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Percutaneous electrical stimulation improves chronic knee pain and function. A Systematic Review and Meta-analyses

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ABSTRACT

Objectives. The aim of this systematic review and meta-analysis was to evaluate the effectiveness of the percutaneous electrical stimulation in the modulation of pain and its implication in the function of patients with a painful knee condition.

Methods. A search was conducted from database inception to September 2023 across PubMed, Web of Science and Scopus databases. Randomized controlled trials were included. Two reviewers performed independent data extraction and methodologic quality assessment of the studies. Study quality was assessed using the PEDro scale and the risk of bias was evaluated with the Cochrane Assessment tool.

Results. Eight studies were included. A significant statistical effect was found ($p< 0.001$) for reducing pain and improving function after treatment. Additionally, a significant statistical effect was presented for reducing pain ($p= 0.009$) and improving function ($p< 0.001$) after follow-up. The risk of bias was low.

Conclusion. This review showed a positive effect of applying the percutaneous electrical stimulation reducing pain and improving function in adults with a painful knee.

KEYWORDS: knee joint, pain, electrical stimulation therapy, systematic review

INTRODUCTION

Knee pain affects up to 25% of the adult population, and its prevalence has increased a 65% in the past 20 years, causing more than 4 million primary care visits annually. [1] This

condition carries a negative effect on the functionality [2] and the mental health, increasing the risk of developing psychological distress. [3]

The modulation of pain with the electrical current has been widely used in many painful conditions. [4] There are different application forms, including transcutaneous electrical nerve stimulation (TENS), neuromuscular electrical stimulation (NMES), interferential current (IFC), etc. Among the different forms of applying, in the last years, percutaneous electrical stimulation is one of the most clinically used. [4]

The percutaneous electrical stimulation consists of the application through a needle, of a biphasic continuous current with a high or low frequency and a specific pulse duration. [5,6] It has been applied in different tissues and different localization, e.g., periosteal, muscle, nerve. [7] These applications have as main effect the analgesia based on Melzack and Wall control gate theory, [8] bringing potential effects on the activation of inhibition descending pathways of pain. [9]

Percutaneous electrical stimulation has been demonstrated to be effective in the pain treatment of different locations as the low back. [10] The study of Nascimento et al. [10] reported that this treatment can improve pain modulation, reducing motor-evoked potential and increasing intracortical inhibition, suggesting positive effects in patients with central sensitization. [9]

However, to date, no systematic review has studied the effects of the percutaneous application in the modulation of chronic knee pain. For this reason, the aim of this systematic review and meta-analysis was to evaluate the effectiveness of the percutaneous electrical stimulation in the modulation of pain and its implication in the function of patients with a painful knee condition.

MATERIAL AND METHODS

Search strategies and selection criteria

This systematic review and meta-analysis adhere to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement. [11] The international Prospective Register of Systematic Reviews (PROSPERO) registration number is CRD42022380071.

An electronic search was conducted using the following electronic databases: PubMed, Web of Science, and Scopus database of randomized controlled trials. Relevant publications were included from inception until September 2023. To define the research question, the PICOS [12] (Participants, Interventions, Comparisons, Outcome and Study design) model was applied.

The search on the different databases was based on: (“Percutaneous electrical stimulation” OR “Intramuscular electrical stimulation” OR “Electrical dry needling” OR “Percutaneous electrical nerve stimulation” OR “Percutaneous TENS” OR “Peripheral nerve stimulation” OR “Percutaneous electric nerve stimulation” OR “Percutaneous electrical nerve stimulation” OR “Percutaneous neuromodulation therapy” OR “Neuromodulation therapy, percutaneous” OR “Percutaneous neuromodulation therapies” OR “Therapy, percutaneous neuromodulation” OR “Percutaneous electrical neuromodulation” OR “Electrical neuromodulation,

percutaneous" OR "Electrical neuromodulations, percutaneous" OR "Neuromodulation, percutaneous electrical" OR "Neuromodulations, percutaneous electrical" OR "Percutaneous electrical neuromodulations") AND ("Knee") . This strategy was modified and adapted for each database.

The inclusion criteria of the article were: (1) Adult's patients with painful knee; (2) percutaneous electrical stimulation interventions focused on knee pain and knee function; (3) the percutaneous electrical stimulation intervention had to be compared to a control intervention; (4) only randomized clinical trials were included. Full texts in English were included.

The participants in selected studies had to be symptomatic adults (≥ 18 years old) with chronic knee pain that was diagnosed as painful knee, including different etiologies.

The trials will be included if they used percutaneous electrical stimulation as a continuous bi-phasic current. The interventions could be compared to any type of stimulation, placebos, or other techniques or a combination of them.

The clinical trials were selected by two reviewers who independently applied the inclusion criteria, initially identified from the title and abstract. the full texts of each trial were also independently evaluated. When there was a disagreement between the reviewers, a third author intervened to resolve the inclusion decision.

Reviewers were not blinded to information relating to the articles reviewed. A standardized formulary was used to extract the data concerning participants, types of intervention, follow-up, clinical outcome measures, and findings. The formulary was elaborated according to the directions of the Cochrane Handbook for Systematic Reviews of Interventions-Version 5.1.0. [13]

The PEDro scale was used independently by the authors to assess the methodological quality of the included studies. The PEDRo scale has proven to be reliable and valid for rating the quality of randomized controlled trials. [14] When available, the PEDro score for each trial was compared with the PEDro database. Another author was consulted in the case of persisting disagreement. Articles were not excluded based on their quality. The PEDro score assesses with 10 items the internal validity and presentation of the statistical analysis of the studies. The presence of indicators of the quality of the evidence is presented as 1 point and not 0 points. A trial was considered of low quality when PEDro score was less than 5 points. [14]

The risk of bias was assessed using the Cochrane Risk of Bias Tool for Randomized Controlled Trials method. [13] It consists of seven elements with six subscales (selection bias, performance bias, detection bias, attrition bias, reporting bias and other bias). It is considered that a study is of high quality when there is low risk for each domain. Fair quality when one criterion does not meet (i.e., high risk of bias for one domain) or two criteria are unclear, and there is no known important limitation that could invalidate the results. Poor quality, when one criterion is not meet or two criteria are unclear, and there are important limitations that could invalidate the results; and when two or more criteria are listed as high or unclear risk of bias.

Data analysis

Review Manager Software (RevMan version 5.1, updated March 2011) was used to pool the results of the studies and perform a meta-analysis. We contacted trial authors if it was possible when data were insufficient for meta-analyses purposes (e.g., no means provided, no standard deviation provided). Ultimately, only those variables for which data were available were included in the meta-analysis. Variables for which the necessary data could not be obtained were ex-cluded from the analysis.When p-values

or 95% confidence intervals were given and standard deviations were missing, these were calculated via the embedded Review Manager calculator. We used I_2 to examine statistical heterogeneity, where the percentages quantified the magnitude of heterogeneity: 25% = low, 50% = medium, and 75% = high heterogeneity. [15] Using this scale, if I_2 was higher than 50%, a random-effects model was used. [15] Forest plots were generated to illustrate the overall effect of interventions.

RESULTS

We identified 351 studies through database searching. After removing duplicates and screening titles and abstracts of all remaining unique articles, 8 were selected. Eight of them were included after the inclusion criteria were checked [16-23]. Five studies analyzed the effects of the periosteal electrical dry needling, [16,19,20,22,23] two studies analyzed the effects of electrical intramuscular stimulation, [18, 21] one study [17] analyzed the effect of ultrasound-guided percutaneous neuromodulation (Figure 1).

Please, insert figure 1

Data studies are detailed in Table 1. A total of 742 individuals with painful knees were recruited. The range of age was 37±9.6 to 71.5±5.6. All studies concerned chronic knee pain; however, the range of pain intensity was 8±3.3 to 10.6±3.4 when WOMAC Pain was used, 5.27±1.91 to 7.921±1.04 when VAS was applied and 56.4±14.56 to 56.9±18.88 when the Numeric rating scale was evaluated. The range of pain duration was 0.58±0.22 to 11.08±1.88 years.

Please, insert table 1

Quality assessment and Risk of Bias

The methodological quality of studies included in this review was assessed according to the PEDro (Physiotherapy Evidence Database) scale. [14] All studies [16-23] reached

the minimum score (6/10) to be considered good quality. The range was from 6/10 to 9/10. The worst quality criteria on which none of the studies reached a positive score was the blinding of physical therapists. The best criteria on which all studies obtained a positive score were in randomization of the sample, the initial comparability of the most important prognostic factors, the follow-up assessment and study point measures and measures of variability. (Table 2).

Please, insert table 2

When Cochrane Risk of Bias Assessment was applied, [13] three of eight studies presented good quality, [18,19,21] and five studies presented poor quality (figure 2). [16,17,20,22,23]

Please, insert figure 2

Table 3 shows the interventions and the results obtained.

Please, insert table 3

Five of the included studies performed PES by stimulating the periosteum with acupuncture needles, [16,19,20,22,23] a protocol of four to nine acupuncture needles was established at symptomatic sites of the knee concert, and two of the studies also included a booster session. Two of the included studies performed an intramuscular ESP procedure . [18, 21] Only one study evaluated direct nerve stimulation by inserting an acupuncture needle into the perineurium of the femoral nerve. [17]

All the studies carried out a 30-minute ESP, [16,18-23] except for the study by García Bermejo et al. [17] which directly stimulated the nerve with periods of 1.5 minutes. In addition, all included studies included pain and functionality as one of their variables. [16-23]

Significant improvements in favor of the PES intervention were found for both pain and functionality in five of the included studies. [16-18,20,23]

Meta-Analysis

Results obtained in pain and functionality have been analyzed across different clinical moments (post-treatment, follow-up).

Effects of percutaneous electrical stimulation on pain modulation

Results obtained in pain modulation have been analyzed as shown in Figure 3.

For after treatment moment, the pooled mean difference (MD) showed significant overall effect of percutaneous electrical stimulation when compared to sham control (MD = -0.47; 95% CI = -0.67, -0.26; $p < 0.00001$), or to other interventions (MD = -0.84; 95% CI = -1.29; -0.39; $p < 0.0003$). The pooled mean difference (MD) showed significant overall effect of the intervention when compared to control groups (MD = -0.68; 95% CI = -0.92, -0.43; $p < 0.00001$). Heterogeneity was medium ($I_2 = 58\%$).

Please, Insert Figure 3a

In a follow-up analysis, the pooled mean difference (MD) didn´t show a significant overall effect of percutaneous electrical stimulation when compared to sham control (MD = -0.22; 95% CI = -0.51, 0.06; $p = 0.12$). However, when percutaneous electrical stimulation was compared to other intervention, the pooled mean difference (MD) showed significant overall effect (MD = -1.22; 95% CI = -2.07; -0.38; $p < 0.00001$). The pooled mean difference (MD) showed significant overall effect of the intervention when compared to control groups (MD = -0.75; 95% CI = 1.25, -0.26; $p = 0.003$). Heterogeneity was high ($I^2 = 89\%$).

Please, Insert Figure 3b

Effects of percutaneous electrical stimulation on functionality

Results obtained in functionality have been analyzed as shown in Figure 4.

When the functionality was analyzed after treatment, the mean difference (MD) showed a significant overall effect of percutaneous electrical stimulation when compared to sham controls (MD = -0.24; 95% CI = -0.46, -0.03; p = 0.03), and to other intervention (MD = -0.65; 95% CI = -0.89, -0.42; p < 0.00001). The mean difference (MD) of the percutaneous electrical stimulation compared to control groups showed significant overall effect (MD = -0.86; 95% CI = -1.29, -0.43; p = 0.0003). Analysis showed high heterogeneity (I^2 = 69%).

Please, Insert Figure 4a

When the functionality was analyzed in the follow-up, the mean difference (MD) didn´t show significant overall effect of percutaneous electrical stimulation when compared to sham controls (MD = -0.2; 95% CI = -0.42, 0.02; p = 0.08), but the mean difference (MD) showed significant overall effect of percutaneous electrical stimulation when compared to other interventions (MD = -1.48; 95% CI = -2.52, -0.45; p < 0.00001). The mean difference (MD) of percutaneous electrical stimulation compared to control groups showed significant overall effect (MD = -0.78; 95% CI = -1.30, -0.25; p = 0.004). Analysis showed medium heterogeneity (I^2 = 90%).

Please, Insert Figure 4b

DISCUSSION

The aim of this systematic review and meta-analysis was to evaluate the effectiveness of the percutaneous electrical stimulation in the modulation of pain and its implication in the function of patients with a painful knee condition. The results showed a positive

effect of the percutaneous electrical stimulation in painful knee conditions, improving pain and function.

The time spent in the treatment was longer than 20 minutes, in most of the included studies, the application time was 30 minutes, [16,18-23] only the study of Garcia-Bemejo et al. presented an application time of 1.5 minutes since the application of the current went directly to the perineurium of the nerve. [17] In a similar way to the study of Hamza et al. [24] that reported significant clinical results with applications of more than 15 minutes.

The needle placement was also heterogeneous. One study [17] applied the needle near the nerve, two studies [18, 21] placed the needles in muscle points, and the rest of the studies applied it in knee periosteal points. [16,19,20,22,23] Nevertheless, in the same line as our results, previous studies [25,26] have already compared that needle placement alters the efficacy of the treatment.

The analysis of the functionality has shown significant improvement after intervention and even showed significant results in the follow-up. [16,19,20,22,23] In this line, previous research has obtained similar results in functionality when electrical currents were applied with percutaneous applications for low back pain [27] and knee arthroplasty. [28]

Limitations

This review has some limitations to comments. Firstly, despite the positive results obtained, they should be interpreted with caution due to the differences in the electrical parameters (frequency, pulse width, duration) and the needle placement. Additionally, more studies that apply PENS are necessary to realize a good evaluation of its effects. Another limitation is that the current systematic review and meta-analysis focus

exclusively on studies categorized as percutaneous electrical stimulation, and other applications as electroacupuncture have not been included. Finally, the follow-up of the studies was carried out at different moments, and it could be confusing, it should be standardized in the future.

Conclusion

In conclusion, the use of percutaneous electrical stimulation was found a positive effect in reducing pain and improving short- and long-term function in adults with painful knee. Future studies are needed to clarify the treatment doses and patient profiles that may benefit most from this intervention.

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Figure 1. Flowchart

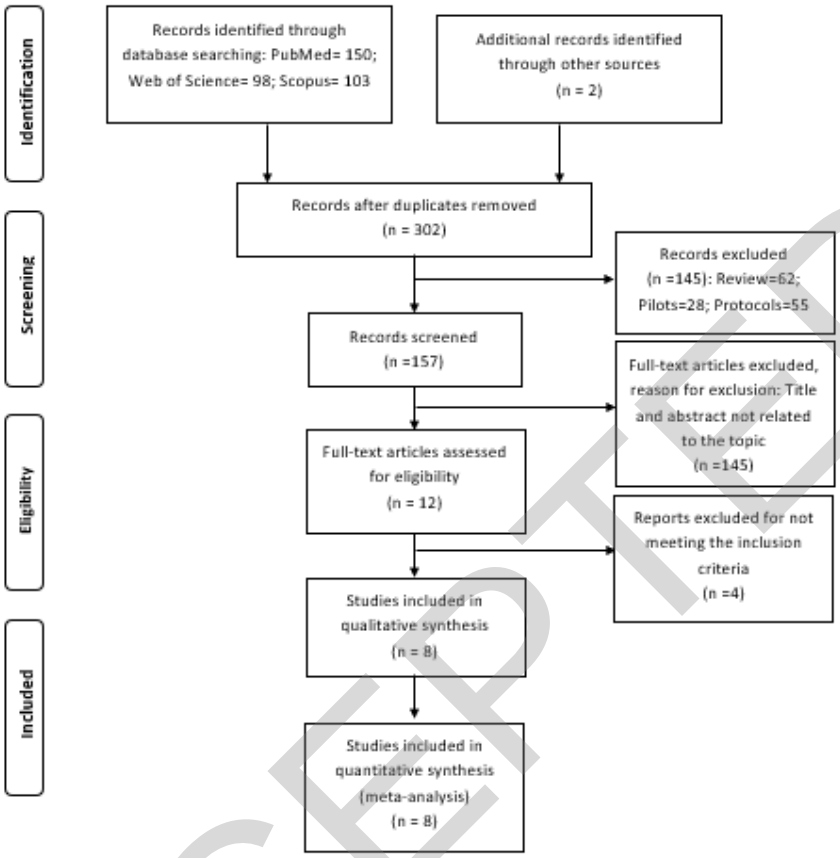
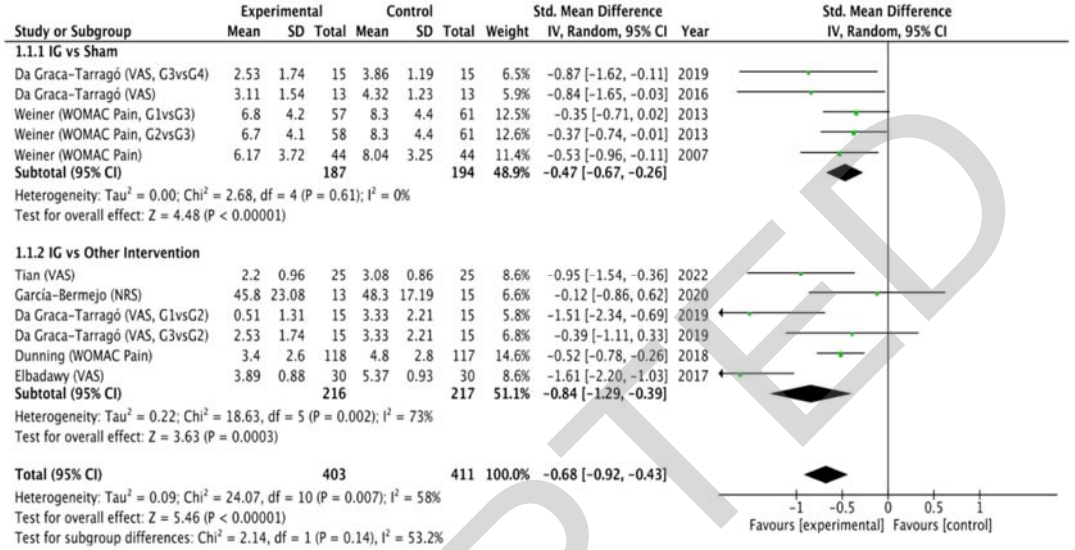


Figure 2. Risk of bias

Figure 3. Pain assessment

Figure 3a. Pain in post-treatment assessment

Figure 3b. Pain in follow-up assessment



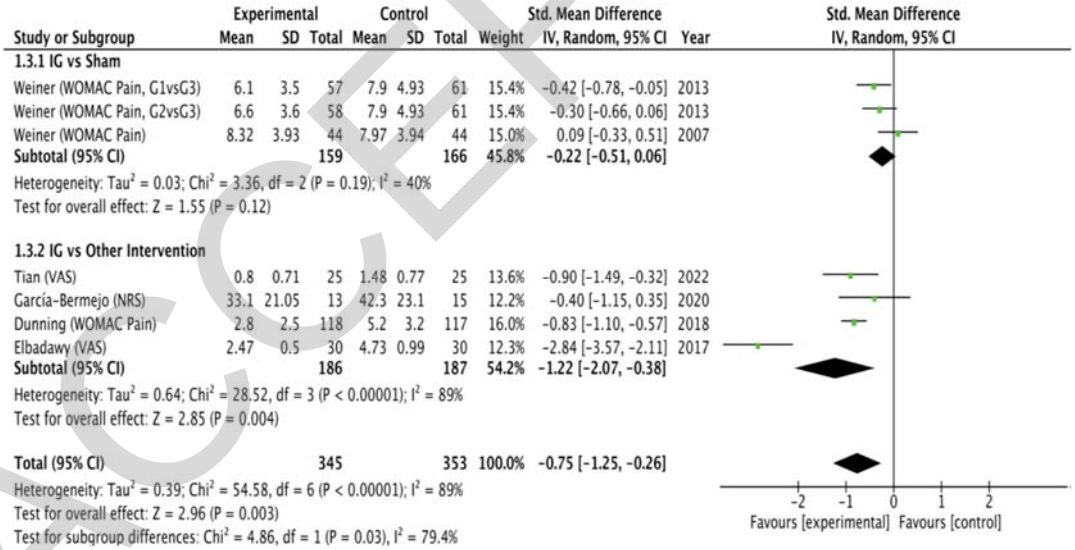
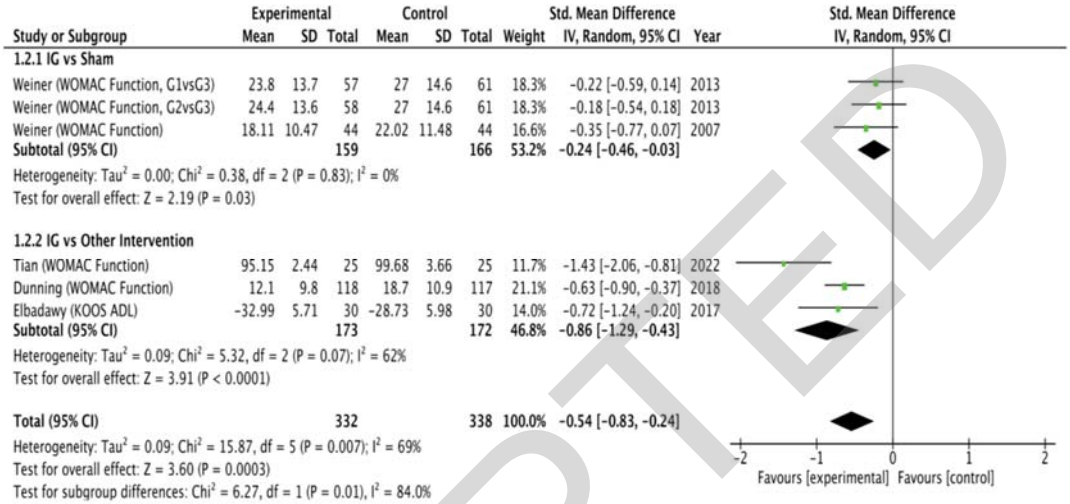


Figure 4. Functionality assessment

Figure 4a. Functionality in post-treatment assessment

Figure 4b. Functionality in follow-up assessment



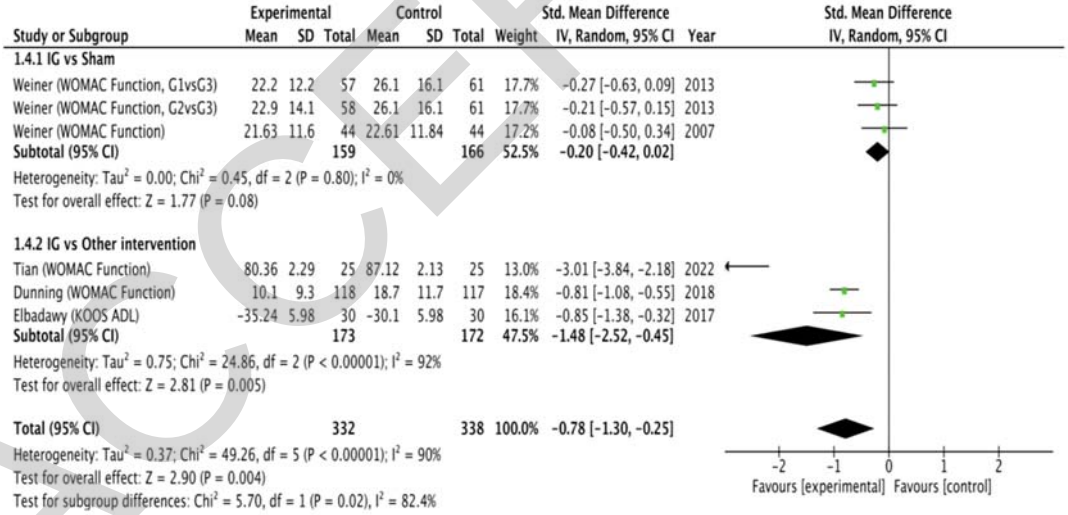


Table 1: Characteristics and quality of the included studies

Study	Knee injury	Design/Participants	Age (Mean± SD)	Sex n(%Men)	Pain duration (year)	Baseline Pain intensity	Quality assessment
Tian et al. (2022) [16]	Knee Osteotomy	RCT/N=50	G_1 = 64.76 ± 6.07 G_2 = 64.84 ± 8.84	G_1= 8 (32) G_2 = 6 (25)	NR	G_1= 7.921 ± 1.04 VAS G_2 = 7.52 ± 0.87 VAS	6/10
García-Bermejo et al. (2020) [17]	Unilateral anterior knee pain	RCT/n = 30	G_1 = 39.3 ± 9.5 G_2 = 37 ± 9.6	G_1= 5 (33.33) G_2 = 4 (26.66)	G_1= 0.6 ± 0.23 G_2 =0.58 ±0.22	G_1= 56.9 ± 18.88 NRS G_2 = 56.4 ± 14.56 NRS	6/10
Da Graca-Tarragó et al. (2019) [18]	Knee Osteoarthritis	RCT/n = 60	G_1 = 66 ± 9.08 G_2 = 64.14 ± 9.82 G_3 = 64.4 ± 6.02	G_1 = 0 (0) G_2 = 0 (0) G_3 = 0 (0) G_4 = 0 (0)	G_1 >0,5 G_2 >0,5 G_3 >0,5 G_4 >0,5	G_1 = 5.59 ± 2.63 VAS G_2 = 6.07 ± 2.42 VAS G_3 = 5.27 ±	9/10

			G_4 = 63.87 ± 7.07			1.91 VAS G_4 = 5.5 ± 2.77 VAS	
Dunning et al. (2018) [19]	Knee Osteoarthritis	RCT/n = 242	G_1 = 57.1 ± 13.2 G_2 = 58.1 ± 13.1	G_1 = 55 (45.45) G_2 = 56 (46.28)	G_1= 4.5 ± 4.7 G_2 = 4.6 ± 5.1	G_1= 8.7 ± 3.2 WP G_2 = 8 ± 3.3 WP	8/10
Elbadawy et al. (2017) [20]	Knee Osteoarthritis	RCT/n = 60	G_1= 59.43 ± 4.17 G_2 = 59.93 ± 4.35	G_1 = 10 (33.33) G_2 = 10 (33.33)	G_1 =11.08 ±1.88 G_2 =10.25 ±2.16	G_1= 7.71 ± 0.76 VAS G_2 = 7.49 ± 0.79 VAS	7/10
Da Graca-Tarragó et al. (2016) [21]	Knee Osteoarthritis	RCT/n = 26	G_1= 62.15 ± 7.44 G_2 = 66.85 ± 7.53	G_1 = 0 (0) G_2 = 0 (0)	G_1= 6.67 ± 1.59 G_2 = 6.49 ± 1.48	G_1 = 6.85 ± 0.38 VAS G_2 = 6.77 ± 0.43 VAS	9/10
Weiner et al. (2013) [22]	Knee Osteoarthritis	RCT/n = 190	G_1 = 67.1 ± 8.9 G_2 = 65.8 ± 8.7	G_1 = 55 (87.3) G_2 = 54 (84.4)	G_1 = 5.7 ± 6.4 G_2 = 6.2 ± 6.8	G_1 = 8.9 ± 3.3 WP G_2 = 9.8 ±	7/10

			G_3 = 66.8 ± 10.4	G_3 = 52 (82.5)	G_3 = 7.2 ± 8.3	3.8 WP G_3 = 10.6 ± 3.4 WP	
Weiner et al. (2007) [23]	Knee Osteoarthritis	RCT/n = 88	G_1 = 71.5 ± 5.6 G_2 = 71.4 ± 5.2	G_1= 18 (40.91) G_2= 22 (50)	G_1 = 7.6 ± 7.4 G_2 = 8.4 ± 7.4	G_1 = 9.3 ± 3.1 WP G_2 = 9 ± 3.4 WP	7/10

SD= Standard Deviation; RCT= Randomized Controlled Trial; G1-4= Group; n= Total sample

Table 2: Complementary table of PEDro Scale

Study	1	2	3	4	5	6	7	8	9	10	TOTAL
Tian et al. (2022) [16]	1	1	0	1	0	0	0	1	1	1	6/10
García-Bermejo et al. (2020) [17]	1	0	1	0	0	1	1	1	0	1	6/10
Da Graca-Tarragó et al. (2019) [18]	1	1	1	1	0	1	1	1	1	1	9/10
Dunning et al. (2018) [19]	1	1	1	0	0	1	1	1	1	1	8/10
Elbadawy et al. (2017) [20]	1	1	1	0	0	1	1	0	1	1	7/10
Da Graca-Tarragó et al. (2016) [21]	1	1	1	1	0	1	1	1	1	1	9/10
Weiner et al. (2013) [22]	1	1	1	0	0	0	1	1	1	1	7/10
Weiner et al. (2007) [23]	1	0	1	0	0	1	1	1	1	1	7/10

Table 3: Studies of the effectiveness of percutaneous electrical stimulation

Study	Intervention	Description of Experimental Intervention	Outcomes	Main Results
Tian et al. (2022) [16]	G_1= PES G_2= UC	Nine-knee point standardized (at least 3 of them: over the medial tibial condyle, the femoral epicondyle, and over the anterolateral crest of the tibial tuberosity); 30 min with acupuncture needle	Pain (VAS); Functionality (WOMAC Physical Function)	Significant differences between groups were found in favor of the experimental group in pain and functionality after intervention
García-Bermejo et al. (2020) [17]	G_1= PES G_2= Sham PES	Intervention of Femoral nerve with an acupuncture needle	Pain (NRS); Functionality (VISA-P; Kujala)	Significant differences between groups were found in favor of the experimental group in pain and functionality

				after intervention
Da Graca-Tarragó et al. (2019) [18]	G_1 = tDCS + PES G_2 = tDCS + Sham PES G_3 = Sham tDCS + PES G_4 =Sham tDCS + Sham PES	tDCS intervention of primary motor cortex: five sessions of 30 min PES intervention of vast medial, rectus femoris, vast lateral, anterior tibialis muscles and the pes anserine bursae. 30 min with acupuncture needle + 12 needles inserted along spinous process at L1-S2	Pain (VAS); Functionality (WOMAC Physical Function)	Significant differences between groups were found in favor of the G1 in pain and functionality after intervention
Dunning et al. (2018) [19]	G_1=PES + EX+ MT G_2=EX + MT	Nine-knee point standardized (at least 3 of	Pain (WOMAC Pain; NRS); Functionality	No differences were found in pain and functionality

		them: over the medial tibial condyle, the femoral epicondyle, and over the anterolateral crest of the tibial tuberosity) 20-30 min with acupuncture needle + manual therapy + exercise	(WOMAC Physical Function)	after intervention. Significant differences between groups were found in favor of the experimental group in pain and functionality in six months follow up assessment.
Elbadawy et al. (2017) [20]	G_1=PES+HEP G_2=TENS+HEP	PES intervention in medial and lateral femoral condyle; medial and lateral tibial condyle; head of fibula and 2 additional needles in the upper third of the tibial shaft; 30min; with	Pain (VAS); Functionality (KOOS)	Significant differences between groups were found in favor of the experimental group in pain and functionality after intervention and in six month follow up assessment

		acupuncture needle		
Da Graca-Tarragó et al. (2016) [21]	G_1=PES G_2=Sham PES	PES intervention of vast medial, rectus femoris, vast lateral, anterior tibialis muscles and the pes anserine bursae:, 30 min with acupuncture needle + 12 needles inserted along spinous process at L1-S2	Pain (VAS); Functionality (WOMAC Physical Function)	Significant differences between groups were found in favor of the experimental group in pain after intervention. No differences were found in functionality
Weiner et al. (2013) [22]	G_1 = PES + PES booster G_2 = PES + control PES booster G_3 = Control PES	PES intervention in periosteum of the medial and lateral femoral condyles, tibial flare and fibular head; 30 min + 5 booster	Pain (WOMAC Pain); Functionality (WOMAC Physical Function)	No differences were found in pain and function after intervention. Significant differences between groups were found in favor of the experimental

		session with the same parameters in G_1		group in functionality in nine months follow up assessment.
Weiner et al. (2007) [23]	G_1= PES G_2= Sham PES	PES intervention in periosteum of the medial and lateral femoral condyles, tibial flare and fibular head; 30 min + 5 booster session with the same parameters in G_1	Pain (WOMAC Pain); Functionality (WOMAC Physical Function)	Significant differences between groups were found in favor of the experimental group in pain and functionality after intervention but no differences between groups were found in three months follow up assessment

G_{1-4}= Group; PES= Percutaneous electrical Stimulation Therapy; UC= Usual Care; NRS= Numeric Rating Scale; VISA-P= Victorian Institute of Sport Assessment; tDCS= Transcranial Direct Current Stimulation; VAS= Visual Analogue Scale; WOMAC= Western Ontario and McMaster Universities Osteoarthritis Index; EX= Exercise; MT= Manual Therapy; HEP= Home Exercise Program; TENS= Transcutaneous Electrical Nerve Stimulation; KOOS= Knee injury and Osteoarthritis Outcome Score