REVIEW PAPER

Physiotherapy Quarterly (ISSN 2544-4395)
2024, 32(2), 1–18

Effectiveness of combined therapy in physical therapy for the management of musculoskeletal pain: a systematic review and meta-analysis

DOI: https://doi.org/10.5114/pq/163383

Hernán Andrés de la Barra Ortiz, Cristóbal Alfaro Leiva, Camilo Alfaro Lillo, Diego Carvajal Álvarez, Bastián Cuéllar Pizarro
Exercise and Rehabilitation Sciences Institute, School of Physical Therapy, Faculty of Rehabilitation Sciences, Universidad Andres Bello, Santiago de Chile, Chile

Abstract

Introduction. Therapeutic ultrasound and electrotherapy are commonly used in physical therapy for musculoskeletal pain (MSP) management. Combined therapy (CT) is a resource that merges both techniques, enhancing the analgesic effects of both treatments, although studies are limited. Objective: To determine the effectiveness of CT in physical therapy for the management of MSP.

Methods. The PubMed, Web of Science, Scopus, Cinahl, Science Direct, and PEDro databases were searched for randomised clinical trials (RCTs) (updated June 5, 2024). RCTs comparing CT with other physical therapy treatments for MSP were included. Thirteen studies met the eligibility criteria, including those of the qualitative synthesis and meta-analysis types. The Cochrane Rob2 tool was used to assess the articles' quality.

Results. RCTs were assessed as having a low risk of bias for all RoB2 domains. Although the qualitative synthesis reports a reduction in pain, an increase in ROM, and less disability in favour of CT, the quantitative analysis only shows large, statistically significant effect sizes (Cohen's d) ($p < 0.05$) for the standardised mean differences (SMD) in pain (SMD = 0.9; CI = 0.8, 1.1) and ROM (SMD = –0.93; CI = –1.1, –0.8). These analgesic and ROM benefits improve when CT is applied with interferential currents (Pain: SMD = –1.54; IC = –1.8, –1.3) (ROM: SMD = 2.28; CI = 1.8, 2.7). Although the analgesic evidence was qualified as important, the heterogeneity obtained in the studies ($I^2 > 75\%$) moderates its degree of recommendation.

Conclusions. This SR shows that CT has better analgesic effects than TENS, interferential currents, or therapeutic ultrasound alone, which supports the idea of a combined analgesic effect. The researchers propose dosage recommendations for clinical practice and future research.

Key words: electrical stimulation therapy, musculoskeletal pain, musculoskeletal diseases, therapeutic ultrasound, transcutaneous electrical nerve stimulation, systematic review

Introduction

Musculoskeletal pain (MSP) is one of the leading causes of disability, affecting more than 1.5 billion people and worsening due to population growth and increased life expectancy [1]. MSP is characterised by movement limitations and loss of functional capacity and is caused by traumatic injuries, overuse, or degenerative diseases [2, 3]. Other alterations, such as fatigue, depression, and anxiety, appear when these conditions evolve chronically, which occurs in at least 20% of cases [1, 4, 5].

The World Health Organization has promoted initiatives to facilitate rehabilitation due to musculoskeletal disorders, promoting evidence-based interventions and providing the resources to develop them [1, 3]. In the same way, the current MSP management guidelines have placed non-pharmacological treatments in the first line due to recurrences, side effects, and dependence on some drugs [4, 6].

Physical therapy deals with MSP, its rehabilitation, and its deficiencies [7– 9]. It includes treatments such as physical agents, manual therapy, and therapeutic exercise for pain management, tissue repair, and range of motion improvement in pursuit of functional capacity recovery [6, 10, 11]. Therapeutic ultrasound (US) and electrotherapy, such as transcutaneous electrical nerve stimulation (TENS) or interferential currents (ITFC), are supported by evidence for treating MSP [12–15]. US is a non-invasive resource that uses mechanical waves with frequencies of 1 or 3 MHz, produced by the vibration of a transducer, at a power density lower than 3 W/cm^2 [16, 17]. US presents thermal and mechanical effects depending on its duty cycle, favouring hyperaemia, collagen synthesis, and changes in nerve conduction velocity [16, 17]. The analgesic effects of US are related to temperature changes at the tissue level [12, 16]. TENS and ITFC are two electrotherapy modalities used for pain reduction by activating sensory fibres (Gate Control theory) or endogenous opioid peptide release [16–19].

Combined therapy (CT) is another intervention described for MSP [20]. It consists of the combination of US with some electrical current, commonly TENS or ITFC, although the equipment allows currents such as 2–5, diadynamic, or faradic [16, 20]. The US acts as an active (mobile) electrode in addition to emitting mechanical waves, while a static electrode is attached to the patient, closing the circuit. CT enables tender point identification, represented as areas of increased excitability due to the lower nociceptive threshold [16]. Tender points are treated by positioning and holding the US over them until their excitability decreases [20, 21]. CT has been described to have a greater analgesic effect than either US or electrotherapy alone, resulting in analgesia by combining both physical agents, which is interesting due to the analgesic potentiation, versatility of the resource (simultaneous

Correspondence address: Hernán Andrés de la Barra Ortiz, Exercise and Rehabilitation Sciences Institute, School of Physical Therapy, Faculty of Rehabilitation Sciences, Universidad Andres Bello, Santiago, 7591538, Chile, e-mail: hdelabarra@unab.cl, handresdelabarra@yahoo.es; https://orcid.org/0000-0002-3927-1743

Received: 09.01.2023
Accepted: 18.04.2023

Citation: de la Barra Ortiz HA, Leiva CA, Lillo CA, Álvarez DC, Pizarro BC. Effectiveness of combined therapy in physical therapy for the management of musculoskeletal pain: a systematic review and meta-analysis. Physiother Quart. 2024;32(2):1–18; doi: https://doi.org/10.5114/pq/163383.

evaluation and treatment of painful points), possibility of thermal effects with electric current delivery, and in some cases, the time saving when both agents are required in each treatment [16, 20, 21]. Unfortunately, even though much electrotherapy equipment allows for its use, CT appears to be unknown or infrequent in clinics.

Although the analgesic efficacy of CT has been supported by a few RCTs in conditions such as knee osteoarthritis (OA), fibromyalgia, and myofascial pain syndrome [20–24], its use in physical therapy is less well-known than individual US and electrotherapy treatments. So, the objective of this systematic review (SR) is to examine the available research on CT and assess its value as a management tool for MSPs.

Design and method

Study design

This SR follows the PRISMA 2020 declaration guidelines (Preference reporting elements for systematic reviews and meta-analyses) [25] and was registered in the International Prospective Registry for SR (PROSPERO) of the National Institute for Health Research (NIHR) (CRD42022332557).

The PICO acronym (patient, intervention, comparison, and outcomes) was used to structure the research question and search algorithm: patients with musculoskeletal pain treated with CT were compared to another physical therapy intervention with or without sham CT, with pain reduction as the main outcome and changes in the range of motion (ROM) and disability as secondary outcomes.

These outcomes were analysed as continuous data, and due to the different measurement instruments, the standardised mean difference (SMD) was used in the meta-analysis (MT-A) to perform the comparisons. The effect size from the SMD values was determined by Cohen's d [26]: less than 0.4 (small effect), 0.4–0.7 (moderate effect), and greater than 0.7 (large effect). An SMD value of 0.5 or greater was considered a minimally important clinical difference (MCID) [26]. The Higgins I^2 statistic was used to assess the heterogeneity between studies [27]: unimportant (0–30%), moderate (40–50%), high (60–75%) or considerable (90–100%). The meta-analysis was performed using Cochrane's Review Manager 5.4 (RevMan).

RCTs selection

The following inclusion criteria were considered: (1) randomised or controlled clinical trials (RCT); (2) studies in humans; (3) participants older than 18 years; (4) articles in English or Spanish; (5) studies using CT alone or with another physical therapy intervention in musculoskeletal disorders; and (6) comparisons with other physical therapy treatments with or without sham CT. Moreover, the exclusion criteria considered were (1) CT treatments in other clinical conditions; (2) pain associated with neurological conditions or disorders; (3) studies with abstracts or incomplete texts; and (4) unavailable articles.

Search strategy

Three independent researchers (CA-L, CA-LV, and BC-P) reviewed clinical trials in six electronic databases, with the last update on June 5, 2024: Medline (via PubMed), Scopus, Web of Science (WoS), Cinahl, Science Direct, and PEDro. The search algorithm was constructed using keywords from the Medical Subject Headings dictionary (MeSH). The following keywords were used to structure the search: 'Transcutaneous Electric Nerve Stimulation', 'Electric Stimulation Therapy', 'Electric Stimulation', 'Interferential currents', 'Ultrasonic Therapy', 'Ultrasound therapy', 'Musculoskeletal Pain', 'Musculoskeletal Diseases', 'Myofascial Pain Syndromes', 'Arthralgia' and 'Pain Management' with the boolean terms 'OR' and 'AND', obtaining the search algorithm: (((((*"Transcutaneous Electric Nerve Stimulation"*) *OR* (*"Electric Stimulation Therapy"*)) *OR* (*"Electric Stimulation"*)) *OR* (*"Interferential currents"*)) *AND* ((*"Ultrasonic Therapy"*) *OR* (*"Ultrasound therapy"*))) *AND* (((((*"Musculoskeletal Pain") OR* (*"Musculoskeletal Diseases"*)) *OR* (*"Myofascial Pain Syndromes"*)) *OR* (*"Arthralgia"*)) *OR* (*"Pain Management"*)) Filters: Clinical Trial, Randomized Controlled Trial.

Searches for each database were analysed using the Rayyan platform (https://rayyan.qcri.org). Firstly, article titles and abstracts were analysed according to the selection criteria, classifying them into three categories (included, maybe, or excluded), and later the full texts of relevant articles were downloaded and reviewed. Any disagreements were resolved by the principal researcher (HDB-O). Then, each researcher reviewed the following characteristics of the RCTs: participant demographics, sessions, assessments, instruments reported, follow-up periods, CT treatment protocol, and outcomes measured.

RCTs' quality and risk of bias

RCTs' quality was reviewed by three researchers (CA-L, CA-LV, and BC-P), who assessed their indexing to the Evidence-Based Physiotherapy Database (PEDro). For PEDro-not-indexed RCTs, quality assessment was determined with the PEDro scale, and any disagreements were resolved as a team. RCTs with scores less than 5 were considered low-quality, while those with scores greater than or equal to 5 were rated as high-quality [28].

The Cochrane Collaboration's RoB2 tool was used to evaluate the risk of bias using six criteria [29]: (1) randomisation process bias; (2) bias due to deviations from planned interventions; (3) missing outcome data bias; (4) outcome measurement bias; (5) reported outcome selection bias; and (6) general bias. Four researchers (CA-L, CA-LV, DC-A, and BC-P) reviewed the studies and rated each criterion for them in the categories 'high risk of bias', 'low risk of bias', 'some concerns', or 'unclear risk of bias' [29]. If no consensus was reached, a fifth evaluator (HDB-O) was included. Studies with two or more high risks of bias were of low quality. After the analysis, box and summary plots were constructed with the Robvis tool (Figure 1) [30]. The researchers' RoB2 degree of agreement was estimated with the Fleiss-Kappa statistic ($\kappa = 0.93$).

The quality of the evidence for interesting outcomes was assessed with the recommendation, evaluation, development, and evaluation (GRADE) grading tool, which rated the collected evidence into high, moderate, low, or very low quality categories [31]. The guideline development tool (GRADEpro, GDT) was used to create the results table summary (https://www.gradepro.org).

Results

Search results

First, a total of 278 articles were obtained from PubMed ($n = 42$), Scopus ($n = 42$), WoS ($n = 93$), CINAHL ($n = 25$), Science Direct ($n = 69$) and PEDro ($n = 7$), resulting in 104 articles for analysis when duplicates where resolved. Sixteen RCTs were obtained after reviewing titles and abstracts ('pos-

Figure 1. Risk of bias summary for included RCTs: researchers' judgement for each criterion is expressed as a percentage

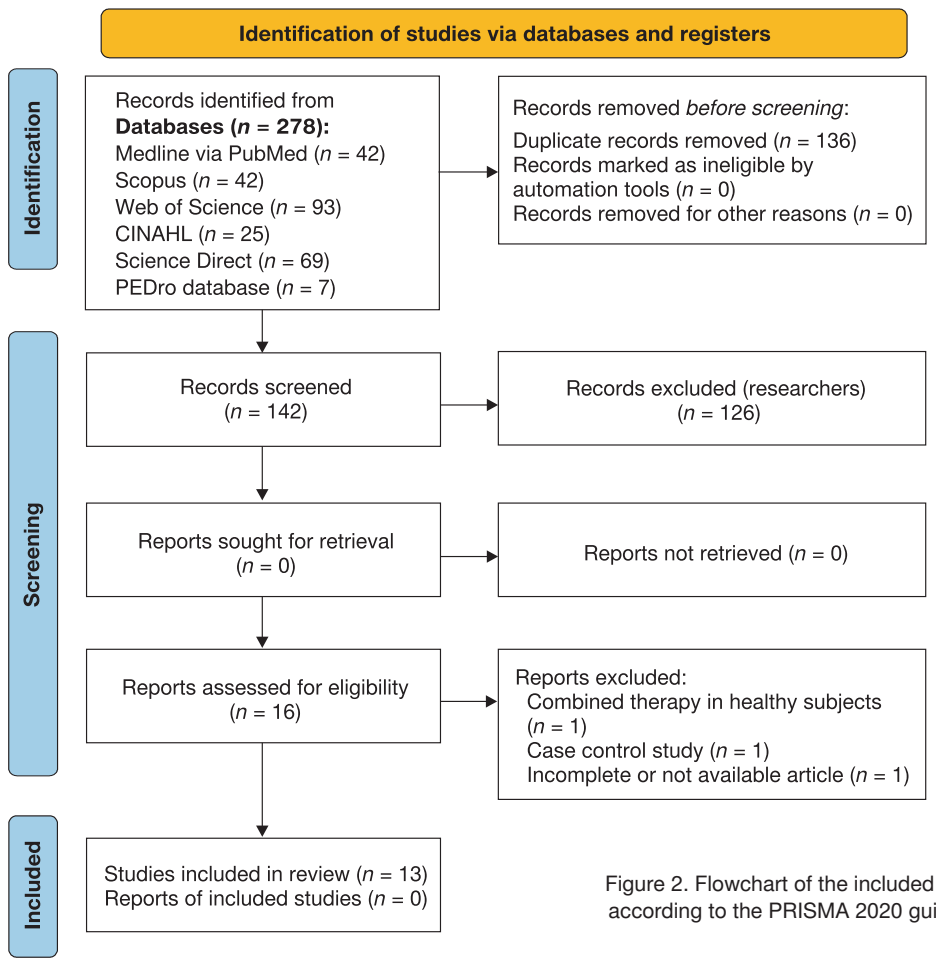


Figure 2. Flowchart of the included studies according to the PRISMA 2020 guidelines

sible' and 'included' categories). Three studies were discarded, resulting in 13 for this SR. The primary reasons for exclusion were the use of CT in healthy subjects ($n = 1$), case-control study ($n = 1$), and an unavailable article ($n = 1$). Figure 2 presents the search strategy summary using the PRISMA flowchart [25]. Appendix 1 shows the results of the search strategy for each electronic database.

Quality and risk of bias results

The quality of the RCTs was assessed using the PEDro scale. 92.3% of the articles were rated as high quality ($n = 12$), with scores equal to or greater than five [27], while only was evaluated as low quality, obtaining three points [32]. Higher scores were obtained for criteria 2 (random assignment), 4 (baseline comparability), 10 (results of between-group statistical comparisons were reported for at least one key outcome), and 11 (the study provides point measures and variability for at least one key result). Moreover, criteria 3 (concealed allocation), 5, and 6 (blind treaters and evaluators) presented the main inconsistencies [27].

The risk of bias assessment is presented in Figure 1: The randomisation process bias was rated as low-risk with 84.61% [21–24, 33–39]; the bias associated with deviations from planned interventions was rated as low-risk with 61.53% [20, 21, 23, 24, 34–36]; missing outcome data bias was rated as low-risk with 53.8% [20, 22, 24, 34, 37, 38]; selection of the reported outcome bias was rated as low-risk with 92.3% [21–24, 33–39]; and the general bias was rated as low-risk with 0.69% [20–24, 33–39].

Qualitative synthesis

The RCTs' qualitative characteristics, along with their outcome measures, are summarised in Table 1. The RCTs were conducted in Brazil ($n = 2$), China ($n = 1$), Korea ($n = 1$), Egypt (n = 2), India ($n = 1$), Israel ($n = 1$), Hungary ($n = 1$), Poland ($n = 1$), Thailand ($n = 2$), and the USA ($n = 1$) between the years 1997 and 2021. The total participants were 789, with an average age of 53.16, including 567 women and 205 men, data that excluded Almeida et al.'s study, which did not report the number of participants according to sex [20]. The musculoskeletal disorders treated were fibromyalgia ($n = 2$) [20, 21], trapezius muscle myofascial trigger points (MTrPs) ($n = 4$) [24, 32, 33, 36], hip osteoarthritis (OA) ($n = 2$) [23, 34], knee OA ($n = 3$) [22, 35, 37, 38] and lumbar herniated nucleus pulposus (HNP) [39]. CT was applied to a total of 318 participants, of whom 252 received the isolated intervention and 66 in conjunction with another treatment: manual therapy (post isometric relaxation technique, PIR) [34], phonophoresis (PhP) [24], stretching exercises [24], therapeutic exercises [23, 38], massage therapy, and balneotherapy [23]. Furthermore, 471 participants served as controls and received treatments such as TENS in knee OA and HNP [22, 39], US in MTrPs, hip and knee OA [23, 24, 32, 37], direct and alternating current in fibromyalgia [32], ischemic pressure in fibromyalgia [33], PIR in hip OA [34], PhP in fibromyalgia and knee OA [38], massage [23], and therapeutic exercises in hip and knee OA [23, 38]. Six studies used CT [20, 36, 39], US [23, 24], or sham TENS [35].

CT interventions were applied to upper trapezius MTrPs in patients with myofascial pain [24, 32, 33, 36], knee and hip in OA [22, 23, 34, 35, 38], and tender points in fibromyalgia [20, 21]. Only one study reported a remote application on the quadriceps femoris in participants with hip OA [37]. Eight studies (61.53%) used CT-TENS (sensory stimulation, frequency higher than 50 Hz, phase duration lower than 100 μs) [22–24, 34–37], and four (23.07%) used CT-ITFC (sensitive stimulation, 4.000 Hz and an amplitude modulated frequency between 100 and 150 Hz) [20, 21, 38, 39]. Only one study combined CT with DC and AC [23].

Regarding the US dose, six trials (46.15%) used continuous delivery (100% duty cycle) [20, 23, 24, 33, 35, 38], and five (38.46%) pulsed emission with duty cycles of 50% [34, 36], 40% [22] and 20% [21, 39]. Two studies did not report their US parameters [32, 37]. The average number of CT sessions ranged from 6 to 12, although some studies report a minimum of 1 [21, 24, 32, 39] and a maximum of 40 [22]. The average treatment times ranged from 8 to 10 min, although 20 min was also reported [22].

Main and secondary outcomes

Twelve RCTs (92.30%) report pain assessment as the main outcome, through changes in pain intensity (PI) or pain pressure threshold (PPT) [20–24, 32–38]. PI was assessed mainly with the visual analogue scale (VAS) [20–23, 32–35, 38] followed by the numerical pain rating scale (NPRS) [37], the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC-section A) [22, 38] and the Laitinen index [34], while the PPT with algometry was assessed [20, 24, 32].

The secondary outcomes included range of motion (ROM) and disability. Neck ROM through goniometry was reported for participants with myofascial pain [24, 32, 33, 36], while hip ROM was measured in OA [34] and HNP [39] through goniometry or an inclinometer. Moreover, disability was assessed in knee and hip OA using the WOMAC index (overall score) or the 6-minute walk test (6_{MWT}) [21–23, 35, 37, 38], while in patients with fibromyalgia, it was done through the Fibromyalgia Impact Questionnaire (FIQ) [21]. Additionally, Király et al. [23] and Kim et al. [22] used the SF-36 questionnaire to assess the quality of life in OA, while Moretti et al. [21] evaluated sleep quality using the Pittsburgh Sleep Quality Index. Some studies report the quantification of the number of tender points and sleep parameters with polysomnography in patients with fibromyalgia [20, 21] and the quantification of cartilage thickness in patients with knee OA [22].

Eleven studies (84.61%) evaluated outcome changes in two instances (before and after treatment), reporting average treatment times of 2 to 4 weeks. Only two studies included a follow-up evaluation after CT treatment [22, 23].

Table 2 summarises the results and statistical comparisons for pain, ROM, and disability between evaluation sessions in CT groups (efficacy) and versus controls at the end of treatment (effectiveness).

When comparing pre-posttreatment measurements after an average of 2–4 weeks, a statistically significant decrease in pain was observed in favour of CT ($p < 0.05$) for VAS [20–23, 33–35, 38], PPT [20, 24–32, 36], NPRS [37], WOMAC (section A) [35], and the Laitinen index [34]. In contrast, Lee et al. [32] did not report analgesic benefits in the EG for VAS and PPT once the treatment ended ($p > 0.05$). Kim et al. [22] also did not report analgesia during treatment ($p = 0.08$) but at they did rest ($p = 0.047$). Moreover, contradictory results appear when comparing the baseline with the follow-up evaluations, showing a statistically significant pain decrease in the Király et al. [23] study (follow-up at week 14) ($p = 0.001$) and a non-significant change for pain at rest in Kim et al.'s [22] study (follow-up at week 11) ($p = 0.134$) [22]. When analysing the pain changes between groups, contrasting results appear, with a statistically significant decrease in favour of CT at the end of the treatment for VAS and PPT in five studies

Table 1. Characteristics of the included studies

No.	Study	Author year country	Musculoskeletal disorder	PEDro score	*n* men women mean age ± *SD*	Groups	Intervention	Sessions	CT-parameters	Evaluations	Outcomes
1	The effectiveness of simultaneous thermotherapy with ultrasound and electrotherapy with combined AC and DC current on the immediate pain relief of myofascial trigger points	Lee et al. 1997 USA [32]	MFP – UT MTrPs	3/10	*n* = 26 ♂ = 12 ♀ = 14 43.7 ± 14.3	EG: 7 (5♀, 2♂) CG1: 6 (3♀, 3♂) CG2: 8 (4♀, 4♂) CG3: 5 (2♀, 3♂)	EG: CT (US + CD/AC) GC 1: Sham CT (US + DC/AC) GC 2: US GC 3: DC/AC	1	AC + DC Parameters: FR 50–100 Hz, CI NS US mode: NS US parameters: NS Time: 6 min Application: UT	T0: baseline (pretreatment) T1: post-treatment	– PI (VAS) – PPT (ALG) – cervical ROM (GNM)
2	The effect of combined therapy (ultrasound and interferential current) on pain and sleep in fibromyalgia	Almeida et al. 2003 Brazil [20]	fibromyalgia	6/10	*n* = 17 ♂ = NS ♀ = NS 56.5 ± 5.5	EG: 9 (NS) CG: 8 (NS)	EG: CT-ITFC GG: Sham CT	12 (3weeks)	ITFC Parameters: CF 4000 Hz, AMF 100 Hz, CI sensitive US mode: continuous US Parameters: FR 1 MHz, DwP 0.5 W/cm^2 Time: NS Application: tender points	T0: baseline (pretreatment) T1: 4 weeks (post-treatment)	– PI (VAS) – PPT (ALG) – no. of sensitive points – subjective sleep parameters (BISD – RS) (VAS) – subjective sleep parameters (MF) (VAS) – sleep parameters: arousals, SSC and WASO (PSG)
3	Effect of combination therapy [TENS & ultrasound] and ischemic compression in the treatment of active myofascial trigger points	Mukkannavar 2008 India [33]	MFP – UT MTrPs	5/10	*n* = 30 men = 15 ♀ = 15 29.5 ± 7.4	EG: 15 (NS) CG: 15 (NS)	EG: CT-TENS CG: ISP	6 (1week)	TENS Parameters: High voltage 300 V, PD 10–40 µs, IC 10 mA US mode: continuous US parameters: FR 1 MHz, DwP 1.5 W/cm^2, ERA NS Time: 5 min Application: UT	T0: baseline (pretreatment) T1: 1 week (post-treatment)	– PI (VAS) – cervical ROM (GNM)
4	Combined therapy (ultrasound and interferential current) in patients with fibromyalgia: once or twice in a week?	Moretti et al. 2012 Brazil [21]	fibromyalgia	6/10	*n* = 50 ♂ = 0 ♀ = 50 52.9 ± 4.8	EG1: 25 (25♀) EG2: 25 (25♀)	EG1: CT-ITFC EG2: CT (US + ITFC)	EG 1: 1 per week EG 2: 2 per week (4weeks)	ITFC Parameters: CF 4000, AMF 100 Hz, CI sensitive US mode: pulsed (DC 20%) US parameters: FR 1 MHz, DwP 2.5 W/cm^2, ERA NS Time: 2 min per TP Application: TP	T0: baseline (pretreatment) T1: 4 weeks (post-treatment)	– PI (VAS) – disability (FIQ) – sleep quality (PSQI) – no. of tender points (palpation)
5	Use of combined therapy (TENS+UD) and postisometric relaxation (PIR) of muscles in seniors with degenerative disease of the hip joint	Podczarska-Głowacka and Łysak 2016 Poland [34]	hip OA	5/10	*n* = 60 ♂ = 11 ♀ = 49 68.0 ± 7.8	EG: 30 (23♀, 7♂) CG: 30 (26♀, 4♂)	EG: CG-TENS + PIR CG: PIR	NS (3weeks)	TENS Parameters: FR 80–100 Hz, PD 100 µs, CI sensitive US mode: pulsed (DC 50%) US Parameters: FR 1 MHz, DwP 0.7 W/cm^2, ERA NS Time: 8 min Application: hip	T0: baseline (pretreatment) T1: 3 weeks (post-treatment)	– PI (VAS) – pain perception (LI) – ROM (GNM)
6	Ultrasound combined transcutaneous electrical nerve stimulation (UltraTENS) versus phonophoresis of piroxicam (PhP) in symptomatic knee osteoarthritis: a randomized double-blind, controlled trial	Boonhong et al. 2017 Thailand [35]	knee OA	8/10	*n* = 61 ♂ = 6 ♀ = 55 63.4 ± 8.1	EG: 31 (28♀, 3♂) CG: 30 (27♀, 3♂)	EG: CT-TENS CG: Sham TENS + PhP	10 (2weeks)	TENS Parameters: FR 100 Hz, PD 100 µs, CI 10–30 mA US mode: continuous US parameters: FR 1 MHz, PwD 1.0W/cm^2, ERA NS Time: 10 min Application: knee	T0: baseline (pretreatment) T1: 2 weeks (post-treatment)	– PI (VAS) – disability (WOMAC)

7	Immediate effects of simultaneous application of transcutaneous electrical nerve stimulation and ultrasound phonophoresis on active myofascial trigger points: a randomized controlled trial	Takla and Rezk-Allah 2018 Egypt [24]	MFP – UT MTrPs	9/10	*n* = 100 ♂ = 46 ♀ = 54 35.7 ± 5.6	EG: 25 (14♀, 11♂) CG1: 25 (12♀, 13♂) CG2: 25 (15♀, 10♂) GC3: 25 (13♀, 12♂)	EG: CT-TENS + PhP + stretching CG 1: PhP + passive stretching CG2: US + passive stretching GC3: Sham US + stretching	1	TENS Parameters: FR 120–200 Hz, PD 200µs, CI sensitive US mode: continuous US parameters: FR 1 MHz, PWD 1.5 W/cm², ERA 4 cm² Time: 10 min Application: UT	T0: baseline (pretreatment) T1: post-treatment	– PPT (ALG) – cervical ROM (ICM)
8	Low-frequency high-intensity versus medium-frequency low-intensity combined therapy in the management of active myofascial trigger points: a randomized controlled trial	Takla 2018 Egypt [36]	MFP – UT MTrPs	6/10	*n* = 70 ♂ = 30 ♀ = 40 34.8 ± 5.7	EG1: 23 (14♀, 9♂) EG2: 25 (13♀, 12♂) CG: 22 (13♀, 9♂)	EG1: CT-TENS EG2: CT-ITFC CG: Sham CT	12 (4weeks)	TENS (EG1), IFC (EG2) Parameters: TENS: FR 100 Hz, PD 200 µs, IC (motor) IFC: CF 4000 Hz, AMF 100–150 Hz, CI sensitive US mode: pulsed (DC 50%) US parameters: FR 1 MHz, PWD 1.2 W/cm², ERA 4 cm² Time: 10 min Application: UT	T0: baseline (pretreatment) T1: 4 weeks (post-treatment)	– PPT (ALG) – cervical ROM (ICM)
9	Does adding transcutaneous electrical nerve stimulation to therapeutic ultrasound affect pain or function in people with osteoarthritis of the knee? A randomized controlled trial	Sangtong et al. 2019 Thailand [37]	knee OA	7/10	*n* = 148 ♂ = 13 ♀ = 135 62.9 ± 7.9	EG: 74 (69♀, 5♂) CG: 74 (66♀, 8♂)	EG: CT-TENS CG: US	10 (2weeks)	TENS Parameters: FR 32–50 Hz, PD 80 µs, CI sensitive US mode: NS US parameters: FR 1 MHz, PWD 1.0 W/cm², ERA NS Time: 10 min Application: QF	T0: baseline (pretreatment) T1: 2 weeks (post-treatment)	– PI (NPRS) – walking speed (6_{MWT})
10	Effects of combination therapy and infrared radiation on pain, physical function, and quality of life in subjects with knee osteoarthritis: a randomized controlled study	Usman et al. 2019 China [38]	knee OA	6/10	*n* = 60 ♂ = 18 ♀ = 42 66.3 ± 8.9	EG: 30 (24♀, 6♂) CG: 30 (18♀, 12♂)	EG: CT-ITFC + isometric exercise (QF) CG: IR + isometric exercise (QF)	36 (12weeks)	ITFC Parameters: CF NS, AMF 100 Hz, CI NS US mode: continuous US parameters: FR 1 MHz, PWD 1.5 W/cm², ERA 5 cm² Time: 10 min Application: knee	T0: baseline (pretreatment) T1: 12 weeks (post-treatment)	– PI (VAS S-R) – disability (WOMAC S-R) – quality of life (HRQoL S-R)
11	Efficacy and safety of a stimulator using low-intensity pulsed ultrasound combined with transcutaneous electrical nerve stimulation in patients with painful knee osteoarthritis	Kim et al. 2019 Korea [22]	knee OA	7/10	*n* = 40 ♂ = 8 ♀ = 32 57.6 ± 8.3	EG: 20 (17♀, 3♂) CG: 20 (15♀, 5♂)	EG: CT-TENS CG: TENS	40 (8weeks)	TENS Parameters: FR 80 Hz, PD 50–100 µs, CI sensitive US mode: pulsed (DC 40%) US parameters: FR 1 MHz, PWD 1.0 W/cm², ERA 3.3 cm². Time: 20 min Application: knee	T0: baseline (pretreatment) T1: 8 weeks (post-treatment) T2: 11 weeks (follow-up)	– PI (VAS) – PI (WOMAC, section A) – knee stiffness (WOMAC, section B) –- functional capacity (WOMAC, section C) – quality of life (SF-36) – cartilage thickness (USG)

12	Effects of various types of ultrasound therapy in hip osteoarthritis – a double blind, randomized, controlled, follow-up study	Király et al. 2021 Hungary [23]	hip OA	8/10	*n* = 71 ♂ = 14 ♀ = 57 66.3 ± 9.0	EG: 15 (13♀, 2♂) CG1: 21 (17♀,4♂) CG2: 17 (13♀, 4♂) GC3: 18 (14♀, 4♂)	EG: CT-TENS + conventional therapy (exercises, massage, balneotherapy) CG1: continuous US + conventional therapy (exercises, massage, balneotherapy) CG2: pulsed US + conventional therapy (exercises, massage, balneotherapy) CG3: Sham US + conventional therapy (exercises, massage, balneotherapy)	10 (2weeks)	TENS Parameters: FR 100 Hz, DF 100 µs, CI NS US mode: continuous US parameters: FR 3 MHz, PWD 0.5 W/cm² Time: 10 min Application: hip	T0: baseline (pretreatment) T1: 2 weeks (post-treatment) T2: 14 weeks (follow-up)	– PI (VAS) – disability (6_{MWT}) – disability (WOMAC) – quality of life (SF-36)
13	The effects of TENS, interferential stimulation, and combined interferential stimulation and pulsed ultrasound on patients with disc herniation-induced radicular pain	Ariel et al. 2021 Israel [39]	HNP	6/10	*n* = 56 ♂ = 32 ♀ = 24 53.5 ± NS	EG: 14 (6♀, 8♂) CG 1: 14 (6♀, 8♂) CG 2: 14 (6♀, 8♂) CG 3: 14 (6♀, 8♂)	EG: CT-ITFC CG1: TENS CG2: ITFC GC3: Sham CT	1	ITFC Parameters: CF 4000 Hz, AMF 30 Hz US mode: pulsed (DC 20%) US parameters: FR 1 MHz, PWD 1.2 W/cm², ERA NS Time: 10 min Application: back	T0: baseline (pretreatment) T1: post-treatment	– SLR ROM (ICM)

(38.46%) ($p < 0.05$) [20, 22, 24, 36, 38] and without differences in the other five trials for VAS, PPT, and NPRS [23, 33–35, 37]. Moretti et al. worked with two EGs without a control [21], whereas Lee et al. [32] did not report intragroup pain changes.

A statistically significant ROM increase was observed in myofascial pain, hip OA, and HNP evaluated with goniometry or an inclinometer ($p < 0.05$) [24, 33, 34, 36, 39]. Lee et al. [32] was the only study than did not report differences in ROM after CT treatment ($p > 0.05$). Moreover, ROM was not assessed in the studies that considered follow-up [22, 23]. The intergroup ROM changes are controversial, with no statistically significant changes in patients with myofascial pain [33] and hip OA [34], and with significant changes in participants with neck myofascial pain [36] and HNP [39].

Concerning disability, statistically significant changes are observed after CT, represented by a decreased WOMAC score [23, 35, 38], an increase in speed or metres in the 6_{MWT} [23, 38], or a reduction in the FIQ score [21]. Follow-up assessments show a statistically significant decrease in the WOMAC score and an increase in metres in 6_{MWT} for Király et al.'s [23] study ($p < 0.01$), but not for Kim et al. [22], who reported no change for WOMAC ($p = 0.886$). Finally, the intergroup disability also shows controversial findings, including a higher proportion of studies with no significant difference between groups ($p > 0.05$) for WOMAC [22, 23, 35] and 6_{MWT} [23, 37] and only one study with significant changes for the WOMAC (physical function section) ($p < 0.01$) [38].

Main outcome and meta-analysis

Means were analysed for VAS, PPT, LI, or WOMAC A section to assess pain changes. Figure 3 shows the MT-A with a fixed effects model for differences in PI at the end of treatment (3A) and four subgroup analyses: PI after 2–4 weeks (3B), PI for follow-up (3C), PI for CT-ITFC studies (3D), and PI for CT-TENS studies (3E). MT-A included the same author more than once because many studies reported more than one measurement instrument to assess pain (Table 2). The studies by Moretti [21] and Lee [32] were excluded from the analysis due to the absence of a control and due to methodological quality and high risk of bias, respectively. Differences in PI show a pooled effect in favour of CT.

For PI at the end of treatment, 20 means were extracted from nine RCTs (Figure 3A): Almeida et al. (VAS and PPT before and after sleep) [20], Kim et al. (VAS during treatment, on movement, and at rest) [22], Király et al. (VAS at rest) [23], Takla and Rezk-Allah (PPT for MTrPs) [24], Takla (PPT for MTrPs with CT-ITFC or CT-TENS) [36], Podczarska-Głowacka and Łysak (VAS and LI) [34], Boonhong et al. (VAS and WOMAC) [35], Sangtong et al. (NPRS) [37], and Usman et al. (VAS and WOMAC) [38]. The difference is statistically significant in favour of CT, but there is statistical heterogeneity (CT = 503; control = 580; SMD = –0.93 [95% CI = –1.07, 0.78], $I^2 = 95\%$).

Treatments between weeks 2 and 4 were pooled, as these were the most common treatment periods. The MT-A included six RCTs, extracting 14 means with their SD (Figure 3B): Almeida (VAS and PPT before and after sleep) [20], Király et al. (VAS at rest) [23], Podczarska-Głowacka and Łysak (VAS and LI) [34], Boonhong et al. (VAS and WOMAC A section) [35], Takla (PPT in MTrPs with CT-ITFC or CT-TENS) [36] and Sangtong et al. (NPRS) [37]. CT has a statistically significant difference with considerable statistical heterogeneity (CT = 343; control = 370; SMD = –0.74 [95% CI = –0.92, –0.57], $I^2 = 95\%$).

Trials with follow-up assessments were pooled and five outcomes were obtained from two studies (Figure 3C): Kim

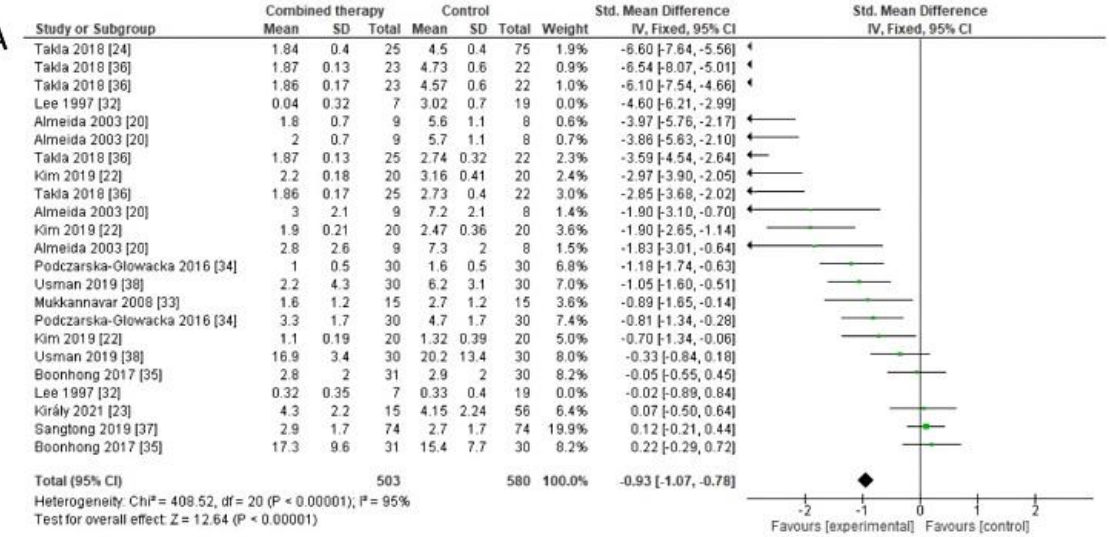
Table 2. Results and statistical comparisons of the outcome measures in the CT groups between the included studies

Study	Outcome-measurement tool	T0: baseline mean ± *SD*	T1: post-treatment mean ± *SD*	T2: follow-up mean ± *SD*	*p*-value intragroup T0–T1	*p*-value Intragroup T0–T2	*p*-value intergroup after treatment	CT efficacy	CT effectiveness
Lee et al. [32]	PI-VAS (cm)	3.32 ± 0.85	0.32 ± 0.35 (1 day)	/	> 0.05	/		N	NE+
	PPT-ALG (kgf/cm^2)	0.02 ± 0.18	3.02 ± 0.68 (1 day)					N	
	Cervical SB ROM-GNM (°)	31 ± 3.6	30.3 ± 5.36 (1 day)					N	
Almeida et al. [20]	PI before sleep-VAS (cm)	6.8 ± 1.4	3.0 ± 2.1 (4 weeks)	/	< 0.01*	/	< 0.01*	Y	Y
	PI after sleep-VAS (cm)	7.4 ± 1.5	2.8 ± 2.6 (4 weeks)					Y	Y
	PPT before sleep-ALG (kgf/cm^2)	2.8 ± 0.4	5.6 ± 1.1 (4 weeks)	/	< 0.01*		< 0.01*	Y	Y
	PPT after sleep-ALG (kgf/cm^2)	3.0 ± 0.1	5.7 ± 1.1 (4 weeks)					Y	Y
Mukkannavar [33]	PI-VAS (cm)	7.0 ± 0.84	1.6 ± 1.17 (1 week)	/	< 0.05*	/	> 0.05	Y	N
	Cervical SB ROM-GNM (°)	30.5 ± 7.33	44.73 ± 11.2 (1 week)					Y	N
Moretti et al. [21]	PI-VAS (cm) CT-ITFC (1 per week)	7.2 ± 2.6	3.1 ± 2.3 (4 weeks)	/	< 0.001*	/	0.162	Y	NE+
	PI-VAS (cm) CT-ITFC (2 per week)	8.8 ± 1.7	1.6 ± 2.3 (4 weeks)					Y	
	Disability-FIQ (score) CT-ITFC (1 per week)	73.6 ± 9.8	48.8 ± 21 (4 weeks)				0.745	Y	
	Disability-FIQ (score) CT-ITFC (2 per week)	65.1 ± 12.2	42.9 ± 18.7 (4 weeks)					Y	
Podczarska-Głowacka and Łysak [34]	PI-VAS (cm)	5.6 ± 1.8	3.3 ± 1.7 (3 weeks)	/	0.001*	/	0.517	Y	N
	PI-LI (score)	2.1 ± 0.7	1.0 ± 0.5 (3 weeks)				0.610	Y	N
	Hip flexion ROM-GNM (°)	59.0 ± 12.4	71.0 ± 16.5 (3 weeks)				0.783	Y	N
	Hip extension ROM-GNM (°)	6.0 ± 1.3	8.8 ± 1.2 (3 weeks)				0.938	Y	N
	Hip abduction ROM-GNM (°)	17.1 ± 2.9	23.0 ± 4.1 (3 weeks)				0.999	Y	N
	Hip adduction ROM-GNM (°)	18.1 ± 4.7	23.5 ± 5.2 (3 weeks)				0.996	Y	N
	Hip external rotation ROM-GNM (°)	26.3 ± 4.2	31.0 ± 4.3 (3 weeks)				0.450	Y	N
	Hip internal rotation ROM-GNM (°)	24.1 ± 4.9	28.7 ± 5.3 (3 weeks)				0.885	Y	N
Boonhong et al. [35]	PI-VAS (cm)	6.5 ± 1.1	2.8 ± 2.0 (2 weeks)	/	< 0.01*	/	0.70	Y	N
	PI-WOMAC pain (score)	30.0 ± 7.0	17.3 ± 9.6 (2 weeks)				0.43	Y	N
	Disability-WOMAC overall (score)	141.2 ± 32.9	78.1 ± 45.4 (2 weeks)				0.61	Y	N

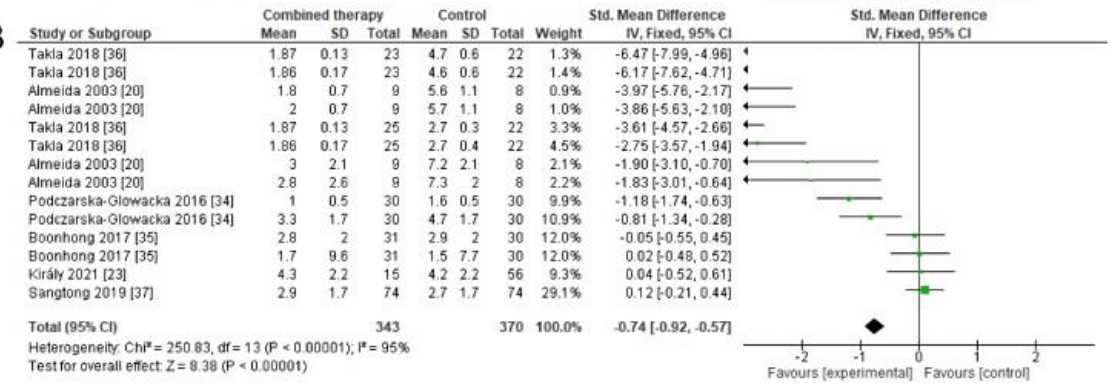
Takla and Rezk-Allah [24]	PPT MTrPs-ALG (kgf/cm^2)	0.85 ± 0.1	4.48 ± 0.39 (1 day)	/	< 0.01*	/	< 0.01*	Y	Y
	Cervical SB ROM-ICM (°)	35.7 ± 1.7	40.2 ± 1.2 (1 day)					Y	Y
Takla [36]	PPT MTrPs 1-ALG (kgf/cm^2) CT-TENS	0.27 ± 0.18	4.57 ± 0.57 (4 weeks)	/	< 0.01*	/	< 0.01*	Y	Y
	PPT MTrPs 2-ALG (kgf/cm^2) CT-TENS	0.73 ± 0.17	4.73 ± 0.59 (4 weeks)					Y	Y
	Right cervical *SD* ROM-ICM (°) CT-TENS	36.5 ± 2.11	52.86 ± 1.86 (4 weeks)					Y	Y
	Left cervical *SD* ROM-ICM (°) CT-TENS	35.8 ± 2.16	53.5 ± 1.87 (4 weeks)					Y	Y
	PPT MTrPs 1-ALG (kgf/cm^2) CT-ITFC	0.75 ± 0.16	2.73 ± 0.35 (4 weeks)					Y	Y
	PPT MTrPs 2-ALG (kgf/cm^2) CT-ITFC	0.70 ± 0.15	2.74 ± 0.32 (4 weeks)					Y	Y
	Right cervical SD ROM-ICM (°) CT-ITFC	35.92 ± 1.93	47.1 ± 1.49 (4 weeks)					Y	Y
	Left cervical SD ROM-ICM (°) CT-ITFC	36.23 ± 2.17	46.99 ± 1.39 (4 weeks)					Y	Y
Sangtong et al. [37]	PI-NPRS (points)	5.8 ± 1.3	2.9 ± 1.7 (2 weeks)	/	<0.05*	/	0.323	Y	N
	Disability-6$_{MWT}$ (gait speed, m/s)	1.10 ± 0.36	1.17 ± 0.39 (2 weeks)				0.551	N	Y
Usman et al. [38]	PI-VAS (cm)	7.1 ± 1.7	2.2 ± 4.3 (12 weeks)	/	< 0.05*	/	< 0.01*	Y	Y
	PI-WOMAC pain (scores)	18.8 ± 2.8	16.97 ± 3.4 (12 weeks)					Y	Y
	Disability-WOMAC PF (scores)	56.1 ± 7.4	45.8 ± 9.1 (12 weeks)					Y	Y
Kim et al. [22]	PI during treatment-VAS (cm)	4.2 ± 0.34	1.9 ± 0.21 (8 weeks)	2.5 ± 0.29 (11 weeks	0.080	0.650	0.036*	N	Y
	PI at movement-VAS (cm)	4.9 ± 0.29	2.2 ± 0.18 (8 weeks)	2.7 ± 0.20 (11 weeks)	0.022*	0.457	0.027*	Y	Y
	PI at rest-VAS (cm)	3.0 ± 0.26	1.1 ± 0.19 (8 weeks)	1.5 ± 0.23 (11 weeks)	0.047*	0.134	0.759	Y	N
	Disability-WOMAC (score)	35.2 ± 3.4	19.1 ± 2.7 (8 weeks)	21.7 ± 3.03 (11 weeks)	0.055	0.886	0.05	N	N
Király et al. [23]	PI-VAS (cm)	6.1 ± 1.8	4.3 ± 2.2 (2 weeks)	3.1 ± 2.2 (14 weeks)	< 0.01*	0.001*	0.689	Y	N
	Disability-WOMAC (score)	1220.33 ± 424.6	993.9 ± 532.2 (2 weeks)	787.7 ± 366.6 (14 weeks)	0.023*	0.001*	0.707	Y	N
	Disability-6$_{MWT}$ (m)	306.1 ± 86.0	338.5 ± 87.0 (2 weeks)	355.4 ± 88.8 (14 weeks)	0.003*	0.0015*	0.653	Y	N
Ariel et al. [39]	SLR ROM-ICM (grades)	46.3 ± 12.0	57.5 ± 17.7 (1 day)	/	< 0.01*	/	< 0.01*	Y	Y

6_{MWT} – 6-minute walk test, ALG – algometry, CT – combined therapy, ICM – inclinometry, ITFC – interferential current, FIQ – Fibromyalgia Impact Questionnaire, kgf – kilograms-force, LI – Lattinen index, NPRS – numeric pain rating scale, PI – pain intensity, PPT – pain pressure threshold, ROM – range of movement; SB – side bending, SLR – straight leg raising, TENS – transcutaneous electrical nerve stimulation, T1,T2… TX – evaluations carried out after treatment, US – therapeutic ultrasound, VAS – visual analogue scale, WOMAC – Western Ontario and McMaster Universities Osteoarthritis Index, NE+ – not evaluated, Y – yes, N – no; $p < 0.05$*

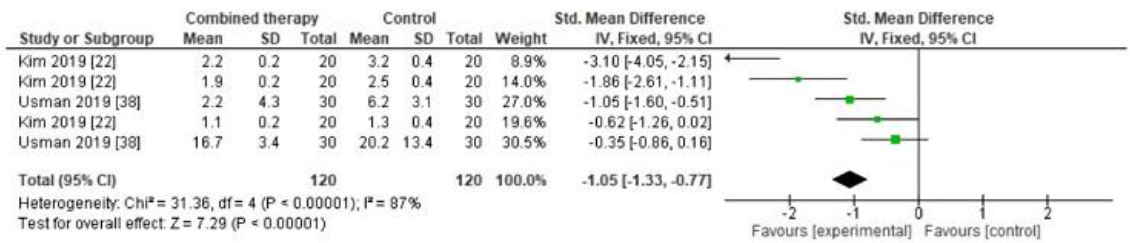
3A



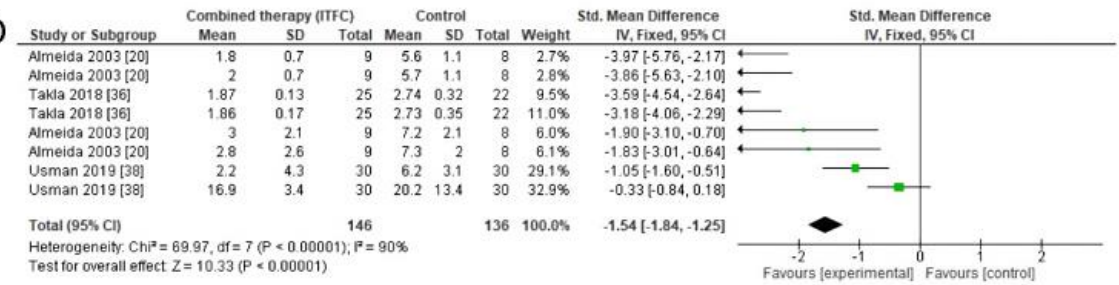
3B



3C



3D



3E

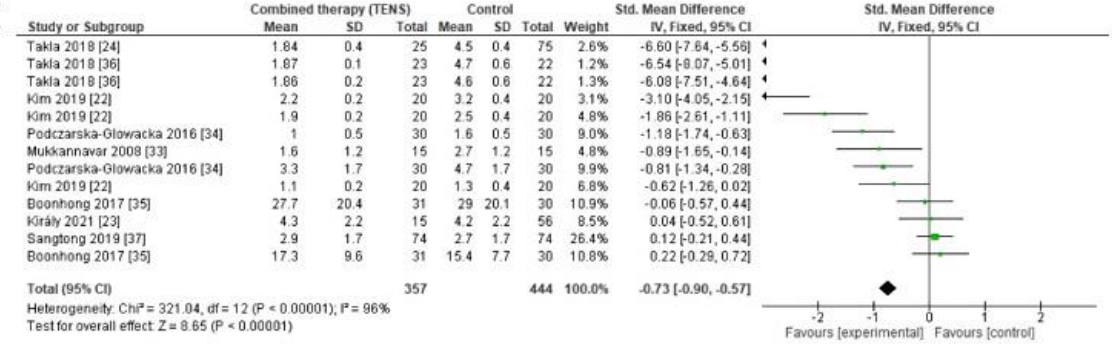


Figure 3. Forest plots for PI at the end of treatment (3A), at 2–4 weeks (3B), at follow-up (3C), at the end of treatment for CT-ITFC studies (3D), and at the end of treatment for CT-TENS studies (3E)

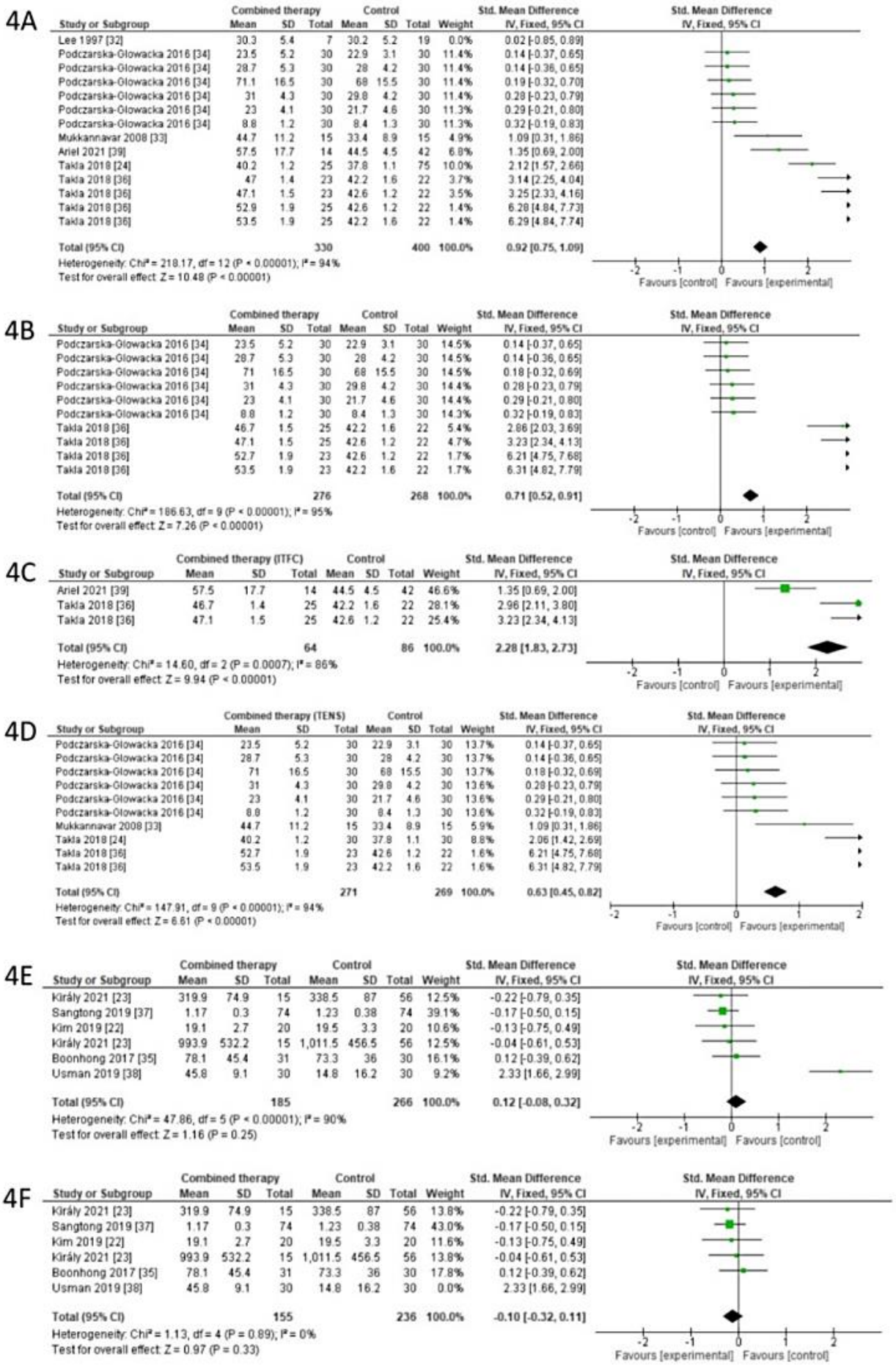


Figure 4. Forest plot for ROM and disability changes: ROM at end of treatment (4A), ROM after 2–4 weeks of treatment (4B), ROM at end of treatment for CT-ITFC studies (4C), end-of-treatment ROM for CT-TENS studies (4E), end-of-treatment disability (4F), and end-of-treatment disability for CT-TENS studies (5B)

et al. (VAS during treatment in motion and at rest) [22], and Usman et al. (VAS and WOMAC) [38]. A statistically significant difference for CT with statistical heterogeneity is observed (CT = 120; control = 120; SMD = –1.05 [95% CI = –1.33, –0.77], I^2 = 87%).

Pain changes using CT with ITFC were analysed with 3 studies and 8 outcomes (Figure 3D): Almeida (VAS and PPT before and after sleep) [20], Takla (PPT for MTrPS) [36], and Usman et al. (VAS and WOMAC) [38]. The results show a statistically significant difference in favour of CT with considerable heterogeneity (CT = 146; control = 136; SMD = –1.54 [95% CI = –1.84, –1.25], I^2 = 90%).

Pain changes using CT with ITFC included seven studies with 13 outcomes (Figure 3E): Kim et al. (VAS during treatment in motion and at rest) [22], Király et al. (VAS at rest) [23], Takla (PPT for MTrPs) [24, 36], Podczarska-Głowacka and Łysak (VAS and LI) [34], Boonhong et al. (VAS and WOMAC) [35], and Sangtong et al. (NPRS) [37]. There is a statistically significant difference in favour of CT and considerable heterogeneity (CT = 357; control = 444; SMD = –0.73 [95% CI = –0.90, –0.57], I^2 = 96%).

Secondary outcomes and meta-analysis

The means with their SD were obtained for the different ROM measurements, while disability is considered by the WOMAC index and the 6_{MWT} reported by RCTs. Figure 4 shows the MT-A with a fixed effects model for ROM and disability differences at the end of treatment and their subgroup analyses. In some cases, the same trial was analysed more than once because many studies assessed several ROMs (Table 2). The study by Lee et al. [32] was excluded from the analysis due to its low methodological quality and high risk of bias. All comparisons show a pooled effect for ROM in favour of CT.

End-of-treatment ROM analysis included five RCTs and 13 outcomes (Figure 4A): Takla and Rezk-Allah (neck side bending) [24], Mukkannavar (neck side bending) [33], Podczarska-Głowacka and Łysak (hip flexion, extension, abduction, adduction, internal, and external rotation) [34], Takla (right and left neck side bending for CT-TENS and CT-ITFC) [36], and Ariel et al. (ROM for the SLR test) [39]. The results show a statistically significant difference for CT with considerable statistical heterogeneity (CT = 330; control = 400; SMD = 0.92 [95% CI = 0.75, 1.09], I^2 = 94%).

Treatments between weeks 2 and 4 were pooled, as these were the most common treatment periods. The analysis included two studies with ten outcomes (Figure 4B): Podczarska-Głowacka and Łysak (hip flexion, extension, abduction, adduction, and internal and external rotation ROM) [34], and Takla (right and left neck side bending for CT-TENS and CT-ITFC) [36]. There is a statistically significant difference for CT and statistical heterogeneity (CT = 276; control = 268; SMD = 0.71 [95% CI = 0.52, 0.91], I^2 = 95%).

ROM changes using CT-ITFC included two studies with three outcome measures (Figure 4C): Takla (right and left neck side bending) [36], and Ariel et al. (ROM with SLR test) [39]. The results show a statistically significant difference for CT and high heterogeneity (CT = 64; control = 86; SMD = 2.28 [95% CI = 1.83, 2.73], I^2 = 86%).

Four trials considered ROM changes using CT-TENS with ten measures (Figure 4D): Takla and Rezk-Allah (neck side bending) [24], Mukkannavar (neck side bending) [33], Podczarska-Głowacka and Łysak (flexion, extension, abduction, adduction, hip internal and external rotation) [34], and Takla (right and left neck side bending) [36]. There is also a statistically significant difference in favour of CT and considerable heterogeneity (CT = 271; control = 269; SMD = 0.63 [95% CI = 0.45, 0.82], I^2 = 94%).

Figure 4 shows a fixed-effects model for disability changes at the end of treatment (4E) and subgroup analysis with CT-TENS (4F). MT-A included the same author more than once because some studies reported more than one instrument for disability changes (Table 2). Disability analysis for CT-ITFC was not performed as there was only one trial [38]. Both disability comparisons show non-significant results that do not favour either group.

For disability, five RCTs and six measures were considered (Figure 5A): Kim et al. (WOMAC score) [22], Király et al. (WOMAC score and 6MWT metres) [23], Boonhong et al. (WOMAC score) [35], Sangtong et al. (6_{MWT} gait speed) [37], and Usman et al. (WOMAC score) [38]. There was considerable heterogeneity with a non-significant difference between groups (p = 0.25) (CT = 185; control = 266; SMD = 0.12 [95% CI = –0.08, 0.32], I^2 = 90%).

Disability changes using CT-TENS considered the same studies and outcomes described above, excluding only the study by Usman et al. because it used CT-ITFC (Figure 5B). There is statistical homogeneity with no significant differences between groups (p = 0.33) (CT = 155; control = 236; SMD = –0.10 [95% CI = –0.32, 0.11], I^2 = 0%).

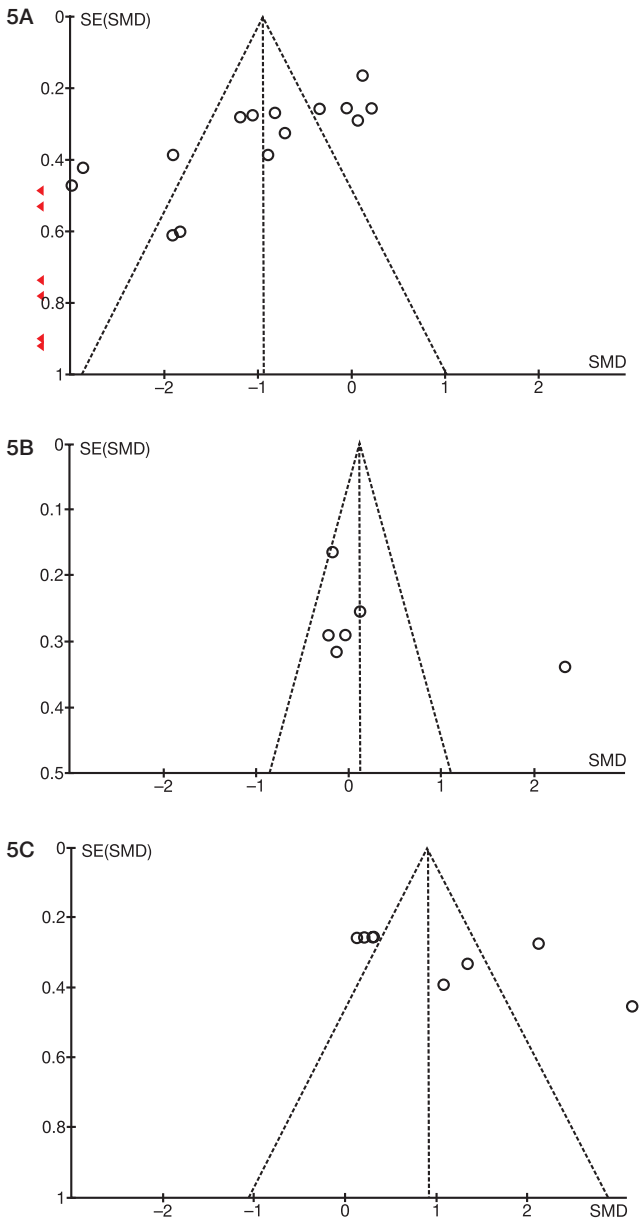


Figure 5. Funnel plots for outcomes of interest: PI (5A), ROM (5B), and disability (5C)

Table 3. Evidence quality by GRADE using CT for pain management, ROM improvement, and disability decrease at the end of treatment

Certainty assessment							No. of patients		Effect		Certainty	Importance
no. of studies	study design	risk of bias	inconsistency	indirectness	imprecision	other considerations	combined therapy	other physical therapy intervention	relative (95% CI)	absolute (95% CI)		
1A. Pain intensity at end of treatment												
10	RCTs	not serious[a]	serious[b]	not serious[c]	serious[d]	publication bias strongly suspected[e]	503	580	–	SMD **0.93 lower** (*SD* 1.07 lower to 0.78 lower)	⊕ very low	important[j]
1B. Pain intensity at end of treatment using CT-ITFC												
3	RCTs	not serious[a]	serious[b]	not serious[c]	not serious[f]	publication bias strongly suspected[e]	146	136	–	*SMD* **1.54 lower** (*SD* 1.84 lower to 1.25 lower)	⊕⊕ low	important[j]
1C. Pain intensity at end of treatment using CT-TENS												
8	RCTs	not serious[a]	serious[b]	not serious[c]	serious[d]	publication bias strongly suspected[e]	357	444	–	*SMD* **0.73 lower** (*SD* 0.9 lower to 0.57 lower)	⊕ very low	important[j]
2A. Changes in ROM at end of treatment												
6	RCTs	not serious[a]	serious[b]	not serious[c]	serious[d]	publication bias strongly suspected[g]	330	400	–	*SMD* **0.92 more** (SD 0.75 more to 1.09 more)	⊕ very low	important[j]
2B. Changes in ROM at end of treatment using CT-ITFC												
2	RCTs	not serious[a]	serious[b]	not serious[c]	not serious[h]	publication bias strongly suspected[g]	64	86	–	*SMD* **2.28 more** (SD 1.83 more to 2.73 more)	⊕⊕ low	critical[j]
2C. Changes in ROM at end of treatment using CT-TENS												
4	RCTs	not serious[a]	serious[b]	not serious[c]	serious[d]	publication bias strongly suspected[g]	271	269	–	*SMD* **0.63 more** (*SD* 0.45 more to 0.82 more)	⊕ very low	important[k]
3A. Changes in disability at end of treatment												
5	RCTs	not serious[a]	serious[b]	not serious[c]	serious[d]	none[i]	185	266	–	*SMD* **0.12 more** (0.08 fewer to 0.32 more)	⊕⊕ low	not important[l]
3B. Changes in disability at end of treatment using CT-TENS												
4	RCTs	not serious[a]	not serious[f]	not serious[c]	serious[d]	none[i]	155	236	–	*SMD* **0.1 lower** (*SD* 0.32 higher to 0.11 higher)	⊕⊕⊕ moderate	not important[l]

CI – confidence interval, RCTs – randomised controlled trial, *SMD* – standardised mean difference

(a) The risk of bias has been identified as not very serious with the Cochrane RoB2 tool, showing as a result a low risk of bias (greater than 50%) for all its domains: bias due to the randomisation process (84.6%), bias due to deviations from interventions (61.5%), missing outcome data bias (53.8%), outcome measurement bias (92.3%), reported outcome selection bias (92.3%), and overall bias (69.2%)
(b) The value for the Higgins I^2 test results in a value greater than 75%. In addition, even though the estimation points are loaded in favour of the CT, there is considerable variation in the results with a wide CI (95%), and for several studies, they crossed the 'no effect' line
(c) The indirectness was assessed as not serious because the studies directly compared the interventions and outcomes. All the studies included in the meta-analysis consider the population, the intervention, the comparison groups, and the report of the outcome;
(d) The range of the confidence interval was used as a criterion to assess the imprecision as well as the crossing of the line of no effect. Some studies show CI ranges that cross the line of no effect
(e) Egger's regression test applied to pain intensity confirms the presence of publication bias (p-value < 0.04)
(f) The range of the confidence interval was used as a criterion to assess the imprecision as well as the crossing of the line of no effect. Only one study shows CI ranges that cross the line of no effect
(g) Egger's regression test applied to pain intensity confirms the presence of publication bias (p-value < 0.09)
(h) The range of the confidence interval was used as a criterion to assess the imprecision as well as the crossing of the line of no effect. No study shows results for MDS that cross the line of no effect
(i) Egger's regression test applied to pain intensity confirms the absence of publication bias (p-value > 0.78)

Publication bias

Figure 5 shows the funnel plots for PI (5A), ROM (5B) and disability (5C) for the RCTs. The figure shows a distribution for each outcome measure (SMD) extending from the mid-funnel to its top, indicating good or fair precision given by the homogeneous sample sizes. However, an asymmetric SMD distribution for PI, ROM and disability appears together with effect sizes outside the confidence interval (CI = 95%) or that come across the no effect line. Egger's regression test confirms publication bias only for PI (*p*-value = 0.04) and ROM (*p*-value = 0.09), which is an indicator of a small study effect, while for disability, publication bias was not significant (*p*-value = 0.78).

Table 3 depicts the GRADE quality of evidence for CT for PI decrease, ROM increase, and disability. Analgesic effectiveness for pooled (CT-TENS or CT-ITFC) and all RCTs has been assessed as important because of the effect size obtained (SMD > 0.7), although with very low or low certainty due to inconsistency (I^2 > 75%) and imprecision (large CI for SMD values across studies). Similarly, the effectiveness of analgesic CT is supported, with the best evidence in favour of CT-ITFC. Moreover, the ROM increase evidence has been valued as important and critical due to the large effect sizes (SMD > 0.8), especially for CT-ITFC (SMD = 2.28), which furnishes proof that it could be of higher quality if the inconsistency were less. Because of its low or moderate certainty, small effect sizes (SMD = 0.2), inconsistency, and impression, disability decrease have been rated as unimportant.

Discussion

CT is a physical therapy resource used for the MSP in conditions such as MTrPs, fibromyalgia, and OA. Its analgesic effects are due to simultaneously combining US with TENS, ITFC, or other low-frequency currents [21, 24, 35–38]. The efficacy of US, TENS, and ITFC for MSP management is supported by evidence when these treatments are applied individually [15, 26, 40, 41], which provides a framework for CT, whose analgesic effects are eventually greater with the combination of two interventions [16, 20, 21]. As a result, this SR was created to evaluate the effectiveness of CT for MSP management, which was accomplished through an MT-A of thirteen RCTs with PI as the primary outcome and ROM and disability as secondary outcomes.

The methodological quality of the RCTs was satisfactory, obtaining a high risk of bias for a single study [32], and a low risk of bias for all domains of the RoB.2 instrument in twelve RCTs [20–22, 33–39]. However, some biases due to deviations from planned interventions and missing data were identified as unclear but with low weighting [29]. This highlights the internal validity of the included studies [29, 30], and it is also consistent with the score rated by PEDro [28].

Twelve studies considered PI changes as the main outcome, six additionally considered changes in ROM, and five considered changes in disability through scales or functional tests. The qualitative synthesis shows analgesic benefits for CT together with increased ROM and decreased disability; however, the quantitative analysis only supported the analgesia and ROM increase, showing a greater effect size for both outcomes in favour of CT [42]. This upholds the CT's analgesia over interventions such as US and ischemic pressure in MTrPs [32, 36] or TENS or PIR in patients with OA of the hip or knee when the interventions are compared separately [22, 32–37]. Also, analgesic effects are observed when CT is added to interventions such as PhP, massages, balneotherapy, stretching, or strengthening exercises for the same conditions [23, 24, 38], promoting its use in a physical therapy plan. These findings suggest an enhanced analgesic effect due to the modulation or removal of pronociceptive mediators by US vasodilatation, as well as the release of endogenous opioid peptides, activation of downstream modulator systems (noradrenergic or serotonergic), or inhibition of nociceptive transmission via the gate control mechanism produced by electrotherapy [18, 19, 43]. Although CT shows favourable results, its greatest benefits are achieved with ITFC, which is probably due to its greater depth and more comfortable perception compared to TENS due to the lower electrical resistance of tissues [44, 45]. So, CT's advantages are its greater depth due to US frequencies (1 or 3 MHz) and the choice of different electrotherapy modalities (depth proportional to current frequency), demonstrating greater depth than TENS or ITFC alone [45].

CT favours tender points scanning, which responds more excitably to low current intensities due to the lowering of their threshold (hyperalgesia) [24, 33, 36]. This allows the clinician to identify a greater number of hyperresponsive points during treatment, as opposed to traditional electrotherapy applications, whose effects tend to be more local [33, 36]. Another analgesic mechanism involves painful point desensitisation, which occurs because of the constant depolarisation-repolarisation cycles induced by electric current [22, 24].

Despite the favourable analgesic efficacy, publication bias and the heterogeneity obtained for the metadata when analysing pain changes should be considered, which may be due to possible differences in sample sizes and the variability of results between studies [27]. This led researchers to rate the quality of the analgesic evidence as important due to the large effect size, but with low certainty [31].

Moreover, an increase in ROM was observed for participants with fibromyalgia, knee OA, and HNP after ending treatment with a large effect size [24, 34, 36, 39]. These trials report on CT at the muscular level (upper trapezius, femoral quadriceps, and paravertebral musculature) for improving neck and hip ROM [24, 34, 36, 39]. Protective muscle spasms accompanied by local ischemia are common in many painful conditions, accompanied by the sensitisation of free nerve endings and, therefore, a greater nociceptive load, a situation described as the 'muscle spasm-pain cycle' (MSPC) [46]. CT can interrupt MSPC by desensitising tender points and promoting muscle relaxation, decreasing both nociception sources [24, 33, 36]. Muscle relaxation is due to the thermal effects of the US, especially for duty cycles equal to or greater than 50%, as applied in the MTrPs and hip OA studies [24, 34, 36]. As a deep thermotherapy, US induces muscle relaxation by increasing viscoelasticity, activating the Golgi tendon organ, and inhibiting the neuromuscular spindle [47]. The above make CT a versatile technique for different conditions, combining the analgesic effects with those of deep thermotherapy [21, 22]. Although an improvement in ROM is observed, more relevant results are found for CT-ITFC, which probably occur due to the lower tissues' electrical resistance for medium-frequency currents (1,000–10,000 Hz) than low ones, which is key to reaching the muscle more easily [15, 44]. Likewise, publication bias and heterogeneity must be considered, which could lead to underestimating or overestimating the results. They were considered to determine the degree of evidence quality, assessing it as critical or important due to the large effect size but low certainty [27, 31].

Regarding disability, no differences were observed between groups, with small effect sizes for CT [42]. Disability assessment is valuable because it translates functional

changes from treatment independent of the techniques, such as CT, which focuses more on analgesia [48]. It should be noted that functional improvements for this type of technique are generally indirect due to decreased pain and improved ROM [21, 22, 24]. A possible explanation for the less clear benefits may be that many studies used CT alone without the addition of interventions with greater functional impact [20–22, 32, 33, 36, 37, 39], such as, for example, therapeutic exercises [49, 50]. Then, CT in the absence of another more specialised therapeutic intervention might not be enough to achieve functional changes, so an application complemented with therapeutic exercises is suggested. Because of the small effect size, the quality of the evidence for disability decrease was rated as unimportant. Moreover, certainty was rated as moderate for CT-TENS due to the absence of heterogeneity and low publication bias, which provide enough information not to recommend it for disability reduction.

It is increasingly common for functional changes to be reported by the patients themselves (patient-reported outcomes measures, or PROMs). PROMs commonly consist of self-report instruments used in clinics, trials, and clinical registries that allow patients to report on their quality of life, daily functioning, symptoms, and other aspects of their health [51]. Examples of PROMs are the WOMAC index, SF-36, and FIQ, which were used by the RCTs in this review and are supported by their reliability (WOMAC ICC:0.84; SF-36 ICC:0.95; FIQ ICC:0.83) [52, 53]. However, one disadvantage of these and similar instruments is the presence of Hawthorne effects, a psychological response phenomenon that can modify behaviour and condition the responses of participants who are aware that they are being studied [54]. To minimise these sources of bias, there is the anonymity of the answers or hidden examination strategies (without the presence of the examiner), which can be reported in a study [54, 55].

Even though CT shows analgesic effectiveness, some discrepancies in its parameters are observed between studies (especially for US therapy). Likewise, it was possible to establish some dosage recommendations:

1. For CT-TENS: electrical current: sensory stimulation, frequency between 80 and 100 Hz, phase duration between 50 and 80 μs. US: 1 MHz, duty cycle between 20 and 50%, and a power density between 0.5 and 2.5 W/cm^2.

2. For CT-ITFC: electrical current: sensory stimulation, carrier frequency of 4,000 Hz, AMF of 100 Hz. US: 1 MHz, duty cycle between 20 and 50%, and power density between 0.5 and 2.5 W/cm^2.

The treatment times in the studies ranged from 5 to 10 min, with the most frequent number of sessions being between 10 and 12. In addition, it seems that the therapeutic benefits are better when CT is used with ITFC than TENS, which could be associated with greater depth and comfort with medium-frequency electrotherapy [15, 44]. Similarly, most of equipments allows CT applications to be configured with other electrical currents, such as Träbert, Diadynamic, or Faradic, achieving other therapeutic benefits because, due to their biophysical properties, they can induce greater or lesser degrees of electrochemical effects typical of galvanic currents, which ITFC and TENS cannot achieve that [56].

Finally, it is suggested for new trials to use the dosages recommended by the researchers due to the good analgesic results reported, and to consider new therapeutic applications with other electric currents.

Limitations for this SR

This SR was the first to evaluate the analgesic effectiveness of CT in MSP using the PRISMA method to assess and report the evidence. The researchers highlight the protocol registration in PROSPERO and the determination of the quality of the evidence according to GRADE. Moreover, the following limitations are recognised: (1) Although six databases were reviewed, only articles in English and Spanish were included, so articles in other languages cannot be ruled out considering that many of the RCTs were conducted in India, Thailand, Egypt, Poland, or Korea; (2) Despite the benefits observed in meta-analysis and reported by the studies, the heterogeneity obtained for PI and ROM can reduce the degree of CT recommendation; (3) The researchers acknowledged the existence of one other CT study but were unable to obtain it.

Conclusions

CT is a technique that combines US with electrotherapy, usually low- and medium-frequency currents, the most common being TENS and ITFC. Its practice is supported by the combination of the analgesic effects of electrotherapy and the thermal or mechanical effects of US, achieving greater therapeutic benefits and different depths than the same techniques separately. Furthermore, it is a technique that allows for both evaluation and treatment in the same session. Despite being available in many electrotherapy devices, it seems to be less well known than resources such as TENS and ITFC. This ignorance may be due to the lack of professional training and to the scarcity of scientific articles on the subject. This motivated the researchers to develop the first CT SR to assess the efficacy of this resource.

CT decreases pain and increases ROM in conditions such as fibromyalgia, MTrPs, and OA when applied alone or in combination with other treatments, showing greater effectiveness than TENS, ITFC, US, massage, or exercises. Although the quality of the evidence was assessed as important, the heterogeneity of the trials affected their degree of recommendation. Moreover, CT appears to improve functionality when applied in conjunction with other treatments, such as exercise, but not by itself; this is encouraging because the primary focus is analgesia, situating it as a complementary resource when it comes to improving the functionality.

Finally, this review shows the need to develop new CT clinical trials, combining it with other low-frequency currents, for MSP management considering that electrochemical effects can be exploited and that, combined with US, could be interesting. It is recommended to use the doses proposed in this review for clinical applications of CT-ITFC or CT-TENS.

Ethical approval

The conducted research is not related to either human or animal use.

Disclosure statement

No author has any financial interest or has received any financial benefit from this research.

Conflict of interests

The authors state no conflict of interest.

Funding

This study received no external funding.

References

[1] Cieza A, Causey K, Kamenov K, Hanson SW, Chatterji S, Vos T. Global estimates of the need for rehabilitation based on the Global Burden of Disease study 2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet. 2021;396(10267):2006–17; doi: 0.1016/S0140-6736(20)32340-0.

[2] Kennedy PC, Purtill H, O'Sullivan K. Musculoskeletal pain in primary care physiotherapy: associations with demographic and general health characteristics. Musculoskelet Sci Pract. 2018;35:61–66; doi: 10.1016/j.msksp.2018.03.001.

[3] Blyth FM, Briggs AM, Schneider CH, Hoy DG, March LM. The Global Burden of musculoskeletal pain-where to from here? Am J Public Health. 2019;109(1):35–40; doi: 10.2105/AJPH.2018.304747.

[4] Trulsson Schouenborg A, Rivano Fischer M, Bondesson E, Jöud A. Physiotherapist-led rehabilitation for patients with chronic musculoskeletal pain: interventions and promising long-term outcomes. BMC Musculoskelet Disord. 2021;22(1):910; doi: 10.1186/s12891-021-04780-x.

[5] Babatunde OO, Jordan JL, Van der Windt DA, Hill JC, Foster NE, Protheroe J. Effective treatment options for musculoskeletal pain in primary care: a systematic overview of current evidence. PLoS One. 2017;12(6):e0178621; doi: 10.1371/journal.pone.0178621.

[6] George SZ, Goode AP. Physical therapy and opioid use for musculoskeletal pain management: competitors or companions? Pain Rep. 2020;5(5):e827; doi: 10.1097/PR9.0000000000000827.

[7] Derry S, Conaghan P, Da Silva JAP, Wiffen PJ, Moore RA. Topical NSAIDs for chronic musculoskeletal pain in adults. Cochrane Database Syst Rev. 2016;4:CD007400; doi: 1002/14651858.CD007400.pub3.

[8] Arribas-Romano A, Fernández-Carnero J, Molina-Rueda F, Angulo-Diaz-Parreño S, Navarro-Santana MJ. Efficacy of physical therapy on nociceptive pain processing alterations in patients with chronic musculoskeletal pain: a systematic review and meta-analysis. Pain Med. 2020;21(10):2502–17; doi: 10.1093/pm/pnz366.

[9] Flynn DM. Chronic musculoskeletal pain: nonpharmacologic, noninvasive treatments. Am Fam Physician. 2020;102(8):465–77.

[10] Fredin K, Lorås H. Manual therapy, exercise therapy or combined treatment in the management of adult neck pain – a systematic review and meta-analysis. Musculoskelet Sci Pract. 2017;31:62–71; doi: 10.1016/j.msksp.2017.07.005.

[11] Geneen LJ, Moore RA, Clarke C, Martin D, Colvin LA, Smith BH. Physical activity and exercise for chronic pain in adults: an overview of Cochrane Reviews. Cochrane Database Syst Rev. 2017;4:CD011279; doi: 10.1002/14651858.CD011279.pub3.

[12] Noori SA, Rasheed A, Aiyer R, Jung B, Bansal N, Chang K-V, Ottestad E, Gulati A. Therapeutic ultrasound for pain management in chronic low back pain and chronic neck pain: a systematic review. Pain Med. 2020;21(7):1482–1493; doi: 10.1093/pm/pny287.

[13] Paley CA, Wittkopf PG, Jones G, Johnson MI. Does TENS reduce the intensity of acute and chronic pain? A comprehensive appraisal of the characteristics and outcomes of 169 reviews and 49 meta-analyses. Medicina. 2021;57(10):1060; doi: 10.3390/medicina57101060.

[14] Gibson W, Wand BM, Meads C, Catley MJ, O'Connell NE. Transcutaneous electrical nerve stimulation (TENS) for chronic pain – an overview of Cochrane Reviews. Cochrane Database Syst Rev. 2019;4:CD011890; doi: 10.1002/14651858.CD011890.pub3.

[15] Fuentes JP, Armijo Olivo S, Magee DJ, Gross DP. Effectiveness of interferential current therapy in the management of musculoskeletal pain: a systematic review and meta-analysis. Phys Ther. 2010;90(9):1219–38; doi: 10.2522/ptj.20090335.

[16] Cameron MH. Physical Agents in Rehabilitation. An Evidence-Based Approach to Practice. 6th ed. Philadelphia: Elsevier – Health Sciences Division; 2022.

[17] Watson T (ed.) Electrotherapy. Evidence-Based Practice. 12th ed. London: Churchill Livingstone; 2019.

[18] Vance CGT, Dailey DL, Chimenti RL, Van Gorp BJ, Crofford LJ, Sluka KA. Using TENS for pain control: update on the state of the evidence. Medicina. 2022;58(10):1332; doi: 10.3390/medicina58101332.

[19] Liebano RE, Rakel B, Vance CGT, Walsh DM, Sluka KA. An investigation of the development of analgesic tolerance to TENS in humans. Pain. 2011;152(2):335–42; doi: 10.1016/j.pain.2010.10.040.

[20] Almeida TF, Roizenblatt S, Benedito-Silva AA, Tufik S. The effect of combined therapy (ultrasound and interferential current) on pain and sleep in fibromyalgia. Pain. 2003;104(3):665–72; doi: 10.1016/S0304-3959(03)00139-8.

[21] Moretti FA, Marcondes FB, Provenza JR, Fukuda TY, de Vasconcelos RA, Roizenblatt S. Combined therapy (ultrasound and interferential current) in patients with fibromyalgia: once or twice in a week?: combined therapy in fibromyalgia. Physiother Res Int. 2012;17(3):142–49; doi: 10.1002/pri.525.

[22] Kim E-D, Won YH, Park S-H, Seo J-H, Kim D-S, Ko M-H, Kim G-W. Efficacy and safety of a stimulator using low-intensity pulsed ultrasound combined with transcutaneous electrical nerve stimulation in patients with painful knee osteoarthritis. Pain Res Manag. 2019;2019:7964897; doi: 10.1155/2019/7964897.

[23] Király M, Gömöri E, Kiss R, Nógrádi N, Nusser N, Hodosi K, Bender T. Effects of various types of ultrasound therapy in hip osteoarthritis – a double-blind, randomized, controlled, follow-up study. Physiother Theory Pract. 2022;38(12):1958–68; doi: 10.1080/09593985.2021.1895386.

[24] Takla MKN, Rezk-Allah SS. Immediate effects of simultaneous application of transcutaneous electrical nerve stimulation and ultrasound phonophoresis on active myofascial trigger points: a randomized controlled trial. Am J Phys Med Rehabil. 2018;97(5):332–38; doi: 10.1097/PHM.0000000000000876.

[25] Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, Shamseer L, Tetzlaff JM, Akl EA, Brennan SE, Chou R, Glanville J, Grimshaw JM, Hróbjartsson A, Lalu MM, Li T, Loder EW, Mayo-Wilson E, McDonald S, McGuinness LA, Stewart LA, Thomas J, Tricco AC, Welch VA, Whiting P, Moher D. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. Syst Rev. 2021;10(1):89; doi: 10.1186/s13643-021-01626-4.

[26] Johnson MI, Paley CA, Jones G, Mulvey MR, Wittkopf PG. Efficacy and safety of transcutaneous electrical nerve stimulation (TENS) for acute and chronic pain in adults: a systematic review and meta-analysis of 381 studies (the meta-TENS study). BMJ Open. 2022;12(2):e051073; doi: 10.1136/bmjopen-2021-051073.

[27] Higgins JPT, Thompson SG. Quantifying heterogeneity in a meta-analysis. Stat Med. 2002;21(11):1539–58; doi: 10.1002/sim.1186.

[28] Cashin AG, McAuley JH. Clinimetrics: physiotherapy evidence database (PEDro) scale. J Physiother. 2020; 66(1):59; doi: 10.1016/j.jphys.2019.08.005.
[29] Sterne JAC, Savović J, Page MJ, Elbers RG, Blencowe NS, Boutron I, Cates CJ, Cheng H-Y, Corbett MS, Eldridge SM, Emberson JR, Hernán MA, Hopewell S, Hróbjartsson A, Junqueira DR, Jüni P, Kirkham JJ, Lasserson T, Li T, McAleenan A, Reeves BC, Shepperd S, Shrier I, Stewart LA, Tilling K, White IR, Whiting PF, Higgins JPT. RoB 2: a revised tool for assessing risk of bias in randomised trials. BMJ. 2019;366:l4898; doi: 10.1136/bmj.l4898.
[30] McGuinness LA, Higgins JPT. Risk-of-bias VISualization (robvis): an R package and Shiny web app for visualizing risk-of-bias assessments. Res Synth Methods. 2021;12(1):55–61; doi: 10.1002/jrsm.1411.
[31] Guyatt GH, Oxman AD, Schünemann HJ, Tugwell P, Knottnerus A. GRADE guidelines: a new series of articles in the Journal of Clinical Epidemiology. J Clin Epidemiol. 2011;64(4):380–82; doi: 10.1016/j.jclinepi.2010.09.011.
[32] Lee JC, Lin DT, Hong C-Z. The effectiveness of simultaneous thermotherapy with ultrasound and electrotherapy with combined AC and DC current on the immediate pain relief of myofascial trigger points. J Musculoskelet Pain. 1997;5(1):81–90; doi: 10.1300/j094v05n01_06.
[33] Mukkannavar PB. Effect of combination therapy [tens & ultrasound] and ischemic compression in the treatment of active myofascial trigger points. J Excercise Sci Physiother. 2012;8(2):95; doi: 10.18376//2012/v8i2/67589
[34] Podczarska-Głowacka M, Łysak A. Use of combined therapy (TENS+UD) and postisometric relaxation (PIR) of muscles in seniors with degenerative disease of the hip jointnt. J Pre-Clin Clin Res. 2016;10(2):95–9; doi: 10.5604/18982395.1227564
[35] Boonhong J, Suntornpiyapan P, Piriyajarukul A. Ultrasound combined transcutaneous electrical nerve stimulation (UltraTENS) versus phonophoresis of piroxicam (PhP) in symptomatic knee osteoarthritis: a randomized double-blind, controlled trial. J Back Musculoskelet Rehabil. 2018;31(3):507–13; doi: 10.3233/BMR-150492.
[36] Takla MKN. Low-frequency high-intensity versus medium-frequency low-intensity combined therapy in the management of active myofascial trigger points: a randomized controlled trial. Physiother Res Int. 2018;23(4): e1737; doi: 10.1002/pri.1737.
[37] Sangtong K, Chupinijrobkob C, Putthakumnerd W, Kuptniratsaikul V. Does adding transcutaneous electrical nerve stimulation to therapeutic ultrasound affect pain or function in people with osteoarthritis of the knee? A randomized controlled trial. Clin Rehabil. 2019;33(7): 1197–205; doi: 10.1177/0269215519838017.
[38] Usman Z, Maharaj SS, Kaka B. Effects of combination therapy and infrared radiation on pain, physical function, and quality of life in subjects with knee osteoarthritis: a randomized controlled study. Hong Kong Physiother J. 2019;39(2):133–42; doi: 10.1142/S1013702519500124.
[39] Ariel E, Levkovitz Y, Goor-Aryeh I, Motti R. The effects of TENS, interferential stimulation, and combined interferential stimulation and pulsed ultrasound on patients with disc herniation-induced radicular pain. J Back Musculoskelet Rehabil. 2022;35(2):363–71; doi: 10.3233/BMR-200302.
[40] Johnson MI, Jones G, Paley CA, Wittkopf PG. The clinical efficacy of transcutaneous electrical nerve stimulation (TENS) for acute and chronic pain: a protocol for a meta-analysis of randomised controlled trials (RCTs). BMJ Open. 2019;9(10):e029999; doi: 10.1136/bmjopen-2019-029999.
[41] Xia P, Wang X, Lin Q, Cheng K, Li X. Effectiveness of ultrasound therapy for myofascial pain syndrome: a systematic review and meta-analysis. J Pain Res. 2017; 10:545–555; doi: 10.2147/JPR.S13148.
[42] Dowdy A, Peltier C, Tincani M, Schneider WJ, Hantula DA, Travers JC. Meta-analyses and effect sizes in applied behavior analysis: a review and discussion. J Appl Behav Anal. 2021;54(4):1317–40; doi: 10.1002/jaba.862.
[43] Mendell LM. Constructing and deconstructing the gate theory of pain. Pain. 2014;155(2):210–216; doi: 10.1016/j.pain.2013.12.010.
[44] Rampazo ÉP, Liebano RE. Analgesic effects of interferential current therapy: a narrative review. Medicina. 2022; 58(1):141; doi: 10.3390/medicina58010141.
[45] Ariel E, Ratmansky M, Levkovitz Y, Goor-Aryeh I. Efficiency of tissue penetration by currents induced by 3 electrotherapeutic techniques: a comparative study using a novel deep-tissue measuring technique. Phys Ther. 2019;99(5):540–48; doi: 10.1093/ptj/pzz005.
[46] Skúladóttir H, Gunnarsdóttir TJ, Halldórsdóttir S, Sveinsdóttir H, Holden JE, Björnsdóttir A. Breaking the vicious circle: Experiences of people in chronic pain on the pain rehabilitation journey. Nurs Open. 2020;7(5):1412–23; doi: 10.1002/nop2.512
[47] Sluka KA, Baxter GD, Basford JR. Overview of other electrophysical and thermal agents. Mechanisms and management of pain for the physical therapist. Philadelphia: Wolters Kluwer/IASP Press; 2016: pp. 191–204.
[48] Roush SE, Sharby N. Disability reconsidered: the paradox of physical therapy. Phys Ther. 2011;91(12):1715–27; doi: 10.2522/ptj.20100389
[49] Bertozzi L, Gardenghi I, Turoni F, Villafañe JH, Capra F, Guccione AA, Pillastrini P. Effect of therapeutic exercise on pain and disability in the management of chronic nonspecific neck pain: systematic review and meta-analysis of randomized trials. Phys Ther. 2013;93(8): 1026–36; doi: 10.2522/ptj.20120412.
[50] Kuru Çolak T, Kavlak B, Aydoğdu O, Şahin E, Acar G, Demirbüken İ, Sarı Z, Çolak İ, Bulut G, Polat MG. The effects of therapeutic exercises on pain, muscle strength, functional capacity, balance and hemodynamic parameters in knee osteoarthritis patients: a randomized controlled study of supervised versus home exercises. Rheumatol Int. 2017;37(3):399–407; doi: 10.1007/s00296-016-3646-5.
[51] Kyte DG, Calvert M, van der Wees PJ, ten Hove R, Tolan S, Hill JC. An introduction to patient-reported outcome measures (PROMs) in physiotherapy. Physiotherapy. 2015;101(2):119–25; doi: 10.1016/j.physio.2014.11.003
[52] Salaffi F, Leardini G, Canesi B, Mannoni A, Fioravanti A, Caporali R, Lapadula G, Punzi L; GOnorthrosis and Quality Of Life Assessment (GOQOLA). Reliability and validity of the Western Ontario and McMaster Universities (WOMAC) Osteoarthritis Index in Italian patients with osteoarthritis of the knee. Osteoarthritis Cartilage. 2003; 11(8):551–60; doi: 10.1016/s1063-4584(03)00089-x.
[53] Wukich DK, Sambenedetto TL, Mota NM, Suder NC, Rosario BL. Correlation of SF-36 and SF-12 component scores in patients with diabetic foot disease. J Foot Ankle Surg. 2016;55(4):693–96; doi: 10.1053/j.jfas.2015.12.009.

[54] Berthelot J-M, Le Goff B, Maugars Y. The Hawthorne effect: stronger than the placebo effect? Joint Bone Spine. 2011;78(4):335–36; doi: 10.1016/j.jbspin.2011.06.001.
[55] Benedetti F, Carlino E, Piedimonte A. Increasing uncertainty in CNS clinical trials: the role of placebo, nocebo, and Hawthorne effects. Lancet Neurol. 2016;15(7):736–47; doi: 10.1016/s1474-4422(16)00066-1.
[56] Ortiz H, Cancino J, Goluboff N, Obando G, Jara M, Vera M. Effects of ascending and descending direct current on grip strength assessed through dynamometry and myofeedback: a randomized controlled trial. Physiother Quart. 2020;28(2):1–8; doi: 10.5114/pq.2020.92471.

Appendix 1. Search strategy (last updated June 5, 2024)

	Key words	PubMed	Scopus	WoS	CINAHL	Science Direct	PEDro	Total
S1	"Transcutaneous Electric Nerve Stimulation"	5,965	5,449	389	2,719	781		1184,133
S2	"Electric Stimulation Therapy"	22,457	19,462	372	16	252		681,919
S3	"Electric Stimulation"	140,369	127,173	4,200	12,447	13,077		297,266
S4	"Interferential currents"	49	394	53	31	577		1104
S5	S1 OR S2 OR S3 OR S4	145,183	131,717	4,599	14,975	14,214		310,688
S6	"Ultrasonic Therapy"	10,577	9,682	294	3,007	834		1151,266
S7	"Ultrasound therapy"	1,216	13,410	1,422	2,379	2,569		20,996
S8	S6 OR S7	11,219	15,686	1,679	3,175	3,243		35,002
S9	"Musculoskeletal Pain"	11,653	19,948	14,727	4,894	20,973		72,195
S10	"Musculoskeletal Diseases"	18,515	48,085	10,173	12,329	10,138		99,24
S11	"Myofascial Pain Syndromes"	2,199	3,156	331	1,739	2,871		340,965
S12	"Arthralgia"	17,513	75,973	7,719	5,142	47,599		153,946
S13	"Pain Management"	81,677	63,508	53,813	36,975	81,091		317,064
S14	S9 OR S10 OR S11 OR S12 OR S13	127,477	200,91	85,073	58,703	153,073		625,236
S15	S5 AND S8 AND S14	42	42	93	25	69	7	278

Search algorithm used for formal databases: („Transcutaneous Electric Nerve Stimulation" OR „Electric Stimulation Therapy" OR „Electric Stimulation" OR „Interferential currents") AND („Ultrasonic Therapy" OR „Ultrasound therapy") AND („Musculoskeletal Pain" OR „Musculoskeletal Diseases" OR „Myofascial Pain Syndromes" OR „Arthralgia" OR „Pain Management")