Pain Medicine, 00(0), 2020, 1–17
doi: 10.1093/pm/pnaa342
Review Article

Effectiveness of Ultrasound-Guided Percutaneous Electrolysis for Musculoskeletal Pain: A Systematic Review and Meta-Analysis

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Funding sources: No funds were received for this study.

Conflicts of interest: The authors have no conflicts of interest to report.

Author contributions: All of the authors contributed to the study concept and design. Marcos J. Navarro-Santana, Guido F. Gómez-Chiguano, and Jose L. Arias-Buría conducted the literature review and performed the main statistical analysis. All of the authors contributed to the interpretation of the data. César Fernández-de-las-Peñas and Joshua A. Cleland wrote the first draft of the manuscript. All of the authors reviewed the intellectual content and read and approved the final version of the manuscript.

Abstract

Objective. To evaluate the effects of ultrasound-guided percutaneous electrolysis alone or as an adjunct to other interventions on pain and pain-related disability for musculoskeletal pain conditions. **Databases and Data Treatment**. Search of MEDLINE database, Allied and Complementary Medicine Database, EMBASE database, Cumulative Index to Nursing & Allied Health Literature database, EBSCO database, PubMed database, Physiotherapy Evidence Database, Cochrane Library database, Scopus database, and Web of Science database. Randomized controlled trials in which at least one group received ultrasound-guided percutaneous electrolysis for treatment of musculoskeletal pain. To be eligible, studies had to include humans and collect outcomes on pain intensity and pain-related disability for musculoskeletal pain syndromes. Data were extracted by two reviewers. The risk of bias was assessed by the Cochrane Guidelines and the quality of evidence was reported using the Grading of Recommendations Assessment, Development and Evaluation approach. Standardized mean differences (SMDs) and random effects were calculated. **Results**. Ten studies were included. The meta-analysis found that ultrasound-guided percutaneous electrolysis reduced the mean pain intensity by –2.06 (95% confidence interval [CI], –2.69 to –1.42) and the pain intensity as assessed with a visual analog scale or a numeric pain rating scale with a large size effect (SMD = –1.15; 95% CI, –1.48 to –0.81) and also improved pain-related disability with a large size effect (SMD = 0.95; 95% CI, 0.73–1.18) as compared with comparison groups. No differences in effect sizes were found among the short-term, midterm, and long-term follow-ups. The risk of bias was generally low, but the heterogeneity of the overall result downgraded the evidence level. Trials included heterogeneous musculoskeletal pain conditions and short-term, midterm, and long-term follow-ups. **Conclusion**. Moderate evidence suggests positive effects of ultrasound-guided percutaneous electrolysis for pain and pain-related disability in musculoskeletal pain conditions relative to a comparison group in the short term, midterm, and long term.

Key words: . Percutaneous Electrolysis; Musculoskeletal Pain; Meta-Analysis

Introduction

Musculoskeletal pain results in a large economic burden, a loss in quality of life, and difficulty during daily activities [1–3]. The incidence of musculoskeletal pain in Europe has been found to be 19% [4], whereas the prevalence ranges from 35% to 51% [5]. Musculoskeletal pain includes a myriad of conditions related to pain arising from bones (fractures), muscles (myofascial pain), ligaments (sprains), or tendons (tendinopathies). It can be primary musculoskeletal pain—i.e., related to a specific pathology, such as knee or hip osteoarthritis—or secondary musculoskeletal pain—i.e., not attributed to a specific identified pathology, such as shoulder or neck pain [6]. When the nerve tissue is affected, it is usually called "neuropathic pain."

Multimodal approaches are typically recommended for musculoskeletal pain. Several nonpharmacologic interventions, including exercise, pain education, and cognitive and psychological approaches, are used for the treatment of chronic musculoskeletal pain [7, 8]. The use of electrical current has also been proposed as a therapeutic strategy for the management of musculoskeletal pain; it was first introduced to the medical community by Wall and Sweet [9]. The most common form of electrotherapy to manage musculoskeletal pain is transcutaneous electrical nerve stimulation, which consists of the application of a pulsed electrical current across the surface of the skin to potentially activate underlying nerves [10]. The application of a pulsed electrical current throughout a needle is called percutaneous electrical nerve stimulation (PENS), which includes a range of applications depending on the frequency of the electrical current (low or high frequency) or the place where the needles are inserted (e.g., dermatome or myotome). Other authors use the term "electro-acupuncture" for the application of a pulsed electrical current with a needle applied over acupuncture points. All of these applications have a common denominator: the use of a pulsed electrical current. PENS uses solid filament needles, whereas other interventions, such as tendon tenotomies, use beveled, cutting-edge needles or an electric scalpel.

One emerging therapeutic strategy that also uses electrical current with a needle is percutaneous electrolysis [11]. Percutaneous electrolysis consists of the application of a galvanic continuous—not pulsed—electrical current through a solid filament needle in a targeted tissue such as the tendon or muscle [11]. Percutaneous electrolysis combines the mechanical effect resulting from the insertion of the solid needle and the biological effect derived from the application of the galvanic current [11]. The theoretical background for applying percutaneous electrolysis is the ability to induce a controlled inflammatory response by a nonthermal electrolytic reaction through a cathodic flow with the aim to facilitate phagocytosis and posterior regeneration of the affected tissue [11]. Due to the use of a continuous galvanic current with the goal of producing a nonthermal electrolytic reaction, percutaneous electrolysis should be ultrasound guided to apply the continuous galvanic current in the targeted tissue [11] (Figure 1). In fact, other invasive procedures, such as percutaneous needle tenotomy, should also be conducted using the direct visual guidance of ultrasound, as it creates small holes and slices in a tendon.

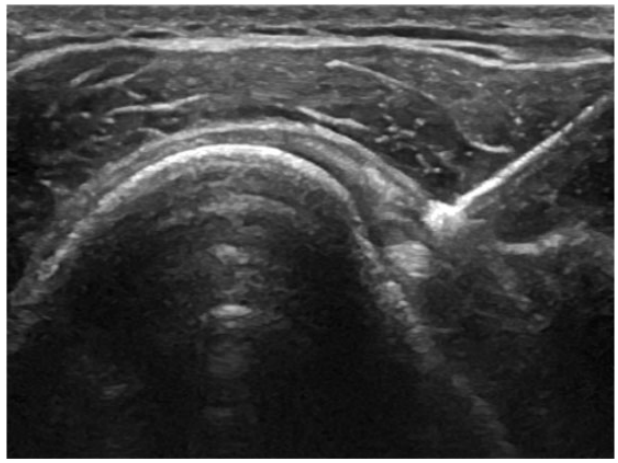

Figure 1. Ultrasound-guided application of percutaneous electrolysis on the supraspinatus tendon. The image shows how the needle reaches the area of the tendon and the nonthermal electrolytic reaction with the application of the continuous galvanic electrical current (white).

Several case studies have suggested that percutaneous electrolysis, combined with exercise, is effective for the management of different musculoskeletal disorders [12–15]. In the last few years, the number of clinical trials in this area has increased, but (to the best of our knowledge) there is not a meta-analysis on this topic in the literature.

Therefore, this systematic review and meta-analysis evaluates the effects of ultrasound-guided percutaneous electrolysis alone or as an adjunct with other interventions on pain intensity and pain-related disability in people with musculoskeletal pain.

Methods

This systematic review and meta-analysis adheres to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [16]. The international OPS Registry registration link is https://doi.org/10.17605/OSF.IO/W359E.

Systematic Literature Search

Electronic literature searches were conducted on the MEDLINE database, Allied and Complementary Medicine Database, EMBASE database, Cumulative Index to Nursing & Allied Health Literature database, EBSCO database, PubMed database, Physiotherapy Evidence Database (PEDro), Cochrane Library database, Scopus database, and Web of Science database from their inception to August 1, 2020. When the searched

databases allowed limits, searches were restricted to randomized clinical trials. We also manually screened the reference lists of the articles identified in the database searches and included these in the analysis. Bibliographical database search strategies were conducted with the assistance of an experienced health science librarian.

Population

The population for this study was composed of adults with a musculoskeletal pain condition, excluding neuropathic conditions, who were older than 18 years.

Intervention

The intervention consisted of any form of percutaneous electrolysis (i.e., the application of continuous galvanic current with a needle). Other interventions using pulsed current, such as PENS or electro-acupuncture, were excluded. For this aim, the search strategy included one of the following key words: *ultrasound-guided percutaneous electrolysis OR needle percutaneous electrolysis OR percutaneous needle electrolysis OR (percutaneous AND electrolysis) OR intratissue percutaneous electrolysis OR ultrasound-guided galvanic electrolysis*.

Comparator

Acceptable comparators were any type of placebo, sham, or no intervention. For this aim, the search strategy included one of these key words: *sham OR placebo OR control OR no intervention*. In addition, we also included a comparison of percutaneous electrolysis with another active intervention.

Outcomes

The primary outcome measure was *pain OR pain-related disability OR function*.

The search strategy for each database is available in Supplementary Data.

Selection Criteria

The systematic review included randomized clinical trials in which at least one group received any form of ultrasound-guided percutaneous electrolysis in a sample of patients with musculoskeletal pain. Patients with systemic medical underlying conditions causing pain, such as infection, neoplasms, metastasis, fracture, rheumatoid arthritis, or osteoporosis, were excluded. Additionally, patients with neuropathic pain or pain associated with neurological disorders were also excluded.

The specific inclusion criteria included 1) adult population (>18 years old) with musculoskeletal pain; 2) one group receiving any type of ultrasound-guided percutaneous electrolysis intervention; 3) an acceptable comparator with a sham, placebo, or control or another active intervention; and 4) pain intensity (e.g., as measured with a visual analog scale [VAS] or a numeric pain rating scale [NPRS]) or pain-related disability (e.g., as assessed with a specific disease questionnaire) as a primary outcome of the study. We excluded clinical trials, including 1) studies that analyzed pain related to neurological disorders; 2) retrospective clinical studies; and 3) studies that were not published as journal articles.

Screening, Selection Process, and Data Extraction

Articles identified from the different databases were independently reviewed by two authors. First, the duplicates were removed. Second, the titles and abstracts of the articles were screened for potential eligibility. Third, a full-text read of potentially eligible studies was conducted. The authors were required to reach a consensus on the included trials. In the case of discrepancy between both reviewers, a third author participated in the process to reach a consensus and to decide whether the study should be included.

Data from each trial were extracted independently by two authors using a standardized form. The data analyzed included the study design, sample size, population, diagnosis, interventions, outcomes, and follow-up periods. Both authors had to reach a consensus on each item on the data extraction form. If disagreement occurred, a third author made the final determination.

Assessment of Methodological Quality and Risk of Bias

Risk of bias and the methodological quality of the included trials were independently assessed by two researchers using the Cochrane Risk of Bias (RoB) assessment tool [17] and the PEDro scale [18], respectively.

The RoB tool includes the following types of bias: selection bias (randomization sequence generation, allocation concealment); performance bias (blinding participants, blinding therapists); detection bias (blinding outcome assessor); attrition bias (incomplete outcome data); reporting bias (source of funding bias or selective outcome reporting); and other bias (sample size) [17]. Each item was classified as low risk, high risk, or unclear according to the Cochrane Collaboration tool [17].

The PEDro scale assessed the following items: random allocation, concealed allocation, between-group similarity at baseline, participant blinding, therapist blinding, assessor blinding, dropout rate, intention-to-treat statistical analysis, between-group statistical comparison, and point measures and variability data [18]. A PEDro score of 6 of 10 points is the cutoff point for determining the high or low quality of a trial.

Quality of Evidence

To evaluate the quality of the evidence for percutaneous electrolysis, we used the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach [19]. The quality of evidence was classified as high, moderate, low, or very low based on the presence

of study limitations (RoB), indirectness of evidence, inconsistency of results or unexplained heterogeneity, imprecision of results, and high probability of publication bias [20]. The quality of evidence was classified as high when all items were negative; moderate when one item included serious risk; low when two to three items showed serious risk or one to two items showed very serious risk; or very low when all items had a serious risk or more than two items showed a very serious risk. This evaluation was independently performed by two authors, with a third author available if the two authors could not reach a consensus.

Data Synthesis and Analysis

The meta-analysis was conducted using Review Manager statistical software (RevMan version 5.3). Data synthesis was categorized by groups according to the follow-up period as short-term (less than 1 month), midterm (1–3 months), and long-term (3–6 months) if the data were available.

We extracted the sample size, means, and standard deviations for each variable. When the trial reported only standard errors, these were converted to standard deviations. When necessary, the mean scores and standard deviations were estimated from graphs. Also, if the study reported a nonparametric value (median and interquartile range), using the method described by Wan et al. [21] and Luo et al. [22], the results were converted to the mean [22] and standard deviation [21].

For the outcome of pain intensity—using either an NPRS or a VAS—we calculated the mean difference (MD) between the percutaneous electrolysis group and the comparison group and converted this to the standardized mean difference (SMD). For pain-related disability, we included any outcome reporting self-perception of function or disability and due to the heterogeneity of the variety of the included outcomes, we decided to use only the SMD for the between-group comparison.

The between-group MDs of the trials were converted to the SMD with a 95% confidence interval (CI). A random-effects model was used to determine the overall effect size (SMD). An effect size (SMD) of 0.8 or greater was considered large, between 0.5 to 0.8 was considered moderate, and between 0.2 to 0.5 was considered small. In general, P values less than 0.05 were considered statistically significant. The overall effect sizes and calculations of the effect size on pain intensity and pain-related disability were obtained for the short term (0–1 months), for the midterm (1–3 months), and for the long term (3–6 months).

The heterogeneity of the studies was assessed using the I^2 statistic. The Cochrane Group has established the following interpretation of the I^2 statistic: 0–40% may not be relevant or important heterogeneity, 30–60% suggests moderate heterogeneity, 50–90% represents substantial heterogeneity, and 75–100% represents considerable heterogeneity [23].

Results

Study Selection

The electronic searches identified 126 potential studies for review. After removing duplicates, 73 studies remained. Fifty-five (n=55) were excluded because study protocols were being reviewed (Supplementary Data) or based on examination of their titles or abstracts, leaving 18 articles for further full-text analysis. Another eight were excluded because congress communication had occurred [24–27], the study included an inadequate comparator group or it was not a randomized clinical trial [13, 28, 29], or the study was a retrospective study [30]. Finally, a total of 10 trials [31–40] were included in the qualitative and quantitative analyses (Figure 2).

Study Characteristics

The characteristics of the participants of the included studies are listed in Table 1. The musculoskeletal conditions were heterogeneous, including nonspecific shoulder pain [32, 33, 36, 40], patellar tendinopathy [31], groin pain [37], plantar heel pain [34], whiplash-associated pain [35], temporomandibular pain [38], and lateral epicondylalgia [39]. All trials applied percutaneous electrolysis, but there was higher diversity in terms of the number or frequency of sessions, the intensity of the electrical current, and the type of comparator. Supplementary Data summarizes the percutaneous electrolysis parameters applied in each trial. Seven studies combined percutaneous electrolysis with an exercise program [31–34, 37, 39, 40], whereas only three trials analyzed the isolated effects of percutaneous electrolysis [35,36,38] (Table 2).

Methodological Quality

The methodological quality scores ranged from 5 to 9 (mean, 6.8; SD = 1.2) out of a maximum of 10 points. Eight studies (80%) were considered to be of high methodological quality (≥6 points). The most frequent biases were blinding of the therapists, followed by allocation concealment and assessor blinding. Table 3 lists the details of the PEDro scale.

Risk of Bias

The details of the risk-of-bias assessment of the included trials are shown in Figure 3. Only one trial was able to blind therapists [34], and six had a substantial risk of bias in the item of blinding participants. In general, the risk of bias of the trials included in this meta-analysis was low, except for the blinding of the participant or therapist.

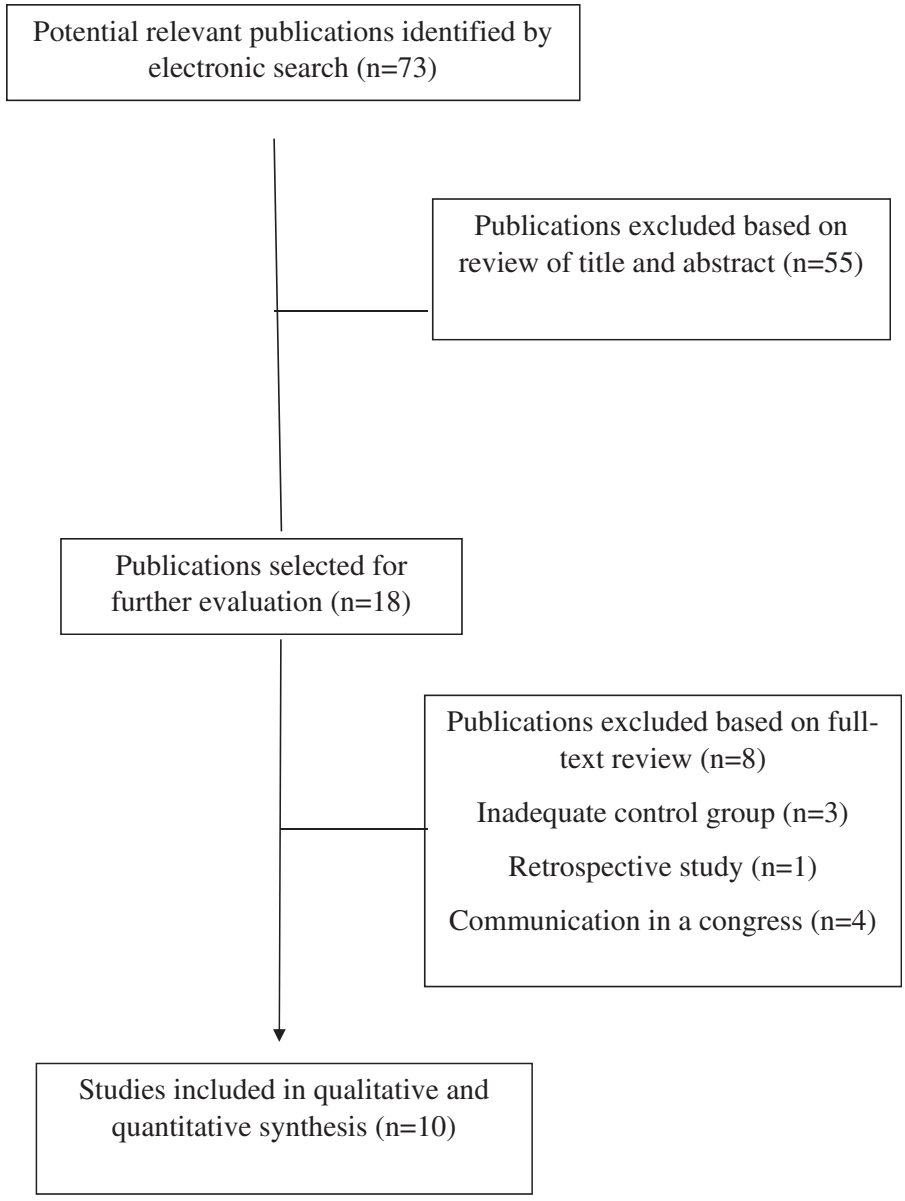

Figure 2. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram.

Effects of Percutaneous Electrolysis on Pain

The overall effect of percutaneous electrolysis vs a comparison group showed a statistically significant ($P<0.001$) effect for reducing pain (MD = –2.06; 95% CI, –2.69 to –1.42; Figure 4) with a large effect of size (SMD = –1.15; 95% CI, –1.48 to –0.81; n=838; $Z=6.67$; $P<0.001$; Figure 5) but with considerable heterogeneity ($I^2=79\%$) between the studies. The results were significant at follow-up each time: the mean reduction of pain (MD) was –1.94 (95% CI, –3.13 to –0.76; n=408; $Z=3.21$; $P=0.001$) in the short term; –2.09 (95% CI, –2.90 to –1.29; n=251; $Z=5.09$; $P<0.001$) in the midterm; and –2.28 (95% CI, –3.27 to –1.30; n=179; $Z=4.54$; $P<0.001$) in the long term, but always with considerable heterogeneity between studies ($I^2>75\%$). All effect sizes were also large at all follow-ups (Figure 5). Table 2 summarizes the main results of each of the included trials.

Effects of Percutaneous Electrolysis on Pain-Related Disability

The overall effect of percutaneous electrolysis vs a comparative group showed a statistically significant ($P<0.001$) large effect size (SMD = 0.95; 95% CI, 0.73–1.18; n=706; $Z=8$–46; $P<0.001$) on pain-related disability with a moderate heterogeneity ($I^2=45\%$) between the trials (Figure 6). Again, significant effect sizes were observed at each follow-up period. In the short term, the effect size was moderate (SMD = 0.76; 95% CI, 0.44–1.07; n=380; $Z=4.71$; $P<0.001$) with moderate heterogeneity ($I^2=50\%$). In the midterm (SMD = 1.21; 95%

Table 1. Participant characteristics of the included trials

Type of Pain	Group	Sample Size	Gender, Male (Female)	Age, Years	Pain Duration
Shoulder Pain					
Arias-Buría et al. [32]	G1	17	4 (13)	58±7	11.2±2.7 months
	G2	19	5 (14)	57±6	10.6±2.6 months
Moreno [36]	G1	10	NR	39.6±3.7	>3 months
	G2	10	NR	40.4±3.2	>3 months
	G3	10	NR	39.9±4.15	>3 months
	G4	10	NR	39.8±4.65	>3 months
de Miguel Valtierra et al. [33]	G1	25	11 (14)	54.9±13.7	12.6±14.4 months
	G2	25	12 (13)	55.3±11.1	11.2±10.6 months
Rodríguez-Huguet et al. [40]	G1	18	16 (2)	39.2±11.35	NR
	G2	18	11 (7)	40.9±8.4	NR
Lateral Elbow Pain					
Rodríguez-Huguet et al. [39]	G1	16	10 (6)	40.45±15.5	NR
	G2	16	10 (6)	35.9±12.1	NR
Patellar Tendinopathy					
Abat et al. [31]	G1	32	27 (5)	31.2±6.5	28.8±32.4 months
	G2	32	24 (8)	30.5±5.9	29.5±31.5 months
Groin Pain					
Moreno et al. [37]	G1	11	11 (0)	26.9±4.5	0–4 weeks: 5 4–10 weeks: 4 10–26 weeks: 2 >26 weeks: 0
	G2	13	13 (0)	25.2±4.9	0–4 weeks: 6 4–10 weeks: 3 10–26 weeks: 3 >26 weeks: 1
Whiplash-Associated Pain					
García-Naranjo et al. [35]	G1	50	20 (30)	35.3±8.1	5.6±1.6 days
	G2	50	16 (34)	40.9±9.2	6.1±1.2 days
Plantar Heel Pain					
Fernández-Rodríguez et al. [34]	G1	38	15 (23)	45.1±11.4	>3 months
	G2	29	10 (19)	46.6±11.1	>3 months
Temporomandibular Pain					
Lopez-Martos et al. [38]	G1	20	5 (15)	38.5 (18–57), IQR	>6 months
	G2	20	2 (18)	36 (19–58), IQR	>6 months
	G3	20	1 (19)	42 (25–62), IQR	>6 months

NR = not reported; IQR = interquartile range.

CI, 0.89–1.52; n=183; Z=7.41; P<0.001) and the long term (SMD = 1.20; 95% CI, 0.84–1.56; n=143; Z=6.53; P<0.001), the effect sizes were large, with no heterogeneity between the trials (I^2=0%). Table 2 summarizes the main results of each of the included trials.

Quality of Evidence (GRADE)

Table 4 lists the details of the GRADE assessment, showing risk of bias, inconsistency of the results, indirectness of evidence, imprecision of results, and high probability of publication bias. The serious inconsistency of the results (heterogeneity) and the series imprecision was downgraded to a moderate level of evidence of the overall effect of ultrasound-guided percutaneous electrolysis for pain and pain-related disability.

Adverse Events of Percutaneous Electrolysis

The most common adverse effect reported was postelectrolysis soreness. Arias-Buría et al. [32] reported that 35% of patients receiving percutaneous electrolysis experienced muscle soreness after the first two interventions, whereas de Miguel Valtierra et al. [33] observed this event in 24% of patients. Postelectrolysis soreness disappeared 24–36 hours after the procedure without treatment [32, 33]. Lopez-Martos et al. [38] reported that one patient presented a self-limiting hematoma. Moreno et al. [37] reported that patients experienced a slight increase in pain intensity the following 12 hours after percutaneous electrolysis intervention, but no adverse events were reported. No adverse events were observed in the studies conducted by Abat et al. [31] and Fernández-Rodríguez et al. [34]. Finally, the remaining four studies [35, 36, 39, 40] did not provide data about adverse events.

Discussion

The objective of this meta-analysis was to determine the effects of ultrasound-guided percutaneous electrolysis on the management of musculoskeletal pain syndromes. The results found moderate-quality evidence that percutaneous electrolysis has a large effect on reducing pain and

Table 2. Effects of percutaneous electrolysis on pain and pain-related disability for musculoskeletal pain conditions

Study	Intervention(s)	Sample Size	Intervention Duration, Sessions or Weeks	Comparison and Outcome Measure	Between-Group Differences (95% CI) [SMD]*
Shoulder Pain					
Arias-Buría et al. [32]	G1: PE and eccentric exercise	17	1 × 4 weeks	Mean pain intensity (0–10)	2 weeks: –1.5 (0.7, 2.2) [–1.2]
	G2: Eccentric exercise	19	1 × 4 weeks	G1 vs G2	5 weeks: –1.70 (–2.80, –0.6) [–0.96]
				G1 vs G2	
				Worst pain intensity (0–10)	2 weeks: –0.3 (2.0, –1.4) [–0.11]
				G1 vs G2	5 weeks: –2.3 (–1.2, 3.3) [–1.34]
				G1 vs G2	
				Worst pain intensity (0–10)	2 weeks: –0.2 (–1.4, 1.1) [–0.10]
				G1 vs G2	5 weeks: –1.1 (–1.5, 0.3) [–0.51]
				G1 vs G2	
				DASH (0–100)	2 weeks: 12.2 (5.6, 18.9) [1.18]
				G1 vs G2	5 weeks: 9.5 (1.9, 17.2) [0.80]
				G1 vs G2	
Moreno [36]	G1: Control group	10	1 × 3 weeks	Pain intensity (VAS)	3 weeks: –3.80 (–4.28, –3.32) [–6.64]
	G2: PE at TrP	10		G2 vs G1	3 weeks: –2.90 (–3.40, –2.40) [–4.85]
	G3: PE at tendon	10		G3 vs G1	3 weeks: –1.75 (–2.65, –0.85) [–1.64]
	G4: PE at TrP and tendon	10		G4 vs G1	
de Miguel Valtierra et al. [33]	G1: Manual therapy, exercise, and PE	25	Manual therapy: 1 × 4 weeks	Mean pain intensity (NPRS)	6 weeks: –1.4 (–2.4, –0.4) [–0.65]
	G2: Manual therapy and exercise	25	Exercise: Twice per day × 5	G1 vs G2	17 weeks: –2.6 (–4.0, –1.5) [–0.91]
			PE: 1 × 5 weeks	G1 vs G2	29 weeks: –2.7 (–4.2, –1.2) [–1.03]
				G1 vs G2	
				Least pain intensity (NPRS)	6 weeks: –1.8 (–2.6, –1.0) [–0.79]
				G1 vs G2	17 weeks: –3.0 (–4.2, –1.8) [–1.15]
				G1 vs G2	29 weeks: –2.8 (–3.6, –2.0) [–1.05]
				G1 vs G2	
				Worst pain intensity (NPRS)	6 weeks: –1.3 (–2.0, –0.6) [–0.56]
				G1 vs G2	17 weeks: –3.2 (–3.8, –2.6) [–1.18]
				G1 vs G2	29 weeks: –3.1 (–3.6, –2.6) [–1.29]
				G1 vs G2	
				Disability (SPADI)	6 weeks: –12.5 (–18.9, –6.1) [–1.06]
				G1 vs G2	17 weeks: –16.9 (–25.2, –8.6) [–1.08]
				G1 vs G2	29 weeks: –17.3 (–25.5, –9.1) [–1.18]
				G1 vs G2	
				Disability (DASH)	6 weeks: 1.7 (–0.3, 3.7) [0.46]
				G1 vs G2	17 weeks: –2.8 (–7.8, 2.2) [–0.20]
				G1 vs G2	29 weeks: –9.9 (–0.3, 3.7) [–0.41]
				G1 vs G2	
Rodríguez-Huguet et al. [40]	G1: PE and eccentric exercise	18	1 × 4 weeks	Pain (NPRS)	4 weeks: –1.38 (–2.75, –0.01) [–0.64]
	G2: DN and eccentric exercise	18	1 × 4 weeks	G1 vs G2	8 weeks: –0.96 (–2.32, –0.91) [–0.45]
				G1 vs G2	52 weeks: –1.65 (–2.7, –0.58) [–0.98]
				G1 vs G2	
Lateral Elbow Pain					
	G1: PE and eccentric exercise	18	1 × 4 weeks	Pain (NPRS)	4 weeks: –1.81 (–2.86, –0.76) [–1.16]

(continued)

Study	Intervention(s)	Sample Size	Intervention Duration, Sessions or Weeks	Comparison and Outcome Measure	Between-Group Differences (95% CI) [SMD]*
Rodríguez-Huguet et al. [39]	G2: DN and eccentric exercise	18	1 × 4 weeks	G1 vs G2 G1 vs G2	12 weeks: –2.18 (–3.34, –1.02) [–1.27]
Patellar Tendinopathy					
Abat et al. [31]	G1: PE and eccentric exercise (VISA-P<90) G2: Conventional physiotherapy (VISA-P<90) G3: PE (VISA-P>90) G4: Conventional physiotherapy (VISA-P>90)	8 19 22 11	0.5 × 6 weeks 3 × 8 weeks 0.5 × 6 weeks 3 × 8 weeks	VISA-P G1 vs G2 VISA-P G3 vs G4	6–8 weeks: 1.40 (–10.27, 13.07) [0.10] 6–8 weeks: 1.90 (0.26, 3.54) [0.93]
Groin Pain					
Moreno et al. [37]	G1: PE and active physical therapy program G2: Active physical therapy program	10 13	Two sessions during phase 1 of the active physical therapy program. The mean of the duration of treatment was 37.9±8.5 weeks The mean of the duration of treatment was 48.8±9.4 weeks	Pain intensity at palpation of the insertion of the adductor longus (NPRS) G1 vs G2 G1 vs G2 G1 vs G2 G1 vs G2 Pain intensity to isometric contraction against resistance (NPRS) G1 vs G2 G1 vs G2 G1 vs G2 G1 vs G2 Patient-Specific Functional Scale (PSFS) G1 vs G2 G1 vs G2 G1 vs G2 G1 vs G2	6–8 weeks: –0.90 (–1.96, 0.16) [–0.65] 14–16 weeks: –1.70 (–2.56, –0.84) [–1.47] 22–24 weeks: –1.30 (–2.04, –0.56) [–1.39] 30–32 weeks: –0.90 (–1.89, 0.09) [–0.68] 6–8 weeks: –0.90 (–1.98, 0.18) [–0.61] 14–16 weeks: –1.50 (–2.61, –0.39) [–1.03] 22–24 weeks: –1.50 (–2.38, –0.62) [–1.25] 30–32 weeks: –1.10 (–1.93, –0.27) [–0.98] 6–8 weeks: 4.10 (0.25, 0.18) [0.80] 14–16 weeks: 12.20 (5.92, 18.48) [1.38] 22–24 weeks: 7.50 (2.66, 12.34) [1.15] 30–32 weeks: 5.50 (1.01, 9.99) [0.91]
Whiplash-Associated Pain					
García-Naranjo et al. [35]	G1: PE G2: Standard physiotherapy	50 50	1 × 3 weeks 5 × 4 weeks	Pain intensity (VAS) G1 vs G2 Disability (NPQ) G1 vs G2	–4 weeks: 0.20 (–0.39, 0.79) [0.13] 3–4 weeks: –6.20 (–12.74, 0.34) [–0.37]
Plantar Heel Pain					
Fernández-Rodríguez et al. [34]	G1: PE plus exercise G2: Sham PE plus exercise	38 29	1 × 5 weeks 1 × 5 weeks	Mean pain intensity (NPRS) G1 vs G2 G1 vs G2 G1 vs G2 Disability (FAAM) G1 vs G2 G1 vs G2 G1 vs G2	6 weeks: –4.00 (–5.16, –2.84) [–1.55] 17 weeks: –3.70 (–4.65, –2.75) [–1.73] 29 weeks: –3.30 (–4.03, –2.57) [–2.08] 6 weeks: 27.40 (18.01, 36.79) [1.36] 17 weeks: 25.90 (–4.65, –2.75) [1.47] 29 weeks: 20.20 (–4.03, –2.57) [1.37]

(continued)

Study	Intervention(s)	Sample Size	Intervention Duration, Sessions or Weeks	Comparison and Outcome Measure	Between-Group Differences (95% CI) [SMD]*
Temporomandibular Pain					
Lopez-Martos et al. [38]	G1: PE	20		Pain on rest (VAS)	4 weeks: –2.53 (–3.95, –1.11) [–1.08]
				G1 vs G2	6 weeks: –1.57 (–2.83, –0.31) [–0.76]
				G1 vs G3	10 weeks: –1.39 (–2.26, –0.52) [–0.91]
				G2 vs G3	4 weeks: –3.07 (–5.00, –1.14) [–0.97]
					6 weeks: –3.97 (–5.45, –2.49) [–1.63]
					10 weeks: –3.50 (–4.76, –2.24) [–1.69]
					4 weeks: –0.54 (–2.03, 0.95) [–0.22]
					6 weeks: –2.40 (–3.66, –1.14) [–1.16]
					10 weeks: –2.11 (–3.28, –0.94) [–1.10]
	G2: Dry needling	20		Pain on mastication (VAS)	4 weeks: –1.53 (–2.70, –0.36) [–0.79]
				G1 vs G2	6 weeks: –1.12 (–2.71, 0.47) [–0.43]
				G1 vs G3	10 weeks: –1.00 (–2.48, 0.48) [–0.41]
				G2 vs G3	4 weeks: –2.71 (–4.74, –0.68) [–0.81]
					6 weeks: –3.97 (–6.23, –1.71) [–1.07]
					10 weeks: –2.44 (–4.47, –0.41) [–0.73]
					4 weeks: –1.18 (–3.00, 0.64) [–0.39]
					6 weeks: –2.85 (–4.73, –0.97) [–0.92]
					10 weeks: –1.44 (–3.47, 0.59) [–0.43]
	G3: Sham dry needling	20			
				Disability (TMJ)	4 weeks: 9.55 (–3.36, 22.46) [0.45]
				G1 vs G2	6 weeks: 14.59 (0.27, 28.91) [0.62]
				G1 vs G3	10 weeks: 16.21 (4.07, 28.35) [0.81]
				G2 vs G3	4 weeks: 26.40 (4.06, 48.74) [0.72]
					6 weeks: 35.85 (14.00, 57.70) [1.01]
					10 weeks: 33.63 (15.59, 51.67) [1.13]
					4 weeks: 16.85 (–3.33, 37.03) [0.51]
					6 weeks: 21.26 (2.85, 39.67) [0.70]
					10 weeks: 17.42 (1.51, 33.33) [0.67]

CI = confidence interval; SMD = standardized mean difference; PE = percutaneous electrolysis; DASH = Disabilities of the Arm, Shoulder, and Hand Questionnaire; VAS = visual analog scale; NPRS = numeric pain rating scale; SPADI = Shoulder Pain and Disability Index; DN = dry needling; VISA-P = Victorian Institute of Sport Assessment—Patella; NPQ = Northwick Park Neck Questionnaire; FAAM = Foot and Ankle Ability Measure; TMJ = Temporomandibular Joint Dysfunction Scale; TrP = Trigger point.

*Follow-up from baseline.

Table 3. Methodological score of randomized clinical trials using the Physiotherapy Evidence Database (PEDro) scale

Study	1	2	3	4	5	6	7	8	9	10	Total
Shoulder Pain											
Arias-Buría et al. [32]	Y	Y	Y	Y	N	N	N	Y	Y	Y	7
Moreno [36]	N	N	Y	N	N	N	Y	Y	Y	Y	5
de Miguel Valtierra et al. [33]	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	9
Rodríguez-Huguet et al. [40]	Y	Y	Y	N	N	Y	Y	N	Y	Y	7
Lateral Elbow Pain											
Rodríguez-Huguet et al. [39]	Y	Y	Y	N	N	Y	Y	N	Y	Y	7
Patellar Tendinopathy											
Abat et al. [31]	Y	N	N	Y	N	N	Y	N	Y	Y	5
Groin Pain											
Moreno et al. [37]	Y	Y	N	N	N	Y	Y	N	Y	Y	6
Whiplash-Associated Pain											
García-Naranjo et al. [35]	Y	Y	Y	N	N	Y	Y	Y	Y	Y	8
Plantar Heel Pain											
Fernández-Rodríguez et al. [34]	Y	N	Y	Y	Y	N	Y	N	Y	Y	7
Temporomandibular Pain											
Lopez-Martos et al. [38]	Y	N	Y	Y	N	N	Y	Y	Y	Y	7

Y = yes; N = no.

1 = random allocation of participants; 2 = concealed allocation; 3 = similarity between groups at baseline; 4 = participant blinding; 5 = therapist blinding; 6 = assessor blinding; 7 = dropout rate less than 15%; 8 = intention-to-treat analysis; 9 = between-group statistical comparisons; 10 = point measures and variability data.

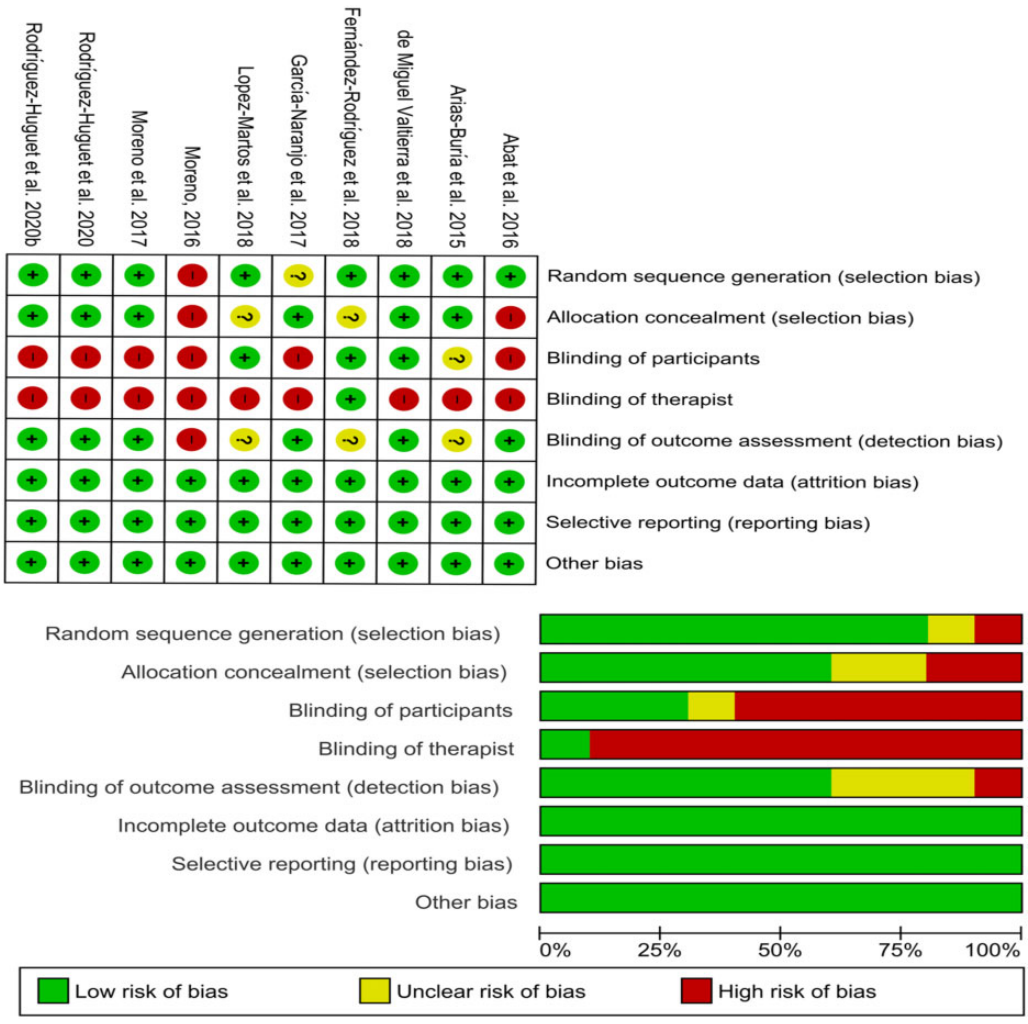

Figure 3. Plots of risk of bias of the included studies.

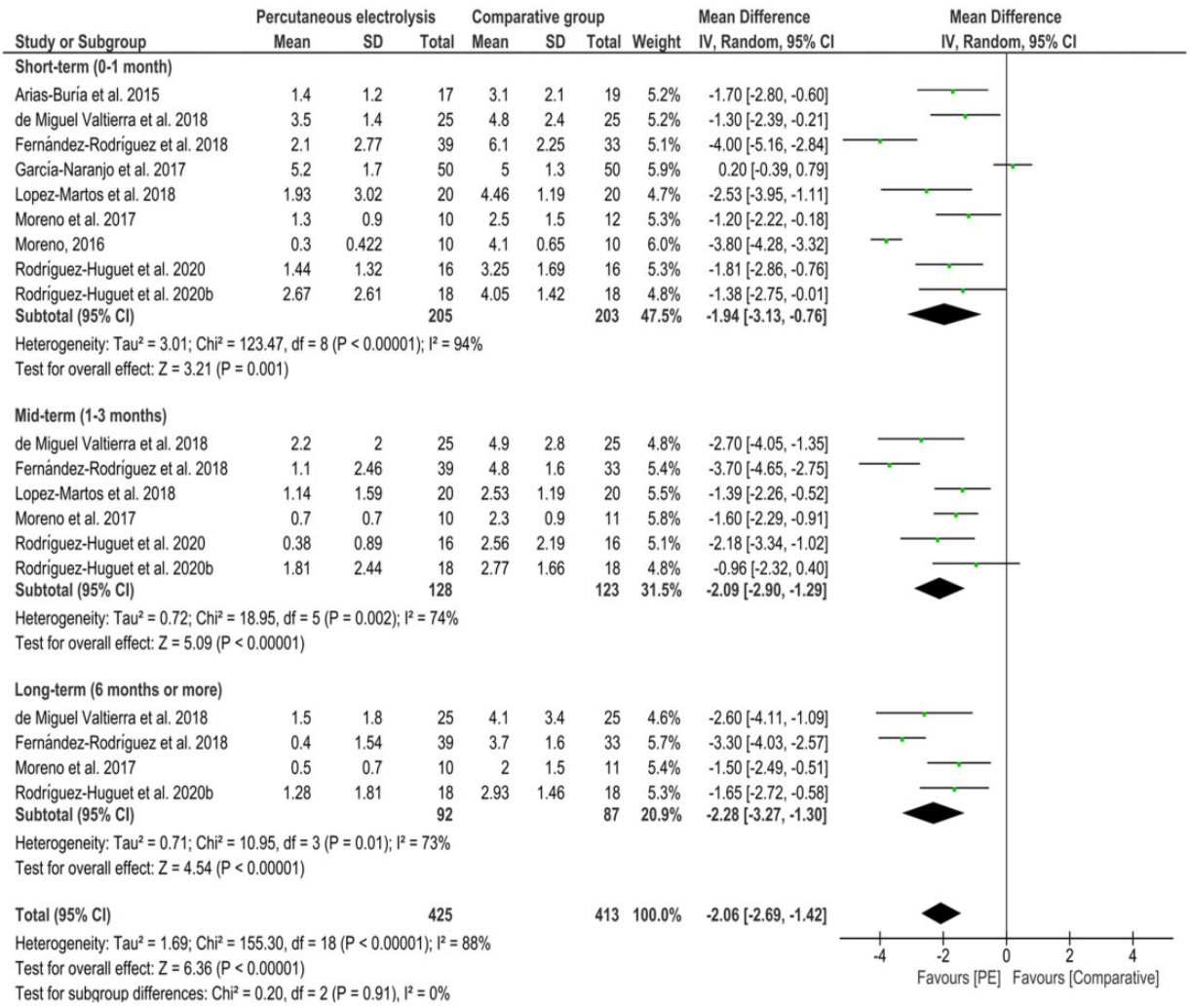

Figure 4. Comparison (mean difference) of the effects of percutaneous electrolysis vs the comparison group on pain intensity.

moderate-quality evidence for a large effect of improving pain-related disability in individuals with musculoskeletal pain. The risk of bias of the trials included in the current meta-analysis was low, but the inconsistency of the results (heterogeneity) downgraded one level of evidence quality (GRADE).

Effectiveness of Percutaneous Electrolysis

This is the first meta-analysis (to the best of our knowledge) analyzing the impact of percutaneous electrolysis on pain intensity and pain-related disability for musculoskeletal pain. Percutaneous electrolysis is a novel therapeutic intervention, different from PENS and electroacupuncture, recently recommended for the treatment of soft tissue pain conditions [11]. We found that ultrasound-based percutaneous electrolysis was more effective than a comparison intervention for pain relief and improved pain-related disability in the short term, mid-term, and long term. Seven trials (70%) used percutaneous electrolysis as an adjunct with another intervention, such as exercise alone [31, 32, 34, 37, 39, 40] or manual therapy and exercise combined [33], whereas three trials (30%) applied percutaneous electrolysis alone [35, 36, 38]. Most trials (90%) reported differences in pain or pain-related disability in favor of percutaneous electrolysis as compared with the comparative group [31–34, 36–40]. Only the study by García-Naranjo et al. [35] reported no differences in the short term when comparing percutaneous electrolysis with multimodal therapy, including an exercise program for individuals with whiplash-associated pain. In this study, both groups reported significant improvements in pain and function; however, considering that the intervention group consisted of three sessions of isolated percutaneous electrolysis, a greater number of treatment sessions may support a better effect in favor of percutaneous electrolysis [35]. All trials compared percutaneous electrolysis with other intervention [31–35, 37–40] except the study by Moreno [36], which compared percutaneous electrolysis with a control group without intervention. This, along with the small sample size, may explain why the study by Moreno [36] reported a size effect that was larger than that of the remaining trials.

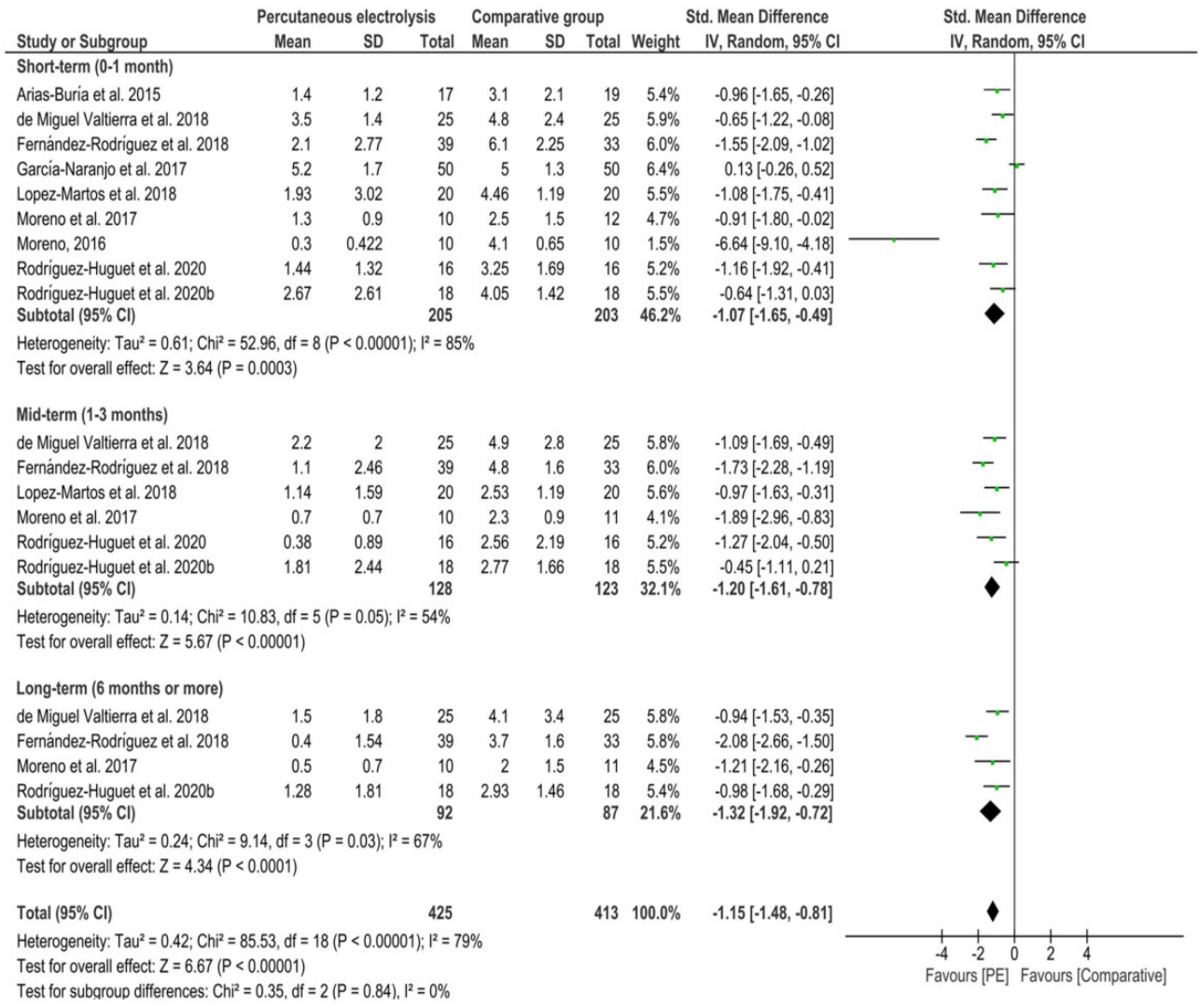

Figure 5. Comparison (standardized mean difference) of the effects of percutaneous electrolysis vs the comparison group on pain intensity.

It is important to determine if the observed changes are clinically relevant. We observed a mean decrease of pain intensity greater than 2 points at the short-term, midterm, and long-term follow-ups, with a decrease in the overall mean score of –2.06 points (95% CI, –2.69 to –1.42). Salaffi et al. [41] reported that a reduction of 1 point or a reduction of 15% from baseline scores represents the minimal clinically important difference (MCID) for the NPRS in patients with musculoskeletal pain. The decrease in pain found with the application of percutaneous electrolysis was higher than the determined MCID of 1 point. Furthermore, specific conditions included in some trials (e.g., shoulder pain [42] or neck pain [43]) have a similar MCID of 1.2 points. These results support the clinical relevance of the observed changes with this intervention.

A potential topic for research may be the cost-effectiveness of ultrasound-guided percutaneous electrolysis. García-Naranjo et al. [35] suggested a possible cost-effective benefit of including percutaneous electrolysis with other physical therapy interventions, but this hypothesis requires further study. Similarly, Minaya-Muñoz et al. [29], in an open-label study, also showed the potential cost benefits of combining percutaneous electrolysis with exercise for people with lateral epicondylalgia. Finally, Iborra-Marcos et al. [30] noted that treatment with corticosteroid injections was more expensive per session than ultrasound-guided percutaneous electrolysis, but no statistical cost analysis was performed.

Mechanisms of Percutaneous Electrolysis

The underlying mechanisms explaining the effects of percutaneous electrolysis are not clearly understood. Percutaneous electrolysis has been shown to be able to activate protein expression of cytochrome C, vascular endothelial growth factor and its receptor 2, and the nuclear transcription factor peroxisome proliferator-activated receptor gamma [44]. It has also been shown to inhibit the action of IL-1, TNF, and COX-2 [45]. All of

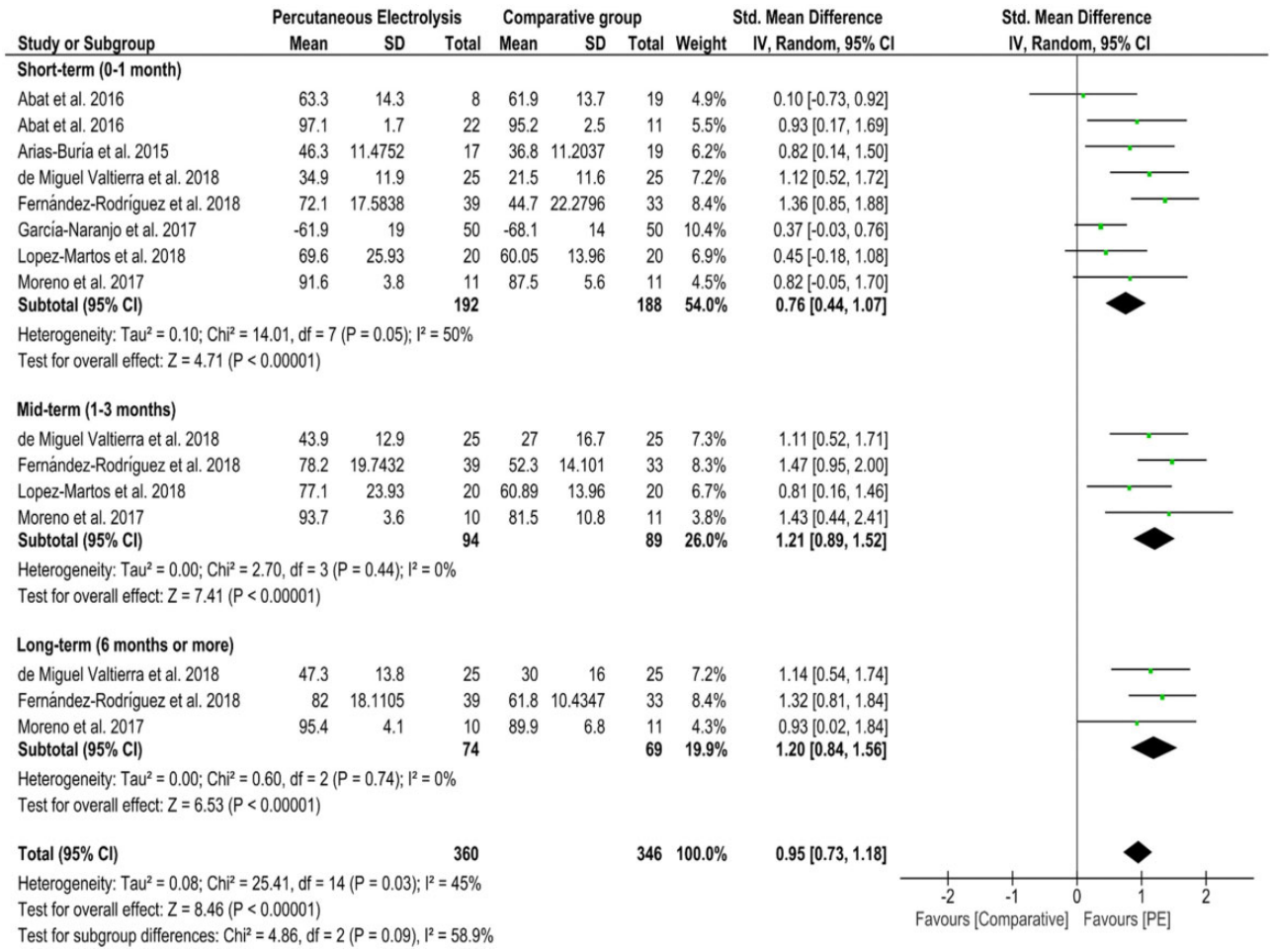

Figure 6. Comparison (standardized mean difference) of the effects of percutaneous electrolysis vs the comparison group on pain-related disability.

these factors are indicative of an inflammatory response that facilitates proper phagocytosis and posterior tissue healing regeneration. Considering that degenerative tissue changes are a common finding in painful tendons [46], it would make sense that this intervention could help in the healing process of chronic tendinopathies. Nevertheless, tissue change is not the only explanation of clinical improvement [47], and many times changes in tendon structure do not predict the evolution of the symptoms [48]. In addition, the degenerative part of the tendon cannot respond properly to mechanical stimuli [49]; therefore, the degenerative area may not be able to adapt and increase its load. These hypotheses are in accordance with the study by Fernández-Rodríguez et al. [34], who found a reduction in plantar fascia thickness after the application of percutaneous electrolysis and exercise in patients with plantar heel pain; however, the observed changes were not sufficiently large to be considered a true improvement. Some case series including individuals with lateral epicondylalgia that received percutaneous electrolysis intervention and eccentric exercise also reported a reduction of 56% of hypoechogenicity [14]. In fact, because tendons have low metabolism, it is difficult to explain the clinical improvement throughout only the changes in the tissue structure in the short term. In such a scenario, neuroplastic changes (induced by the mechanical stimulus of percutaneous electrolysis or exercise) and muscle adaptations (induced by exercise therapy) [50] could explain the clinical effects. Future studies should investigate tissue changes and their association with clinical outcome changes after the application of percutaneous electrolysis.

A second potential mechanism of percutaneous electrolysis is neurophysiological. Ronzio et al. [27] found a significant hypoalgesic effect (increase pressure pain threshold) in the group receiving percutaneous microelectrolysis when compared with a sham group (needle insertion without electrical current), suggesting that percutaneous electrolysis may have immediate effects on pain modulation. In fact, some studies have reported autonomic activation after application of percutaneous electrolysis by observing parasympathetic activation during the intervention [51, 52].

Table 4. GRADE evidence for percutaneous electrolysis to treat pain and pain-related disability for musculoskeletal pain conditions

Number of Studies	Risk of Bias*	Inconsistency†	Indirectness of Evidence‡	Imprecision§	Publication Bias¶	Quality of Evidence	MD or SMD (95% CI)
Percutaneous Electrolysis vs Comparative Intervention on Pain							
Overall effects, nine trials (n=838)	No	Serious (I^2=79%)	No	No	No	Moderate	MD = –2.06 (–2.69 to –1.42) SMD = –1.15 (–1.48 to –0.81)
Short-term effects, nine trials (n=408)	No	Very serious (I^2=94%)	No	No	No	Moderate	MD = –1.94 (–3.13 to –0.76) SMD = –1.07 (–1.65 to –0.49)
Midterm effects, five trials (n=251)	No	Serious (I^2=74%)	No	No	No	Moderate	MD = –2.09 (–2.90 to –1.29) SMD = –1.20 (–1.61 to –0.78)
Long-term effects, four trials (n=179)	No	Serious (I^2=73%)	No	Serious	No	Low	MD = –2.28 (–3.27 to –1.30) SMD = –1.32 (–1.92 to –0.72)
Percutaneous Electrolysis vs Comparative Intervention on Pain-Related Disability							
Overall effects, seven trials (n=707)	No	Serious (I^2=45%)	No	No	No	Moderate	SMD = 0.95 (0.73–1.18)
Short-term effects, seven trials (n=380)	No	Serious (I^2=50%)	No	No	No	Moderate	SMD = 0.76 (0.44–1.07)
Midterm effects, four trials (n=183)	No	No (I^2=0%)	No	Serious	No	Moderate	SMD = 1.21 (0.89–1.52)
Long-term effects, three trials (n=143)	No	No (I^2=0%)	No	Serious	No	Moderate	SMD = 1.20 (0.84–1.55)

GRADE = Grading of Recommendations Assessment, Development and Evaluation; MD = mean difference; SMD = standardized mean difference.

*"No" = most information is from results at low risk of bias; "Serious" = crucial limitation for one criterion or some limitations for multiple criteria sufficient to lower confidence in the estimate of effect; "Very serious" = crucial limitation for one or more criteria sufficient to substantially lower confidence in the estimate of effect.

†"Serious" = $I^2 > 40\%$; "Very serious" = $I^2 > 80\%$.

‡No indirectness of evidence was found in any study.

§Based on sample size. "Serious" = n<250 subjects; "Very serious" = n<250 and the estimated effect is little or absent.

¶Based on funnel plots. No publication bias was found. Funnel plots are not shown because the number of trials was less than 10.

Safety of Percutaneous Electrolysis

Because this is a new intervention, we wondered if percutaneous electrolysis would be a safe intervention that would not produce serious adverse effects. The most common adverse effect was postelectrolysis soreness (30% of patients). This adverse event may be mostly produced by the insertion of the needle (as is also common during other procedures such as dry needling) [53] or the application of a galvanic electrical current; however, this postelectrolysis soreness disappeared without any treatment after 12–36 hours [32, 33, 37]. One trial reported the presence of postelectrolysis hematoma in one patient [38]. No other adverse events were reported. The retrospective study by Iborra-Marcos et al. [30] described two individuals with a vasovagal episode. All of the observed events can be categorized as minor [54]. Therefore, it seems that percutaneous electrolysis could be considered a safe intervention. In addition, the fact that percutaneous electrolysis is recommended to be ultrasound guided increases its safety. Future studies should investigate if the ultrasound-guided application is beneficial in relation to adverse events as compared with the application of non–ultrasound-guided techniques.

Strengths and Limitations

Although this is the first (to the best of our knowledge) meta-analysis analyzing the effects of ultrasound-guided percutaneous electrolysis on pain or pain-related disability in musculoskeletal pain conditions, the results should be considered in light of potential strengths and limitations. The strengths of this meta-analysis include a comprehensive literature search, methodological rigor, data extraction, rigorous statistical analysis, and the inclusion of randomized controlled trials of high quality in the quantitative analysis. However, the number of randomized controlled trials examining the effects of percutaneous electrolysis on musculoskeletal pain was relatively small (n=10; e.g., only one trial for plantar heel pain, whiplash-related pain, or lateral epicondylalgia). In addition, not only was the number of trials small, but the trials also evaluated the application of percutaneous electrolysis with different dosages (i.e., time, sessions, electrical current intensity). Another potential limitation is the heterogeneity and imprecision of the results of some of the included trials; therefore, the results should be considered with caution at this stage.

Clinical Implications

This meta-analysis found a moderate level of evidence supporting the application of ultrasound-guided percutaneous electrolysis for musculoskeletal pain in general. However, this should be considered with caution, as we do not know if percutaneous electrolysis could potentially be beneficial in some subgroups of patients with musculoskeletal pain. In fact, the current meta-analysis included several musculoskeletal pain conditions, and

only one study has been published on some of them. Furthermore, the pain conditions included in this meta-analysis were heterogeneous. According to suggested mechanisms proposed for explaining the effects of percutaneous electrolysis, it is expected that musculoskeletal pain conditions with an involvement of the tendon would benefit from this intervention. In fact, percutaneous electrolysis was originally developed for the management of chronic tendinopathies with the aim to promote and/or facilitate the healing process after the induction of the nonthermal electrolytic reaction [11]. In this meta-analysis, most of the trials included musculoskeletal pain conditions where the tendon could be partially (i.e., shoulder pain or lateral epicondylalgia) or completely (i.e., patellar tendinopathy or plantar heel pain) involved in the symptoms. Clinicians should apply proper clinical reasoning for the application of percutaneous electrolysis.

In addition, we do not currently know the real effects of percutaneous electrolysis when compared with sham percutaneous electrolysis. Some of the trials included in this meta-analysis compared percutaneous electrolysis with a needling approach without the application of the electrical current, suggesting that at least some clinical effects are related to the continuous galvanic electrical current. There is a need for well-designed randomized clinical trials examining the effects of percutaneous electrolysis vs sham and the combination of percutaneous electrolysis with other interventions. In fact, a study protocol investigating this topic in patients with patellar tendinopathy has recently been published [55].

One of the most important topics to consider for the proper clinical application of percutaneous electrolysis is the appropriate parameters (i.e., treatment duration, intensity of electrical current, or number of sessions), and studies should be conducted to create reproducible results. We do not have enough data to determine which treatment parameters are the most effective for the application of percutaneous electrolysis on each particular pain condition. A recent animal study reported that higher doses of electrical current are more effective for decreasing electromyographic findings of myofascial trigger points in rats [56]. Future studies should investigate the appropriate parameters of percutaneous electrolysis for the management of different musculoskeletal pain conditions.

Conclusion

This meta-analysis found moderate evidence suggesting a large positive effect of percutaneous electrolysis for reducing pain and moderate evidence for a large decrease in pain-related disability for musculoskeletal pain conditions in the short term, midterm, and long term. Future studies are needed to clarify the dosage and which musculoskeletal pain conditions would be most likely to benefit from this intervention.

Supplementary Data

Supplementary Data may be found online at http://painmedicine.oxfordjournals.org.

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