International Journal of Kinesiology & Sports Science
ISSN: 2202-946X
www.ijkss.aiac.org.au

The Effectiveness of Neural Mobilization in Patients with Tarsal Tunnel Syndrome: A Systematic Review and Meta-Analysis

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ARTICLE INFO

Article history
Received: July 26, 2024
Revised: September 29, 2024
Accepted: October 25, 2024
Published: October 30, 2024
Volume: 12 Issue: 4

Conflicts of interest: None.
Funding: None.

ABSTRACT

Background: Tarsal Tunnel Syndrome (TTS) is a compression neuropathy, occurring when the distal branches of the posterior tibial nerve become entrapped within the tarsal tunnel, with no definitive evidence for its conservative management. Neural mobilization, a therapeutic approach involving joint and peripheral nerve movement, seeks to restore the nervous system's homeostasis. There is currently insufficient evidence to determine the efficacy of neural mobilization. **Objectives:** Analysis of data from randomized controlled trials (RCTs) examining the efficacy of neural mobilization techniques (NMT) in TTS patients. **Methods:** A thorough search was carried out from inception until September 2024 utilizing four scientific databases (PubMed, Scopus, EMBASE, and Physiotherapy Evidence Database-PEDro) and the Google Scholar search engine. Relevant English-language research was retrieved, assessed, and given an independent methodological quality rating (PEDro scale). Meta-analyses were conducted for select outcomes, where possible. **Results:** 745 studies were eliminated from the total of 748 because they were duplicates or did not fit the inclusion criteria. Three RCTs were finally included, rated on average with 6.67/10 for methodological quality (PEDro scale). NMT led to a highly significant improvement of the nerve's physiological sensitivity ($p<0.001$), measured with the Tinel's sign, based on evidence of high methodological quality (7.5/10) and no heterogeneity. NMT did not lead to a significant diminution of pain intensity ($p=0.21$) based on evidence of moderate methodological quality (6.67/10). Significant improvements in favour of NMT, however measured in one out of three studies, were identified for 2-point discrimination and light touch, the Neuropathic Pain Questionnaire, and the Functional Foot Index ($p<0.05$). No adverse events were reported. All studies measured change immediately post-treatment. **Conclusion:** NMT significantly improved the tibial nerve's mechanosensitivity. Moreover, as part of the treatment of patients with TTS, high-quality RCTs are necessary to examine the short and longer-term effects of NMT.

Key words: Tarsal Tunnel Syndrome, Nerve Compression Syndromes, Flatfoot, Entrapment Neuropathy, Tibial Neuropathy, Rehabilitation

INTRODUCTION

Tarsal tunnel syndrome (TTS) is a less common type of nerve compression and one of several nerve compression conditions affecting the ankle. The syndrome, was first described over sixty years ago (Kopell & Thompson, 1960), is often referred to as "tarsal tunnel syndrome" (Lam, 1962). While precise prevalence rates are not available, studies suggest it is frequently underdiagnosed or misdiagnosed. Based on comparative estimates, TTS ranks as the fifth most common entrapment syndrome (Vij et al., 2022). TTS can affect individuals of any age group, but it tends to occur more frequently in active individuals, possibly due to repetitive stress on the ankle joint, and in females (Nelson, 2021).

TTS resembles carpal tunnel syndrome, as the tibial nerve or its branches (medial calcaneal and plantar nerves) are entrapped within the tarsal tunnel (Kim & Cho, 2024), a fibro-osseous passage between the medial malleolus and the calcaneus (Nelson, 2021). The plantar nerves provide the plantar foot with motor, sensory, and autonomic fibers. In 25% of cases, there may be a variation in the medial calcaneal nerve, which supplies sensory innervation to the heel via passing through the flexor retinaculum. In some cases, the nerve may come from the lateral plantar nerve, branch before, or travel superficially to the flexor retinaculum (Kim & Cho, 2024). Among the structures that traverse via the tarsal tunnel are the tibial nerve, the posterior tibial artery and vein, the posterior tibial tendon, the flexor

Published by Australian International Academic Centre PTY.LTD.

http://dx.doi.org/10.7575/aiac.ijkss.v.12n.4p.63

digitorum longus tendon, and the flexor hallucis longus tendon.

TTS often results from extrinsic factors like trauma or repetitive stress in activities like running and soccer, particularly in individuals with ankle instability, hyperpronation or poor running mechanics, poorly fitting shoes, overweight, or with systemic disease (Ferkel, Davis, & Ellington, 2015; Kim & Cho, 2024). Foot and ankle eversion and inversion movements could decrease the tarsal tunnel's compartment volume, putting additional strain on the posterior tibial nerve and perhaps exacerbating tarsal tunnel syndrome symptoms (Bracilovic et al., 2006). Tendinopathy/tenosynovitis, space-occupying structures like ganglion cysts, perineural fibrosis, calcaneal osteochondroma, tumors, lipomas, arterial insufficiency, varicose veins, or auxiliary muscles are examples of intrinsic causes that can also result in compression. In some cases, multiple sites of nerve compression can lead to a "double-crush phenomenon," which may radiate proximally, causing symptoms. In 20% of instances, tarsal tunnel syndrome is categorized as idiopathic since the underlying etiology is unknown (Kim & Cho, 2024).

To track the success of rehabilitation therapy, a thorough diagnostic strategy must be used for individuals with TTS. Weight-bearing radiographs (Nelson, 2021) and MRI can be valuable tools in identifying the underlying cause of symptoms and electrophysiological evidence of decreased nerve conduction (electromyography or nerve conduction studies) (Oh, Sarala, Kuba, & Elmore, 1979). Patient history is the most important step to make an accurate diagnosis (Nelson, 2021). A physical examination may show discomfort or abnormal sensations in the region supplied by the tibial nerve, as well as soreness and a positive Tinel's sign (Nelson, 2021; Rinkel et al., 2018). The main sensory symptoms that people with TTS experience are pain, burning, tingling, and numbness in the plantar foot aspect. Symptoms worsen with standing, walking, or running (Ferkel et al., 2015). It is an often-overlooked syndrome because its symptoms can be similar to those of other lower extremity neuropathies, such as diabetic sensorimotor polyneuropathy (Rinkel et al., 2018).

Despite the fact that TTS patients have traditionally been treated with traditional physiotherapy, including electrical stimulation, iontophoresis, phonophoresis, ultrasound, orthotic insoles, nonsteroidal anti-inflammatory drugs, corticosteroid injections, use of a night splint or removable walker boot,for immobilization, vitamin B supplements, or flexor retinaculum surgical release (Bracilovic et al., 2006), a considerable number of patients do not fully recover and may benefit from surgery (Nelson, 2021).

Neural mobilization techniques (NMT) involve a series of joint movements that promote the gliding or tensioning of neural structures, including the nerve itself and associated tissues. Sliding techniques entail reciprocal movements performed in a manner that simultaneously elongate neural tissue at one joint while shortening it at another. Conversely, a tensioning technique occurs when both ends of the neural tissue are displaced in opposite directions or when one end is stretched while the other remains in place (Brown et al., 2011; Coppieters & Butler, 2008).

Sliding techniques allow for gentler nerve movement, potentially helping to retrain the brain and reduce learned pain associations (Coppieters & Butler, 2008; Shacklock, 1995). Greater range of motion exercises appear to assist in remapping the pain region and decreasing fear of movement (Shacklock, 1995). In contrast, tensioning techniques have shown promise in improving pressure pain thresholds and reducing intraneural edema (Brown et al., 2011; Coppieters & Butler, 2008).

Several neurophysiological (intraneural microcirculation alteration, axonal transport and nerve impulse transmission), biomechanical, psychological, and other non-specific mechanisms, therefore, might be stimulated via NMT to improve clinical outcomes in patients with TTS. Following a thorough search of the scientific literature databases PubMed, PEDro, EMBASE (Science Direct), and Scopus, we observed a gap in the existing body of knowledge about the efficacy of NMT in TTS patients. Three systematic reviews have examined research on the efficacy of neurodynamic techniques in TTS patients (Basson et al., 2017; de Magalhães, Ribeiro, de Mendonça Cardoso, & de Amoreira Gepp, 2022; Vij et al., 2022), but none of them evaluated the clinical significance of the suggested intervention or performed a meta-analysis. Additionally, more randomized controlled studies examining the efficacy of NMT on TTS have been published since the publication of these reviews.

Thus, this review's goal was to evaluate the efficacy of NMT in TTS based on results pertaining to pain, nerve function deficit, and other associated pathophysiological reactions like Tinel's sign or two-point discrimination. Regarding the effectiveness and therapeutic relevance of NMT in TTS, we expected that an updated systematic review with meta-analysis would offer more conclusive findings.

In light of these findings and several hypotheses interpreting the dysfunction found in TTS patients, the aim of this systematic review was to examine the following issues:

(1) How effectively does neural mobilization perform in combination or in relation to other methods for measuring clinical outcomes in TTS patients?
(2) Does incorporating the evaluation of clinical outcome measures to the tracking of TTS patients' progress offer any extra advantages?

MATERIALS AND METHODS

Study Design

This systematic review was conducted using the PEDro scale for methodological quality evaluation of the clinical trials (da Costa, Hilfiker, & Egger, 2013; Maher, Sherrington, Herbert, Moseley, & Elkins, 2003) and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 requirements (Page et al., 2021). This review has been registered in the INPLASY database (Registration Number: INPLASY202490077).

Inclusion and Exclusion Criteria

Randomized controlled trials (RCTs), published in English, that (a) were relevant to the NMT intervention, which included sliding and tension techniques, and (b) included only patients with TTS, aged between 18-65 years, with positive Tinel's sign or/and Tenderness grading more than 2/4 were included in the current systematic review.

Non-randomized controlled clinical trials, studies without control or other intervention groups, and case reports or case studies were not included in the current systematic review. Additionally, studies that included participants with any of the following conditions were disqualified: plantar fasciitis, heel pain, Morton's syndrome, ankle instability, rheumatoid arthritis, spondyloarthropathy, cancer, any neuropathy, comorbidities of the ankle and foot, and any other inflammatory disease. Although there were no language restrictions when searching the database, papers authored in languages other than English were not included in the screening process.

Search Strategy

From inception to September 2024, an electronic database search was conducted using PubMed, the Physiotherapy Evidence Database, Scopus, EMBASE (Science Direct), and Google Scholar. Additional searches included a manual search of the included studies' reference lists. The PEDro database (advanced search) and the Scopus database both used the keywords in different combinations and in line with the PICO Model for Clinical Questions (Table 1).

All titles and/or abstracts were separately assessed by two reviewers (PIT, GAK), who then examined the studies that were selected for inclusion. Disagreements were resolved by consensus between the two reviewers, and if not possible, a third reviewer (EG) was required.

Methodological Quality Assessment

Two reviewers (PIT and IP) assessed the methodological quality of the included trials using the PEDro scale (de Costa et al., 2013). Discrepancies were reevaluated by a third reviewer (IP). The PEDro scale is a reliable and useful tool for assessing the quality of physical therapy and rehabilitation trials (de Costa et al., 2013; Maher et al., 2003). The scale includes eight items for internal validity and two items for assessing whether statistical requirements are met. Each item satisfied provides one point to the total PEDro score (range 0–10 points). However, no points are given for ambiguous items.

Table 1. PICO model of the current systematic review

Patient/Client group	"tarsal tunnel syndrome" OR "nerve compression syndromes" OR "nerve entrapment" OR "flatfoot" AND
Intervention	"neural mobilization" OR "nerve mobilization exercises" OR "tibial nerve mobilization" OR "Tibial nerve stretch AND
Comparison	"control group" OR "conventional physiotherapy" OR "sham" AND
Outcomes	"pain" OR "Functional Foot Index" OR "range of motion" OR "muscle strength" OR "nerve tissue assessments" AND
Study	"randomized clinical trial" OR "systematic review"

The PEDro scale items were used to calculate the overall (Maher et al., 2003) and individual (da Costa et al., 2013; Maher et al., 2003) scores for all research. The effectiveness of each study was also evaluated separately for each of the review's outcome measures.

Data Extraction

The abstracts and titles of the extracted studies were evaluated by one reviewer (PIT). When the abstract did not contain enough information, the entire article was examined. Data about the year of publication, inclusion-exclusion criteria of individuals, demographics of participants (sample size, study population, sex, and age), type, number of sessions and duration of each intervention, outcomes, follow-up, and results of each included study were extracted by two reviewers (PIT) and (SV) in accordance with PRISMA (Page et al., 2021).

Data Synthesis and Analysis

The Review Manager (RevMan) Web online platform was used to summarize the effects of NMT on all outcomes that could be combined to a meta-analysis. Subgroup analyses were not performed for outcomes of included studies, as comparisons of interest included NMT with or without parallel interventions versus a control or parallel or sham intervention. Categorization of studies based on follow-up time points was not performed, as all included studies measured the effect of interventions immediately post-treatment, without including any short or long-term follow-up. The quantitative synthesis for this study was carried out using the pre-post means and standard deviations for continuous outcomes and odds ratios (ORs) for dichotomous outcomes from each selected study for the between-group comparisons, in accordance with the "Cochrane Handbook for Systematic Reviews of Interventions" (Deeks, Higgins, & Altman, 2023). The data used were obtained from the articles or, if needed, derived using the RevMan Web online calculator. The between-group mean difference (MD) and 95% of confidence intervals (CI) were used for continuous outcomes and ORs for categorical outcomes. A random-effects inverse variance or Mantel-Haenszel model was selected for meta-analysis, to identify the clinical effect of NMT, for each outcome. Since populations were expected to differ across studies, the random-effects model was preferred to the fixed-effects. Heterogeneity was assessed using the I^2 statistic, with values >50% interpreted as substantial and >75% as considerable heterogeneity (Deeks et al., 2023). The overall treatment effect could not be compared with its Minimum Clinically Important Difference (MCID), as no previous research reporting MCID values for any outcome in patients with TTS could be located.

RESULTS

Studies' Identification

There were 748 studies retrieved via an electronic search. A total of 445 studies were obtained from Google Scholar, 187 from EMBASE (Science Direct), 5 from the PEDro database, 76 from Scopus, and 35 from PubMed. Many studies (n=225) were eliminated due to their identical nature, non-English language, and title. After evaluating the abstract, the remaining studies were filtered eliminated. Other studies were removed according to the current systematic review's inclusion and exclusion criteria, and the ones that remained were obtained for full-text review. Finally, three publications have been included to the current systematic review. Figure 1 illustrates a detailed flowchart.

Methodological Quality

On average, the methodological quality score of all included studies rated with the PEDro scale (table 2) was 6.67/10. Specifically, one study was rated with 8/10 (Leblebicier, Yaman, Saracoglu, & Ozkaya, 2022), one with 7/10 (Kavlak & Uygur, 2011), and one with 5/10.

When examining each of the 10 PEDro scale items independently, the three main areas of risk of bias were subject, therapist, and assessor blinding. These sources of bias were not addressed in more than or as many as 50% of research (Figure 2).

Participants

Table 3 displays the participant details. The precise number of patients assigned to each group, their BMI, and the duration of their symptoms were all provided in all of the included trials. Furthermore, for one of their primary outcome measures, every included study had calculated the sample size a priori in order to attain a power level of at least 80% at a significance level of a=0.05.

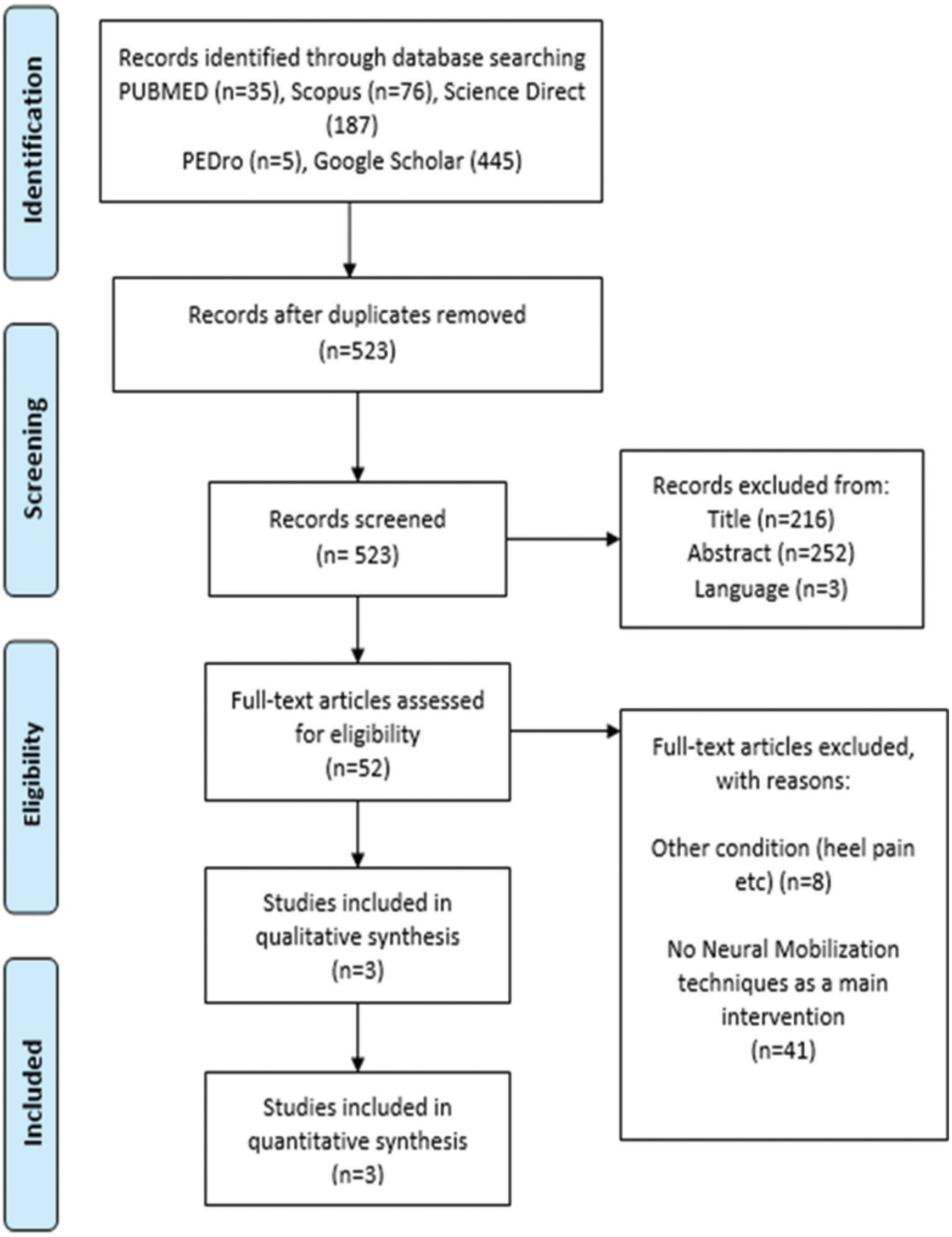

Figure 1. PRISMA flowchart illustrating the selection process of studies for this systematic review

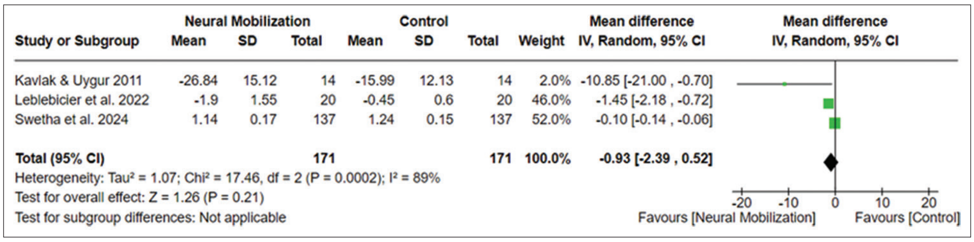

Figure 2. Forest plot of the effect of neural mobilization techniques with or without other parallel interventions on pain intensity

Table 2. PEDro scale individual and overall scores of methodological quality for the included studies

Studies	Items										Total Score
	1	2	3	4	5	6	7	8	9	10	
Leblebicier et al. 2022	√	√	√			√	√	√	√	√	8/10
Kavlak & Uygur 2011	√	√	√	√			√		√	√	7/10
Swetha et al. 2024	√		√					√	√	√	5/10

Items correspond to the following criteria, 1: random allocation, 2: concealed allocation, 3: baseline comparability, 4: blind subjects, 5: blind therapists, 6: blind assessors, 7: adequate follow up, 8: management as planned or intention-to-treat analysis, 9: between-group comparisons, 10: point estimates and variability.

Interventions

The experimental group used Neural Mobilization techniques as an intervention in all of the included trials. Other treatment modalities (exercise, conventional physiotherapy) were compared with these interventions. (Kavlak & Uygur, 2011) or home exercise program (Leblebicier et al., 2022) or strengthening exercise along with ultrasound (Swetha, Senthilkumar, Kumaresan, Kumaran, & Alagesan, 2024). The intervention frequency and duration were also provided (Table 3).

Outcome Measures

Pain intensity outcome measures included the Visual Analogue Scale (VAS) (Kavlak & Uygur, 2011; Leblebicier et al., 2022), the Neuropathic Pain Questionnaire (NPQ) (Leblebicier et al., 2022). Provocation tests of tibial nerve entrapment were assessed: Tinel's test (Kavlak & Uygur, 2011; Leblebicier et al., 2022; Swetha et al., 2024), tibial nerve stretch test (Kavlak & Uygur, 2011) and Tenderness grading scale (Swetha et al., 2024).

Kendall and McCreary's examination of the strength of the foot muscles, innervated by the tibial nerve and its branches, was used to determine the total muscular strength of each patient (Kavlak & Uygur, 2011).

The range of motion of the ankle and subtalar joints was measured using a universal goniometer (Kavlak & Uygur, 2011).

The Functional Foot Index (FFI) was used to evaluate functional status (Leblebicier et al., 2022).

Light touch was evaluated with monofilaments applied to three distinct foot regions, for 2-point discrimination an esthesiometer was used, and the presence of paresthesia was examined (Kavlak & Uygur, 2011).

Comparability of Interventions

Every study that was included was randomized, had a control group, and had a sufficient number of participants. A quantitative synthesis was carried out for part of the included studies, despite the fact that there was notable clinical heterogeneity across the included studies, which was explained by: (a) variations in the neural mobilization techniques used to target the tibial nerve, (b) variations in the duration of interventions, and (c) variations in the outcomes evaluated between studies. Heterogeneity among the research populations was also noted. To illustrate the differing characteristics of participants across the different trials, one study (Swetha et al., 2024) recruited male and female middle-aged (on average) patients, whereas the other two studies selected younger (21–30 years old) pregnant women with diabetes and TTS.

Content of Interventions and Control Group

In every study that was included, the experimental group used neural gliding techniques with tension and elongation to incorporate NMT as an intervention. (Swetha et al., 2024), or as a posterior gliding compressor (Kavlak & Uygur, 2011; Leblebicier et al., 2022). A true control group (wait and see, sham, or no intervention) or other forms of therapy (conventional physiotherapy, exercise, and therapeutic patient education) were contrasted with these treatments. Intervention duration ranged from 4 to 6 weeks.

Effects of Interventions

Effects of NMT on pain

The effect of NMT in patients with tarsal tunnel syndrome, with or without other parallel interventions, on pain intensity were compared in three studies (Kavlak & Uygur, 2011; Leblebicier et al., 2022; Swetha et al., 2024) that included 342 patients in total (Figure 2). A MD (95% CI) = -0.93 (-2.39 to 0.52) favoring neural mobilization was found, however not statistically significant (Z = 1.26, p = 0.21) and with very high statistical heterogeneity (I^2 = 89%, p = 0.0002), based on a moderate 6.67/10 mean PEDro scale rating of methodological quality score (Table 1).

Effects of NMT on the nerve's mechanosensitivity (Tinel's Sign)

The effect of NMT in patients with tarsal tunnel syndrome, with or without other parallel interventions, on whether the

Table 3. Characteristics of the systematic review's randomized controlled studies

RCT	METHODS	CRITERIA	INTERVENTIONS	OUTCOMES	RESULTS
Kavlak & Uygur 2011 Aim: Effectiveness of nerve mobilization exercises in the conservative treatment of TTS	Randomized controlled trial, Participants: 28 (Female: 24, Male: 4), Age: A) 40.71±12.84 years, B) 43.64±14.72 years, Height: A) 163.07±9.47 cm, B) 163.35±9.60 cm, Weight: A) 69.92±12.28 kg B) 76.35±10.95 kg Duration: 6 weeks (1st week with physiotherapist and 2nd-6th week advised to perform auto-NMT at home daily)	Inclusion criteria: i) not having an indication for surgery, ii) cooperative, and understand the aims of study, understanding and following the prescribed exercise protocols iii) able to attend therapy and follow-up sessions and iv) older than 18 years Exclusion criteria: i) comorbidities or orthopedic or postural problems that could confound the outcomes ii) other entrapment neuropathies iii) previous surgery related to the lower extremity or lumbar spine iv) regular alcohol intake and v) addiction to smoking	Intervention group A (n=14): home exercise program (TheraBand's) and tibial nerve mobilization exercises as described by Meyer *et al.* every day. Control group B (n=14): the same home exercise program (TheraBand's) Duration: 6 weeks	ROM: universal goniometer Muscle Strength: Manual muscle test – individual and total Pain: VAS Sensory measurement: esthesiometer for determining 2-point discrimination Light touch: Semmes-Weinstein monofilaments Provocative symptoms of tibial nerve entrapment: Tinel test, tibial nerve stretch test, Existence of paresthesia All outcomes evaluated at baseline, and 6 weeks of treatment Sample size calculation performed	Significant difference in favor of posttreatment values for ROM, muscle strength, and pain in both groups (p<0.05). Intergroup comparisons showed no difference between the groups for these parameters. Significant results were attained in the study group for 2-point discrimination and light touch and Tinel sign after treatment (p<0.05).
Leblebicier et al. 2022 Aim: Effectiveness of tibial nerve mobilization in addition to home exercise on the tibial nerve area in patients with TTS	Randomized controlled trial, Participants: 40, (Female: 19, Male: 1), Age: 18-65 years, BMI: A) 25.03±3.40), B) 25.57±3.45 Duration: 4 weeks (2 days/week)	Inclusion criteria: i) ages of 18-65 ii) diagnosed with TTS in the last 6 months, iii) having at least 2 or more foot-ankle pain complaints iv) voluntary participation Exclusion criteria: i) previous foot-ankle surgery, ii) electrodiagnostic examination, iii) no commorbidities, iv) systematic inflammatory disease v) central nervous system disease, vi) hearing impairment	Intervention group A (n=20): Tibial nerve mobilization 5 sets of 10 reps with 1-minute rest period/set and the same home exercise program Control group B (n=20): Home exercise program 10 Reps, stretching exercises 20-30 sec each with 10 sec of rest in-between	Nerve Conduction Studies: EMG Tinel's sign: Manual test Tibial nerve's diameter: ultrasound with a 6-18 MHz linear probe Pain intensity: (VAS) Neuropathic pain status: Neuropathic Pain Questionnaire (NPQ) and Functional: Functional Foot Index (FFI) Outcomes evaluated at baseline and at 4 weeks after treatment Sample size calculation performed	Significant between-group differences favouring the IG group for: - Positive Tinel's (Odds ratio: 0.11 95% CI: 0.03 to 0.46). - Pain intensity (Mean difference: 1.45; 95% CI: 0.69 to 2.20), - NPQ (Mean difference: 0.70; 95% CI: 0.36 to 1.03), - FFI Pain Subscale (Mean difference: 10.0; 95% CI: 4.33 to 15.66) and - Total FFI score (Mean difference: 20.60; 95% CI: 0.53 to 40.66). No adverse events reported.

(*Contd...*)

Table 3. (*Continued*)

RCT	METHODS	CRITERIA	INTERVENTIONS	OUTCOMES	RESULTS
Swetha et al. 2024 Aim: Effectiveness of strengthening and nerve mobilization on TTS among pregnant women	Randomized controlled trial, pilot Participants: 274, (all female), Age: 21-30 years, Duration: 4 weeks (5 days/week - 2 session/day)	Inclusion criteria: i) Tinel's sign positive ii) Tenderness grading more than 2 and III) Pregnant women age 21-30 years Exclusion criteria: i) past history of fracture of injury and ii) other neurological disorders iii) recent surgeries in lower limb	Intervention group A (n=137): Strengthening exercises (TheraBand's) 10 reps, 1-min Pause/Set, Ultrasound mode-continuous and intensity - 2.0 W/m2, 10 min/session Intervention group B (n=137): NMT, Strengthening Exercises 10 reps, 1 min Pause/set, accompanied by the same ultrasound intervention	Tinel's sign: Manual test Tenderness grading scale All outcomes evaluated at baseline and at 4 weeks after treatment Sample size calculation performed	Both IGA and IGB improved their tenderness grading scale scores, IGA had significant improvement in tenderness grading (p<0.0001) compared with IGB (p<0.0001)

CG: control group, FFI: Foot Functional Index, IG: Intervention group, NMT: Nerve Mobilization Techniques, NPQ: Neuropathic Pain Questionnaire, Rep: Repetition, sec: seconds, ROM: Range of Motion, TTS: Tarsal Tunnel Syndrome, VAS: visual analogue scale

Tinel's sign was elicited post-treatment or not, were compared in two studies (Kavlak & Uygur, 2011; Leblebicier et al., 2022) that included 68 patients in total (Figure 3). An OR (95% CI) = 0.10 (0.03 to 0.34) favoring neural mobilization was found, which was highly statistically significant (Z = 3.72, p = 0.0002) with no statistical heterogeneity noted (I2 = 0%, p = 0.79), based on a moderate 6.67/10 mean PEDro scale rating of methodological quality score (Table 1).

Other significant between group improvements from individual studies

In addition to the statistically significant improvements in nerve mechanosensitivity (Tinel's sign), neural mobilization techniques also demonstrated between-groups statistically significant improvements in other outcome measures, however from one of the three studies included, therefore a meta-analysis could not be performed. Specifically, in one of the studies (Kavlak & Uygur, 2011), significant improvements in favour of the NMT group were reported for two-point discrimination and light touch (p<0.05). Also, another study reported significant between-group differences in the NPQ and in the total score and the pain subscale of the FFI, favoring the group that received neural mobilization techniques (Leblebicier et al., 2022). Importantly, no adverse events were reported in any of the included studies.

DISCUSSION

The effectiveness of NMT in treating TTS patients was examined in the current systematic study. In contrast to the interventions delivered in the control conditions, the NMT interventions were implemented in various combinations. According to Shacklock, the experimental groups were given several NMTs with varying combinations, application methods, and strategies (Kavlak & Uygur, 2011; Leblebicier et al., 2022), and one study (Swetha et al., 2024) did not specify the precise approach used. For patients with TTS the NMT techniques were applied at the tibial nerve. Two studies (Kavlak & Uygur, 2011; Leblebicier et al., 2022) combined NMT with strengthening or stretching activities, while one study (Swetha et al., 2024) combined NMT with ultrasound and strengthening exercises.

Specifically, regarding the dosage of NMT, the study by Kavlak & Uygur (2011) received the highest treatment dosage (6 weeks in total, the 1st week daily, under the supervision of a physiotherapist and from the 2nd to the 6th week advised to perform auto-NMT at home daily). The other two studies provided NMT for 4 weeks, with frequencies ranging from daily (Swetha et al. 2024) to twice/week (Leblebicier et al. 2022). The effect of treatment dosage (frequency, repetitions per NMT administered, type of NMT administered, relating to the intensity each of the techniques) may have to be standardized in future studies. In addition, if exercises are to be administered at home, a compliance diary has to be kept, to ensure to an extent that exercises are performed when intended to. For the studies included a diary of exercises performed by patients was not kept, therefore the exercise dosage delivered for each participant could not be verified.

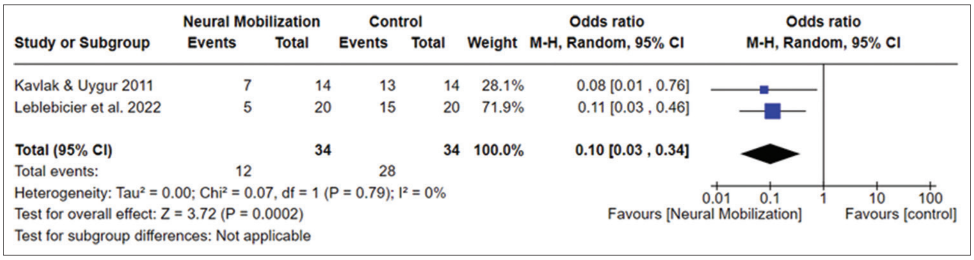

Figure 3. Forest plot of the effect of neural mobilization techniques with or without other parallel interventions on the number of patients with a positive Tinel's sign

The present systematic review is the only review that has been carried out considering NMT in patients with TTS with respect to pain, disability nerve function and other related pathophysiological responses, such as Tinel's sign or two-point discrimination. Three systematic reviews evaluated the effectiveness of NMT. One review focused on the comparison between surgical vs conservative treatment in reducing the symptoms of the syndrome (de Magalhães, Ribeiro, de Mendonça Cardoso, & de Amoreira Gepp, 2022). They observed a rate of good-excellent pain control of 68% (n=204) for open surgery (n=299), 100% (n=8) for endoscopic surgery (n=8), and 7% (n=2) for conservative treatments (n=28). One study included in that review (Kavlak & Uygur, 2011) is also included and analyzed in the present review. No other included study in that previous review met the inclusion criteria for the present study.

Another review described current conservative management treatment options (Vij et al., 2022) including two studies on NMT, one of which (Kavlak & Uygur, 2005) has been written in Turkish, while the other is included in our study also (Kavlak & Uygur, 2011). The review concluded that conservative management remains a viable option for many patients with tarsal tunnel syndrome (Vij et al., 2022), often leading to symptom resolution. A systematic review with meta-analysis referred to the effectiveness of NMT for neuromusculoskeletal conditions in general, combining under 'other conditions' plantar heel pain with tarsal tunnel syndrome (Basson et al., 2017). They concluded that NMT improves pain in tarsal tunnel syndrome and plantar heel pain (low-risk-of-bias evidence from a single study) (Kavlak & Uygur, 2011). Another narrative review by (Kratter, 2024) analyzed the therapeutic management of the painful nerve and mentioned only one study (Kavlak & Uygur, 2011) for the treatment of TTS.

Finally, as a result we can conclude that all the systematic reviews until now did not focus on the effectiveness of NMT in patients with TTS, and included only one relevant study to this review, which is included herein (Kavlak & Uygur, 2011), and highlight the lack of evidence and varying methodological quality in studies they included. Regarding one previous study identified as possibly relevant to this review, this was most likely reported in Turkish and was therefore excluded (Kavlak & Uygur, 2005).

Neural mobilization techniques are commonly used for entrapment neuropathies (Paraskevopoulos et al., 2023), neuromusculoskeletal conditions (Basson et al., 2017) and generally for pain syndromes (Shacklock, 1995) but the mechanisms responsible for the improvement outcomes remain unclear. Body movements naturally involve interactions between mechanical and physiological mechanisms within the nervous system. The sequence and combination of bodily motions, as well as local anatomical and mechanical elements, all influence the nerve system's mechanical function. Sliding, elongation, tension, and pressure changes are examples of mechanical forces acting on neural tissues (Shacklock, 1995).

Physiological alterations in blood flow, axonal transport, nerve impulse transmission, and sympathetic activation are the nervous system's reactions to these mechanical stresses (Shacklock, 1995). In human cadaveric specimens, passive mobilization—which includes plantar flexion to end range and ankle dorsiflexion—significantly enhances fluid dispersion inside the tibial nerve. According to Brown et al. (2011), this implies that neural mobilization strategies could help maintain nerve function by reducing the development of intraneural fluid and mitigating the negative consequences of intraneural edema.

A study excluded from this review, as it was performed on twenty-four symptom-free participants with bilateral flatfeet, investigated the effect of neural tissue mobilization on tibial nerve mobility, reporting a significant difference in mean straight leg raise (SLR) favouring the NMT group (Kaydawala & Sheth, 1989). Because of the close association between flat feet and TTS, flat feet may be considered a predisposing factor, and the finding of this study may suggest that neural tissue mobilization that can improve SLR range of motion, could also be effective in preventing tibial nerve compression in individuals with TTS.

Finally, while conducting this review of NMT on patients with TTS, this topic seems to be of increasing interest in the research community, as we identified two published RCT protocols for studies that are currently underway on similar topics (Ashoori, Pourahmadi, Hashemi, Dadgoo, & Hosseini, 2024; Goyal, Esht, & Mittal, 2019).

This systematic review with meta-analysis is the first to evaluate the effectiveness of neural mobilization techniques in managing tarsal tunnel syndrome. It is the sole review to assess the impact of these techniques on pain, disability, nerve function, and other relevant pathophysiological responses, such as Tinel's sign and two-point discrimination. The review incorporates two novel studies not included in previous systematic reviews, also highlighting the dearth of research on this significant condition. The study emphasizes the importance of the correct application and dosage of these techniques.

This study provides a strong rationale for integrating neural mobilization techniques into evaluating and treating tarsal tunnel syndrome. It underscores the unique characteristics of tarsal tunnel syndrome in specific populations, such as pregnant women and individuals with diabetes.

This review's limitations included the inclusion of research with a wide range of methodological quality and sample size, as well as language limits (only English-language studies were included). Additionally, there are very few studies on this topic so far; therefore, the results obtained may be subject to change. More high-quality research is required on this treatment technique, searching for the appropriate therapeutic dosage for this pathology.

CONCLUSIONS

Evaluating the existing clinical trials, we conclude that up to now there is some emerging evidence that neural mobilization techniques are appropriate in patients with TTS. This may be due to the relief of abnormal nerve tension with appropriate movements of the neural tissue, which should be taken into consideration in clinical reasoning and home-exercise prescription in this patient group. Supplementing existing neural mobilization techniques with other relevant techniques such as strengthening exercises in patients with TTS may also have a significant therapeutic benefit. However, further research studies of high methodological quality and a greater number of participants are required, focusing on the evaluation of the effectiveness of neural mobilization techniques in this pathology.

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