



SYSTEMATIC REVIEW

Effectiveness of non-invasive therapies on pain, maximum grip strength, disability, and quality of life for lateral elbow tendinopathy: A systematic review and meta-analysis

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KEYWORDS

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Meta-analysis;
Tendinopathy;
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Abstract

Background: Lateral elbow tendinopathy is a common musculoskeletal disorder. Effectiveness of non-invasive therapies for this health condition are unclear.

Objective: To investigate the effectiveness of non-invasive therapies on pain, maximum grip strength, disability, and quality of life for lateral elbow tendinopathy.

Methods: Searches were conducted on MEDLINE, Embase, CINAHL, AMED, PEDro, Cochrane Library, SPORTDiscus and PsycINFO without language or date restrictions up to May 3rd, 2023. Randomized trials investigating the effectiveness of any non-invasive therapy compared with control or other invasive interventions were included. Two independent reviewers screened eligible trials, extracted data, and assessed the risk of bias of included trials and certainty of the evidence.

Results: Twenty-two different therapies investigated in 47 randomized trials were included in the quantitative analysis. Moderate certainty evidence showed that betamethasone valerate medicated plaster may reduce disability (mean difference -6.7 ; 95% CI -11.4 , -2.0) in the short-term when compared with placebo. Low certainty evidence showed that acupuncture may reduce disability (MD -9.1 ; 95% CI -11.7 , -6.4) in the short-term when compared with sham. Moderate to very low certainty of evidence also showed small to no effect of non-invasive therapies on pain intensity, maximum grip strength, and disability outcomes in the short-term compared to control or invasive interventions. Most therapies had only very low certainty of evidence to support their use.

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Conclusions: Decision-making processes for lateral elbow tendinopathy should be carefully evaluated, taking into consideration that most investigated interventions have very low certainty of evidence. There is an urgent call for larger high-quality trials.

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Introduction

Lateral elbow tendinopathy is one of the most prevalent musculoskeletal conditions involving the upper extremities,^{1,2} resulting in high levels of disability.³ The injury occurs as a result of frequent microtraumas of the extensor carpi radialis brevis tendon due to overuse, triggering degenerative processes at the origin of the tendon.⁴ Associated with repetitive and strenuous movements,⁵ lateral elbow tendinopathy affects both athletes (e.g., tennis and other racket sports) and the general population.⁶ About 1% to 3% of the global population is annually diagnosed with lateral elbow tendinopathy,⁷ resulting in substantial costs related to disability, loss of productivity, and absenteeism.^{8,9}

Non-invasive therapies should be the first choice management option for lateral elbow tendinopathy^{9,10} and may include exercises, bracing, acupuncture, manual therapy, and oral drugs.¹¹ But, invasive treatment options are also commonly prescribed (e.g., platelet-rich plasma injection, corticosteroid injections, or surgery).^{12,13} Although non-invasive therapies are used as the first choice treatment, the effectiveness and clinical benefits compared with control and invasive therapies are still unclear.¹⁴ Some systematic reviews addressing the effectiveness of individual non-invasive therapies have been published,^{15,16} but a review of the effectiveness of all available therapy options for pain intensity, grip strength, disability, and quality of life has yet to be performed.¹⁷ In addition, previous systematic reviews on the effectiveness of non-invasive therapies in lateral elbow tendinopathy are methodologically limited (i.e., inappropriate comparisons, narrow search strategy, and heterogeneous groups) which sometimes make their conclusions misleading.^{18,19}

This systematic review aims to investigate the short- and long-term effectiveness of non-invasive therapies on pain intensity, maximum grip strength, disability, and quality of life in people with lateral elbow tendinopathy. Moreover, we aim to compare the effectiveness of non-invasive with invasive therapies. Certainty of the evidence was summarized using the Grading of Recommendations, Assessment, Development and Evaluations (GRADE) approach.²⁰

Methods

This systematic review follows the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA)²¹ and Cochrane recommendations.²² The protocol was prospectively registered at PROSPERO (CRD42020202285) and at the Open Science Framework (<https://osf.io/72rzy/>).

Search strategy

An electronic search was conducted up to May 3rd, 2023 on MEDLINE, Embase, CINAHL, AMED, PEDro, Cochrane Library,

SPORTDiscus, and PsycINFO without language or date restrictions. Descriptors were related to “randomized controlled trial” and “lateral elbow tendinopathy.” To maximize the sensitivity of the search strategy and consequently avoid exclusions of potential therapies of which we are not aware, descriptors related to non-invasive therapies were not used. Detailed information on the search strategy is provided in Supplementary material 1. In addition, reference lists of previous systematic reviews and the clinical trials registers (www.clinicaltrials.gov, www.anzctr.org.au) were manually searched to maximize the identification of all eligible trials.

Eligibility criteria

Randomized or quasi-randomized controlled trials (e.g., trials with allocation by hospital record number, date of birth, or alternation) that investigated the effectiveness of any non-invasive therapy on the outcomes of pain intensity, disability, maximum grip strength, and quality of life in patients with lateral elbow tendinopathy were included. The intervention of interest was defined as any non-invasive intervention, including oral medications. Lateral elbow tendinopathy was defined as constant tendon pain and reduced function related to mechanical loading of the lateral elbow tendons,²³ epicondylar tenderness, and pain with resisted wrist extension and stretching of the radial wrist extensors.²⁴ To be included, trials had to compare any non-invasive therapy with control (i.e., placebo, sham, waiting list, or no intervention) or invasive interventions (i.e., any type of injection or surgery). In this meta-analysis, placebo and sham were combined as a control group, and no intervention and waiting list were combined as another control group. Crossover randomized controlled trials were included if data from the first phase were reported separately. Trials comparing different modalities of non-invasive therapies were excluded. Pain intensity, maximum grip strength, disability, and quality of life were assessed using any valid instrument: for pain intensity (e.g., Numerical Rating Scale - NRS²⁵ or Visual Analogue Scale - VAS²⁵); maximum grip strength (e.g., Hand Grip Dynamometer²⁶); disability (e.g., Disabilities of the Arm, Shoulder and Hand - DASH²⁷ or Patient-Rated Tennis Elbow Evaluation - PRTEE²⁸); and quality of life (e.g., Short Form Health Survey - SF-36²⁹).

Selection process

After searches, the identified references were exported to an Endnote® file and duplicates were removed. Then, two independent reviewers screened titles and abstracts, and evaluated potential full texts using the eligibility criteria outlined above. Between-reviewer discrepancies were resolved by a third reviewer.

Risk of bias assessment

When available, we extracted scores directly from the PEDro database (<http://www.pedro.org.au/>). When not available, the risk of bias of included trials was assessed by two independent reviewers using the 0–10 Physiotherapy Evidence Database (PEDro) scale.³⁰ Discrepancies were resolved by a third reviewer. The PEDro scale is a reliable and valid tool to evaluate risk of bias of trials investigating non-invasive therapies.^{30–32}

Data extraction

Two independent reviewers extracted data from included trials: source of participants; sex; type and dosage for non-invasive therapy and comparator; outcome data; and time points. The extracted outcome data included means and standard deviations (SDs) post-intervention and sample sizes for all groups of interest to investigate the short- and long-term effectiveness. The short-term effect was considered a follow-up of up to 12 weeks after randomization, and the long-term effect was considered a follow-up more than 12 weeks after randomization. When more than one time point was available in the same follow-up period, the one closer to the end of the intervention was considered. Following Cochrane's recommendations,²² when trials evaluated more than one similar non-invasive therapy or more than one form of similar comparator, outcome data of similar trial arms were combined.³³ When data were not reported, attempts to contact the authors was made up to three times within a one week interval to obtain further information. In trials in which SD was not reported, missing data were calculated from 95% confidence interval (CI), standard error, p-value, baseline change, graphic representation, medians and inter-quartile ranges, or SD from baseline.²² When imputations were not possible, trials were excluded from the quantitative analysis. Between-reviewer discrepancies during the data extraction process were resolved by a third reviewer.

Data analysis and synthesis

Meta-analysis was conducted using a random-effects model (DerSimonian and Laird method), when possible. Mean differences (MDs) and 95% CIs were presented for each specific non-invasive therapy in forest plots. The effect was evaluated by the Z test, and a p-value <0.05 was considered statistically significant. The clinical importance of therapies were interpreted by comparing the estimated effect sizes and 95% CI in association with the minimal clinically important difference (MCID) of the outcome of interest.³⁴ The MCIDs considered were: 19 points on the 0–100 points scale for pain intensity^{35,36}; 17 kgs (kg) for maximum grip strength³⁷; and 11 points on the 0–100 points scale for disability.^{15,36,38}

Data were converted to a common scale before being combined in the meta-analysis. The common scale ranged from 0 to 100 points for pain intensity, disability, and quality of life.²² For maximum grip strength, different units of measurement were converted to kg.²²

To reduce clinical heterogeneity, we chose to group only non-invasive interventions with similar protocols. Otherwise, studies were renamed according to the experimental group and analyzed individually.^{39,40}

Assessment of the certainty of the evidence using the grading of recommendations, assessment, development and evaluation (GRADE) approach

Two independent reviewers assessed the certainty of the evidence using the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach^{20,41} in a Microsoft Excel® sheet. Between-reviewer discrepancies were resolved by a third reviewer. According to the four-levels GRADE system, evidence may range from high to very low certainty, with lower levels indicating that future high-quality trials are likely to change estimated outcomes.⁴¹ In the present review, evidence began at high certainty and was downgraded by one or two levels for each of the following issues related to risk of bias, inconsistency, indirectness, imprecision, and publication bias:

Risk of bias

- 25% participants from high overall risk of bias trials (i.e., PEDro score <6 out of 10): downgrade by one level⁴²; and
- ≥50% participants from high overall risk of bias trials: downgrade by two levels.

Inconsistency

- Important unexplained heterogeneity or $I^2 > 50\%$: downgrade by one level;
- When pooling was not possible²²: downgrade by one level; and
- Serious inconsistency (i.e., $I^2 > 75\%$): downgrade by two levels.

Indirectness

- Participants outside target group >50%: downgrade by one level; and
- There was no downgrade by two levels for this domain.

Imprecision

For dichotomous outcomes

- Total events <300 or only one trial: downgrade by one level;
- 95% CI includes no effect and appreciable benefit/harm: downgrade by one level; and
- Imprecision due to both above reasons: downgrade by two levels.

For continuous outcomes

- Total sample size <400 or only one trial: downgrade by one level;
- 95% CI includes no effect and crosses standardized mean difference (SMD) = 0.5 or MD >10%: downgrade by one level; and
- Imprecision due to both above reasons: downgrade by two levels.

Publication Bias

- Funnel plots asymmetry (i.e., when pooling ≥10 trials)^{43,44}; downgrade by one level; and
- There was no downgrade by two levels for this domain.

Sensitivity analyses were performed to assess whether the high risk of bias impacted the estimated effectiveness. We performed separate meta-analyses removing trials with the PEDro score <6 from the meta-analysis. Meta-regression was not possible because of the small number of included trials.²² All analyses were conducted using the Comprehensive Meta-analysis software, version 2.2.04 (Biostat, Englewood, NJ).

Results

Study selection

Searches identified 4810 references. Following removal of duplicates 2904 titles and abstracts were screened, 141 potential full texts were assessed using the eligibility criteria, and 52 original trials were included in the review. Of the 52 included trials, 47 trials were included in the quantitative analysis. Five trials were excluded from the quantitative analysis because outcome data were not reported, and imputations were not possible.⁴⁵⁻⁴⁹ The flow of studies through the review is in Figure 1.

Study characteristics

Fifty-two randomized controlled trials published between 1985 and 2022 were included in the qualitative analyses. Trials were conducted in Asia ($n = 22$, 42.3%),⁴⁷⁻⁶⁸ Europe ($n = 22$, 42.3%),^{33,39,45,46,69-86} North America ($n = 3$, 5.7%),⁸⁷⁻⁸⁹ Oceania ($n = 3$, 5.7%),^{40,90,91} South America ($n = 1$, 1.9%),⁹² and one multicenter trial conducted concurrently in Asia, Europe, and Oceania ($n = 1$, 1.9%).⁹³ Sample sizes of included trials ranged from 12 to 199 participants.

Twenty-two different non-invasive therapies were investigated in the 47 trials: non-pharmacological therapies ($n = 37$)^{50-62,65-68,71-74,76-81,83-89,91-93}; combination of two or more non-pharmacological therapies ($n = 7$)^{39,40,56,57,63,82,90}; combination of non-pharmacological and pharmacological therapy ($n = 1$)⁵⁶; and pharmacological therapies ($n = 6$).^{33,63,64,69,70,75} Thirty-four (72.3%) of the included trials compared non-invasive therapy with control (i.e., no intervention, waiting list, placebo, or sham) and 17 trials (36.2%) compared non-invasive with invasive intervention (i.e., autologous blood injection, corticosteroid injection, leech therapy, neural therapy, non-steroidal anti-inflammatory drugs injection, prolotherapy injection, and tenotomy). Pain intensity was investigated in 38 of 47 trials (80.9%),^{33,39,40,50,52-67,69-76,78,79,81,82,85,86,90,91,93,94} maximum grip strength was

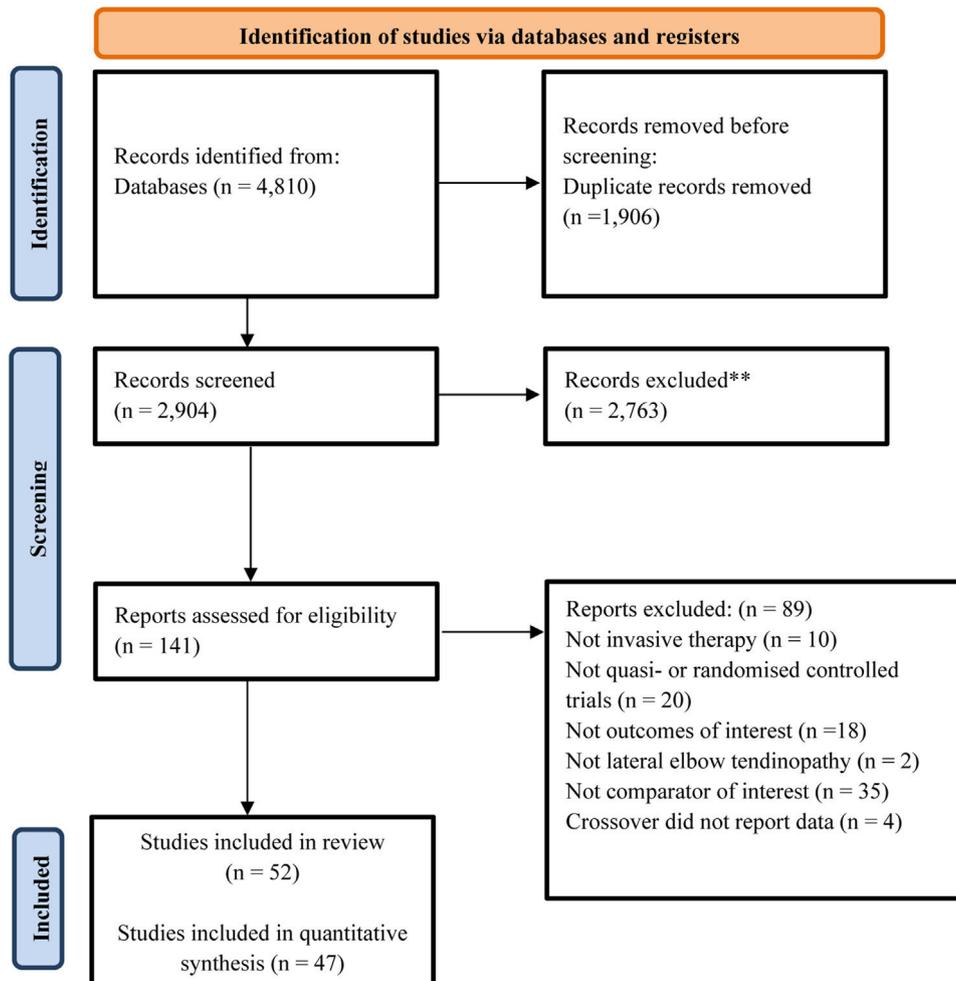


Fig. 1 PRISMA flowchart.

investigated in 21 trials (44.7%),^{39,50,52,54-59,63,65-67,69,72,73,80,81,84,88,89} disability was investigated in 31 trials (65.9%),^{33,39,40,50,51,53-55,58-62,66-70,72,73,77,81-84,86,88,90,91,93,94} and quality of life was investigated in five trials (10.6%).^{40,54,69,83,87} All trials included in the quantitative analysis investigated only short-term effectiveness (i.e., ≤12 weeks after randomization). Supplementary material 2 shows detailed characteristics of the included trials (n = 52).

Risk of bias of included trials

The mean risk of bias of the 52 included trials was 7.0 points on the 0 to 10 points PEDro scale, with scores ranging from 3 to 9 points. Of the 47 trials included in the quantitative analysis, 37 trials (78.7%) were considered to have low risk of bias (i.e., PEDro score ≥6 out of 10). The main methodological issues of included trials were absence of concealed allocation (n = 22, 47.8%), absence of participant blinding (n = 31, 66.1%), and absence of therapist blinding (n = 43, 91.5%). In addition, 31 trials (66.1%) did not report intention-to-treat analysis (Supplementary material 3).

Effectiveness of non-invasive therapy on pain intensity, maximum grip strength, disability, and quality of life

Effect estimates are presented as MDs on a scale of 0–100 points (i.e., pain intensity, disability, and quality of life) or kilograms (i.e., maximum grip strength). We found no high certainty of evidence for the effectiveness estimates of non-invasive interventions for pain intensity, disability, maximum grip strength, or quality of life in this review. The main reasons for downgrading the certainty of the

evidence were imprecision (88 of 88 comparisons, 100%), inconsistency (82 of 88 comparisons, 93.2%), and risk of bias (31 of 88 comparisons, 35.2%). None of the estimates were downgraded due to publication bias and indirectness. Supplementary material 4 shows complete forest plots of the analyses for interventions rated as moderate, low, and very low certainty of evidence.

Non-invasive therapy versus control (i.e., placebo, sham, waiting list or no intervention)

For pain intensity in the short term, moderate certainty evidence suggests that betamethasone valerate (BMV) medicated plaster likely results in a slight reduction in pain when compared with placebo (MD -10.7, 95% CI: -18.4, -3.0, two trials,^{33,70} n = 261 participants). The estimated effect for BMV medicated plaster did not reach clinical relevance (i.e., 19 points on the 0–100 point scale). Low certainty evidence shows that extracorporeal shockwave therapy (ESWT) does not reduce pain intensity when compared with placebo or sham in the short-term (MD -3.3, 95% CI: -11.9, 5.1, three trials,^{72,81,85} n = 194 participants) (Figure 2).

For maximum grip strength in the short-term, moderate certainty evidence suggests that ESWT likely results in little increase in strength when compared with placebo or sham (MD 4.9 kg, 95% CI: 1.2, 8.6, four trials,^{72,81,84,88} n = 311). The estimated effect for ESWT did not reach clinical relevance of 17 kg. Low certainty evidence shows that laser therapy does not increase strength (MD 5.0 kg, 95% CI: -2.3, 12.3, two trials,^{54,89} n = 76 participants) when compared with placebo or sham (Figure 3).

For disability, moderate certainty evidence shows that BMV medicated plaster likely reduces disability (MD

PAIN INTENSITY

A - Non-invasive therapies x Control (i.e., placebo, sham, waiting list or no intervention)

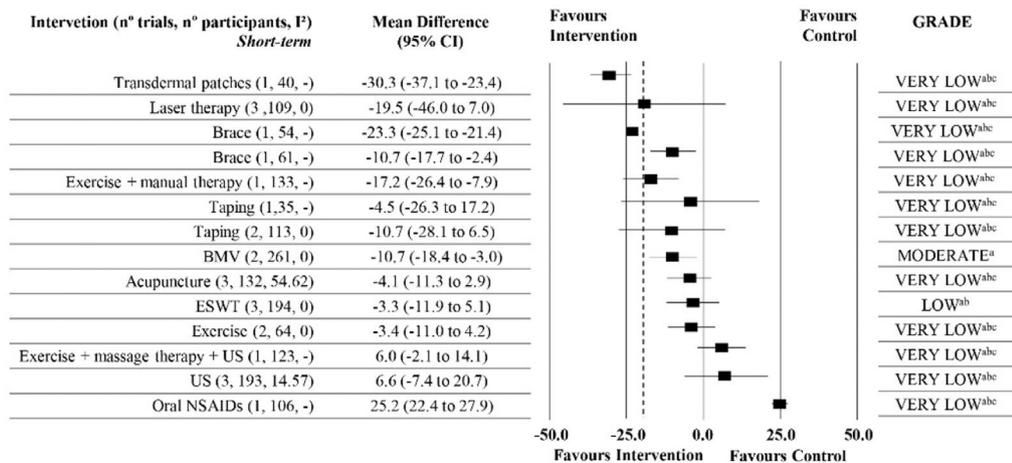


Fig. 2 Summary of Moderate, Low, and Very Low-Certainty of Evidence on Pain Intensity in Lateral Elbow Tendinopathy. Dashed line indicates the minimum clinically important difference. BMV, betamethasone valerate medicated plaster; ESWT, extracorporeal shockwave therapy; NSAIDs, nonsteroidal anti-inflammatory drugs; US, ultrasound therapy.

^aDowngraded owing to imprecision: less than 400 participants included in the meta-analysis or 95% CI includes no effect and crosses SMD = 0.5 or MD > 10%. ^bDowngraded owing to inconsistency: I² statistic was higher than 50%, absence of overlap between CI or pooling was not possible. ^cDowngraded owing to risk of bias: more than 25% of the participants in the meta-analysis were from trials with a high risk of bias (i.e., PEDro score <6 out of 10).

MAXIMUM GRIP STRENGTH

A - Non-invasive therapies x Control (i.e., placebo, sham, waiting list or no intervention)

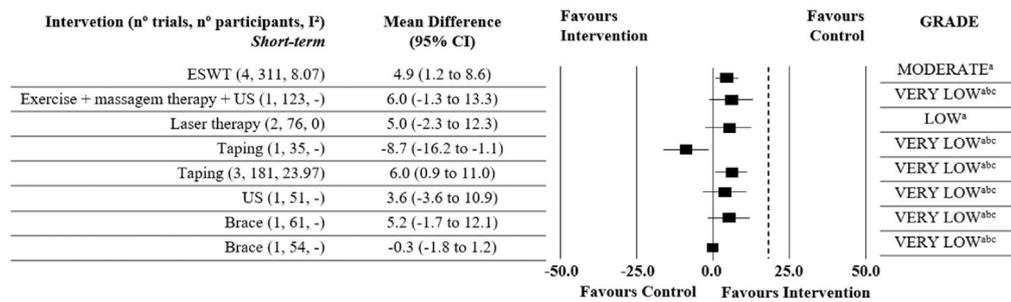


Fig. 3 Summary of Moderate, Low, and Very Low-Certainty of Evidence on Maximum Grip Strength in Lateral Elbow Tendinopathy. Dashed line indicates the minimum clinically important difference. ESWT, extracorporeal shockwave therapy; NSAIDs, nonsteroidal anti-inflammatory drugs; US = ultrasound therapy.

^aDowngraded owing to imprecision: less than 400 participants included in the meta-analysis or 95% CI includes no effect and crosses SMD = 0.5 or MD > 10%. ^bDowngraded owing to inconsistency: I² statistic was higher than 50%, absence of overlap between CI or pooling was not possible. ^cDowngraded owing to risk of bias: more than 25% of the participants in the meta-analysis were from trials with a high risk of bias (i.e., PEDro score <6 out of 10).

-6.7, 95% CI: -11.4, -2.0, two trials,^{33,70} n = 261 participants) when compared with placebo in the short-term. The estimated effect may reach clinical relevance of 11 points on the 0–100 point scale. Also, with an effect that may reach a clinical relevance, low certainty suggests that acupuncture reduces disability when compared with sham in the short-term (MD -9.1, 95% CI: -11.7, -6.4, three trials,^{62,77,93} n = 178 participants) (Figure 4). Low certainty evidence shows that ESWT does not reduce disability (MD 2.9, 95% CI: -5.9, 11.7, four trials,^{72,81,84,88} n = 311 participants) when compared with

placebo in the short-term. Very low certainty evidence for quality of life is reported in Figure 5.

Non-Invasive therapy versus invasive interventions

Low certainty evidence indicates that there is no significant difference between dry needling and corticosteroid injection in reducing disability in the short-term (MD -10.9, 95% CI: -29.9, 9.3, two trials,^{58,68} n = 149 participants). In all other comparisons with invasive interventions, the evidence is very low on certainty for outcomes of interest. Detailed results are reported in Supplementary material 4.

DISABILITY

A - Non-invasive therapies x Control (i.e., placebo, sham, waiting list or no intervention)

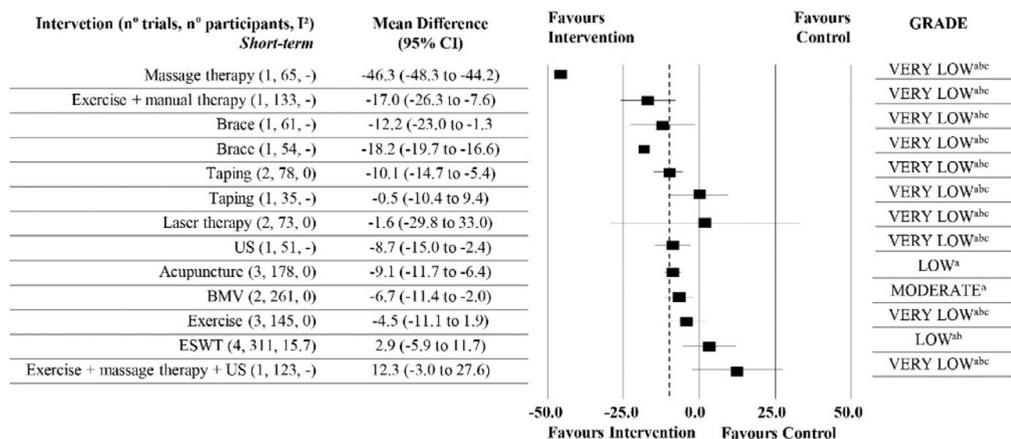


Fig. 4 Summary of Moderate, Low, and Very Low-Certainty of Evidence on Disability in Lateral Elbow Tendinopathy. Dashed line indicates the minimum clinically important difference. BMV, betamethasone valerate medicated plaster; ESWT, extracorporeal shockwave therapy; NSAIDs = nonsteroidal anti-inflammatory drugs; US = ultrasound therapy.

^aDowngraded owing to imprecision: less than 400 participants included in the meta-analysis or 95% CI includes no effect and crosses SMD = 0.5 or MD > 10%. ^bDowngraded owing to inconsistency: I² statistic was higher than 50%, absence of overlap between CI or pooling was not possible. ^cDowngraded owing to risk of bias: more than 25% of the participants in the meta-analysis were from trials with a high risk of bias (i.e., PEDro score <6 out of 10).

QUALITY OF LIFE

A - Non-invasive therapies x Control (i.e., placebo, sham, waiting list or no intervention)

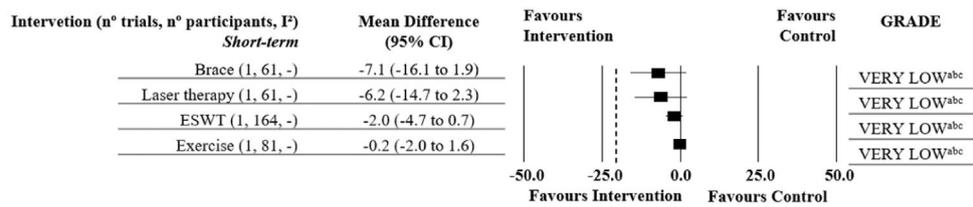


Fig. 5 Summary of Very Low-Certainty of Evidence on Quality of Life in Lateral Elbow Tendinopathy.

Dashed line indicates the minimum clinically important difference. ESWT, extracorporeal shockwave therapy; NSAIDs, nonsteroidal anti-inflammatory drugs.

^aDowngraded owing to imprecision: less than 400 participants included in the meta-analysis or 95% CI includes no effect and crosses SMD = 0.5 or MD > 10%. ^bDowngraded owing to inconsistency: I^2 statistic was higher than 50%, absence of overlap between CI or pooling was not possible. ^cDowngraded owing to risk of bias: more than 25% of the participants in the meta-analysis were from trials with a high risk of bias (i.e., PEDro score <6 out of 10).

Sensitivity analysis

Detailed qualitative sensitivity analyses conducted by removing high risk of bias trials (i.e., PEDro score <6 points out of 10) to investigate potential impact of poor methodological quality trials on the estimated effectiveness are presented in Supplementary material 5. Significant effect changes were found for laser therapy to reduce pain (MD -9.1, 95% CI: -16.3, -1.9, one trials,⁵⁴ $n = 61$ participants) and disability (MD -14.6, 95% CI: -25.2, -3.9, one trial,⁵⁴ $n = 61$ participants) when compared to sham in the short-term. However, such effect estimates are based on comparisons with very low certainty evidence, making the results uncertain.

Discussion

This systematic review with meta-analysis investigated the effectiveness of non-invasive therapies on pain intensity, maximum grip strength, disability, and quality of life in people with lateral elbow tendinopathy, when compared with control and invasive interventions. Our results indicate that the most promising non-invasive therapy for improving short-term disability is the BMV medicated plaster compared to placebo. Low certainty evidence also supports acupuncture for disability in the short-term compared to sham. None of the identified trials investigated the long-term effectiveness, moreover much of the evidence has very low certainty, demonstrating the lack of evidence on the treatment of lateral elbow tendinopathy. Estimates with very low certainty of evidence will likely change in the future with larger, high-quality trials.

The defined questions to be answered in our study differ from those of other reviews already conducted, making a direct comparison between estimates impossible. Thus, previous reviews investigating the effectiveness of specific interventions allowed an indirect comparison between results. Our review identified moderate effects that may reach clinical relevance in favor of BMV medicated plaster for disability in the short-term compared to placebo. Although other reviews have already investigated the effectiveness of BMV medicated plaster,⁹⁵ our review was the first

to reveal its effectiveness on lateral elbow tendinopathy. Potentially clinically important effects were also found in favor of acupuncture for disability. Recent studies have shown the benefits of acupuncture on lateral elbow tendinopathy in the short-term; however, the disability outcome had not yet been investigated until our review was conducted.^{96,97}

Several systematic reviews have been published to date to investigate the effect of ESWT on lateral elbow tendinopathy, but current evidence is still conflicting. Yao et al.⁹⁸ gathered 13 clinical trials, showing effective pain relief and improved grip strength as results. Similarly, Karanasios et al.⁹⁹ showed estimates in favor of the ESWT for grip strength. In our review, we found a small non-clinically relevant effect to no effect for ESWT. The use of this resource in clinical practice must be carefully analyzed, taking into account the intended outcome.

Among the clinical trials selected for inclusion, we found none that investigated the long-term effectiveness of non-invasive therapies. Even with follow-up of the sample above the 12-week time point, the intervention protocols did not persist for the long term.^{80,100,101} It is known that most patients with lateral elbow tendinopathy evolve to a chronic clinical condition, accompanied by persistent pain, increased disability, and a remarkable reduction in quality of life.^{102,103} Future clinical trials evaluating long-term effectiveness is necessary to guide health professionals during clinical practice.

The lateral elbow pain and muscle function impairments guideline recommends the use of interventions such as manual therapy, medications, and taping for the management of lateral elbow tendinopathy.¹⁰⁴ However, the trials presented to support such argument have unreliable estimates, accompanied by inadequate comparators to establish effectiveness and low methodological rigor. In contrast, our review rigorously evaluated the available evidence, considering suitable comparators and criticizing the feasibility of practical application according to clinically important estimates.

Strengths and limitations

This systematic review used strong methodological rigor, following the Cochrane recommendations to investigate the

effectiveness of non-invasive therapy in lateral elbow tendinopathy. We performed a careful analysis classifying all interventions according to the evidence established by the GRADE classification system, which makes our review transparent and reliable.

However, our review presents some potential limitations. Due to the variety of identified interventions, it was often not possible to group included trials. In most cases, interventions entitled “physical therapy” addressed different therapies in the experimental group, making grouping impossible. Thus, we chose to rename the interventions according to the protocol applied and group those that were similar, reducing clinical heterogeneity. Relatedly, the small number of trials included in the meta-analysis made it impossible for us to explore heterogeneity and publication bias. Although several individual trials have produced statistically and clinically relevant positive results, they have all been downgraded to very low certainty of evidence due to imprecision (i.e., small sample sizes) and inconsistency (i.e., pooling was not possible).

Conclusion

We found moderate certainty evidence that BMV medicated plaster may reach clinically relevant effects on disability in the short-term compared to placebo. Low certainty evidence also suggests potential clinically relevant effects of acupuncture on disability in the short-term compared to sham. No evidence was found for the long-term effectiveness of non-invasive therapies. The results of this meta-analysis should be carefully evaluated by clinicians, stakeholders, and researchers, taking into consideration that most investigated interventions have currently very low certainty. Our findings expose the need to develop new larger trials with high methodological quality.

Conflict of interest

The authors declare no conflicts of interest.

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Supplementary materials

Supplementary material associated with this article can be found in the online version at [doi:10.1016/j.bjpt.2024.100596](https://doi.org/10.1016/j.bjpt.2024.100596).

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