Effectiveness of manual therapy in carpal tunnel syndrome: Systematic review and meta-analysis

Efectividad de la terapia manual en el síndrome del túnel carpiano: Revisión sistemática y metaanálisis

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Short title:
Manual therapy in carpal tunnel syndrome

How to cite this article:
Cereceda-Muriel, C., Ramírez-Donoso, S., Cárdenas-Caniuqueo, M., Silva-Alfaro, V., & Concha-Valdevenito, D., (2024). Effectiveness of manual therapy in carpal tunnel syndrome: Sistematic review and meta-analysis. *Cultura, Ciencia y Deporte, 19*(59), 145-180. https://doi.org/10.12800/ccd.v19i59.2025

Received: 28 February 2023 / **Accepted**: 16 January 2024

Summary

The aim of this systematic review is to determine the effectiveness of manual therapy applied alone on pain, function, symptom severity, nerve conduction and strength in people with carpal tunnel syndrome. We searched MEDLINE, WOS, SCOPUS, PEDro, CENTRAL, LILACS and Epistemonikos. Twelve studies met the eligibility criteria and nine were included in the quantitative synthesis. Pain had a standardized mean difference of - 1.83 (95% *CI* = - 2.62, - 1.03, *p* = < .00001), function a mean difference of - 0.88 (95% *CI* = - 1.05, - 0.71, *p* = < .00001), symptom severity a mean difference of - 0.94 (95% *CI* = - 1.58, - 0.30, *p* = .004), sensory conduction velocity a mean difference of 7.46 (95% *CI* = - 0.11, 14.98, *p* = .05), motor conduction velocity a mean difference of 1.85 (95% *CI* = 0.68, 3.01, *p* = .002), motor latency a mean difference = - 0.57, (95% *CI* = - 0.96, - 0.17, *p* = .005), grip strength a mean difference = - 0.24, 95% *CI* = - 2.22, 1.74, *p* = .81) and grip strength a mean difference = 0.21 (95% *CI* = - 0.42, 0.83, *p* = .52). Finally, it is concluded that manual therapy applied alone is an effective short-term option for people with mild to moderate carpal tunnel syndrome.

Keywords: Median neuropathy, musculoskeletal manipulation, physiotherapy, pain.

Resumen

El objetivo de esta revisión sistemática es determinar la efectividad de la terapia manual aplicada de forma aislada en el dolor, la función, la severidad de síntomas, la conducción nerviosa y la fuerza en personas con síndrome del túnel carpiano. Se realizó una búsqueda en MEDLINE, WOS, SCOPUS, PEDro, CENTRAL, LILACS y Epistemonikos. Doce estudios cumplieron los criterios de elegibilidad y nueve fueron incluidos en la síntesis cuantitativa. El dolor obtuvo una diferencia de media estandarizada de -1.83 (*IC* al 95% = - 2.62, - 1.03, *p* = < .00001), la función una diferencia de media de - 0.88 (*IC* al 95% = - 1.05, - 0.71, *p* = < .00001), la severidad de síntomas una diferencia de media de - 0.94 (*IC* al 95% = - 1.58, - 0.30, *p = .004*), la velocidad de conducción sensitiva una diferencia de media de 7.43 (*IC* al 95% = - 0.11, 14.98, *p = .05*), la velocidad de conducción motora una diferencia de media de 1.85 (*IC* al 95% = 0.68, 3.01, *p* = .002), la latencia motora una diferencia de media = - 0.57, (*IC* al 95% = - 0.96, - 0.17, *p = .005*), la fuerza de agarre una diferencia de media = - 0.24, *IC* al 95% = - 2.22, 1.74, *p = .81*) y la fuerza de pinza una diferencia de media = 0.21 (*IC* al 95% = - 0.42, 0.83, *p* = .52). Finalmente, se concluye que la terapia manual aplicada de forma aislada es una opción efectiva a corto plazo para personas con síndrome del túnel carpiano leve a moderado.

Palabras clave: Neuropatía mediana, manipulación musculoesquelética, fisioterapia, dolor.

Introduction

Carpal tunnel syndrome (CTS) is a condition involving entrapment of the median nerve in the carpal tunnel area of the wrist (Foley et al., 2007), is one of the most common peripheral neuropathies of the upper extremity with a prevalence ranging from 1-5% of the general population (Thiese et al., 2014), and increases to 11.7% in more specific symptomatic and working class populations (Bland et al., 2003; Thiese et al., 2014), affecting women more frequently, with a three to ten times higher prevalence than men (Kozak et al., 2015; Lewanska & Walosiak-Skorupa, 2014). Diseases such as diabetes, obesity, osteoarthritis and rheumatoid arthritis could be contributing factors to the development of this pathology (Pourmemari & Shiri 2016; Pourmemari et al., 2018; Shiri, 2016). It's a etiology is based on theories such as Lundborg's, which proposes that intraneural blood microcirculation, myelin sheath, axons and supporting connective tissue are disturbed (Lundborg, 1988) or the double crush theory, which mentions that proximal compression of a nerve can disrupt axoplasmic transport in other areas. Others mention the relevance of local inflammatory changes, mechanical deformation of the nerve fibres and decreased mobility due to oedema or inflammation (Ettema et al., 2004; Oh et al., 2006; Schmid, 2015). Occupational mechanical factors are a relevant cause to consider, as there is an increased risk of CTS in activities that require a high degree of repetition and forced exertion (Kozak & Schedlbauer, 2015). Diagnosis is based primarily on clinical criteria such as pain, loss of function, altered sensation with paraesthesia in phalanges I, II and III and in more advanced stages loss of strength in the tenar area (Vogt & Scholz, 2002), and is usually complemented by tests such as the Phalen, Tinel, Paley/McMurley, among others (Palumbo & Szabo, 2002). Tests such as ultrasound, magnetic resonance imaging and electromyography are used to complement and confirm the diagnosis obtained through clinical criteria (Corlobé, 2004; Cudlip et al., 2002; Jarvik et al., 2008).

Treatment options are varied, and conservative treatment generally focuses on treating the main clinical symptoms, where pain, function, strength and nerve conduction are relevant for improving activities of daily living, quality of life and ultimately reducing healthcare costs (Bland & Rudolfer, 2003; Mondelli et al., 2002). One of the most widely used conservative treatment options is manual therapy (MT), which is widely used in musculoskeletal system disorders and CTS (Akalin et al., 2002; Carlesso et al., 2014; Pettman, 2007). The most commonly used TM techniques in CTS are neurodynamic manoeuvres, joint mobilisation or manipulation techniques, massage or soft tissue management techniques, and instrumental manual therapy (Klokkari & Mamais, 2018). Although there are studies that support the application of TM techniques in CTS, its mechanism of action is still unclear, as TM is a complex intervention based on the interaction of several complementary systems, and independent of the technique used, the effects of TM could be due to a neurophysiological mechanism, which states that a mechanical stimulus generates a cascade of neurophysiological responses at the peripheral and central levels that ultimately produces a decrease in musculoskeletal pain (Bialosky et al, 2009; Bialosky et al., 2018).

In recent years, there has been an increase in the scientific literature on the application of TM in CTS, which has led to various systematic reviews (SR). On the one hand, there are those by Medina and Yancosek (2008), Lim et al. (2017) and Araya et al. (2018), which focus on neural mobilisation techniques, presenting contradictory results, as Medina and Yancoseek (2008) and Lim et al. (2017) conclude that there is insufficient evidence to support the use of neurodynamic techniques in users with CTS, while the SR of Araya et al. (2018) determines that there is moderate evidence to support the application of neurodynamic techniques for the improvement of pain and function in subjects with CTS. On the other hand, the SR of Sault et al. (2020) and Du et al. (2022) focus on establishing the effects of TM applied alone or in combination with other therapies (exercise, laser, ultrasound, etc.), demonstrating that TM combined with other interventions are effective for functional recovery, decreased pain, increased joint range, improved sensory and motor function. Finally, the SR with meta-analysis (MA) by Jiménez et al. (2022) is the only SR that includes clinical studies applying TM techniques in isolation, concluding that it is effective in reducing pain, improving function and nerve conduction. However, it includes few studies and does not incorporate all published clinical trials. For this reason, the aim of this SR is to determine whether there is scientific evidence to support the use of TM techniques applied in isolation or in combination with other TM techniques on pain, function, symptom severity, nerve conduction and strength in users with CTS.

Methodology

Protocol

This systematic review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) statement and considered the recommendations of the Cochrane Collaboration manual (Higgins & Green, 2008; Liberati et al., 2009; Moher et al., 2009).

Elegibility criteria

Studies related to manual therapy intervention in carpal tunnel syndrome were eligible if they met the following criteria: 1) population: people with a diagnosis of carpal tunnel syndrome confirmed by clinical criteria (pain, loss of function, hand paresthesia, etc.), radiological criteria (ultrasound, magnetic resonance imaging) or electromyographic criteria (nerve conduction). 2) Type of intervention: Manual therapy alone or in combination with other manual therapy techniques (joint techniques, neurodynamic, soft tissue management, etc.). The technique must be applied by a certified physiotherapist.

3) Type of comparison: Other therapies, other manual therapy techniques, placebo interventions, surgery or no intervention control group. 4) Type of outcomes: clinical variables such as pain, strength, joint range, function, sensation, nerve conduction, etc. 5) Type of study: Randomised clinical studies published in English or Spanish. Exclusion criteria were: 1) Studies combining treatments other than manual therapy in the experimental group (ultrasound, laser, exercise, pharmacology, splinting, etc.). 2) Studies that included subjects with other pathologies of the upper extremity (shoulder, arm, elbow, forearm, wrist and hand). 3) Studies scoring <5 points on the PEDro scale.

Sources of information

The databases used for the electronic search of articles were MEDLINE (via PubMed), Web of science, SCOPUS, the Physiotherapy Evidence Database (PEDro), Cochrane Central Register of Controlled Trials (CENTRAL), Literatura Latinoamericana y del Caribe en Ciencias de la Salud (LILACS) and Epistemonikos, being these consulted until September 2022.

Electronic search

An advanced computerised search strategy including Medical Subjects Heading (MeSH) terms and free text terms was used for the article collection process. On the one hand, the MeSH terms used were: Carpal tunnel syndrome, musculoskeletal manipulation, clinical trial and randomized controlled trial. While the free text terms were: carpal tunnel, manual therapy, manipulation, mobilization and massage therapy. All terms used were combined with "AND" and "OR" booleans according to their nature. For the MEDLINE database search we used the sensitive search strategy proposed by Cochrane (Moher et al., 2009). The search was performed by two independent reviewers (CC-M and SR-D) and a third reviewer was consulted in case of disagreement (MC-C). Table 1 presents the search commands for each database.

Table 1. Search Commands for the databases

Base de datos	Comando de búsqueda
Medline	(((("Carpal Tunnel Syndrome"[Mesh]) OR (carpal tunnel)) OR (median nerve entrapment)) AND ((((("Musculoskeletal Manipulations"[Mesh]) OR (manual therapy)) OR (manipulation)) OR (mobilization)) OR (massage))) AND (("Clinical Trial" [Publication Type]) OR ("Randomized Controlled Trial" [Publication Type]))
Scopus	(TITLE-ABS-KEY ("carpal tunnel syndrome") OR TITLE-ABS-KEY ("carpal tunnel") OR TITLE-ABS-KEY ("median nerve entrapment") AND TITLE-ABS-KEY ("musculoskeletal manipulation") OR TITLE-ABS-KEY ("manual therapy") OR TITLE-ABS-KEY (manipulation) OR TITLE-ABS-KEY (mobilization) OR TITLE-ABS-KEY (massage) AND TITLE-ABS-KEY ("clinical trial"))
Web of Science	(((ALL = (carpal tunnel syndrome)) OR ALL = (carpal tunnel)) AND ALL = (manual therapy)) AND ALL = (clinical trial)
PEDro	Abstract & title: Syndrome carpal tunnel; Therapy: stretching, mobilization, manipulation, massage; body part: Hand or wrist; Subdiscipline: musculoskeletal
CENTRAL	MeSH descriptor: [Carpal Tunnel Syndrome] explode all trees AND MeSH descriptor: [Musculoskeletal Manipulations] explode all trees AND trials
LILACS	(carpal tunnel syndrome) OR (carpal tunnel) AND (musculoskeletal manipulation) OR (manual therapy) AND (clinical trial)
Epistemonikos	(title: (carpal tunnel syndrome) OR abstract: (carpal tunnel syndrome)) AND (title: (manual therapy) OR abstract: (manual therapy)) OR (title:(manipulation) OR abstract: (manipulation)) OR (title: (mobilization) OR abstract: (mobilization)) OR (title: (massage) OR abstract: (massage)) AND (title: (clinical trial) OR abstract: (clinical trial)) OR (title: (randomized controlled trial) OR abstract: (randomized controlled trial))

Study selection

Two independent reviewers (CC-M and SR-D) screened articles by title and abstract, relevant articles were then reviewed in full text and inclusion and exclusion criteria were applied, in case of disagreement a third reviewer (MC-C) was involved.

Data collection

Two independent reviewers (MC-C and VS-A) performed the extraction of results from the selected articles. Criteria included: 1) author and year of publication, 2) study design, 3) sample characteristics (number of participants, age, sex), 4) type of intervention and dose used in the experimental group (TM, dose, time, etc.), 5) type of intervention in the comparison group (TM, surgery, physical agents, etc.), 6) follow-up, 7) variables, 8) outcomes.

Risk of bias assessment

Two independent reviewers conducted the risk of bias assessment of the included studies (SR-D and VS-A) and a third reviewer was involved in case of disagreement (CC-M). The assessment was conducted according to the recommendations of the Cochrane Collaboration handbook (Moher, et al., 2009) and the risk of bias (RoB) tool (Higgins & Green, 2011) was used. This tool assesses risk of bias across seven domains: generation of the random sequence, concealment of the randomization sequence, blinding of participants and treatments, blinding of the evaluation of the results, incomplete results data, selective reporting of results and other biases. Each of these aspects can be categorised as "low risk of bias" (green), "nuclear risk of bias" (yellow) or "high risk of bias" (red).

Statistical methods

The DerSimonian and Laird random-effects or Mantel-Haenszel fixed-effects method was used, depending on heterogeneity (DerSimonian & Kacker, 2007; Mantel & Haenszel, 1959). For pooled estimation, mean difference (MD) or standardised mean difference (SMD) with 95% confidence interval (CI) was used for pain, strength, symptom severity, functionality and nerve conduction. Statistical heterogeneity was assessed using the I2 statistic (Higgins & Thompson, 2002), which considers 0-40% heterogeneity as unimportant, 30-60% moderate, 50-90% substantial and 75-100% as considerable heterogeneity (Higgins & Green, 2008). Meta-analysis (MA) was performed with RevMan 5.4 software considering significant differences with an alpha value < .05.

Results

Study selection

A total of 364 studies were found in the electronic search process (figure 1), where finally 12 ECAS met the selection criteria to be included in the SR (Beddaa et al., 2022; Fernández et al., 2015; Hains et al., 2010; Jimenez et al., 2018; Jiménez et al., 2022; Moraska, et al., 2008; Talebi et al., 2018; Wolny et al., 2016; Wolny et al., 2017; Wolny & Linek, 2018a; Wolny & Linek, 2018b, Wolny & Linek, 2019).

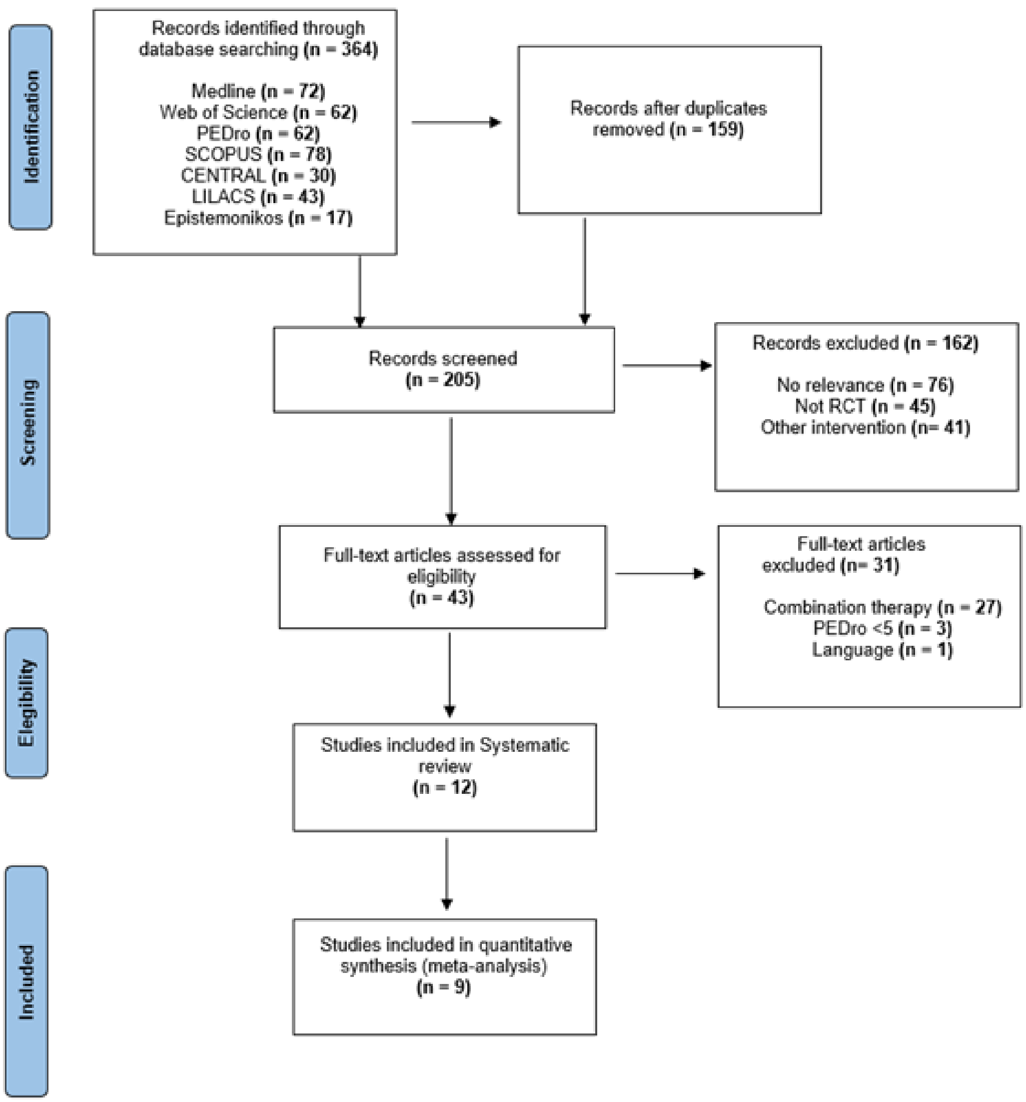

Figure 1. Flow diagram for study selection process

Studies characteristics

The summary of included studies is presented in table 2. The total population included 1,198 treated hands with a diagnosis of CTS (626 in the TM-treated groups and 572 in the groups treated with other interventions). Eighty-six per cent of all treated persons were female and had an average age of 50 years.

In all included studies the diagnosis was mainly based on clinical criteria such as pain in the wrist or hand, paresthesias related to the median nerve pathway, increased symptoms at night and positive Phalen's or Tinel's test. In addition, alteration in electrophysiological aspects was considered through the measurement of nerve conduction in electromyography, where three ECAS considered the recommendations of the "American Academy of Physical Medicine and Rehabilitation", and the diagnosis was confirmed with a conduction velocity < 40 m/s and a motor latency > 4.20 m/s (Fernández et al., 2015; Jiménez et al., 2018; Jiménez et al., 2022), while five articles confirmed the diagnosis with conduction velocity levels < 50 m/s and motor latency > 4 m/s (Wolny et al., 2016; Wolny et al., 2017; Wolny & Linek, 2018a; Wolny & Linek, 2018b; Wolny & Linek, 2019). Exclusion criteria were mainly based on subjects with previous surgeries, corticosteroid injection treatments and other drugs, pregnancy, trauma and systemic comorbidities (cervical radiculopathies, fibromyalgia, osteoarthritis, arthritis, thyroid disorders, diabetes, etc.). Only one study excluded subjects with depression with a score > 8 on the Beck Depression Inventory II (BDI-II) (Fernández et al., 2015). Only the article by Talebi et al. (2018) incorporated a population with CTS and associated diabetes. Finally, ten SCAS included subjects with mild or moderate diagnosis (Beddaa et al., 2022; Jiménez et al., 2018; Jiménez et al., 2022; Moraska, et al., 2008; Talebi et al., 2018; Wolny et al., 2016; Wolny et al., 2017; Wolny & Linek, 2018a; Wolny & Linek, 2018b; Wolny & Linek, 2019) while only one included user with mild, moderate or severe CTS (Fernandez et al., 2015).

Ten studies performed sample size calculations to select their (Beddaa et al., 2022; Fernández et al., 2015; Jiménez et al., 2018; Jiménez et al., 2022; Talebi et al., 2018; Wolny et al., 2016; Wolny et al., 2017; Wolny & Linek, 2018a; Wolny & Linek, 2018b, Wolny & Linek, 2019) and all met ethical safeguards and were approved by ethics committees.

Tabla 2. Characteristics of the studies included in the systematic review and meta-analyses

Author	Manual therapy				Other intervention				Results
	N (women%)	Aged *(SD)*	Intervention	Sessions (time per session)	*N* Women %)	Aged *(SD)*	Intervention	Sessions (time per session)	Between groups difference
Beddaa (2022)	62 (100%)	52.5 (10.6)	Carpal bone mobilization and neurodynamics for median nerve	20 (UE)	62 (100%)	52.5 (10.6)	Sham carpal bone mobilization and sham neurodynamics for median nerve	20 (UE)	**During Treatment (5 semanas)** BSTQ-FS *p* = .0001* NPRS *p* = .001* GS *p* = .05l **End of treatment** BCTQ-FS *p* = .003* NPRS *p* = .0001* GS *p* = .02*
Fernández (2015)	60 (100%)	47 (10)	Neurodynamic median nerve Soft tissue management Joint mobilization of the spine	3 (30 min)	60 (100%)	46 (9)	Surgery	NA	**1 and 3 month follow-up:** NPRS *p* < .001* BCTQ-SS *p* >.05 BCTQ-FS *p* < .01* **6 and 12 month follow-up:** NPRS *p* >.1 BCTQ-SS *p* > .05 BCTQ-SF *p* > .3 GROC *p* > .1
Hains (2010)	37 (70%)	46 (6.7)	Biceps ischemic compression therapy	15	18 (44%)	47 (7.2)	Shoulder and clavicle ischemic compression therapy	15	**End of treatment** PIS *p* = .02*
Jiménez (2018)	30 (80%)	44.9 (9.3)	Diacutaneous fibrolysis	5 (20 min)	30 (83%)	48.8 (7.9)	Sham diacutaneous fibrolysis	5 (20 min)	**End of treatment** SCV *p* < .01* DML *p* = .029* VAS *p* < .01* DASH *p* <.01* **1 month follow-up:** VAS *p* < .01* DASH *p* <.01*

Jiménez (2022)	30 (80%)	44.2 (10)	Diacutaneous fibrolysis	5 (20 min)	30 (87%)	48.9 (8.7)	Sham diacutaneous fibrolysis	5 (20 min)	**End of treatment** VAS, CSA (cross-sectional área) TCL $p < .01$* TCL (transversal carpal ligament) $p < .03$*
Moraska (2008)	14 (71%)	47 (8.8)	Targeted massage (probable sites of nerve entrapment along the afflicted upper extremity)	12 (30 min)	13 (92%)	50.3 (15.1)	General massage (back, neck, arms)	12 (30 min)	**End of treatment** GS $p = .001$* PS $p = .11$ FSS $p = .34$ SSS (symptom severity scale) $p = .80$ GPT $p = .41$
Talebi (2018)	15 (UE)	49 (10.2)	Neurodynamics for median nerve Soft tissue management Carpal bone mobilization	12 (25 min)	15 (UE)	50.2 (10.2)	TENS + TU	12 (25 min)	**End of treatment** VAS $p < .1$ BCTQ-SS $p = .006$* BCTQ-FS $p = .04$* MNT $p = .000$*
Wolny (2016)	70 (89%)	53 (8.7)	Neurodynamics for median nerve wrist opening and closing techniques Trapezious functional massage	20 (30 min)	70 (86%)	51.5 (10.3)	Láser + TU	20 (25 min)	**End of treatment** 2PD: DS: Finger I, II, III $p > .05$ RDS: Finger I $p < .001$*, II $p < .02$*, III $p < .001$*
Wolny (2017)	70 (89%)	53 (8.7)	Neurodynamics for median nerve wrist opening and closing techniques Trapezious functional massage	2 (25 min)	70 (86%)	51.5 (10.3)	Láser + US	20 (25 min)	**End of treatment** SCV, MCV, ML, $p > .05$ VAS $p < .01$* BCTQ-SS $p < .01$* BCTQ-FS $p < .01$*
Wolny (2018a)	102 (88%)	52.6 (9.3)	Neurodynamics for median nerve wrist opening and closing techniques Trapezious functional massage de muñeca	20 (45 min)	87 (91%)	53.1 (8.9)	No intervention	NA	**End of treatment** SF-36 (physical): PF $p < .001$* RF $p < .001$, BP $p < .01$* GH $p < .001$* SF-36 (mental): RE $p < .01$* VT $p < .001$* MH $p <.03$* SF $p < .001$* PCS $p <.001$* MCS $p <.001$*
Wolny (2018b)	78 (90%)	54.2 (9.5)	Neurodynamics for median nerve¿	20 (20 min)	72 (90%)	52.2 (10.4)	Sham neurodynamics for median nerve	20 (20 min)	**End of treatment** SVC, MCV, ML $p < .01$* D2P (finger I, II, III) $p < .01$* VAS $p < .01$* BCTQ-SS/FS $p < .01$* GS $p = 0.1$ PG $p = 0.9$
Wolny (2019)	58 (90%)	54.6 (9.1)	Neurodynamics for median nerve	20 (20 min)	45 (89%)	53.1 (10.1)	No intervention	NA	**End of treatment** GS, PG $p > .05$ BCTQ-FS $p < .01$* BCTQ-SS $p < .01$* NPRS $p < .01$* ML $p < .01$* SCV $p = .01$* MCV $p = .83$

Nota: BCTQ = Boston Carpal Tunnel Questionnaire, BCTQ-FS = Boston Carpal Tunnel Questionnaire-Function severity, BCTQ-SS = Boston Carpal Tunnel Questionnaire-Symptom severity, BP = Bodily Pain, CSA = Cross-Section Area, DASH =

Disability Arm, Shoulder and Hand, DS = discrimination sensation, DML = Distal motor latency, FSS = Functional Status Scale, GH = General Health, GPT = Grooved Pegboard test, GROC = Global Rating of Change, GS = Grip Strength, MCS = Mental Component Summary, MCV = Motor Conduction Velocity, MH = Mental Health, MNT **=** median neurodynamic test, ML = Motor Latency, NA **=** not applicable, NPRS = Numeric Pain Rating Score, PCS Physical Component Summary, PG = Pinch Grip, PIS = Perceived Improvement Scores, 2PD = 2 point discrimination, RDS = Relative Discrimination Sensation, RE = Role limitations because of Emotional problems, RF = Rol Limitations because of physical health problems, SSS = Symprom Severity Scale, SF **=** Social Functioning, SF-36 = Short Form (Quality of life), SVC = Sensory Conduction Velocity, TENS = Transcutaneous electrical nerve stimulation, TU = Therapeutic Ultrasound, UE = Unspecified, VAS = Vidual Analogue Scale, VT = Vitality, * = Significant differences.

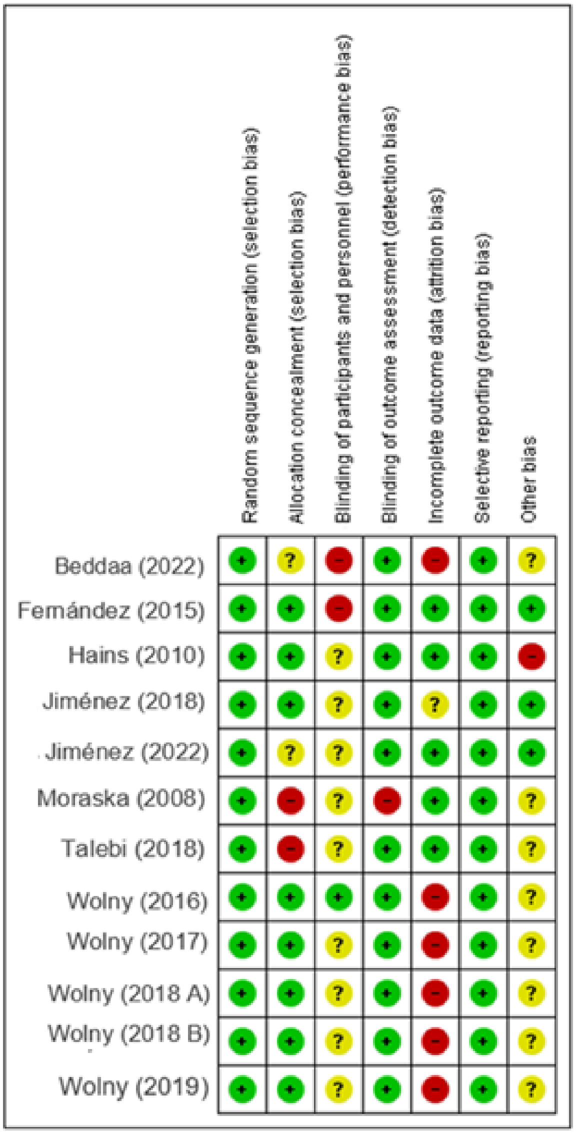

Figure 2. Risk of bias summary for each included study

Risk of bias

The risk of bias analysis is presented in figure 2 and 3, where 100% of the studies present a low risk of bias (Beddaa et al., 2022; Fernández et al., 2015; Hains et al., 2010; Jiménez et al., 2018; Jiménez et al., 2022; Moraska, et al., 2008; Talebi et al., 2018; Wolny et al., 2016; Wolny et al., 2017; Wolny & Linek, 2018a; Wolny & Linek, 2018b; Wolny & Linek, 2019), while random sequence blinding obtained a 67% low risk of bias (Fernández et al., 2015; Hains et al. 2010; Jiménez et al., 2018; Wolny et al., 2016; Wolny et al. 2017; Wolny & Linek, 2018a; Wolny & Linek, 2018b; Wolny & Linek, 2019). In blinding participants and staff, it is noted that 75% had unclear risk of bias (Hains et al., 2010; Jiménez et al., 2018; Jiménez et al., 2022; Moraska et al., 2008; Talebi et al., 2018; Wolny et al., 2017; Wolny & Linek, 2018a; Wolny & Linek, 2018b, Wolny & Linek, 2019). Outcome assessors were adequately blinded and at low risk of bias in 92% of studies (Beddaa et al., 2022; Fernández et al., 2015; Hains

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et al., 2010; Jiménez et al., 2018; Jiménez et al., 2022; Talebi et al., 2018; Wolny et al., 2016; Wolny et al., 2017; Wolny & Linek, 2018a; Wolny & Linek, 2018b, Wolny & Linek, 2019). In incomplete data reporting 50% of the studies had a high risk of bias (Beddaa et al., 2022; Wolny et al., 2016; Wolny et al., 2017; Wolny & Linek, 2018a; Wolny & Linek, 2018b, Wolny & Linek, 2019). 100% of the studies performed selective reporting of the data (Beddaa et al., 2022; Fernández et al., 2015; Hains et al., 2010; Jiménez et al., 2018; Jiménez et al., 2022; Moraska et al., 2008; Talebi et al., 2018; Wolny et al., 2016; Wolny et al., 2017; Wolny & Linek, 2018a; Wolny & Linek, 2018b, Wolny & Linek, 2019) and finally, 67% of the studies present unclear risk in other biases (Beddaa et al., 2022 Moraska et al., 2018; Talebi et al., 2018; Wolny et al., 2016; Wolny et al., 2017; Wolny & Linek, 2018a; Wolny & Linekb, 2018; Wolny & Linek, 2019).

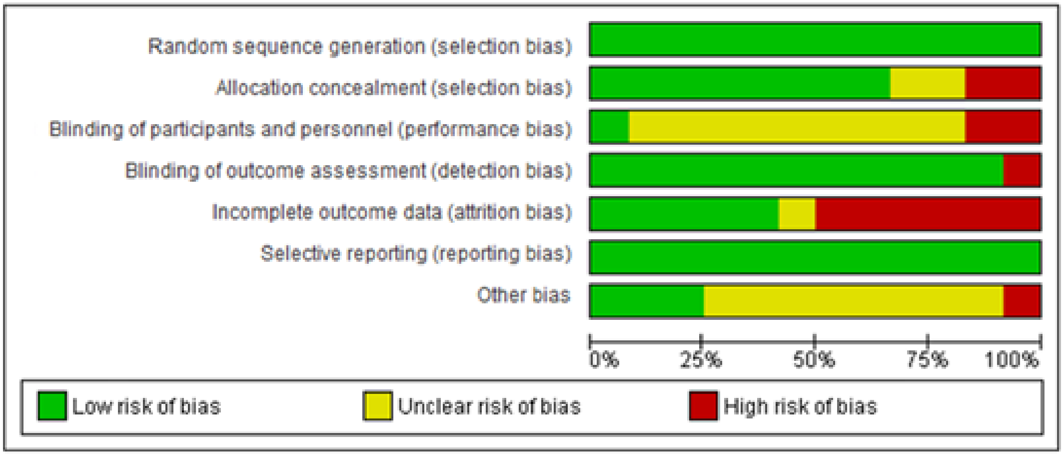

Figure 3. Risk of bias graph presented as percentages across all included studies

Synthesis of results

Of the 12 studies, four assessed grip strength Beddaa et al., 2022; Moraska et al., 2008; Wolny & Linek, 2018b; Wolny & Linek, 2019) and three assessed grip strength (Moraska et al., 2008; Wolny & Linek, 2018b; Wolny & Linek, 2019), where all specified that it was measured with a dynamometer expressed in kilograms (kg) and reported the data needed to perform the MA. Eight assessed (Beddaa et al., 2022; Fernández et al., 2015; Jiménez et al., 2018; Jiménez et al., 2022; Talebi et al., 2018; Wolny et al., 2017; Wolny & Linek, 2018b; Wolny & Linek, 2019), where five measured it with the numerical scale (ENA) (Beddaa et al., 2022; Fernández et al., 2015; Wolny et al., 2017; Wolny & Linek, 2018b; Wolny & Linek, 2019) and the other three assessed it with the visual analogue scale (VAS) (Jiménez et al., 2018; Jiménez et al., 2022; Talebi et al., 2018). All reported data for inclusion in the MA.

Symptom function and severity was assessed with different instruments by nine studies (Beddaa et al., 2022; Fernández et al., 2015; Hains et al., 2010; Jiménez et al., 2018; Moraska, et al., 2008; Talebi et al., 2018; Wolny et al., 2017; Wolny & Linek, 2018b, Wolny & Linek, 2019). However, five studies assessed function with the Boston carpal tunnel questionnaire (CBTC-SF) (Beddaa et al., 2022; Fernández et al., 2015; Wolny et al., 2017; Wolny & Linek, 2018b; Wolny & Linek, 2019) and reported data for necessary to be included in the MA. While four RCTs assessed symptom severity with the Boston Carpal Tunnel Questionnaire for Symptom Severity (CBTC-SS) and reported data for inclusion in the MA (Fernández et al., 2015; Wolny et al., 2017; Wolny & Linek, 2018b; Wolny & Linek, 2019). Nerve conduction (NC) was assessed by four ECAS (Jiménez et al., 2018; Wolny et al., 2017; Wolny & Linek, 2018b; Wolny & Linek, 2019), only three specified that it was with surface electromyography (Wolny et al., 2017; Wolny & Linek, 2018b; Wolny & Linek, 2019), while the other mentions that it was through neurophysiological parameters (Jiménez et al., 2018), of the four studies that assessed CN, all reported the data needed to perform the MA for sensory conduction velocity (SCV) and motor latency (LM) (Jiménez et al., 2018; Wolny et al., 2017; Wolny & Linek, 2018b; Wolny & Linek, 2019 while for motor conduction velocity (MCV), three reported the data to be included in the MA (Wolny et al., 2017; Wolny & Linek, 2018 b; Wolny & Linek, 2019).

Strength

The four studies included in the strength MA demonstrate *MD* with no significant difference between the TM groups compared to the group that applied other interventions on grip strength (MD = -0.24, 95% CI = - 2.22, 1.74, p = .81) (Beddaa et al., 2022; Moraska et al., 2008; Wolny & Linek, 2018b; Wolny & Linek, 2019) and gripper strength (MD = 0.21, 95% CI = -0.42. 0.83, p = .52), (Moraska et al., 2008; Wolny & Linek, 2018b; Wolny & Linek, 2019) where both show substantial heterogeneity ($I2$ = 69%, p = .02 and $I2$ = 62%, p = .07, respectively).

Table 3. Summary comparison manual therapy versus other interventions for grip strength and pinch grip after treatment

	Manual therapy			**Other intervention**				
Autor (year)	Mean	*SD*	*N*	Mean	*SD*	*N*	Weigth	Mean difference, 95% *CI*
Grip Strength								
Beddaa (2022)	20.84	3.56	62	20.33	3.29	62	35.5%	0.61 [- 0.60, 1.82]
Moraska (2008)	30.52	8.76	14	24.0	9.01	13	7.2%	6.52 [- 0.19, 13.23]
Wolny (2018 B)	28.4	6.11	78	30.3	5.38	72	30.2%	-1.90 [3.74, - 0.06]
Wolny 2019	28.8	5.62	58	30.1	5.74	45	27.1%	- 1.30 [- 3.51, 0.91]
Total			212			192	100%	-0.24[- 2.22, 1.74]
Heterogeneity: Tau^2 = 2.49; Chi^2 = 9.81, *df* = 3 *p* = .02; I^2= 69%								
General effect test: *Z* = 0.24 (0.81)								
Pinch Grip								
Moraska (2008)	8.58	2.06	14	6.91	1.77	13	14.1%	1.67 [0.22, 3.12]
Wolny (2018 B)	8.16	1.49	78	8.25	1.24	72	45.3%	- 0.09 [- 0.53, 0.35]
Wolny (2019)	8.36	1.44	58	8.33	1.34	45	40.6%	0.03 [- 0.51, 0.57]
Total			120			130	100%	0.21 [- .42, 0.83]
Heterogeneity: Tau^2 = 0.17; Chi^2 = 5.22, *df* = 2; *p* = 0.07; I^2 = 62%								
General effect test: *Z* = 0.65 (0.52)								

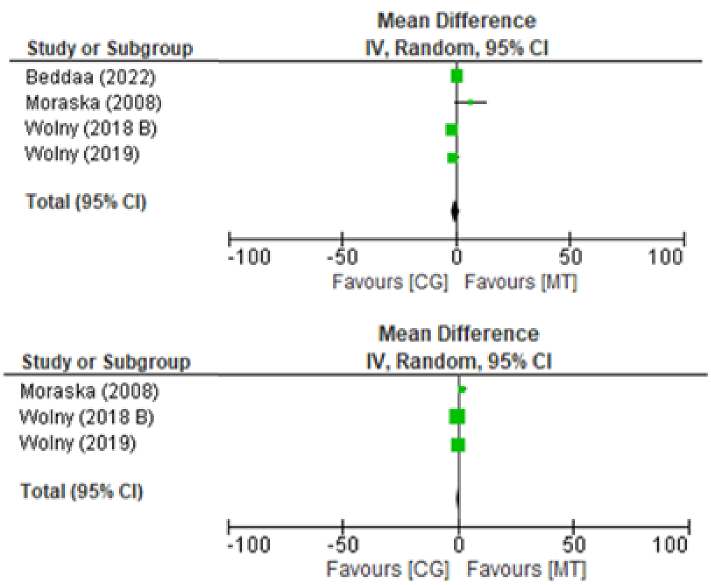

Figure 4. Forest plot comparison manual therapy versus other interventions for grip strength and pinch strength after treatment

Pain

The eight studies included in the MA of pain show a SMD with significant differences in favour of the TM group compared to the group with other interventions at the end of treatment (*SMD* = - 1.83, 95% *CI* = -2.62, - 1.03, *p* = < .00001), with considerable heterogeneity (*I2* = 95%, *p* = < .00001) (Beddaa et al., 2022; Fernandez et al, 2015; Jimenez et al., 2018; Jimenez et al. 2022; Talebi et al., 2018; Wolny et al., 2017; Wolny & Linek, 2018b; Wolny & Linek, 2019).

Table 4. Summary of manual therapy compared to other intervention for pain interventions after treatment

	Manual therapy			Other intervention				
Author (year)	**Mean**	***SD***	***N***	**Mean**	***S***	***N***	**Weigth**	**Mean Difference, 95% *CI***
				Pain				
Beddaa (2022)	1.52	1.5	62	5.52	1.76	62	12.9%	- 1.22 [- 1.60, - 0.83]
Fernández (2015)	1.4	1.9	55	3.4	2.3	56	12.9%	- 0.94 [- 1.33, - 0.55]
Jiménez (2018)	0.42	0.82	30	3.48	2.67	30	12.4%	- 1.53 [- 2.11, - 0.95]
Jiménez (2022)	0.23	0.54	30	2.87	2.5	30	12.4	- 1.44 [- 2.01, - 0.87]
Talebi (2018)	3.75	2.22	15	4.44	1.31	15	12%	- 0.37 [- 1.09, 0.35]
Wolny (2017)	1.47	1.2	70	3.58	1.93	70	12.9%	- 1.31 [- 1.67, - 0.94]
Wolny (2018b)	1.42	1.02	78	5.42	0.99	72	12.5%	- 3.96 [- 4.51, - 3.40]
Wolny (2019)	1.38	1.01	58	5.46	1.05	45	12.1%	- 3.94 [- 4.61, - 3.27]
Total			398			380	100%	- 1.83 [- 2.62, - 1.03]
Heterogeneity: $Tau^2 = 1.24$; $Chi^2 = 144.28$, $df = 7$ ($p = <0.00001$); $I^2 = 95\%$								
General effect test: $Z = 4.51$ ($p < .00001$)								

Table 5. Summary comparison manual therapy versus other interventions for function severity (BCTQ-FS) and symptom severity (BCTQ-SS) after treatment

	Manual therapy			Other intervention				
Author (year)	**Mean**	***SD***	***N***	**Mean**	***SD***	***N***	**Weigth**	**Meam differenc, *CI* 95%**
				Function Severity (BCTQ-FS)				
Beddaa (2022)	1.4	0.4	62	2.24	0.88	62	19.8%	- 0.84 [- 1.08, - 0.60]
Fernández (2015)	1.5	0.4	55	2.3	0.7	56	21.8%	- 0.80 [- 1.01, - 0.59]
Wolny (2017)	1.9	0.62	70	2.55	0.95	70	18.1%	- 0.65 [- 0.92, - 0.38]
Wolny (2018b)	1.94	0.61	78	3.09	0.68	72	22.1%	- 1.15 [- 1.36, - 0.94]
Wolny (2019)	1.96	0.64	58	2.87	0.71	45	18.2%	- 0.91 [- 1.17, - 0.65]
Total			323			305	100.0%	- 0.88 [- 1.05, - 0.71]
Heterogeneity: $Tau^2 = 0.02$; $Chi^2 = 10.06$, $df = 4$ ($p = 0.04$); $I^2 = 60\%$								
General effect test: $Z = 10.28$ ($p = < .00001$)								
				Symptom severity (BCTQ-SS)				
Fernández (2015)	1.6	0.5	55	1.7	0.5	56	25.3%	- 0.10 [- 0.29. 0.09]
Wolny (2017)	1.78	0.47	70	2.57	0.77	70	25.1%	- 0.79 [- 1.00, - 0.58]
Wolny (2018b)	1.77	0.48	78	2.86	0.72	72	25.2%	- 1.09 [- 1.29, - 0.89]
Wolny (2019)	1.08	0.86	58	2.87	0.68	45	24.4%	- 0.94 [- 1.58, - 0.30]
Total			261			243	100%	- 0.94 [- 1.58, - 0.30]
Heterogeneity: $Tau^2 = 0.41$; $Chi^2 = 105.09$, $df = 4$ ($p = <0.00001$); $I^2 = 97\%$								
General effect test: $Z = 2.86$ ($p = .004$)								

Function and symptom severity

The five studies included in the MA of function and symptom severity show a *MD* with significant differences in favour of the TM group compared to the group using other interventions at the end of treatment for the two variables assessed; on the one hand CBTC-SF (*MD* = - 0. 88, 95% *CI* = - 1.05, - 0.71, *p* = < .00001) and on the other, the CBTC-SS (*MD* = - 0.94, 95% *CI* = - 1.58, - 0.30, *p* = .004), with substantial significant (I2 = 60%, *p* = .04) and considerable significant heterogeneity (I2 = 97%, *p* = < .00001) respectively (Beddaa et al., 2022; Fernández et al., 2015; Wolny et al., 2017; Wolny & Linek, 2018 b; Wolny & Linek, 2019).

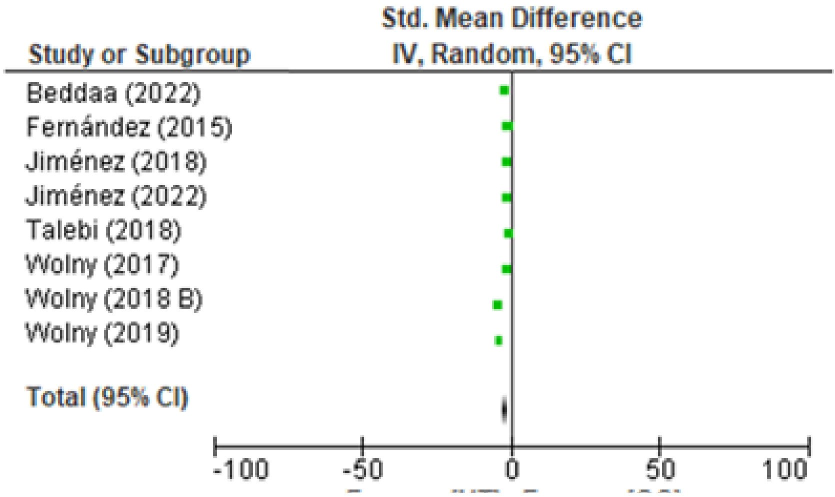

Figure 5. Forest plot comparison manual therapy versus other interventions for pain after treatment

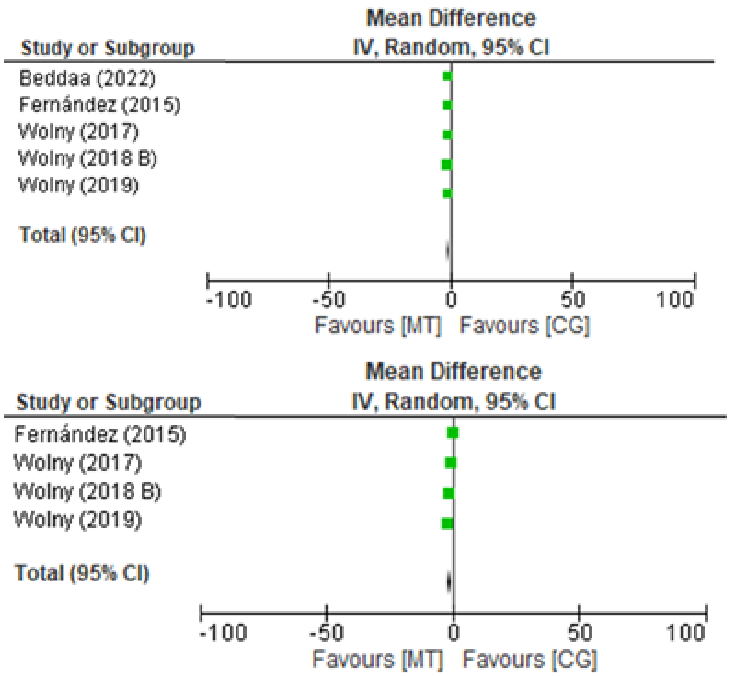

Figure 6. Forest plot comparison manual therapy versus other interventions for function severty (BCTQ-FS) and symptom severity (BCTQ-SS)

Nerve conduction

The four studies included in the MA of nerve conduction show a *MD* with significant differences in favour of the TM group compared to the group with other interventions at the end of treatment for CMV and LM, but not for SVC. On the one hand, VCM with *MD* = 1.85 (95% *CI* = 0.68, 3.01, *p* = .002) and non-significant heterogeneity (*I2* = 0%, *p* = .80) (Wolny et al., 2017; Wolny & Linek, 2018b; Wolny et al., 2019) and LM with *MD* = - 0.57, 95% *CI* = -9.96, - 0.17, *p* = .005) and substantial heterogeneity (*I2* = 86%, *p* = < .0001). On the other hand, VCS presented a *MD* = 7.43 (95% *CI* = -0.11, 14.98, *p* = .05) and substantial heterogeneity (*I2* = 96%, *p* = < .00001) (Jiménez et al., 2018; Wolny et al., 2017; Wolny & Linek, 2018b; Wolny & Linek, 2019).

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Table 6. Summary comparison manual therapy versus other interventions for nerve conduction (sensory conduction velocity, motor conduction velocity and motor latency) after treatment

	Manual therapy			Other intervention				
Author (year)	**Mean**	***SD***	***N***	**Mean**	***SD***	***N***	**Weigth**	**Mean difference, *CI* 95%**
Sensory conduction velocity (SVC)								
Jiménez (2018)	46.9	5.78	30	40.39	5.82	30	25.3%	6.51 [3.57, 9.45]
Wolny (2017)	35.1	12.1	70	39.2	11.9	70	24.6%	- 4.10 [- 8.08, - 0.12]
Wolny (2018 B)	39.8	11.3	78	25.1	7.77	72	25.2%	14.70 [11.62, 17.78]
Wolny (2019)	38.3	11.1	58	25.9	7.72	45	24.8%	12.40 [8.76, 16.04]
Total			236			217	100%	7.43 [- 0.11, 14.98]
Heterogeneity: *Tau*^{2} = 56.23; *Chi*^{2} = 60.22, *df* = 3 (*p* < .00001); *I*^{2} = 95%								
General effect test: *Z* = 1.93 (*p* = .05)								
Motor conduction velocity (MCV)								
Wolny (2017)	56.5	7.8	70	55.3	5.7	70	26.5%	1.20 [- 1.06, 3.46]
Wolny (2018 B)	56.1	6.52	78	54.1	4.32	72	43.9%	2.00 [0.24, 3.76]
Wolny (2019)	55.8	6.92	58	53.6	4.08	45	29.6%	2.20 [0.06, 4.34]
Total			206			187	100%	1.85 [0.68, 3.01]
Heterogeneity: *Chi*^{2} = 0.45, *df* = 2 (*p* = .80); *I*^{2} = 0%								
General effect test: *Z* = 3.11 (*p* = .002)								
Motor latency (ML)								
Jiménez (2018)	3.74	0.49	30	3.99	0.39	70	27.6%	- 0.25 [- 0.45, - 0.05]
Wolny (2017)	5.02	1.13	70	5.24	1.17	70	23..2%	- 0.22 [- 0.60, 0.16]
Wolny (2018 B)	4.43	0.18	78	5.33	1.13	72	26.2%	- 0.90 [- 1.16, - 0.64]
Wolny (2019)	4.49	0.72	58	5.41	1.18	45	22.9%	- 0.92 [- 1.31, - 0.53]
Total			236			257	100%	- 0.57 [- 0.96, - 0.17]
Heterogeneity: *Tau*^{2} = 0.14; *Chi*^{2}= 21.45, *df*= 3 (*p* = < .0001); *I*^{2}= 86%								
General effect test: *Z* = 2.83 (*p* = .005)								

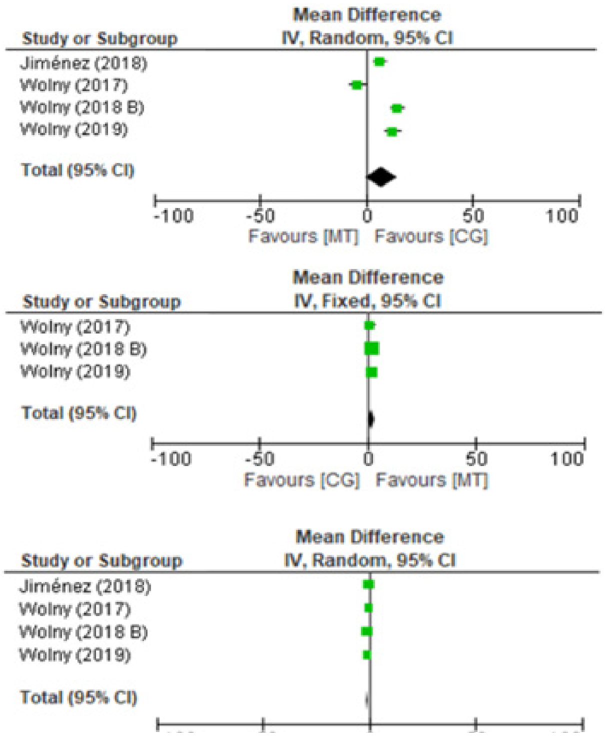

Figure 7. Forest plot comparison manual therapy versus other interventions for nerve conduction (sensory conduction velocity, motor conduction velocity and motor latency) after treatment

Discussion

This SR with MA kprovides a synthesis of the evidence regarding the effectiveness of MT when applied in isolation compared to other interventions for pain, function, symptom severity, nerve conduction, and strength. Significant differences favoring MT were found in all variables except for grip strength and pinch strength. Currently, the favorable effects of MT have not been fully understood; however, Bialosky et al. (2009) proposed a model applicable to all MT approaches, including neurodynamic techniques, joint mobilizations, and massages. The approach suggests that the mechanical stimulus of an MT intervention generates a neurophysiological chain at the central and peripheral levels, ultimately resulting in pain inhibition and, consequently, improvement in other variables. This occurs because MT alters the sensory processing of supraspinal structures, a concept supported by functional magnetic resonance imaging studies. Research has demonstrated that after the application of MT, changes occur in the activation and interaction of cortical areas linked to sensory discrimination, affective regions, and nociceptive processing regions (Gay et al., 2014; Meier et al., 2014; Sparks et al., 2013). Bialosky et al. (2018) updated model incorporates the therapist's personal attributes (preferences, expectations, beliefs about pain, and clinical experience) and how these interact with the patient, emphasizing that they could influence the outcomes of individuals treated with MT. On the other hand, a more specific explanation of neural mobilizations indicates that the positive effect of neurodynamic techniques focuses on reducing edema and intraneural pressure. Nuñes de Arenas-Arroyo et al. (2022) demonstrate in their MA that neurodynamic maneuvers are effective in peripheral neuropathies, noting that tension techniques significantly increase fluid dispersion, and sliding techniques could have a positive effect on reducing intraneural edema. This is relevant because intraneural circulation and axoplasmic flow could compromise microvascular permeability and increase endoneural fluid pressure. However, it should be noted that the five studies included in the MA by Nuñes de Arenas-Arroyo et al. (2022) were conducted on cadavers, and these presented moderate methodological quality.

One relevant factor to consider in clinical aspects is the number of sessions used in treatments. Despite this SR with MA incorporating studies with varying treatment frequencies of Manual Therapy (MT), the results seem to be independent of the number of sessions used. Studies that implemented 20 sessions found significant results in favor of the groups applying MT in most outcomes (Beddaa et al., 2022; Wolny et al., 2016; Wolny et al., 2017; Wolny & Linek, 2018a; Wolny & Linek, 2018b; Wolny & Linek, 2019). Similarly, Randomized Controlled Trials (RCTs) with three sessions (Fernández et al., 2015), five sessions (Jiménez et al., 2018; Jiménez et al., 2022), 12 sessions (Moraska et al., 2008; Talebi et al., 2018), and 15 sessions (Hains et al., 2010) also demonstrated significant results in most variables in favor of the MT groups. Therefore, the optimal minimum dose to achieve results in pain, function, and symptom severity reduction was obtained with three sessions (Fernández et al., 2015). Another clinically relevant aspect to consider is understanding clinical prediction rules to identify individuals who might benefit from MT techniques. Fernández et al. (2016) study aimed to determine if the status of a clinical prediction rule could predict individuals benefiting from an MT program. Initially, the rule's status indicated that a lower pain threshold to pressure in the cervical area and a lower pain threshold to temperature in the affected wrist were related to beneficial effects after an MT program. This was justified by the potential superiority of segmental sensitization over central sensitization (Fernández et al., 2010). Ultimately, the study concluded that the outcome could not be predicted, as women with both negative and positive status in the clinical prediction rule showed similar findings. All studies included in this SR had samples with a high prevalence of females, exceeding 80% in most studies. This is largely related to the high prevalence of this condition in women. Few studies have focused on samples predominantly consisting of males. In the case of the RCTs included in this review, Hains et al. (2010) study had a higher percentage of men in the control group (56%), so the results found in the meta-analyses of this review should be considered more applicable to a female population. In contrast to previous systematic reviews, it can be established that the favorable results towards MT found in this study are similar to earlier reviews for the mentioned variables. However, it should be noted that only Jiménez et al. (2022) review included RCTs where MT was applied in isolation, which demonstrated favorable results in pain, function, symptoms, and nerve conduction through its meta-analysis. The systematic reviews by Araya et al. (2018), Du et al. (2022), Lim et al. (2017), Medina y Yancosek (2008) and Sault et al. (2020), included studies that applied MT in combination with other therapies, showing that the inclusion of MT in programs with ultrasound, laser, exercises, and splints is effective for individuals with Carpal Tunnel Syndrome (CTS). However, Lim et al. (2017) and Medina and Yancosek (2008) concluded that, despite a favorable trend for programs using neurodynamic techniques, more studies are needed, while Araya et al. (2018) systematic review determined that there is moderate evidence supporting the use of neurodynamic techniques in combination with other interventions for pain reduction and improved function.

Grip strength and pinch strength have not been addressed in previous meta-analyses involving isolated MT treatment, likely due to intervention-related heterogeneity. Previous studies have suggested that the application of MT techniques may not be a significant factor in increasing strength in individuals with CTS, as most have shown that adding neurodynamic techniques to other interventions does not provide additional benefits in strength (Bialosky et al., 2009; Hamzeh et al., 2021; Ijaz et al., 2022; Sheereen et al., 2022). Fernández et al. (2017) is one of the few authors who found beneficial effects for increasing pinch strength after applying five sessions of cervical mobilization, soft tissue management, and cervical stretching exercises. However, these effects only persisted during the first month after therapy, as no differences were observed with surgery at three, six, and twelve months. These results are likely due to the passive and therapist-assisted nature of MT, which does not allow for active engagement of the involved musculature (Bruder et al., 2013). In addition, this SR included Talebi et al. (2018) study, which involved individuals with CTS and associated diabetes diagnosis. It found positive findings and significant differences compared to an ultrasound and laser program in function, symptoms, and neural tissue dynamics after applying a twelve-session program of joint mobilization in carpal bones, soft tissue management, and neurodynamic techniques. However, it is the only study conducted on diabetic individuals with CTS, as for all others included in this systematic review, metabolic diseases were an exclusion criterion.

Regarding the studies and variables not included in the MA, the study by Wolny and Linek (2018a) stands out as the sole assessment of overall health using the SF-36 instrument. It demonstrated a significant improvement in both physical (27%) and mental (13%) components after twenty treatment sessions compared to a non-intervention group. Additionally, the studies by Wolny and Linek (2018b) and Wolny et al. (2016) showed beneficial and significant effects on two-point discrimination and relative two-point discrimination in fingers I, II, and III, respectively. These improvements were observed following a twenty-session program of neurodynamic techniques, massage, and opening and closing techniques.

Limitations

The limitations of this study are as follows: 1) the search process was conducted in seven databases and in two languages, potentially missing relevant articles for the review. 2) the limited number of included studies. 3) methodological limitations, such as adequate concealment in the randomization process, blinding of participants and therapists, loss of individuals in the research process, intention-to-treat analysis, and follow-up, which could overestimate the effects of the therapy used. 4) the high degree of clinical and statistical heterogeneity, likely due to variations in intervention protocols (technique, dose, number of sessions used). 5) there was an intention to perform subgroup analyses by age, sex, severity, and TM technique used. Finally, despite several reviews yielding similar results, these findings should be approached with caution due to the mentioned limitations, and it is suggested that future systematic reviews may address and improve upon these aspects.

Conclusion

Based on the results of this SR with MA, it can be determined that, in the short term, isolated application of MT is an option that yields favorable effects in individuals with mild to moderate CTS, resulting in reduced pain and symptom severity, increased function, and improved electrophysiological parameters of nerve conduction compared to other interventions. Additionally, it may be an option to enhance two-point sensory discrimination. However, grip strength and pinch strength do not show benefits when applying a MT protocol. A validated clinical prediction rule regarding who may benefit from a MT program has not been identified. Therefore, it is essential to conduct new studies to identify the most optimal protocol, including technique, dose, and the number of sessions for effective rehabilitation of individuals with CTS in the short, medium, and long term.

Conflict of interest

The authors declare no potential conflict of interest concerning the research, authorship, and/or publication of this article.

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