12 wk.	At 12 wk, there was a significantly greater improvement in VAS pain level in the MWM group compared with the US group $P < .05$; there was a significant increase in maximum grip strength within the MWM group but not in the US group.
Vicenzino et al (2001)	2b	24 patients with unilateral, chronic lateral epicondylalgia >6 wk. Mean age: 46.43 years; SD: 1.68	Group 1: A lateral glide MWM treatment technique for the elbow Group 2: Firm manual contact Group 3: No manual contact	Pain-free grip strength and pressure pain threshold were tested before, during, and after application	Significant and substantial increase in pain-free grip during intervention (58% of preintervention strength) and 46% postintervention strength for group 1. Small but significant change (10%) in pressure pain threshold observed after treatment

LE = lateral epicondylalgia; MWM = mobilization with movement; PRTEE = patient rated tennis elbow evaluation; VAS = visual analog scale; PPT = pressure pain threshold; LET = lateral elbow tendinopathy; SD = standard deviation; PT = physical therapy; BP = blood pressure; HR = heart rate; PFGS = pain-free grip strength.

on improving grip strength. Heterogeneity was not present as Cochrane's Q was 0.94 ($P = .62$), and $I^2 < 0.001$. See Figure 5 for a funnel plot of the pooled grip strength data across all time points.

Kochar et al[61] found a mean increase in maximum grip strength by 7.78 kg at 3 weeks and by 8.83 kg at 12 weeks when compared to baseline measures. The within-group changes were reported as significant ($P < .01$) at each time period, whereas there were no significant differences in grip strength between the control and US group when they were compared to the MWM group. Pain-free grip strength increased 41% when measured immediately after application of the MWM intervention compared to an increase of 10% in a placebo group in the Vicenzino et al[21] study, but raw values were

Table 5
Mills manipulation article summaries

Author (year)	Level of evidence	Sample characteristics	Interventions and dosages	Outcome measures	Results
Olaussen et al (2015)	1b	177 patients with signs and symptoms of acute LE; 2-wk to 3-mo duration of symptoms. Age range: 18-70 y.	Group 1: Physiotherapy With 2 corticosteroid injections (10 mg triamcinolone acetonide) Group 2: Physiotherapy with 2 placebo injections Group 3: Wait and see (control) Injections were administered at the first visit and at a 3-wk follow-up. Physiotherapy consisted of 2 visits a week for 6 wk. Physiotherapy consisted of 15 min of deep transverse friction massage, Mills manipulation, stretching, and eccentric exercises.	Treatment success measured by a self-reported 6 point Likert scale measured at 6, 12, 26, and 52 wk	There was no significant difference between the groups at 52 wk. Corticosteroid injections combined with physiotherapy might be considered for patients needing a quick improvement initially.
Viswas et al 2012	2b	$n = 20$; patients clinically diagnosed with lateral epicondylitis with duration of symptoms between 8 and 10 wk and between the ages of 30-45.	Group 1: Static stretching and eccentric training of the common wrist extensors. Group 2: 10 min of cross friction massage followed by Mill's manipulation. All groups were seen 3 visits per week for 4 wk.	Tennis elbow functional scale and VAS Pain (0-10)	The exercise program resulted in greater improvement in comparison to those who received Cyriax treatments; however, both groups reported meaningful improvements from initial encounter to discharge.
Nagrale et al 2009	1b	60 patients with teno-periosteal variety of LET for greater than a mo; age range 30-60 y.	Group 1: Phonophoresis with diclofenac gel over the lateral epicondyle for 5 min plus supervised exercise Group 2: (experimental group) 10 min of deep transverse friction and single application of Mill's manipulation. Both groups received 3 sessions every week for 4 wk.	PFGS, Tennis Elbow Functional Scale and VAS pain measured at baseline, 2 wk, 4 wk, 8 wk	Both the groups improved in all measures with Cyriax treatment significantly better. Medium effect favoring Cyriax for pain free grip and function; large effect on pain
Stasinopoulos et al 2006	2b	75 patients with clinical diagnosis of LET of at least 4 wk duration. Age range: 30-60 y.	Group 1: Cyriax physiotherapy Group 2: Supervised exercise program Group 3: Polarized polychromatic noncoherent light (Bioptron light). All 3 groups received 3 sessions/wk for 4 wk.	VAS pain; VAS function; PFGS measured at baseline, 4 wk (immediately after treatment), then 1, 3, and 6 mo after treatment ended	The supervised exercise program produced the largest effect in the reduction of pain and in the improvement of function at the end of the treatment and at any of the follow-up time points.
Verhaar et al 1995	2b	106 patients with LET − average symptom duration of 33 wk. Mean age: 43 y; SD 9	Group 1: Cyriax PT for 12 visits in 4 wk and additional 2-wk restricted activity Group 2: 1 or more injection	Severity of pain; occurrence of pain; return to work; grip strength; and patient satisfaction measured at baseline, 6 wk, 1 y	No difference between groups at 1 y; injection group better at 6 wk.

LET = lateral elbow tendinopathy; PFGS = Pain free grip strength; VAS = Visual Analog Scale; SD = standard deviation.

Table 6
Regional mobilization study characteristics

Author (year)	Level of evidence	Sample characteristics	Interventions and dosages	Outcome measures	Results
Neck					
Fernandez-Carnero et al (2011)	2b	18 subjects diagnosed with clinical signs of unilateral LE of the dominant arm. Mean age: 45 y.	Group 1: Rotational HVLA cervical manipulation targeting C5-C6. Group 2: Posterior to anterior HVLA thoracic manipulation targeting T5-T8. Both groups: A maximum of 2 attempts for a cavitation were performed	PPT over the lateral epicondyle; PFGS on affected arm; MGF on unaffected arm. Outcomes measured immediately after manipulation	The group receiving cervical manipulation demonstrated greater changes in PPT than thoracic spine manipulation. There were no differences between groups for PFG or MGF.
Fernandez-Carnero et al (2008)	2b	10 subjects diagnosed with clinical signs of unilateral LE of the dominant arm. Mean age: 42 y	Group 1: Rotational HVLA cervical manipulation targeting C5-C6. A maximum of 2 attempts for a cavitation were performed. Group 2: Manual contact intervention (simulated cervical manipulation). Each participant received the other intervention at least 48 h after the first intervention	PPT and thermal pain thresholds over the lateral epicondyle; PFGS on affected arm; MGF on unaffected arm. Outcomes measured 5 min after the treatment	Cervical manipulation produced a greater increase of PPT on both sides compared with the manual contact intervention. Cervical manipulation produced a greater increase of PFG on the affected side compared with the manual contact intervention
Cleland et al (2005)	2b	10 patients, 5 in each group, with a diagnosis of LE. Symptom duration approximately 13 wk. Mean age: 40 y.	Group 1: Local treatment (local mobs, stretching, and progressive strengthening, HEP). Group 2: Same local treatment + cervical/thoracic grade 3 or 4 mobs. Both groups: 30 min total treatment.	NPRS, DASH, global rating of change, and pain-free grip strength. Outcomes measured at discharge (6 wk) and a 6-mo follow-up.	Patients in both groups exhibited clinically meaningful changes for all outcome measures. There was a clinically meaningful improvement for the group receiving cervical/thoracic mobilization for the DASH at DC and pain free grip at DC and the 6-mo follow-up.
Vicenzino et al(1996)	1b	15 patients with signs and symptoms of LE. Mean duration of symptoms 8 wk. Mean age: 44 y	Experimental: Contralateral grade 3 side glide at C5-6 on same side as affected limb with ULTT 2b. Placebo: Manual contact but no oscillation or ULT position Control: same as placebo but no manual contact. All treatments were 30 s in duration	Upper limb tension test 2b, pain-free grip, pressure pain threshold, current pain and pain over 24 h (VAS). Outcomes measured after application	The experimental group experienced significant improvement in all outcome measures compared to the other groups.
Forearm					
Hsu et al (2006)	2b	$n = 35$; patients with LET with duration of symptoms greater than 2 mo; mean age: 44.81 y; SD: 7.30 (group 1); mean age: 45.89 y; SD: 5.99 (group 2).	Group 1: Radial manipulation. Group 2: Acupuncture treatment Both groups received treatment 2 times/wk for 2 wk.	Maximum grip strength; PFGS; VAS Pain and DASH were administered at baseline, end of treatment, and at 2 and 8 wk after treatment.	Manipulation treatment provided better pain relief than acupuncture treatments during the first few treatments, but there was no difference between the 2 groups at the 8-week mark.
Wrist					
Joshi et al (2013)	2b	10 patients, 5 in each group, with a diagnosis of LE. Symptom duration between 6 wk and 6 mo	Group 1: Ventral scaphoid manipulation with passive wrist extension, 10 times, 15-20 min total treatment. Group 2: Pulsed ultrasound, 10-min friction massage, exercise, stretching Both groups: Total treatment was a maximum of 5 visits over 3 wk	Hand dynamometer, VAS. Outcomes measured at discharge (3 wk).	The overall patient success rate and overall improvement in pain was higher in the groups receiving manipulation compared to the groups receiving other therapeutic interventions.
Struijs et al (2003)	1b	31 patients with signs and symptoms of LE. Duration of symptoms 14 wk (group 1), 9 wk (group 2). Mean age: 46 y (group 1) and 48 y (group 2)	Group 1: Ventral scaphoid manipulation with passive wrist extension, 15 times, 15-20 min total treatment Group 2: Pulsed ultrasound, 10-min friction massage, exercise, and stretching Both groups: Total of 9 treatment sessions	Primary: Global measure of improvement. Secondary: Severity of pain complaint, pain during exam, pain during day, and inconvenience during daily activities	The group receiving manipulation demonstrated a significant improvement in overall success rate (62% vs 20% for the control group). At 6 wk, there was a significant improvement in pain during the day for the manipulation group.

LE = lateral epicondylalgia; PPT = pressure pain threshold; PFGS = pain free grip strength; MGF = max grip force; HVLA = high-velocity low amplitude; VAS = visual analog scale; DC = discharge; DASH = disability of the arm shoulder and hand questionnaire; HEP = Home exercise program; NPRS = numeric pain rating scale; ULT = upper limb tension.

not provided. A similar finding of 37% increase in pain-free grip strength was found in the MWM group compared with a 1.3% decrease in the placebo group in the study by Paungmali et al.[20] This difference was reported to be significant between the MWM and other 2 groups ($P < .05$), but no significant difference was reported between the placebo and no manual contact groups.[20] Three studies did not use grip strength as an outcome.[3,23,53]

Effects of MWM on function

Studies looking at the immediate effects of MWM did not include measures of function as outcomes.[20,21] One other study did not assess function as an outcome.[61] The short-term effect of MWM on function was assessed in the remaining studies; however, considerable variability existed in how function was measured and reported. Two studies[23,53] examined the

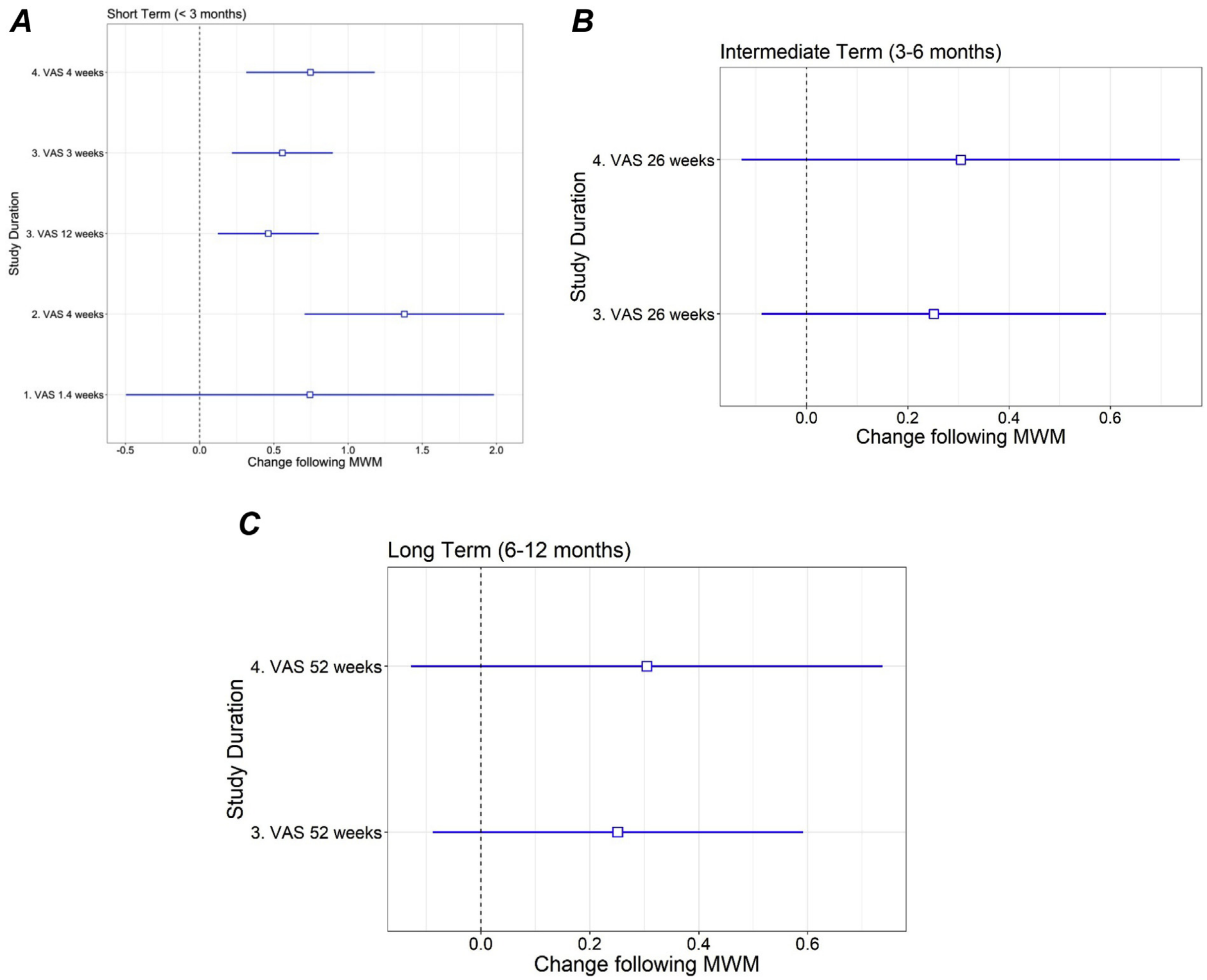

Fig. 2. (**A**) Forest plot of short-term effect sizes (<3 months) of mobilization with movement (MWM) for pain assessed with the Visual Analog Scale (VAS). Author key: 1. Kim et al; 2. Amro et al; 3. Bisset et al; 4. Coombes et al. (**B**) Forest plot of intermediate-term effect sizes (3-6 months) of MWM for pain assessed with the VAS. Author key: 3. Bisset et al; 4. Coombes et al. (**C**) Forest plot of long-term effect sizes (>6 months) of MWM for pain assessed with the VAS. Author key: 3. Bisset et al; 4. Coombes et al.

effects on individual questions of the patient-rated tennis elbow evaluation with no composite score comparisons provided. Coombes et al[3] reported a medium positive effect of MWM on pain and disability as measured by the patient-rated tennis elbow evaluation in the short term (SMD = 0.77 [95% CI: 0.81-1.37]).

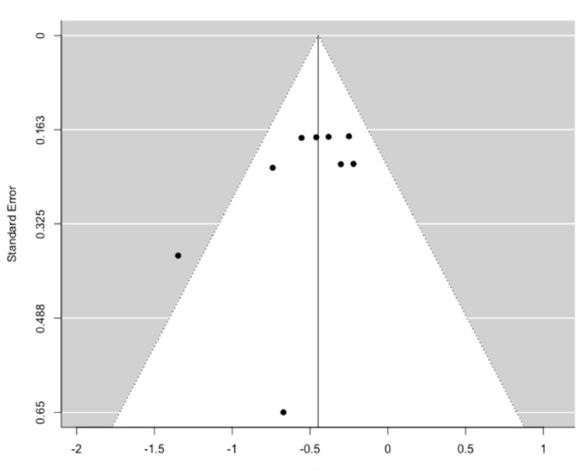

Fig. 3. Funnel plot of meta-analysis for mobilization with movement (MWM) for pain assessed with the Visual Analog Scale (VAS) across all time periods (short, intermediate, and long term).

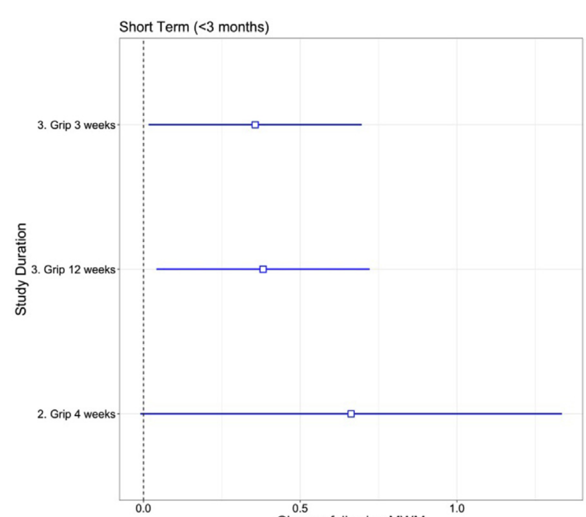

Fig. 4. Forest plot of short-term effect sizes (<3 months) of mobilization with movement (MWM) for grip strength. Author key: 2. Amro et al; 3. Bisset et al.

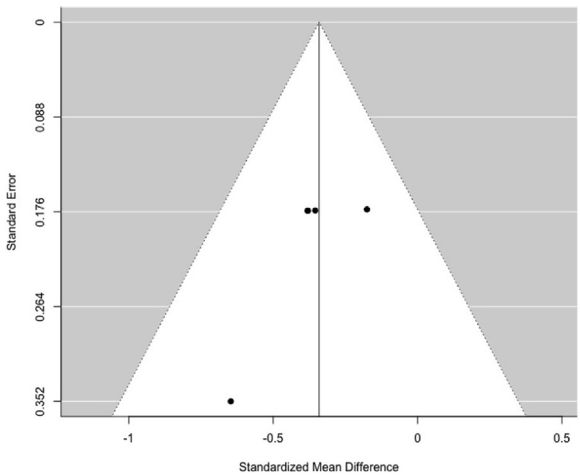

Fig. 5. Funnel plot of meta-analysis for mobilization with movement (MWM) for grip strength across all time periods (short, intermediate, and long term).

Mill's manipulation synthesis of evidence

A total of 5 studies that examined the effectiveness of Mill's manipulation on symptoms of LET were included in this review. The details of individual studies are outlined in Table 5. The review represents a total of 438 participants across the 5 studies. Quality assessment ratings ranged from 7 to 11 on the PEDro scale, with the average rating equal to 8.6 out of a possible 11. The experimental intervention of interest was the Mill's manipulation technique as described by Viswas et al[55] and Nagrale et al.[58] The manipulation was performed with the patient in a seated position with the affected arm internally rotated and abducted at the shoulder such that the olecranon faced the ceiling, while holding the patient's wrist in full flexion and forearm in pronation, the therapist applied a high-velocity low-amplitude thrust at the end range of elbow extension.[55,58] All studies performed the manipulation in the context of Cyriax physical therapy which consisted of 10 minutes of deep transverse friction massage to the common extensor tendon of the elbow plus a single application of the Mill's manipulation maneuver.

All but 1 study[24] examined this intervention in isolation. Olaussen et al[24] combined the Cyriax physical therapy with stretching and a home exercise program of eccentric strengthening of radial wrist extensors and included a "wait-and-see" group as the control condition. The active therapeutic treatment group in the other studies or comparisons included a variety of interventions including eccentric exercise and stretching,[55,62] phonophoresis plus eccentric exercise and stretching,[58] or cortisone injections.[13,24] The clinical settings were similar for 3 studies—an outpatient physical therapy clinic.[24,55,58] While one study[62] recruited participants from a rheumatology and rehabilitation center, the other study recruited from a hospital setting.[13]

Inclusion criteria required subjects to have had symptoms greater than 2-[24] or 4-week[58,62] duration in this group of studies. One study limited inclusion to only those participants with a reported symptom duration between 8 and 10 weeks.[55] The mean duration of symptoms of participants for the included studies ranged from 8 weeks to 8.25 months. Two studies limited age of participants to between 30 and 60 years, 1 limited to 30-45 years, resulting in a mean age of participants ranging from 38.6 to 46.9 years old for Mill's manipulation.

Effects of Mill's manipulation on pain

Out of the 5 studies, 2 studies[24,62] qualified for VAS data extraction and effect size computation with pooling (see Appendix B for explanation of studies excluded from meta-analysis). Their pooled data (random-effects model, $P < .05$) demonstrated a mean effect size of 0.47 (95% CI: 0.11-0.82) across all time periods, which shows a moderate effect of Mill's manipulation on improving VAS pain rating. Heterogeneity was not present: Cochrane's Q was 0.68 ($P = .41$) and $I^2 < 0.001$. The individual studies and their effect sizes for the VAS time periods are shown in the forest plots (Figs. 6A and 6B). Funnel plot of the pooled VAS data is presented in Figure 7.

Viswas et al[55] found that in the short term both the experimental and the active control groups demonstrated significant improvements in pain; however, the supervised exercise group had significantly greater decreases in pain on the VAS than the Mill's manipulation group ($P = .009$). In contrast, Nagrale et al[58] calculated a large effect (0.81) of Mill's manipulation over the supervised exercise group on pain intensity as measured by VAS at 8 weeks. Neither study examined mid- or long-term effects. Verhaar et al[13] examined pain on a 4-point pain severity scale and reported significant differences in favor of cortisone injection at 6 weeks, but no significant differences in pain severity between the injection group and Mill's manipulation group at 1 year.

Effects of Mill's manipulation on grip strength

Three of the 5 studies[13,24,62] qualified for PFGS data extraction and effect size computation with pooling (see Table 3). Their pooled data ($P > .05$, random-effects model) demonstrated a mean effect size of −0.01 (95% CI: −0.27 to 0.26) across all time periods, which shows that Mill's manipulation did not improve PFGS. Heterogeneity was not present: Cochrane's Q was 2.4 ($P = .30$) and $I^2 = 16.84\%$. The individual studies and their effect sizes for grip strength time periods are shown in the forest plot (Fig. 8A and 8B). Funnel plot of the pooled grip strength data is presented in Figure 9.

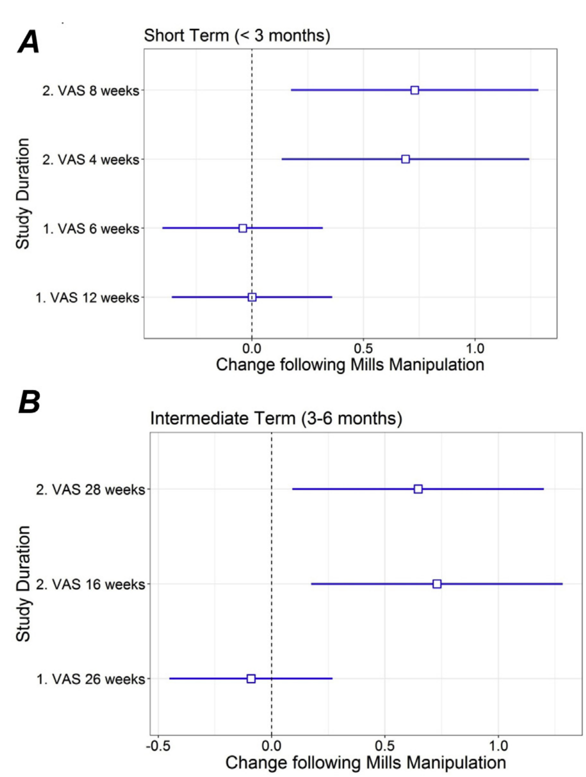

Fig. 6. (**A**) Forest plot of short-term effect sizes (<3 months) of Mill's Manipulation for pain assessed with the Visual Analog Scale (VAS). Author key: 1. Olaussen et al; and 2. Stasinopoulos et al. (**B**) Forest plot of intermediate-term effect sizes (3-6 months) of Mill's Manipulation for pain assessed with the VAS. Author key: 1. Olaussen et al; and 2. Stasinopoulous et al.

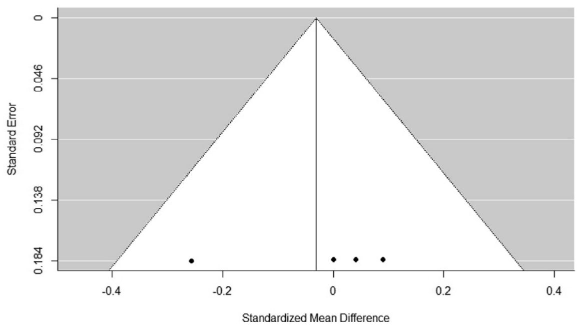

Fig. 7. Funnel plot of meta-analysis for Mill's Manipulation for pain assessed with the Visual Analog Scale (VAS) across all time periods (short and intermediate term).

Nagrale et al[58] found a medium effect (0.74) favoring Mill's manipulation over a supervised exercise group at 8 weeks on grip strength, whereas Viswas et al[55] did not measure grip strength as an outcome.

Effects of Mill's manipulation on function

Studies examining the effect of Mill's manipulation on function used a variety of self-reported functional outcome tools including a 10-cm VAS scale,[24,62] the Tennis Elbow Function Score,[55,58] the Pain-Free Function Index.[24] Verhaar et al[13] did not assess functional changes. Due to the heterogeneity of functional measures used, functional outcomes could not be pooled. Nonetheless, Stasinopoulos et al[62] and Viswas et al[55] found larger improvements in self-reported function in their respective supervised exercise groups than the Mill's manipulation at 8,16, and 28 weeks ($P < .05$)[62] and at week 4 ($P = .002$).[55] Nagrale et al[58] reported a moderate effect (0.74) favoring Mill's manipulation over phonophoresis plus supervised exercise. Olaussen et al[24] demonstrated no effect of Mill's manipulation over a wait-and-see control group on self-reported function as measured on a VAS scale at any time frame.

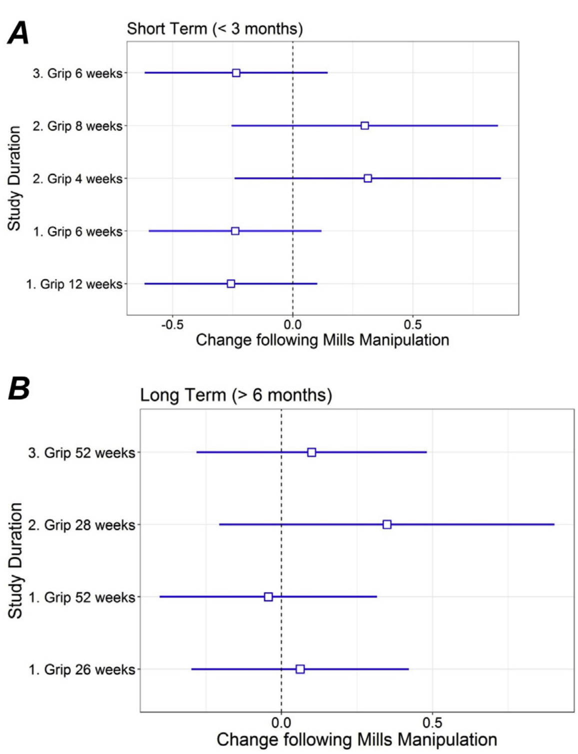

Fig. 8. (**A**) Forest plot of short-term effect sizes (<3 months) of Mill's Manipulation for grip strength. Author key: 1. Olaussen et al; 2. Stasinopoulos et al; and 3. Verhaar et al. (**B**) Forest plot of long-term effect sizes (>6 months) of Mill's Manipulation for grip strength. Author key: 1. Olaussen et al; 2. Stasinopoulous et al; and 3. Verhaar et al.

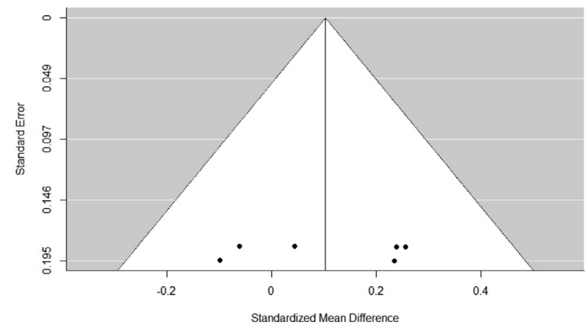

Fig. 9. Funnel plot of meta-analysis for Mill's Manipulation for grip strength across all time periods (short and long term).

Regional mobilizations' synthesis of evidence

A total of 7 studies specifically examined the effectiveness of regional mobilizations on symptoms of LET. The study characteristics are outlined in Table 6. The included studies examined ventral scaphoid manipulation (total $n = 38$)[25,63] that used similar methodology comparing it to an active control condition of pulsed US, cross friction massage, and strengthening exercises administered over 9 visits in 6 weeks. All participants in the wrist manipulation studies were required to have symptom duration between 6 weeks and 6 months. Median or mean duration of symptoms in participants of the other studies ranged between 13 weeks and 8 months. A single study examined the effects of a novel radial bone adjustment manipulation ($n = 16$) compared to acupuncture provided twice a week for 2 weeks.[59]

Four studies examined mobilization to the cervical spine with 3 different techniques. The immediate effects of rotational high-velocity low amplitude thrust manipulation of C5-6 segment of the cervical spine included a total of 18 participants.[54,56] One examined the immediate effects of grade 3 slide glides of C5-6 segment of the cervical spine ($n = 15$).[57] No short-, mid-, or long-term effects were examined for any of these studies that looked at immediate effects. One study examined grade 3 or 4 mobilizations of the cervical or thoracic spine according to impairments found at initial evaluation ($n = 10$).[52] In this study, both groups received local therapy and the mobilization which included grade III or IV passive accessory intervertebral movements and passive physiological intervertebral movements of the affected cervical and thoracic segments provided in 10 sessions spread across 6 weeks. All studies recruited participants from the general population, except one[59] that received referrals from hospital physicians and hospital-wide advertisements. All but one study[57] included 2 group comparisons. The mean age of participants in the studies examining regional mobilizations ranged from 40.4 to 47.5 years.

Effects of regional mobilization on pain

All studies except one reported on only the immediate or short-term effectiveness of regional mobilization in relieving pain in LET. Only Cleland et al[52] looked into the effectiveness in the medium term. Only 2 studies[25,63] reported significant difference in pain after manipulation and both used ventral scaphoid mobilization as the intervention. Struijs et al[63] found that at 6-week follow-up, the wrist mobilization group demonstrated a significantly greater decrease (MD = 5.2 [SD = +2.4]) in "pain during day" compared with the group receiving US, transverse friction massage, and exercise [MD = 3.2 (SD = ±2.1)]. In a similar study, Joshi et al[25] found that at 3-week follow-up, the wrist mobilization group demonstrated a significantly greater decrease (MD = 2.5) in "pain during day" compared with the group receiving US and transverse friction massage (MD = 1.7) on the 10-cm VAS scale; no measures of variability were reported. Hsu et al[59] reported no between-group comparisons but found that there were no significant differences in VAS scores for the acupuncture group ($P = .165$) from baseline to week 10, but the radial bone manipulation group demonstrated a significant decrease in pain ($P = .001$) in a similar timeframe.

Vicenzino et al[57] found improvements in pain levels favoring contralateral lateral glide at the C5-6 segment immediately following treatment, but there were no significant differences between groups. One day after treatment, the experimental group demonstrated a significant decrease in pain levels on the VAS scale compared with the control group ($P < .01$). Cleland et al[52] looked at short and intermediate effects of local treatment compared to local treatment plus grade III and IV intervertebral mobilizations of the cervical or thoracic spine. No significant between-group differences were found at 6 weeks (MD = 1.6 [95% CI: −0.2 to 3.4]) or at 6 months (MD = 2.2 [95% CI: −0.6 to 5.0]).[52]

Effects of regional mobilization on grip strength

All studies have reported their respective manipulations to be effective in improving grip strength in the short term.[52,54,56,57,59,63] Only Cleland et al[52] looked into the effectiveness in the medium term and reported statistically significant improvement in grip strength. The authors reported the manipulation to be effective in the short (MD = 14.6 kg [95% CI: 9.3-19.9]) and medium term (MD = 19.6 kg [95% CI: 1.6-37.6]) in improving grip strength after application.[52]

Effects of regional mobilization on function

A variety of outcome measures were used to measure function in the included studies. These include self-report of inconvenience during activities, functional ability on a VAS scale, and disability of the arm shoulder and hand. Three studies[25,52,63] reported significant improvement in function in the short term. While Cleland et al[52] reported that there were no significant differences in function as measured by the disability of the arm shoulder and hand at 6 months (MD = 14.4 [95% CI: −3.0 to 31.8]).

Discussion

According to the Oxford Centre for Evidence-Based Medicine,[33] there is level 1b and 2b evidence that both MWM and Mill's manipulation techniques are more beneficial than comparison groups at improving pain on the VAS in the short term (<3 months) and intermediate term on patients with LET. Meta-analytic pooling found statistically significant models for both techniques on the VAS, and the heterogeneity between the studies was low. In addition, there is level 1b and 2b evidence that MWM is more beneficial than control groups at improving grip strength in the short term on patients with LET. Meta-analytic pooling found a statistically significant model for MWM on grip strength with low heterogeneity. Based on the available body of evidence of this meta-analysis, the authors recommend the clinical use of MWM or Mill's manipulation directed at the elbow for a moderate positive effect on self-reported pain and decreased pain-free grip strength in the short term.

Parameters for the application of the mobilization techniques did vary considerably among the studies making it challenging to provide a standard dosing recommendation. The most commonly reported frequency of application of the MWM technique was 3 times per week while the treatment duration ranged from 2 to 8 weeks with the most common duration being 4 weeks. The studies examining Mill's manipulation were more consistent with dosing parameters. Mill's manipulation was most commonly described as a single application of a high-velocity, low-amplitude thrust to the extended elbow, whereas the forearm was positioned in pronation and the wrist in flexion. The frequency of its application was 3 times per week over a period of 4 weeks.

There is also a growing body of evidence supporting the use of regional mobilizations for managing patients with LET. More specifically, cervical mobilization/manipulation has a positive short-term effect on improving a variety of self-reported pain measures and grip strength. However, because of the heterogeneity in patient populations, research design, and outcome measures, we were unable to perform meta-analytic pooling. Most cervical manipulation studies were also limited in sample size and thus few performed inferential statistical analyses. As to the effectiveness of other regional mobilizations, there appears to be some merit to both ventral scaphoid and radial bone mobilization for improving pain in the short term, but more research is needed to make a better recommendation. Overall, the authors recommend clinicians consider the use of regional mobilization in the management of patients with LET; however, due to the variety of treatment techniques used, dosage recommendations are not outlined in this article.

Recent systematic reviews support the use of mobilizations for the cervical spine,[64] low back,[65] and nonspecific shoulder pain as well as ankle sprains.[66] More specific to the elbow, a recent qualitative systematic review on the effectiveness of mobilization to improve clinical outcomes in hand therapy reported that there was moderate evidence to support MWM at the elbow in the management of LET in both the short and long term.[19] However, with the successful pooling of data into effect sizes and the addition of several studies, the authors of the current review conclude that there are now objective data to support the use of MWM or Mill's manipulation in the management of LET for moderate positive effects on pain and grip strength.

In addition, the aforementioned systematic reviews generally concluded that the effect of mobilization on the outcomes measured appears to be enhanced by active exercise. Due to the lack of clear guidance on dosage for exercise prescription and the resultant variety of exercise programs used for managing LET in the literature, we did not ask a question comparing the effectiveness of mobilization techniques to exercises for symptom relief. Most studies included in this review reported some combination of exercise along with the mobilization. A notable exception was the Viswas et al[55] study that compared an active control group exposed to an eccentric exercise program to Mill's manipulation. Their findings favored supervised exercise over Mill's manipulation for pain relief and function as measured by the Tennis Elbow Function Score. However, due to the dearth of studies examining isolated treatments, like the previous systematic reviews, we cannot speak to the isolated effects of mobilizations but rather in combinations of other therapies and most specifically exercise. One may argue that the multimodal approach taken by most of the studies included in this review would increase the generalizability of the results to the clinic environments.

The mechanisms by which mobilizations improve both patient pain perception and functional strength have long been discussed.[67] Although the exact mechanism is not clearly known, the most compelling argument for the immediate effect of pain relief and strength improvement is through a complex interaction between the mechanical stimulus at the joint and a neurophysiological reflex mechanism.[68] The direct effects on joint structures including the stimulation of mechanoreceptors and proprioceptors may trigger sympathetic sensory and motor function changes through afferent and efferent pathways in the spinal cord and/or brain that may result in pain modulation and improvement of grip strength.

Implications for practice

Regardless of the physiological mechanism of mobilizations on pain relief and improvement in grip function, our results have significant implications for clinical practice. The data from our meta-analysis demonstrate moderate effect sizes in favor of both Mill's manipulation and MWM on patients with LE for short, mid, and long term. In the short term (>3 months), none of the effect size CIs crossed 0 for either treatment with pain as an outcome, indicating that we are 95% confident that the true mean effect size will favor the mobilization.

To the authors' knowledge, no other systematic review in the past 10 years, other than those related to cortisone injections, has pooled data related to specific interventions for the treatment of LET. Given the outcomes of this study, the authors can confidently recommend mobilization as a treatment for LET in the immediate, short, and intermediate terms. When symptoms of LET become chronic, the tissue pathology can be complicated by complex and multifaceted pain mechanisms leading to long-term disability[3]; therefore, early management of symptoms is important. Furthermore, our results provide substantial quantitative data to third-party payers that a form of manual therapy is beneficial in the early management of LET. Given recent evidence supporting the cost-effectiveness of conservative therapy management of LET, including joint mobilization, future studies are needed to confirm these results and to more thoroughly examine the long-term effects and associated recurrence rates.[14]

Limitations

By accepting scores of 5 or greater on the 11-point PEDro, we included some lower/moderate-quality evidence and thus have a larger risk of introducing study selection bias.[49] However, no studies with <5/11 on the PEDro were included in the pooling of data, and several studies with strong methodology (>8/11 on the PEDro) were included in the pooling of data.[3,22,24,62] As a whole, the studies examining MWM were of lower quality when compared to those examining Mill's manipulation or regional mobilization.

Despite including higher quality studies in the data pool, there were challenges in the collection and pooling of data. First, a true control group did not exist for many of the studies; therefore, an active control group was used as a comparison for some studies in the meta-analysis. Second, there were very few studies with similar research design, outcomes, or follow-up time periods. Although the replication of studies is often viewed as unpopular because of the inherent lack of originality, there is a need for homogenous study designs in different populations to be able to statistically pool results and present higher level evidence. Several well-designed high-quality studies are included in this review that include a true control in the form of a placebo or wait-and-see condition that have not yet been replicated in other populations.

Another barrier observed in homogenizing our findings was in the variability in the clinical presentation of LET. LET is usually diagnosed via clinical examination; however, one could argue that it is a diagnosis of exclusion. Most studies examined in this review did not include a clear methodology for exclusion based on a physical differential diagnosis examination, with a few exceptions.[3,21,52,59,60] For example, many of the studies indicated that they excluded individuals with concomitant pathology, but a physical screen is not described for identification of pathology including underlying cervical involvement, radial nerve irritation at the supinator, or posterolateral instability of the radial head. There are multiple conditions that cause lateral elbow pain, and therefore, a careful differential diagnostic examination is necessary to exclude causes of lateral elbow pain not related to local tendinopathy. Additionally, few studies examined participants for other upper extremity impairments that may regionally impact elbow mechanics and thus contribute to symptoms of LET. Shoulder, elbow, forearm range of motion deficits or hypermobility, strength deficits or muscular imbalances of the scapular stabilizers, or rotator cuff musculature have been demonstrated to be present in individuals with LET.[69-71] If these impairments exist, individuals with LET may benefit from targeted intervention in addition to local treatment.

The multifactorial etiology of LET is likely associated with the difficulty that many clinicians have in managing this condition, even after ruling out other potential sources of pain. Multiple intrinsic and extrinsic factors contribute to the excessive stress at the common extensor tendon.[72] Therefore, the management of LET may differ among individuals. This is especially important for those individuals with more strenuous functional demands through a work environment or sport and for those with regionally related strength or range of motion impairments.

Most of the studies included in this review, do not specify or classify participants in terms of severity, acuity, or irritability of symptoms and the course of symptoms (isolated, recurrent, or persistent symptoms). Although some studies included a requirement related to participant inclusion related to the duration of symptoms, it is difficult to get a clear picture of patient presentation based on chronologic classification alone.[73] A subclassification system could improve the specificity of treatment within the more broad diagnosis of LET.[74] For example, chronic pain complaints may be related less to local pathology and more to the presence of pain-causing chemicals in the area and potentially pain system changes in the peripheral and central nervous system.[75] Therefore, pain education, patient-directed goals, overall health and wellness, cardiovascular endurance, and graded exposure should be more of an emphasis in this subpopulation of patients.

Because of the complexity and multifactorial etiology of this condition, best practice management should probably include a subclassification of patients to enhance effective clinical decision-making. Recent attention in the literature has been placed on the importance of establishing a clear classification system,[73,74,76,77] but as of yet, no consensus has been reached. Attempts at subgroup analyses within a single RCT are often hampered by insufficient statistical power to reveal differences in treatment effects among subgroups, limiting the likelihood for these to be performed. However, if higher quality research is replicated in other settings, pooling of individual patient data from more than one RCT will increase the statistical power and may increase the possibility of identifying relevant subgroup effects.[78] An initial attempt has been made to develop a clinical prediction rule to identify characteristics of individuals with LET that would respond favorably to MWM plus exercise. Additional research is needed to validate that preliminary work.[79]

Conclusions

There is compelling evidence that joint mobilizations directed at the elbow improve both pain and functional grip scores across all time frames compared to control groups in the management of LET. Preliminary evidence suggests that regional joint mobilizations may also be beneficial. Because of variability in the patient populations presenting with LET across individual studies, we highly recommend future studies work toward subcategorization of this condition in order to improve the efficiency and effectiveness of managing LET. There is a need for replication of higher quality studies in different settings, the inclusion of true control groups, and more explicit physical screening of participants for the exclusion of unrelated disorders that cause lateral elbow pain.

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Quiz: # 613

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#1. The following can be said of lateral epicondylitis
  a. the etiology is likely multifactorial
  b. it is characterized by a proliferation of fibroblasts, vascular hyperplasia, and immature collagen fibers
  c. its clinical management is often problematic
  d. all of the above

#2. The design of the study is
  a. a prospective cohort
  b. a case series
  c. a systematic review
  d. RCTs

#3. How many articles met the inclusionary criteria?
  a. 20
  b. 10
  c. 50
  d. 100

#4. The positive effects of manual therapy for LET patients appears to be
  a. nonexistent
  b. enhanced by active exercise
  c. associated with complete remission
  d. enhanced by pulsed ultrasound

#5. The authors recommend not using MWM or Mill's manipulation techniques in the management of LET
  a. true
  b. false

When submitting to the HTCC for re-certification, please batch your JHT RFC certificates in groups of 3 or more to get full credit.

Appendix A

Electronic search strategy example for PubMed: (((((tendinitis OR tendonitis OR tendinopathy OR tendinosis OR peritendinitis OR enthesopathy) AND elbow AND (mobiliz* OR manipula* OR musculoskeletal manipula*))) OR (Lateral Epicondyl* AND manipulation)) OR (Lateral Epicondyl* AND manual therapy)) OR ((“Tennis Elbow”[Mesh]) AND “Musculoskeletal Manipulations”[Mesh]). Limits: English language articles.

SEARCH RESULTS.

Date conducted	PubMed	CINHAL	PEDro	Total reviewed
3/7/17	160	38	56	32

Appendix B

Explanations of why pooling of data were not possible

Author	Reason(s) precluding data extraction
Mobilization with movement studies	
Afzal et al. (2016)	Raw data were not reported separately for control and intervention groups.
Paungmali et al. (2003)	Assessed immediate effects only, no follow-up; pain-pressure threshold
Vicenzino et al. (2001)	Assessed immediate effects only, no follow-up; pressure pain threshold; data reported in figures only (nonextractable)
Kochar (2002)	Data reported in figures only (nonextractable)
Mill’s manipulation studies	
Nagrale et al. 2009	Data reported as change scores (nonextractable)
Viswas et al. 2012	Data reported as ranks and sum of ranks (nonextractable)