Pain Research and Management

Minimally Invasive Techniques for Pain and Dysfunction Management

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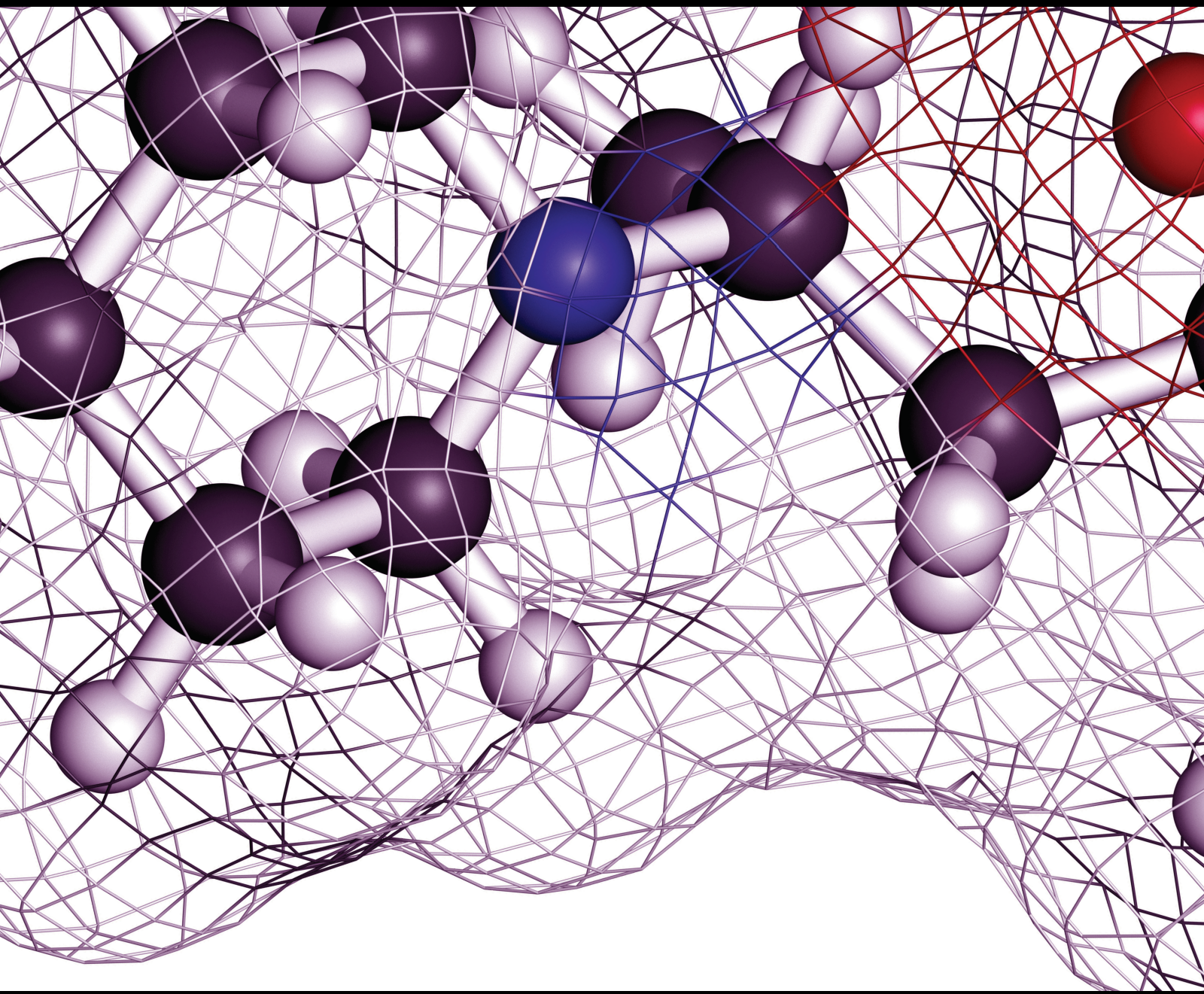

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Research Article

Effectiveness of Dry Needling in Improving Pain and Function in Comparison with Other Techniques in Patients with Chronic Neck Pain: A Systematic Review and Meta-Analysis

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The purpose of this systematic review and meta-analysis was to assess the short-, mid-, and long-term effectiveness of dry needling in improving pain and functional capacity of patients with chronic neck pain. Search strategy was performed on PubMed, Web of Science, Scopus, PEDro, and Cochrane Library Plus biomedical databases. The risk of bias was assessed using the RoB2 tool. Randomised controlled clinical trials in which at least 1 of the groups received dry needling were included. 662 studies were found; 14 clinical trials were selected for qualitative analysis and 13 for quantitative analysis. The quality of most of the studies included was "high." All the studies reported improvements in cervical pain and/or disability, regardless of the protocol followed and the muscles targeted. No serious adverse effects were reported. Dry needling showed to be more effective when compared with other therapies in both women and men, without differences by sex. When the analysis was carried out by age, patients over 40 years old benefitted more than those below 40 years old. Our meta-analysis supports the use of dry needling to improve pain and functional capacity in patients with chronic neck pain at short- and mid-term intervals.

1. Introduction

Neck pain is suffered by at least 30% of adults worldwide with a prevalence of 24439 to 61512 cases per 100000 population [1, 2]. Chronic symptoms are developed by 44% of the patients [3], and this condition is as important as lumbar pain in prevalence and duration [4]. When the problem turns chronic, there is an elevated economic and healthcare cost [5, 6].

Myofascial pain syndrome is defined as a set of autonomic, motor, and sensory signs and symptoms provoked by myofascial trigger points (MTPs) [7]. It often contributes to the appearance of mechanical neck pain [8] and it is associated with the chronification of the symptoms. A MTP is defined as a hyperirritable area in a skeletal muscle associated with a hypersensitive palpable nodule located in a taut band of muscle fibres [7]. The area is painful when subjected to mechanical deformation through compression, stretching, muscle contraction, or other stimuli; it can cause referred pain, hypersensitivity, motor dysfunction, and autonomic phenomena [7–10].

Different treatment strategies have been proposed to manage MTPs, being dry needling (DN) one of the most used [11]. The DN procedure consists of inserting a filiform, solid, nonbevelled needle into the MTP, without injecting or extracting any substance. DN is known to have a mechanical

effect, provoking the disruption of dysfunctional motor endplates, and it is used to treat different pathologies [9]. DN has demonstrated to be effective in reducing myofascial pain in the upper [12] and lower quarter [13] in the short term. Moreover, DN has shown to be an effective and useful procedure complementary to conventional physiotherapy [14], either alone or in combination with pharmacological treatments [15] for headache management. In the case of neck pain, the current scientific evidence suggests that DN can be effective, although only in the short term [16]. Seventeen systematic reviews were published in relation to patients with neck pain and DN effectiveness. However, in the case of chronic neck pain, there are no reviews that have assessed the effectiveness of this technique. Moreover, sex and age characteristics are not usually considered when studying the effects of DN. Therefore, the objective of this systematic review and meta-analysis was to assess the short-, mid-, and long-term effectiveness of DN to improve chronic neck pain and functional capacity in comparison with other physiotherapy techniques or placebo. Secondary, the effectiveness of DN by subgroups, based on sex and age characteristics, was assessed.

2. Materials and Methods

This systematic review was conducted according to the PRISMA statement [17], designed and published to improve systematic reviews and meta-analyses. This review was registered on the Open Science Framework Registry digital platform: DOI 10.17605/OSF.IO/U6QRZ (https://osf.io/ywjbp). Abstract and PRISMA 2020 checklist can be found in Figures S1 and S2.

The PubMed, Web of Science, Scopus, PEDro, and Cochrane Library Plus electronic databases were included. In addition, a search of the grey literature was carried out (Google Scholar and ResearchGate). The search was performed from 15th September to 23rd December, 2021.

Our search strategy was established according to the recommendations of the Cochrane Back and Neck Group [18]. In agreement with these recommendations, three search categories were established (which were combined later) as follows: The purpose of the first category was to perform a sensitive search for the type of studies to be included: randomised controlled clinical trials or controlled clinical trials. The second category was designed to carry out a specific search for the condition of cervicalgia (neck pain or cervical pain). The purpose of the third category was to search specifically for the intervention of DN. See Figure S3 in the Supplementary Materials for Search Strategy. Search terms were established after a preliminary literature search, identifying the keywords and MeSH terms search. To identify additional registers, the search process ended with in-depth review of the bibliographic references included in the articles that underwent full text review.

Our systematic review included randomised controlled clinical trials in which at least 1 of the groups received DN as a treatment for chronic neck pain. The specific inclusion criteria included the following: (1) adult population (>18 years old); (2) chronic neck pain (>3 months); (3) superficial or deep DN technique; (4) description of the DN technique applied; (5) primary variables that included the intensity of the pain; the functional capacity or pain sensitivity (measured with pressure pain threshold); (6) articles written in English, Italian, French or Spanish languages. The exclusion criteria were as follows: (1) patients with neurological pain; (2) patients presenting headaches (tension-type headache, migraine or cervicogenic headache); (3) studies in which acupuncture was performed or mentioned as an intervention technique; (4) postoperative neck pain; and (5) studies published before 2010.

The articles extracted from each database were reviewed independently by two authors (M.H.S. and H.A.B.). Duplicate articles were eliminated using Covidence software. Selection of articles was carried out in three different steps: by title, abstract, and full text. Two independent reviewers (M.H.S. and H.A.B.) performed this selection and if a consensus was not reached, a third reviewer (S.B.A.) decided whether to include the article or not. Cohen's kappa index was calculated to assess the interrater agreement between the two primary reviewers [19].

The data on the studies selected were extracted by the two independent authors (M.H.S. and H.A.B.), filling in a standardised register excel sheet. The study characteristics recorded included the number of participants, the muscles on which the intervention was applied, the parameters used in the DN application, outcomes measured, and results achieved.

Both reviewers assessed the methodological quality and risk of bias independently. Methodological quality was evaluated using the scale of the Physiotherapy Evidence Database (PEDro) [20]. 11 items were assessed, giving each one a score from 1 to 0 depending on whether the item was fulfilled in the study or not, respectively. This scale establishes external validity using Item 1, internal validity using the items from 2 to 9, and result interpretability using Items 10 and 11. The first item was not taken into account in the final score, and 10 points was the maximum obtainable in this scale. Each article was classified according to the score obtained in the following manner: «high quality» if the score was greater than or equal to 6, «moderate quality» if the score was 4-5, and «low quality» if its score is less than 4.

The risk of bias 2 tool (RoB2) is the second version of the Cochrane tool to assess the risk of bias in clinical trials. The biases are evaluated in 5 domains: (1) randomization process; (2) effect of being assigned to intervention; (3) missing outcome data; (4) measurement of the outcome; and (5) reported results. Within each domain, 1 or more questions must be answered. These answers lead to the judgements of "low risk of bias," "some concerns," or "high risk of bias" [21].

All analyses were performed using RevMan Manager 5.4 software (The Cochrane Collaboration, 2012). The sample size, means, and standard deviation for each outcome were extracted. The mean difference (MD) with a 95% confidence interval (CI) was calculated for continuous data. In the cases, where different tools were used to assess pain or function, standard mean difference (SMD) was chosen. Sources of heterogeneity were investigated by subgroup analyses

comparing results based on age (<40 years old, >40 years old. or NR, not reported); sex (mainly female, mainly men, and NR, not reported); and intervention (DN vs other intervention, DN vs DN + physical therapy (PT), and DN + PT vs PT). The heterogeneity of the studies was tested using the I^2 statistic. This statistic describes the variance between studies as a proportion of the total variance. A value <25% indicated low heterogeneity, from 25 to 50% moderate, from 50 to 75% high heterogeneity, and >75% very high heterogeneity [22]. Funnels plots were performed for pain and function outcomes to explore any publication bias. In addition, a graphic display of heterogeneity (GOSH) was used, which plots the pooled effect size on the x-axis and the between-study heterogeneity on the y-axis, which allows looking for specific patterns or clusters with different effect sizes and amounts of heterogeneity (see Supplementary Materials, Figures S4–S6).

3. Results

3.1. Study Selection. The search and the selection process of the relevant studies are shown in Figure 1. After the initial literature search, 662 studies were obtained. After eliminating the duplicated articles, the total number of articles left was 322. Of these, 232 studies were excluded based on the analysis of the title and summary/abstract. Finally, 14 studies were selected for the qualitative analysis and 13 for quantitative analysis. The kappa index between each author was 0.81 (95% CI: 0.65–0.91) [22].

3.2. Characteristics of the Studies. The studies characteristics are presented in Table 1. The DN technique was performed in the posterior cervical area (only one study did not specify the musculature involved) in all studies (22–35). The upper trapezius muscle was treated in 8 studies [23, 26, 27, 29–31, 33–35], levator scapulae in 5 studies [23, 25–27, 33, 35], the splenius and multifidus in 3 studies [25, 34, 35], and medium and lower trapezius in 3 studies [27, 32, 34].

The methodology of the technique application was not homogeneous, as there were variations regarding the number of local twitch responses produced, the duration of DN application, and the number of needle manipulations.

4. Effectiveness for Pain and Function

At short term (immediately after treatment—1 month), DN was more effective to decrease pain in 9 of the studies. In those studies, DN was compared with stretching ($p < 0.001$; 0.006) [25, 31], manual therapy ($p < 0.001$) [34], myofascial release (MR) ($p < 0.001$) [33], and electrotherapy using transcutaneous electrical nerve stimulation (TENS) with ultrasound (US) ($p = 0.023$) [24]. However, DN did not show statistically significant differences compared to extracorporeal shock wave therapy (ESWT) ($p = 0.856$) [30]. DN technique did not show any difference when percutaneous electrical nerve stimulation (PENS) ($p = 0.504$) [29], education ($p > 0.05$) [35], and manual therapy ($p > 0.05$) [23] were added. Moreover, DN showed to be more effective than miniscalpel-needle (MNS) ($p < 0.001$) [36]. As for the functional capacity, DN showed better results than stretching ($p < 0.05$) [31].

At mid term (1–3 months), both pain and functional capacity showed better results in the DN groups in all studies, except for the study of Stieven et al. that only showed improvements in the case of pain outcome. However, this was not the case when DN was compared with the miniscalpel-needle, in favour of the last one ($p < 0.001$) [36]. Moreover, no differences were found in the functional capacity when DN was compared with stretching ($p > 0.05$) [25]. In fact, worse results were found comparing DN alone versus DN combined with pain education [35], manual therapy ($p > 0.05$) [23], or PENS ($p > 0.05$) [28, 29]. In the case of pain, a better evolution was seen when DN was compared with stretching techniques ($p < 0.05$) [23].

At long term (>3 months), the results were contradictory. On the one hand, DN showed statistically significant improvements in pain reduction and functional capacity in all studies except for the one performed by Stieven et al. [34], which did not report significant improvements of DN versus MT combined with exercise ($p = 0.13$). On the other hand, statistically significant differences were found in favour of other treatments, such as MNS ($p < 0.001$) [36], MT ($p < 0.001$) [23], and PENS ($p < 0.05$) [28, 29], when it was compared to DN.

In the analysis of secondary variables, there was an improvement in the pressure pain threshold in the short- and mid-term intervals in all the studies in which this was measured [23, 25–33].

5. Methodological Quality

The mean score of the studies was 8.7, with 13 of the 14 selected studies having a high methodological quality and only one having a moderate quality. Therapist blinding was not achieved in any of the studies, while patient blinding was found in only 4 studies [24, 26, 27, 32]. Regarding the evaluator blinding, all studies had a blinded evaluator except one of them [27]. The details of the methodological quality scores of the articles assessed according to the PEDro scale can be found in Table 2.

The RoB2 tool shows that the features with the worst methodological quality were biased due to deviations from intended intervention, with approximately 25% being high risk. Bias in the measurement of the outcome was the domain with the best methodological quality in the set of studies, being more than 75%. The details regarding the risk of bias are presented in Figure 2.

6. Pain Meta-Analysis

As shown in Figure 3, DN is effective to improve pain (MD: −0.45; 95% CI: −0.90; −0.01). However, heterogeneity was very high for the overall of studies ($I^2 = 88\%$; $p < 0.01$).

As shown in Figure 4, the majority of studies followed a symmetrical distribution. So, it could be that the studies included in the analysis had no publication bias. In addition, the effect size was high for the majority of studies.

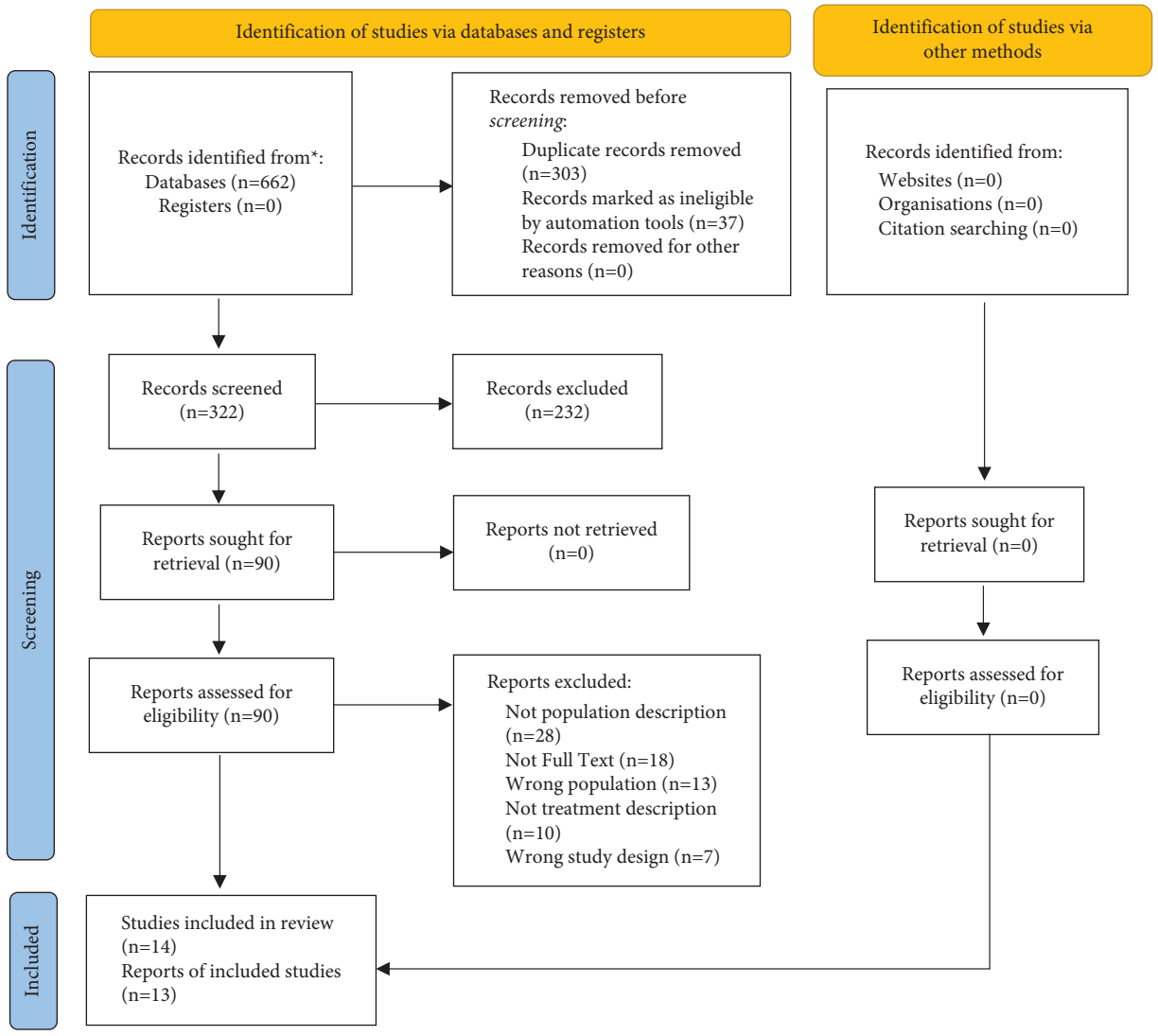


Figure 1: Flow diagram.

6.1. Subgroup Sex (Pain). A subgroup analysis by sex was also carried out. No significant effects on pain were observed in the studies including mainly men (MD: −0.490; 95% CI: −1.713; 0.733) or mainly women (MD: −3.122; 95% CI: −5.309; 0.936). Only one study did not report the sex of the population. In this study, a significant effect on pain for the DN technique was not observed (MD: −1.380; 95% CI: −2.686; 0.074).

6.2. Subgroup Age (Pain). A subgroup analysis by age was performed, showing that DN was effective to improve pain in the studies in which the mean age was over 40 years old (MD: −0.74; 95% CI -1.47; −0.01). Nevertheless, no significant effects on pain were observed in the studies where the mean age was under 40 years old (MD: −0.16; 95% CI: −0.75; 0.43). Results are shown in Figure 5. Heterogeneity was very high and significant for studies in which mean age was over 40 years old ($I^2 = 91\%$) and high for those with a mean age under 40 years old ($I^2 = 84\%$).

As shown in Figure 6, the majority of studies did not follow a symmetrical distribution as shown in the funnel plot.

6.3. Subgroup Interventions (Pain). As shown in Figure 7, DN combined with physical therapy (PT) significantly reduced pain compared to physical therapy alone (MD: −1.14; 95% CI: −2.07; −0.22). Nevertheless, no significant differences were shown for DN alone compared to DN + PT (MD: 0.173; 95% CI: −0.549; 0.895) and DN compared to other interventions (MD: −1.236; 95% CI: −2.897; 0.425). Heterogeneity was very high and significant for studies comparing DN + PT vs PT ($I^2 = 84\%$; $p < 0.01$).

As shown in Figure 8, all studies did not follow a symmetric distribution as shown in the funnel plot. So, probably, the studies included in the analysis had publication bias.

Table 1: Studies characteristics.

Study	*N* (age)	Intervention	Muscles involves	Dosage and follow-up	Outcomes	Results
Campa-Moran et al. [23]	*N*: 36 (18–75 y)	G1 (n: 12): DN + stretch G2 (n: 12): MT G3 (n: 12): soft tissue treatment	Upper trapezius bilateral Levator scapulae bilateral	Tt: 2 ss (break of 48 h) DN: at least 3 LTR (2 min each point) Needle: 0.26 × 25 mm Follow-up: baseline, post 1st ss, post 2nd ss, and 1 week	VAS NDI (B, 1 wk) PPT ROM PCS (B, 1 wk) AE	G1: improved NDI, VAS, and flexion at 1 wk G2: improved in all outcomes and follow-ups G3: not improved G2 > G1 fx-Ext ROM + PPT (C5-C6) G2 > G3 PPT + ROM AE: no
Ceballos-Laita et al. [24]	*N*: 21 (30–65 y)	G1 (n: 7): DN + control G2 (n: 7): DNs + control G3 (n: 7): control (TENS + US)	Active MTrPs (at most 3 pts that reproduce symptoms)	G1/G2: G3 + 1 ss/wk (2 wk) G3: 5 ss/wk (2 wk)-15 min TENS + 5 min US + 10 education DN: reach LTR Needle: 0.25 × 40 mm Follow-up: baseline and postintervention	VAS NDI TSK PCS HADS GROC	G1 improved in all outcomes except HADS G1 > G2 and G3 for VAS, NDI and PCS G1 ⟶ 71.4% "great deal better" G2 + G3 ⟶ "moderately better" (71.4%; 42.9%)
Cerezo-Tellez et al. [25]	*N*: 138 (>18 y)	G1 (n: 64): DN + stretch G2 (n: 64): stretch	Trapezius Levator scapulae Splenius cervicis Multifidi	Tt: 2 ss/wk (2 wk) DN: 4-5 LTR Needle: 0.32 × 40 mm Follow-up: baseline, 1 wk, 3 wk, 1 m, 2 m, 4 m, 7 m	VAS NDI PPT ROM Strength AE	G1 and G2 improved in all outcomes G1 > G2 in all outcomes and follow-ups| AE: no
Gallego-Sendarrubias et al. [26]	*N*: 50 (18–60)	G1 (n:25): DN G2 (n:25): DNs	Upper trapezius	Tt: 1 ss DN: 3-4 LTR Needle: x Follow-up: baseline, 1 d, 1 wk	VAS PPT GROC AE	G1 > G2 in all outcomes G1 ⟶ GROC ≧+5 AE: mild
Gallego-Sendarrubias et al. [27]	*N*: 101 (18–55 y)	G1(n: 47): DN + MT G2 (n: 53): DNs + MT	Upper + lower trapezius Levator scapulae	Tt: 1 ss/wk (2 wk) 55 min (5 min DN + 50 MT) DN: 10s up & down Needle: 0.32 × 40 mm Follow-up: baseline, postintervention, and 1 m	NPRS NDI (*B* + 1 m) PPT ROM AE	G1 and G2 improved NPRS, NDI and PPT all follow-ups G1 > G2 in all outcomes AE: no
Garcia-De-Miguel et al. [28]	*N*: 44 (>18 y)	G1 (n: 22): DN G2 (n: 22): DN + PENS	Levator scapulae	Tt: 1 ss 55 min (5 min DN + 50 MT) DN: 8–10 needle insertions Needle: 0.25 × 25 mm Follow-up: baseline, postintervention, 48 h, and 1 wk	VAS NDI (1 wk) PPT ROM Strength	G1 and G2 improved in all outcomes G2 > G1 on NDI and PPT for all follow-ups
Leon-Hernandez et al. [29]	*N*: 62 (18–48 y)	G1 (n: 31): DN G2 (n: 31): DN + PENS	Upper trapezius	Tt: 1 ss DN: 2 LTR Needle: 0.32 × 40 mm Follow-up: baseline, postintervention, 24 h, 48 h, and 72 h	VAS (postDN soreness [24,48, 72 h] & pain [post, 72 h]) NDI (post, 72 h) PPT (post, 72 h) ROM (post, 72 h)	G1 and G2 on pain, soreness, NDI, ROM extension & lateral flexions in all follow-ups G2 > G1 on pain and PPT in postintervention. Not differences between groups for other outcomes

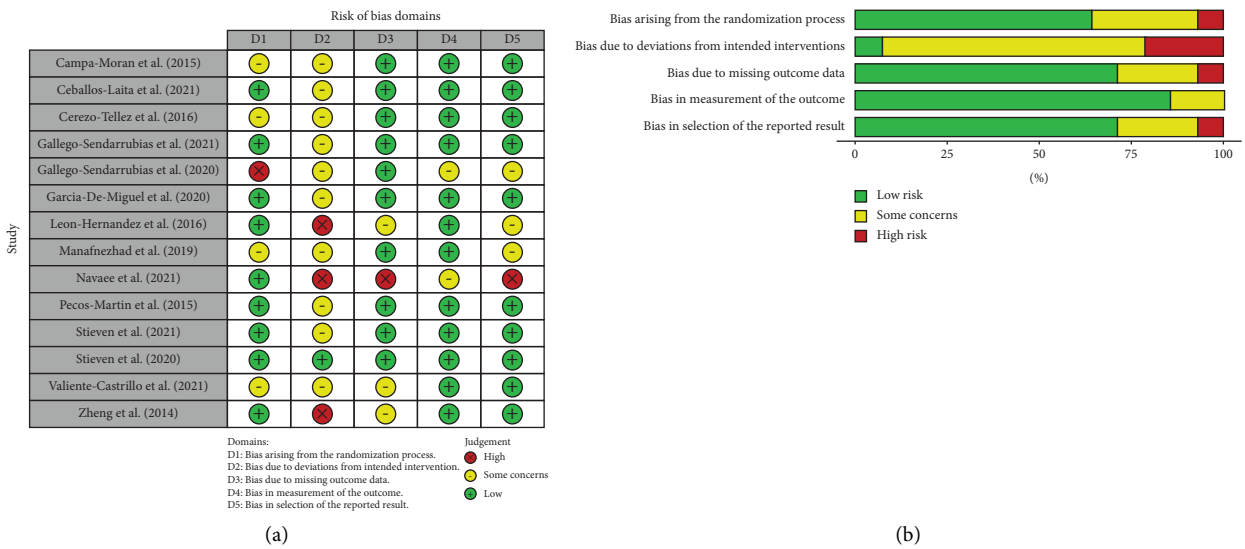
Table 1: Continued.

Study	*N* (age)	Intervention	Muscles involves	Dosage and follow-up	Outcomes	Results
Manafnezhad et al. [30]	*N*: 72 (>18 y)	G1 (n: 36): DN G2 (n: 36): ESWT	Upper trapezius	Tt: 1 ss/wk (3 wk) DN: 1-2 LTRs Needle: 0.32 × 40 mm Follow-up: baseline, 1 wk	NPRS NDI PPT	G1 and G2 improved in all outcomes G1 > G2 in NDI
Navaee et al. [31]	*N*: 40 (18–35 y)	G1 (n: 20): DN G2 (n: 20): stretch	Upper trapezius	Tt: 2 ss/wk (3 wk) DN: until LTRs finished Needle: 0.3 × 50 mm Follow-up: baseline and 1 wk	VAS PPT	G1 and G2 improved in all outcomes and follow-ups G1 > G2
Pecos-Martin et al. [32]	N:72	G1 (n: 36): DN G2 (n: 36): control (1.5 cm of TrP)	Lower trapezius	Tt: 1 ss DN: 8–10 needle insertions Needle: 0.25 × 25 mm Follow-up: baseline, postintervention, 1 wk, and 1 m	VAS NPQ PPT	G1 improved in all outcomes and follow-ups G1 > G2
Stieven et al. [33]	*N*: 44 (18–50 y)	G1(n: 15): DN G2 (n: 14): MR G3 (n: 15): DNs	Upper trapezius	Tt: 1 ss DN: 3 LTR Needle: 0.25 × 30 mm Follow-up: baseline, immediately postintervention, and 10 min after	NPRS PPT NDI (B) FABQ (B) AE	G1 + G2 improved in all outcomes and follow-ups. Not G3 G1/G2 > G3 G1 > G2 AE: no
Stieven et al. [34]	*N*: 116 (18–65 y)	G1 (n: 58): DN + PT G2 (n: 58): PT	Upper and middle trapezius Cervical multifidi Splenius cervicis Levator scapulae	Tt: 4-6 ss/4 wk 40 min DN: 6 LTR Needle: 0.25 × 40 mm Follow-up: baseline, 1 m, 3 m, and 6 m	NPRS NDI GPES PSQI PCS PSEQ AE	G1 > G2 all outcomes at 1 m. Not for 3 m and 6 m AE: mild
Valiente-Castrillo et al. [35]	*N*: 62 (18–65 y)	G1 (n:21): DN G2 (n:21): DN + education G3 (n:20): usual care (electrotherapy)	Upper trapezius Cervical multifidi Splenius cervicis Levator scapulae	G1: 3 ss/wk (2 wk) G2: G1 + 3 ss education G3: 5 ss/wk (2 wk) DN: 5 LTR Needle: 0.32 × 40 mm Follow-up: baseline, postintervention, 1 m, and 3 m	VAS NDI TSK PCS FPQ SOPA PASS-20 AE	G1 and G2 improved et al. follow-ups. G3 only postintervention G1/G2 > G3 for all follow-ups G2 > G1 for postintervention AE: no
Zheng et al. [36]	*N*: 169 (>18 y)	G1 (n: 81): DN (UG) G2 (n: 88): MNS (UG)	Posterior to the articular process of C6	Tt: 1 ss/wk (3 wk) DN: 2-3 insertions Needle: x Follow-up: baseline, 3 m, and 6 m	VAS NDI SF-36 AE	All outcome improved for both groups et al. follow-ups G2 > G1 for all outcomes and follow-ups AE: mild

*AE: adverse event; DN: dry needling; DNs: sham dry needling; ESWT: extracorporeal shock wave therapy; FABQ: fear-avoidance beliefs questionnaire; FPQ: fear pain questionnaire; GROC: global rating of change scale; GPES: global perceived effect scale; HADS: hospital anxiety and depression scale; LTR: local twitch response; MT: manual therapy; m: month; MR: myofascial release; NPRS: numeric pain rating scale; NPQ: neck pain questionnaire; NDI: neck disability index; PPT: pressure pain threshold; PCS: pain catastrophizing scale; PSQI: Pittsburgh sleep quality index; PSEQ: pain self-efficacy questionnaire; PASS-20: 20-point pain anxiety symptoms scale; PENS: percutaneous electrical nerve stimulation; PT: physical therapy; ROM: range of motion; SF-36: health status scale; ss: sessions; SOPA: survey of pain attitudes; TSK: Tampa scale of Kinesiophobia; TENS: transcutaneous electrical nerve stimulation; Tt: treatment; TrP: trigger point; US: ultrasound; VAS: visual analogue scale; wk: week; y: years.

Table 2: PEDro scale.

Study	1	2	3	4	5	6	7	8	9	10	11	Total	Quality
Campa-Moran et al. (2015)	■	■		■			■	■		■	■	7	High
Ceballos-Laita et al. (2021)	■	■	■	■	■		■	■		■	■	9	High
Cerezo-Tellez et al. (2016)	■	■		■			■	■		■	■	7	High
Gallego-Sendarrubias et al. (2021)	■	■	■	■	■		■	■			■	8	High
Gallego-Sendarrubias et al. (2020)	■	■	■	■	■			■			■	7	High
Garcia-De-Miguel et al. (2020)	■	■	■	■			■	■		■	■	8	High
Leon-Hernandez et al. (2016)	■	■	■	■			■	■		■	■	8	High
Manafnezhad et al. (2019)	■	■		■			■	■		■	■	7	High
Navaee et al. (2021)	■	■	■	■			■					5	Moderate
Pecos-Martin et al. (2015)	■	■	■	■	■		■	■		■	■	9	High
Stieven et al. (2021)	■	■	■	■			■	■	■	■	■	9	High
Stieven et al. (2020)	■	■	■	■			■	■	■	■	■	9	High
Valiente-Castrillo et al. (2021)	■	■	■	■			■	■	■	■	■	9	High
Zheng et al. (2014)	■	■	■	■			■	■		■	■	8	High
Average												8/11	High



(a) (b)

Figure 2: (a) Summary of risk of bias 2.0. (b) Risk of bias 2.0. graph.

Study	Intervention Mean	SD	Total	Control Mean	SD	Total	Weight (%)	Std. Mean Difference IV, Random, 95% CI
Campa-Moran et al	20.50	23.86	12	15.90	23.86	12	5.4	0.19 [-0.62; 0.99]
Ceballos-Laita	-1.80	0.92	7	-0.60	0.99	7	4.4	-1.17 [-2.34; -0.01]
Ceballos-Laita et al	1.10	0.99	7	2.10	0.85	7	4.5	-1.01 [-2.15; 0.12]
Cerezo-Tellez et al	-4.80	2.00	64	-1.57	2.00	64	6.5	-1.61 [-2.01; -1.21]
Gallego-Sendarrubias et al	-25.00	10.20	25	3.50	12.76	25	5.6	-2.43 [-3.17; -1.69]
Gallego-Sendarrubias et al. (2)	-3.41	2.13	47	-1.67	2.48	53	6.5	-0.74 [-1.15; -0.34]
García-de-Miguel et al	2.76	1.55	22	2.85	1.29	22	6.1	-0.06 [-0.65; 0.53]
León-Hernández et al	-2.50	5.12	31	-3.00	11.71	31	6.3	0.05 [-0.44; 0.55]
Valiente-Castrillo	-3.41	2.64	20	-4.35	2.12	20	6.0	0.38 [-0.24; 1.01]
Valiente-Castrillo et al	-3.41	2.64	20	-1.41	2.79	20	5.9	-0.72 [-1.36; -0.08]
Navaee et al	-3.29	1.61	15	-1.91	2.01	15	5.6	-0.74 [-1.48; 0.01]
Pecos-Martín et al	-2.70	2.34	36	-0.30	2.26	36	6.3	-1.03 [-1.52; -0.54]
Zheng et al	-2.90	2.34	73	-3.50	2.00	73	6.7	0.27 [-0.05; 0.60]
Manafnezhad et al	-1.09	3.27	35	-1.78	2.68	35	6.4	0.23 [-0.24; 0.70]
Stieven et al	-4.14	1.08	58	-2.81	1.62	58	6.6	-0.96 [-1.34; -0.57]
Stieven et al (1)	0.92	0.87	15	0.34	0.69	14	5.6	0.72 [-0.04; 1.47]
Stieven et al (2)	0.92	0.87	15	0.11	1.22	15	5.6	0.74 [-0.00; 1.49]|
Total (95% CI)			*502*			*507*	*100.0*	*-0.45 [-0.90; -0.01]*
Prediction interval								[-2.14;1.24]

Heterogeneity: tau² = 0.5857; chi² = 137.86, *df* = 16 ($P < 0.01$); I^2= 88%

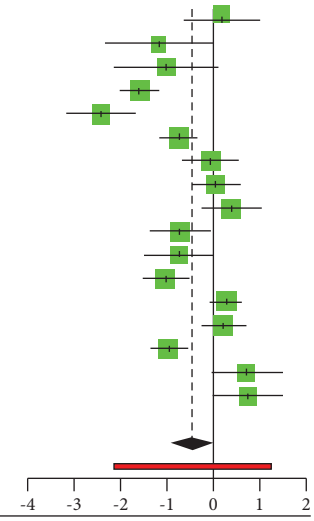


Figure 3: Pain analysis.

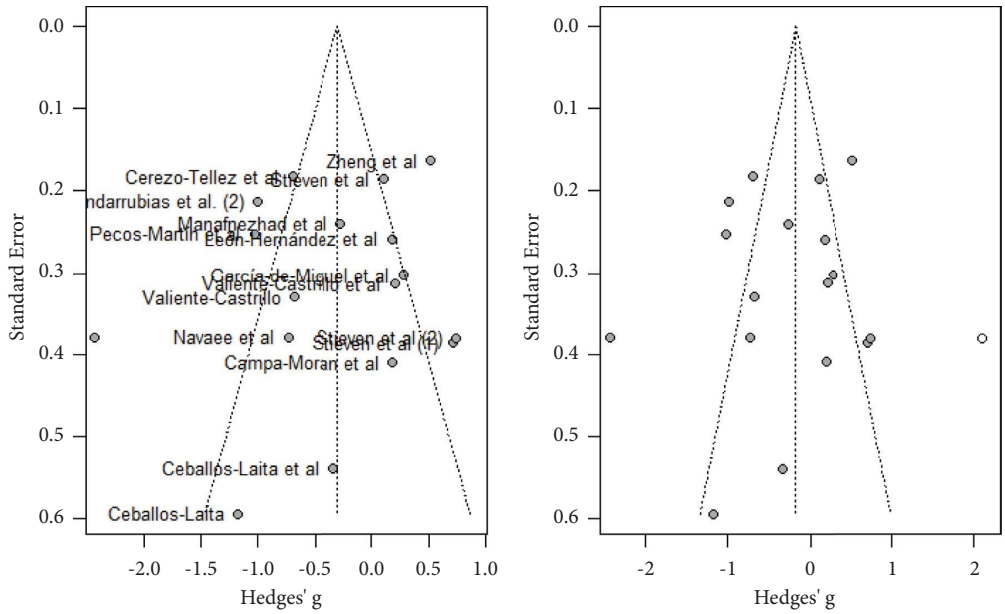


Figure 4: Pain analysis funnel plot.

7. Function Meta-Analysis

As shown in Figure 9, DN was not statistically significant associated with improvements in function (MD: −0.20; 95% CI: −0.51; 0.22). Moreover, heterogeneity was very high for the overall of studies ($I^2 = 84\%$; $p < 0.01$).

As shown in Figure 10, the majority of studies did not follow a symmetrical distribution. So, it could be that the studies included in the analysis had publication or information bias. The effect size was high for the majority of studies.

7.1. Subgroup Sex (Function). A subgroup analysis by sex was carried out. DN was not significantly associated with improvements on function in studies in which the population was mainly females (MD: −1.701; 95% CI: −3.492; 6.894). Moreover, no significant effects on function were observed in the studies including mainly males (MD: −3.875; 95% CI: −8.058; 0.308). Heterogeneity was high for studies including mainly females ($I^2 = 86.07\%$) and for studies including mainly males ($I^2 = 78.42\%$).

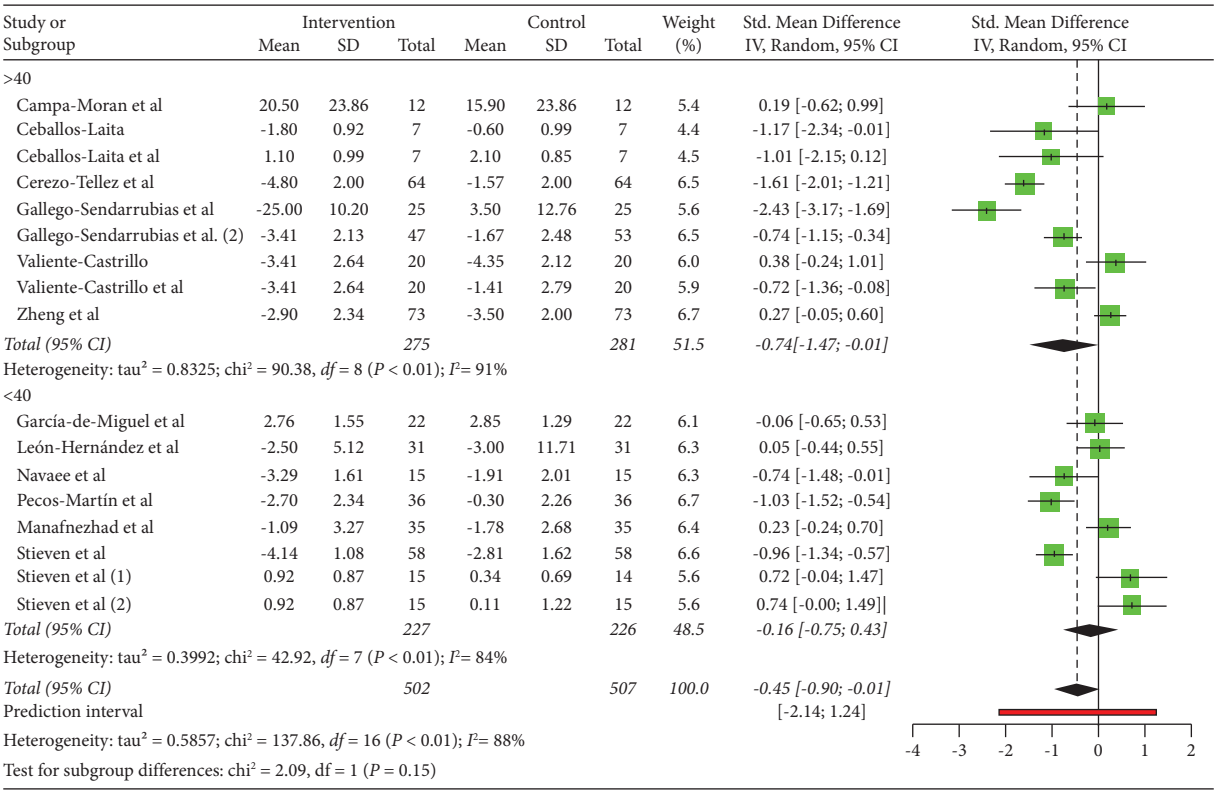


Figure 5: Pain subgroup analysis by mean age (<40 years old, >40 years old).

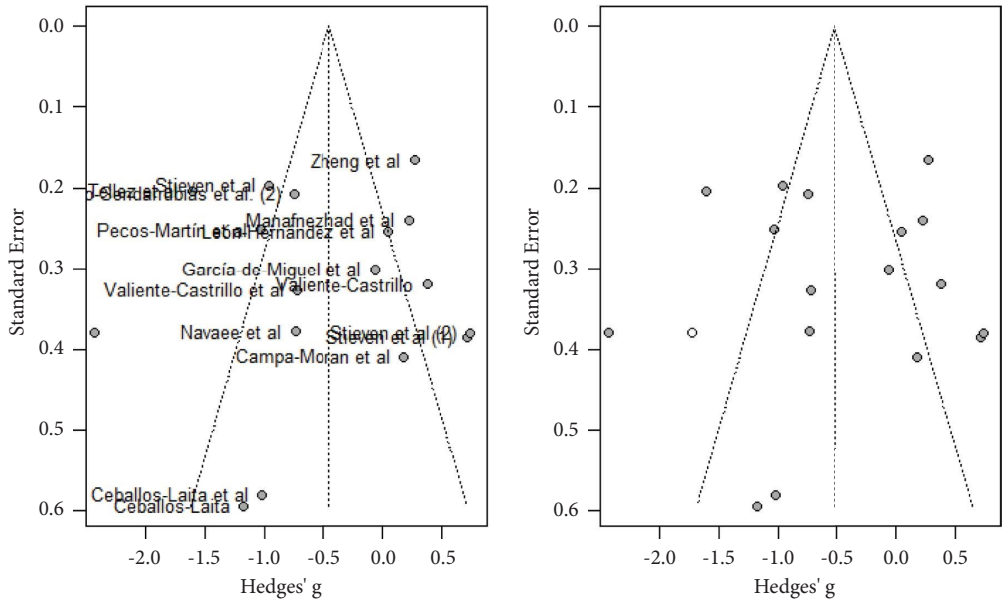


Figure 6: Pain subgroup analysis by mean age (<40 years old, >40 years old). Funnels plot.

7.2. Subgroup Age (Function). Regarding the subgroup analysis by age, DN was not significantly associated with improvements on function in studies where the mean age was over 40 years old (MD: −2.299; 95% CI: −6.611; 2.013). Additionally, no significant effects on function were observed in the studies where the mean age was under 40 years old (MD: −2.897; 95% CI: −10.611; 4.817). Heterogeneity was high for studies in which mean age was over 40 years old ($I^2 = 85.53\%$) and for those with a mean age under 40 years old ($I^2 = 85.14\%$).

Study	Intervention Mean	SD	Total	Control Mean	SD	Total	Weight (%)	Std. Mean Difference IV, Random, 95% CI
Campa-Moran et al	20.50	23.86	12	15.90	23.86	12	16.5	0.19 [-0.62; 0.99]
Ceballos-Laita	-1.80	0.92	7	-0.60	0.99	7	13.1	-1.17 [-2.34; -0.01]
Ceballos-Laita et al	1.10	0.99	7	2.10	0.85	7	13.3	-1.01 [-2.15; 0.12]
Cerezo-Tellez et al	-4.80	2.00	64	-1.57	2.00	64	20.0	-1.61 [-2.01; -1.21]
Gallego-Sendarrubias et al	-25.00	10.20	25	3.50	12.76	25	17.1	-2.43 [-3.17; -1.69]
Gallego-Sendarrubias et al. (2)	-3.41	2.13	47	-1.67	2.48	53	20.0	-0.74 [-1.15; -0.34]
Total (95% CI)			*162*			*168*	*100.0*	*-1.14 [-2.07; -0.22]*
Prediction interval								[3.40; 1.11]

Heterogeneity: tau² = 0.5436; chi² = 30.85, *df* = 5 (*P* < 0.01); I^2 = 84%

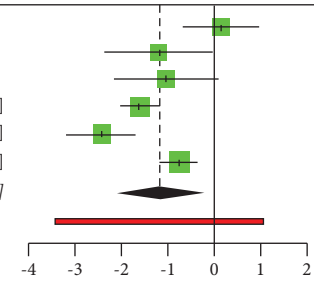


Figure 7: Pain subgroup analysis by intervention (DN + PT vs PT).

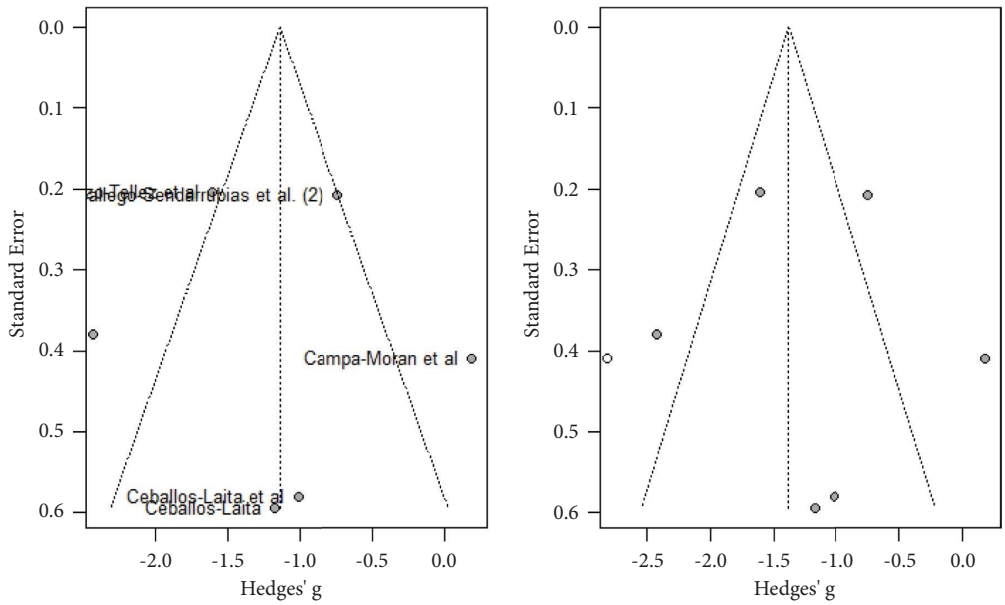


Figure 8: Pain subgroup analysis by intervention (DN + PT vs PT). Funnels plot.

Study	Intervention Mean	SD	Total	Control Mean	SD	Total	Weight (%)	Std. Mean Difference IV, Random, 95% CI
Ceballos-Laita et al	-1.80	2.82	7	-0.80	2.77	7	7.3	-0.34 [-1.39; 0.72]
Cerezo-Tellez et al	-17.30	16.48	64	-6.47	14.16	64	12.6	-0.70 [-1.06; -0.34]
Gallego-Sendarrubias et al. (2)	-24.34	11.94	47	-12.17	12.22	53	12.2	-1.00 [-1.42; 0.87]
García-de-Miguel et al	-6.53	10.44	22	-9.82	12.74	22	10.8	0.28 [-0.32; 0.87]
León-Hernández et al	-3.00	10.00	31	-5.00	11.68	29	11.5	0.18 [-0.33; 0.69]
Valiente-Castrillo	-8.23	7.72	20	-2.36	9.15	19	10.4	-0.68 [-1.33; -0.03]
Valiente-Castrillo et al	-6.60	7.65	20	-8.23	7.72	21	10.6	0.21 [-0.41; 0.82]
Zheng et al	-7.20	7.03	73	-11.50	9.09	82	12.9	0.52 [0.20; 0.84]
Manafnezhad et al	-12.95	13.51	35	-8.92	15.79	35	11.8	-0.27 [-0.74; 0.20]
Total (95% CI)			*319*			*332*	*100.0*	*-0.20 [-0.61; 0.22]*
Prediction interval								[-1.61; 1.22]

Heterogeneity: tau² = 0.3157; chi² = 49.69, *df* = 8 (*P* < 0.01); I^2 = 84%

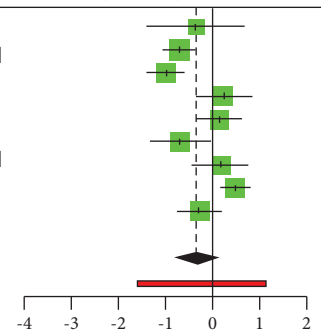


Figure 9: Function analysis.

7.3. Subgroup Interventions (Function). As shown in Figure 11, DN combined with physical therapy (PT) significantly improved function compared to physical therapy alone (MD: −0.80; 95% CI: −1.36; −0.23). Moreover, no significant differences were shown for DN alone compared to DN + PT (MD: 1.785; 95% CI: −1.807; 5.376) and DN compared to other interventions (MD: 1.922; 95% CI: −2.837; 6.682). However, heterogeneity was high for all the studies (I^2 = 80.08%).

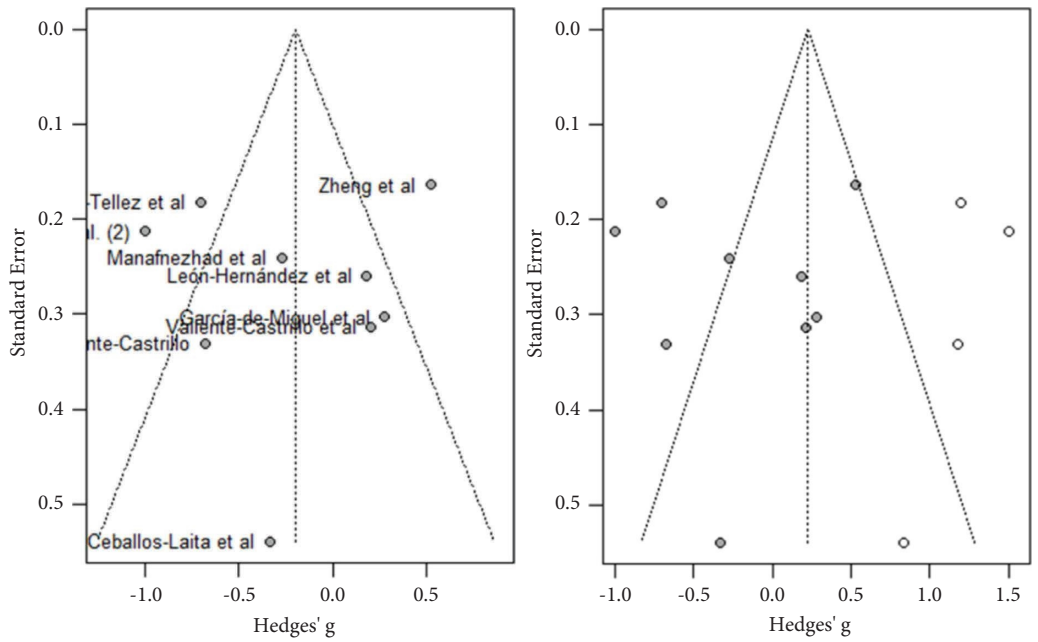


Figure 10: Function analysis funnels plot.

Study	Intervention Mean	SD	Total	Control Mean	SD	Total	Weight (%)	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI
Ceballos-Laita et al	1.80	2.82	7	-0.80	2.77	7	6.2	-0.34 [-1.39; 0.72]	
Cerezo-Tellez et al	-17.30	16.48	64	-6.47	14.16	64	54.1	-0.70 [-1.06; -0.34]	
Gallego-Sendarrubias et al. (2)	-24.34	11.94	47	-12.17	12.22	53	39.7	-1.00 [-1.42; -0.58]	
Total (95% CI)			*118*			*124*	*100.0*	*-0.80 [-1.36; -0.23]*	
Prediction interval								[-2.50; 0.91]	
Heterogeneity: $tau^2 = 0$; $chi^2 = 1.91$, $df = 2$ ($P < 0.38$); $I^2 = 0\%$									

Figure 11: Function subgroup analysis by intervention (DN + PT vs PT).

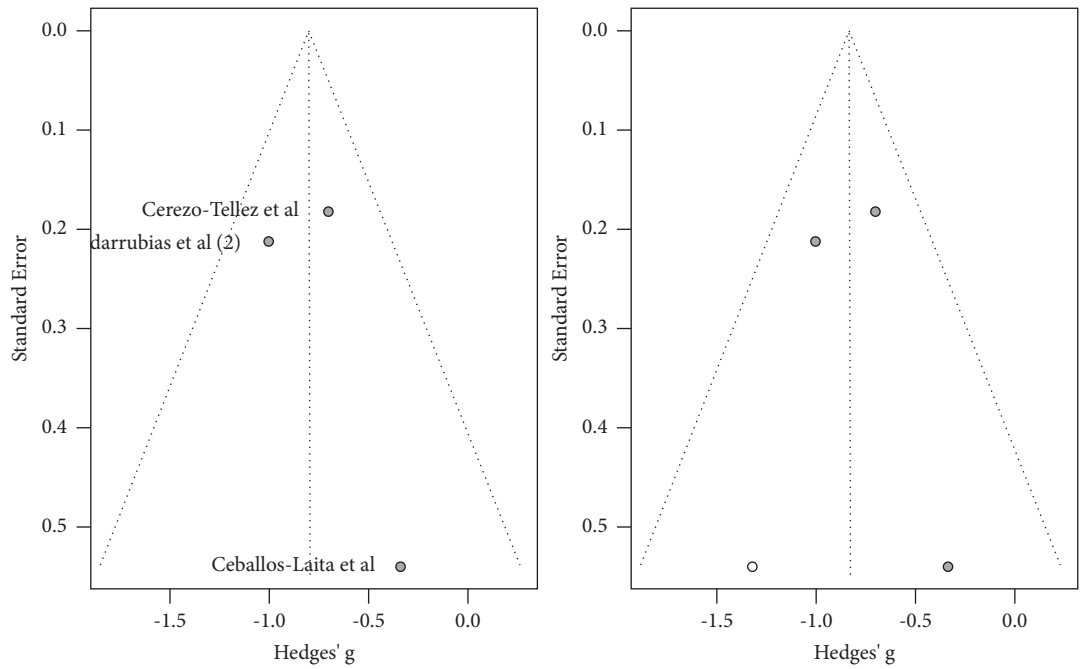


Figure 12: Function subgroup analysis by intervention (DN + PT vs PT). Funnels plot.

Heterogeneity was moderate for studies in which DN was compared to other interventions ($I^2 = 58.29\%$). Moreover, a low heterogeneity was found for subgroups DN vs DN + PT ($I^2 = 0\%$) and for subgroups DN + PT vs PT ($I^2 = 0\%$).

Finally, as shown in Figure 12, all studies followed a symmetric distribution. Nevertheless, the studies included in the analysis probably had publication bias or were simply devoted to the analysis. Moreover, the effect sizes of two studies were high.

8. Discussion

The objective of this meta-analysis was to compare the effectiveness of DN on pain and function, combined or alone, in patients with chronic neck pain at short-, mid-, and long-term intervals. We found high to moderate evidence suggesting a positive effect of including DN into physical therapy treatment for improving pain intensity and functional disability at short term when compared with other techniques such as US, MT, DN + PT, or stretching alone. In addition, this meta-analysis showed that DN alone improved pain intensity and functional capacity at mid and long term but there were not better results if DN was compared to stretching, MT and exercise at mid and long term. A recent meta-analysis from Fernández-De-Las-Peñas et al. [37] showed the effectiveness of DN techniques to treat neck pain, regardless of chronicity, when compared to other techniques. However, our meta-analysis also showed this effect in the case of chronic neck pain, providing evidence about its effectiveness depending on age and sex.

Liu et al. [38] researched the effects of DN alone at short- and mid-term intervals, showing that wet needling was more effective than DN. However, our study showed differences supporting positive changes at pain intensity and function when performing DN. The presence of studies showing that wet needling (WN) was more effective than DN makes WN an alternative to DN to be considered in future studies. Moderate to low evidence was obtained about the efficacy of DN for pain and function, according to Navarro-Santana et al. [39]. However, positive results on these variables after DN techniques were observed at short term (2–12 weeks) in our meta-analysis. Our meta-analysis showed improvements in pain and function, in contrast with Liu et al. [38], who only showed improvements in pain intensity. The samples included in our meta-analysis differ greatly from that of Liu et al. [38], which analysed a sample of poststroke subjects. The sample from our study was joined by subjects with chronic neck pain, providing updated evidence of DN in chronic neck pain.

Authors such as Navarro-Santana et al. [39] and Cagnie et al. [40] only reported short- and mid-term effects with DN, whereas our meta-analysis also showed that DN was effective in the long term for pain and function. In addition, Navarro-Santana et al. [39] only established a comparison between isolated DN versus other therapies, while our study showed the comparison of DN (alone or combined with other techniques) versus other therapies. Finally, we would like to highlight the homogeneity of the professional performing DN in our study given that 100% of the cases were performed by physiotherapists, in contrast to the 50% reported by Navarro-Santana et al. [39].

Similarly to Liu et al. [38], our study verified that DN is effective for neck pain, at least at short term, for patients with chronic neck pain. Further studies are required to extrapolate these positive effects in the mid and long term. Unlike Liu et al., our study showed that combining DN with other techniques showed significant effects for treating pain and dysfunction in patients with chronic neck pain. These findings could be related to practical guideline recommendations [41] for multimodal treatment for patients with chronic pain.

All studies included in our meta-analysis showed long-lasting effects of DN, either alone or combined with other therapies. This is contrary to Cagnie et al. [40], who found this finding in only one of the studies [33]. Moreover, most of the studies reviewed in our meta-analysis had a dosage of 1 to 3 sessions of DN for 2 weeks (at most). However, Cagnie et al. [40] applied 1 to 6 sessions of DN for 10 weeks. This dosage variability demonstrates that the exact dosage needs to be further studied to obtain benefits with DN.

Our results should be analysed, taking into consideration the strengths and weaknesses of this meta-analysis. The strengths include a thorough and updated search of the scientific literature on the subject that it has been carried out with methodological rigour, that it covers randomised clinical trials of high methodological quality, and that the muscles involved are detailed in almost all the studies. Among the limitations, the DN procedure was not described homogenously throughout the studies, and patient blinding was not assessed and/or achieved in most of the studies, being one of the most common biases in physiotherapy studies. DN should be applied with a diagnosis of MTPs. However, some of the studies analysed in our meta-analysis did not consider the diagnosis of a hyperirritable area in a skeletal muscle associated with a hypersensitive palpable nodule located in a taut band of muscle fibre [7] in their inclusion criteria. It would be interesting to take this diagnosis into account for future studies of chronic neck pain patients. Moreover, the choice of studies published after 2010 as selection criteria may have influenced the inclusion of studies. This bias was mitigated by a previous search of all possible studies for inclusion, noting that those published before 2010 were not directly related to chronic neck pain. In addition, previous systematic reviews published on dry needling and neck pain included these studies. Also, the results in heterogeneity may be affected by the low number of studies, having to interpret the results carefully.

For future research, there is a lack of research about the effectiveness of DN in chronic neck pain at long term. Likewise, some standardised protocols are necessary, which may include the parameters of applying the DN technique for chronic neck pain, the definition of dosage criteria based on the type of patient, and the establishment of an adequate sham DN technique. In addition, it may be interesting to observe the effects between performing superficial and deep DN.

9. Conclusion

Our meta-analysis supports the use of dry needling to improve pain and functional capacity in patients with chronic neck pain at short- and mid-term intervals. However, at long term, the number of studies were less numerous, and their results are contradictory. Positive effects in favour of dry needling versus other therapies were found in the studies including patients with a mean age over 40 years in terms of pain, but the same did not occur for the population below 40 years, in which no positive effects were observed. In relation to the interventions, dry needling combined with physical therapy showed to be effective to decrease pain, whereas isolated dry needling did not demonstrate significant improvements in the analysed studies.

Moreover, dry needling did not show to have a different effectiveness to improve function depending on the sex and age. Finally, as for pain, dry needling combined with physical therapy was the therapy that showed the most benefits in function in the analysed studies.

Data Availability

Data of the systematic review and meta-analysis are available from the corresponding author upon request.

Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of this paper.

Supplementary Materials

Figure S1. PRISMA 2020 abstracts checklist. Figure S2. PRISMA 2020 checklist. Figure S3. PICO search strategy followed in different electronic document databases. Figure S4. Gosh plot of age in pain outcome. Figure S5. Gosh plot of intervention in pain outcome. Figure S6. Gosh plot of intervention in function outcome. (*Supplementary Materials*)

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Research Article

A Potential Objective Sign of Central Sensitization: Referred Pain Elicited by Manual Gluteus Minimus Muscle Exploration is Coincident with Pathological Autonomic Response Provoked by Noxious Stimulation

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Referred pain/sensation provoked by trigger points suits the nociplastic pain criteria. There is a debate over whether trigger points are related to a peripheral phenomenon or central sensitization (CS) processes. Referred pain is considered a possible sign of CS, which occurs probably mainly due to the abnormal activity of the immune and autonomic nervous systems. To confirm abnormal autonomic reactivity within the referred pain zone of active trigger points, a new diagnostic tool, the Skorupska Protocol® (the SP test®), was applied. The test uses noxious stimulation (10 minutes of dry needling under infrared camera control) as a diagnostic tool to confirm abnormal autonomic nervous system activity. A response to the SP test® of healthy subjects with referred pain sensations provoked by latent trigger points (LTrPs) stimulation was not explored before. The study aims at examining if LTrPs can develop an autonomic response. *Methods*. Two groups of healthy subjects, (i) gluteus minimus LTrPs with referred pain ($n = 20$) and (ii) control ($n = 27$), were examined using the SP test®. *Results*. Abnormal autonomic activity within the referred pain zone was confirmed for all analyzed LTrPs subjects. 70% of control subjects had no feature of vasodilatation and others presented minor vasomotor fluctuations. The size of vasomotor reactivity within the referred pain zone was LTrPs 11.1 + 10.96% vs. control 0.8 + 0.6% ($p < 0.05$). *Conclusions*. Noxious stimulation of latent TrPs induces abnormal autonomic nervous system activity within the referred pain zone. The observed phenomenon supports the concept of central nervous system involvement in the referred pain patomechanizm.

1. Introduction

In the last decade, a growing interest in myofascial pain syndrome (MPS), characterized by sensory, motor, and autonomic symptoms provoked by trigger points (TrPs), is observed. Importantly, some subtypes of MPS described by Travell and Simons [1, 2] (e.g., cervical, thoracic, and lumbar pain related to TrPs) were included in the 11th Revision of the International Classification of Diseases [3]. Trigger points are defined as hyperirritable painful spots within taut bands of skeletal muscles that are painful on compression, stretch, overload, or contraction of the tissue which usually

respond with referred pain that is perceived distant from the spot. Active and latent TrPs are distinguished. The active form of differentiation is based on spontaneous, recognizable pain mainly [4].

Currently, pain specialists hotly debate whether TrPs are a central or peripheral phenomenon and what are the MPS pain pathomechanisms [5]. One hypothesis states that the central sensitization (CS) processes is involved in TrPs development. This theory is supported by two phenomena, such as referred pain provoked by TrPs (secondary hyperalgesia) together with lower pressure pain thresholds within the muscle fiber affected by TrPs (primary hyperalgesia) [6–8]. The sympathetic activity depended on the referred pain presence was also demonstrated. This additionally confirms the CS involvement in TrPs development [9–11]. The other theories postulate that trigger points are just nociceptive peripheral sensation, denying their clinical importance or even questioning their existence [12]. Functional impairments of the autonomic and immune systems are indicated as a possible reason of the processes of central sensitization [13, 14]. The most commonly accepted hypothesis of TrPs development was presented by Simons [15]. The authors proposed 5-6 stages of the TrPs development. Still, they pointed out the last stage as the one which might result in development/maintenance of TrPs symptoms and induced by the autonomic nervous system (ANS) activity.

To examine abnormal autonomic activity within referred pain and possibly to confirm TrPs objectively, a new diagnostic method, the Skorupska Protocol (SP) test®, was established lately. The test is based on the observation of noxiously provoked amplified vasomotor reactivity coincident with the referred pain zone established previously by Travell and Simons [1, 2, 10, 16].

The abnormality of the ANS response-observed during the SP test® is based on the fact that, in normal conditions, the noxious stimulation of nociceptors in skeletal muscles induces only a local vasomotor reaction limited to the area of the noxious stimulation. On the contrary, the stimulation of the active TrPs within the gluteus minimus provoked distant vasomotor reactivity spreading down the lower extremities. Furthermore, according to the current knowledge about the physiology of the ANS integrative functioning, the elicitation of vasomotor reactivity in the lower extremities demands ANS activity at the level of the spinal cord and/or hypothalamus [17]. This fact further supports the hypothesis of the central nervous system's involvement in the TrPs patomechansim. The amplified vasomotor phenomenon within the thigh and calf, on the low back pain patients, confirmed by SP test®, occurred probably due to a pathological spinal reflex characteristic of TrPs exclusively, i.e., the so-called twitch response that is linked to the ANS [18]. It is worth mentioning that there is no link between vagal control/regulation and gluteal blood supply; this provides further evidence for the abnormal ANS involvement.

Still, it must be remembered that referred pain is also typical for asymptomatic, pain-free healthy subjects with latent TrPs, and it can be provoked by mechanical muscle pressure or needle irritation [19, 20]. A recent study by Ambite-Quesada et al. supports the involvement of central sensitization in referred pain from latent trigger points by applying the quantitative sensory testing technique [21]. Nevertheless, based on the assumption that referred pain is a sign of central sensitization, it is necessary to reveal if latent trigger points are likely to provoke pathological autonomic reactivity within the referred pain zone just like active trigger points.

Thus, the aim of the study was to examine referred pain from latent trigger points towards the presence of pathological autonomic reactivity among healthy subjects.

2. Material and Methods

The study was approved by the Ethics Committee of the Poznan University of Medical Sciences (resolution number 689/20) and was conducted in accordance with the Declaration of Helsinki. Before data collection, all subjects gave written informed consent to participate in the study. A detailed description of all examinations was provided to the participants who had the right to refuse the SP test® performance and withdraw from the study at any time without penalty.

2.1. Participants. Seventy-five healthy subjects were assessed for eligibility.

The inclusion criteria were as follows: (1) for LTrPs subjects: general good health condition (pain-free, without any medical diagnosis of permanent disease or surgery in the past, current fever, or infection), age between 20 and 60 (inclusive), both lower limbs present, and latent trigger points within the gluteus minimus muscle that developed the referred pain pattern due to muscle pressing; (2) for the control subjects: general good health condition, age between 20 and 60 (inclusive), both lower limbs present, and the lack of (i) latent trigger points within the gluteus minimus muscle or (ii) local or referred unrecognized pain after cross-fiber flat palpation of the gluteus minimus/medius/maximus muscle.

The key exclusion criteria were as follows: previous back surgery, spinal tumors, scoliosis, and pregnancy.

2.2. Methods. All subjects enrolled in the study were diagnosed towards latent trigger points presence by two independent therapists experienced in myofascial pain diagnosis. Then, the SP test® was performed using a thermovision touchless camera NEC-AVIO TVS-200EX (measurement error $\pm 2\%$ in the range of the temperatures between 0–100 Celsius degree) with 8–14 μm wave band, temperature resolution better than 0.080°C, sensitivity of 80 mK, and working in real time. The camera was equipped with a high-speed (60 Hz) uncooled FPA 320×240 (H × V) pixels VOx (vanadium oxide) microbolometer. For thermal images analysis, the specialist program "Thermography Studio 2007 Professional" was used.

2.2.1. Diagnostic Criteria for Trigger Point Presence. According to Travell and Simons [1, 2], the taut band (one of the essential clinical criteria) is unlikely to be palpated for the

gluteus minimus muscle because it lies deeper than the gluteus maximus and gluteus medius muscles. However, TrPs spot tenderness can be clearly localized. Additionally, the referred pain pattern is more likely to be observed when the needle encounters TrPs rather than when sustained pressure on the tender spot is applied.

Thus, the diagnosis of latent TrPs within the gluteus minimus muscle was based on Travell and Simons [2] diagnostic criteria, supported by the confirmation of referred pain elicited by deep snapping palpation through the gluteus minimus zone. Next, healthy subjects were rediagnosed using the new Delphi criteria for latent trigger points [22]. The criteria included: local or referred unrecognized pain occurrence, painful sensations only when palpated, the lack of reproduction of symptoms experienced by the patient, and no recognition of the symptoms previously caused by cross-fiber flat palpation [22]. All subjects who tested positive for both clinical criteria were then examined using the SP test® by the same experienced myofascial therapist who had diagnosed the patients before.

2.2.2. The SP Test® Description. A new diagnostic tool, the Skorupska Protocol®, was established to examine abnormal autonomic activity within the trigger points referred pain. The method has undergone the validation and reliability process [23]. The test allows the registration of amplified vasomotor reactivity (vasodilatation and/or vasoconstriction) in the patient's daily complaint area, coincident with referred pain from trigger points located in the tested muscle. The SP test® provides information about the following: (i) the size of the observed phenomenon expressed as a percentage of the examined part of the body; (ii) the changes in the average temperature increase within the observed phenomenon $-\Delta\overline{T}^{\circ}$; (iii) the time interval within the examination when the autonomic phenomenon occurred.

The muscle examination is based on the noxious stimulation (10 minutes of fast-in-fast-out dry needling followed by 6 minutes of further observation of the patient at rest) under infrared thermal (IRT) camera control to detect the expected referred pain zone in the examined muscle. The two SP test® phases (stimulation–10′ and observation–6′) are consistent with active dynamic thermography protocol demands [24]. To determine if noxious stimulation of the muscle provoked abnormal autonomic activity within the referred pain zone defined for the examined muscle by Travell and Simons [2], the analysis of a series of 320 thermal pictures was performed. The time interval between the consecutive thermograms was 3 seconds, and the amplified vasomotor reactivity above/under the cutoff point was recorded. The cutoff point is the smallest subarea of the highest/lowest temperature before stimulation (state at rest).

2.2.3. The Terms for the Confirmation of Abnormal Autonomic Nervous Activity Related to TrPs. Amplified vasomotor activity is confirmed if the SP test® provokes the development of a new thermal subarea above (amplified vasodilatation) or under (amplified vasoconstriction) the cutoff point within the expected referred pain zone. The second condition is that this new subarea provoked by the noxious TrPs stimulation is characterized by average temperature changes of more than 0.3°C, compared to the average temperature of the subarea defined as the cutoff. To calculate the size of the autonomic phenomenon and $\Delta\overline{T}^{\circ}$ changes, the automated segmentation of all collected thermograms towards the presence of specific subareas above/under the cutoff was performed by MATLAB. Based on the occurrence of the new thermal subarea above/under the cutoff, it is possible to examine if the noxious stimulation of given TrPs provokes amplified vasomotor reactivity within the referred pain zone.

2.2.4. A Short Description of the SP Test®

(1) Trigger points examination according to palpatory diagnostic criteria.

(2) Examination according to a typical IRT protocol to evaluate if a patient additionally presents features of the neuropathic pain pathomechanism (possible mixed pain syndrome), i.e., side-to-side comparison under infrared thermal camera control to examine the pain region toward a temperature decrease of more than 0.5°C.

(3) The SP test®, i.e., the IRT-controlled examination of referred pain from the analyzed muscle:

  (a) Noxious, nociceptive muscle stimulation under infrared thermal camera control of the area with expected muscle-referred pain (10 minutes), where noxious stimulation is fast-in-fast-out dry needling of TrPs or two areas that were the most tender to pressure within the examined muscle

  (b) Poststimulation resting phase, i.e., further thermal observation of the patient at rest (6 minutes)

(4) MATLAB analysis of the collected data to calculate two SP test® parameters: (i) the size of the observed vasomotor phenomenon (AURP cutoff) and (ii) the average temperature increase within the observed phenomenon ($\Delta\overline{T}^{\circ}$).

(5) The results are based on the segmentation of each thermogram and the calculation of both parameters for the observed anatomical body parts. The first parameter, called autonomic referred pain (AURP cutoff), is the size of the subarea with vasomotor reactivity expressed as a percentage of the observed anatomical area. This parameter reflects a limited subarea, whose size is defined by a region with a temperature that is not registered for the patient before the stimulation (cutoff). The second parameter is the exact value of the average temperature changes ($\Delta\overline{T}^{\circ}$) within the observed phenomenon.

(6) Final statistical analysis of SP test® results and confirmations of the autonomic phenomenon measured every 3 seconds of the procedure.

An illustration of the SP test® protocol and an example of the test results are shown in Figure 1.

2.2.5. MATLAB Protocol Development. A detailed protocol description, the method's validation, reliability, and the MATLAB procedure established for the SP test® were presented previously [10, 16, 23]. The procedure for the calculation of the final the SP test® results is additionally presented in Figure 2.

In the first step, the region of interest (ROI) is determined for every subject based on the initial thermogram and a manually created ROI mask for the thigh and calf. A representative ROI mask is depicted in Figure 3. The masks were created by hand and further used during the automatic procedure applied for ROI detection. In the next step, all gathered data underwent the cleaning procedure, where outliers and faulty thermograms were deselected from the final data set.

Based on the final data set of AURP cutoff and $\Delta\overline{T}^{\circ}$ values, the final results of the SP test® were calculated. For each thermogram, the AURP cut-off value was calculated as a percentage of the LEG surface with a temperature greater than the maximum temperature registered for the subject before the stimulation and the $\Delta\overline{T}^{\circ}$ value was calculated as a change in the average temperature. The first image registered before the stimulation for the subject at rest was used as a reference point for both parameters.

In the final step, the SP test® results were provided. To confirm autonomic phenomenon occurrence (the SP test® positive results)–the size of the possible amplified vasomotor reactivity was calculated for each thermogram based on the confirmation of two SP test® parameters: (i) AURP cutoff occurrence within the observed area, and (ii) $\Delta\overline{T}^{\circ}$ value greater than 0.3°C.

2.3. Statistical Analysis. For an exact test at a significance level of 0.05 with a beta power of 0.95, the lowest possible sample size is $n = 19$. Exact two-tailed Mann–Whitney U tests with corrected ties were performed to assess the differences between the gluteus minimus LTrPs patients ($n = 20$) and healthy controls ($n = 27$). The tests were applied to compare the final SP test® results between the aforementioned groups and additionally for both SP test® parameters (AURP cutoff and $\Delta\overline{T}^{\circ}$) separately. To check the significance of the p values, a post hoc Dunn test was performed. Due to the multiple comparison problem, the aforementioned test was corrected using the Holm–Sidak procedure. The Dunn test was prepared using the Dunn. test package in *R*. All values, figures, and tables in the text are expressed as the means ± standard deviations (SD) or as quartiles with the median. The significance level was set for all tests at $p < 0.05$. To obtain relevant sample size G ∗ Power 3.1.9.7 calculator was used. The effect size was fixed at the 0.35 level. Statistical analysis was performed using IBM SPSS Statistics version 26 and MATLAB version R2021.

3. Results

3.1. Subjects Examined by the SP Test®. Twenty-five of the subjects assessed for the SP test® eligibility were excluded: seven ($n = 7$) declined to participate and eighteen ($n = 18$) did not meet the inclusion criteria. Twenty subjects with latent gluteus minimus trigger points (LTrPs) ($n = 20$) and thirty healthy subjects with no gluteus minimus trigger points (control) ($n = 30$) were included in the study. During the SP test®, three subjects ($n = 3$) from the control group reported referred pain sensations in the referred pain zone typical for the gluteus minimus muscle. Thus, these three subjects were excluded and the control group consisted of twenty-seven healthy subjects ($n = 27$).

3.2. General Results of the SP Test® Examination. Amplified vasodilatation (necessary for a positive results of the SP test®) was confirmed for the LTrPs subjects exclusively. As many as 70% of the control group showed no vasomotor reactivity. The remaining 30% of the control subject ($n = 9$) presented small temperature fluctuations. The size of amplified vasodilatation in the LTrPs group was significantly bigger compared to the control subjects who presented small vasomotor reactivity ($p < 0.05$; Mann–Whitney U test). The results obtained at two measurement points of the test, i.e., (i) the end of the noxious stimulation and (ii) the end of the poststimulation observation phase of the test and are shown in Table 1.

A key characteristic of the observed autonomic phenomenon among SP test® positive subjects was as follows: (i) the LTrPs subjects presented its further development after the end of the noxious stimulation with the maximum percentage size of amplified vasodilatation reached at $15'43''$ (observation phase of the test); (ii) amplified vasodilatation seen in the LTrPs subjects lasted from $1'00'$ to $16'00''$ (93.8% of the test duration) ($p < 0.05$). The MATLAB trends that present the size of the vasomotor response to the SP test® measured every three seconds are shown in Figure 4.

3.3. Results of the SP Test® Examination Depending on the Anatomical Part of the Leg. All LTrPs subjects (100%; $n = 20$) developed a response in the thigh, and some of them additionally presented amplified phenomenon in the calf (20%; $n = 4$). For the control subjects ($n = 9$) who presented vasomotor reactivity, a series of small hot spots was observed in the thigh ($n = 9$) and calf ($n = 7$). Due to the small number of subjects presenting a vasomotor response on the calf, the statistical analysis of the results characteristic of this group was not possible.

The SP test® results for the thigh were as follows: (i) at the end of the noxious stimulation ($10'$ of the SP test®): LTrPs median 8.7 (0.5, 35.8), 10.1 ± 8.98% vs. control median 1.0 (0.1, 6.6), 2.3 ± 2.37%, and (ii) at the end of the poststimulation observation phase ($16'$ of the SP test®): LTrPs median 13.3 (0.07,45.59), 16.47 ± 15.8% vs. control median 2.4 (0.3, 8.3), 3.2 ± 2.8%.

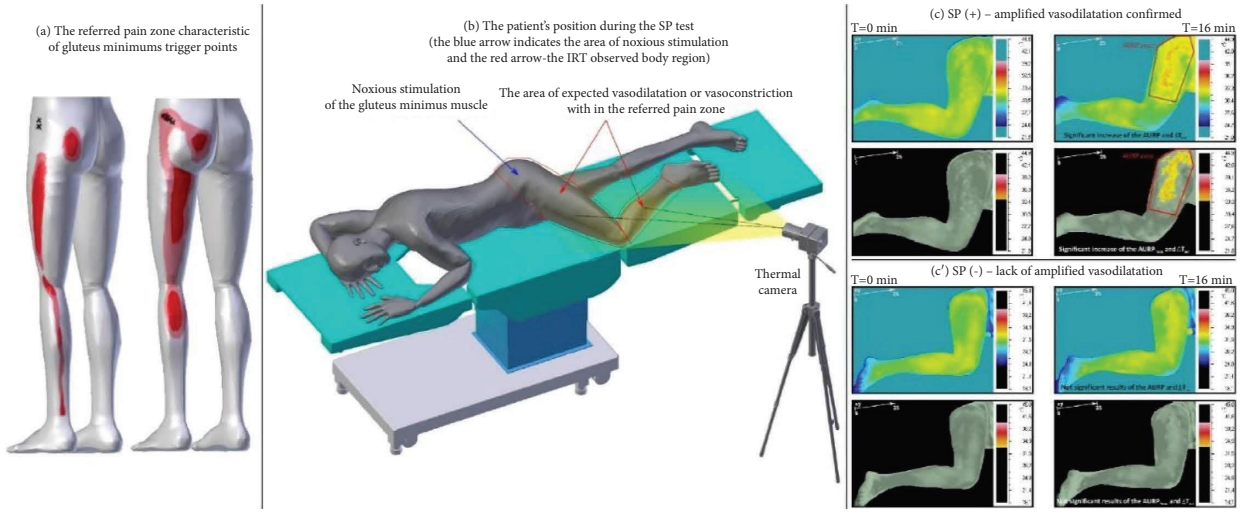


Figure 1: An illustration of the SP test® applied to latent trigger points of healthy subjects: (a) the referred pain zone characteristic of gluteus minimus trigger points; (b) the patient's position during the SP test® (the blue arrow indicates the area of gluteus minimus noxious stimulation and the red arrow shows the body region, that is, coincident with the gluteus minimus referred pain zone, and that was observed for possible autonomic reactivity using an infrared thermal camera; (c) an example of an LTrPs patient's response to the SP test®; (c′) an example of a healthy subject's response to the SP test®.

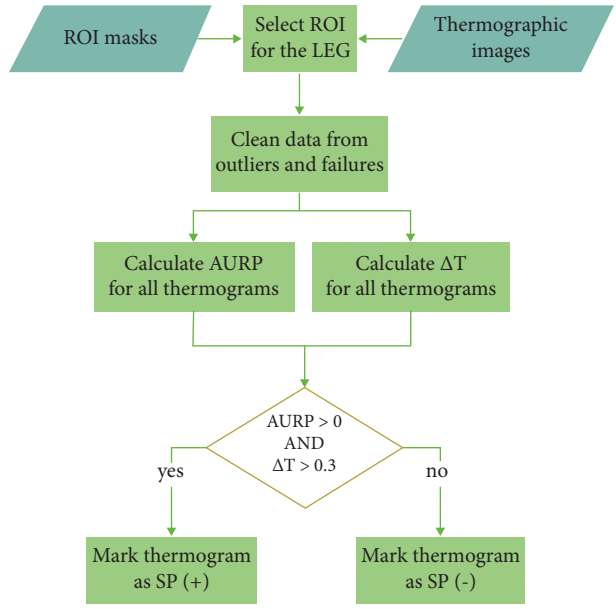


Figure 2: The procedure applied for calculating the final results of the SP test®.

3.4. The Results of the Average Temperature Changes in the Observed Lower Leg According to Conservative Medical Thermography Assessment. The average temperature changes (for LTrPs ($n = 20$) vs. control ($n = 27$)) were measured in the thigh and calf, and were calculated as one region of interest (ROI). $\Delta\overline{T}^{\circ}$ results for both examined groups were as follows: (i) at the end of the noxious stimulation (10′ of the SP test®): LTrPs ($n = 20$) median 0.6 (−0.4, 1.2), $0.5 \pm 0.47^{\circ}$C vs. control ($n = 27$) median 0.08 (−1.1, 1.07), $0.02 \pm 0.56^{\circ}$C ($p < 0.05$; Mann–Whitney U test, and (ii) at the end of the poststimulation observation phase (16′ of the SP test®): LTrPs median 0.6 (−0.02, 1.4), $0.7 \pm 0.44^{\circ}$C vs. control median 0.11 (−1.3, 0.8), $-0.12 \pm 0.61^{\circ}$C ($p < 0.05$; Mann–Whitney U test. The development of $\Delta\overline{T}^{\circ}$ observed for the examined groups every three seconds of the SP test® are shown in Figure 5.

4. Discussion

The SP test® was developed to diagnose abnormal autonomic activity within the trigger points (TrPs) referred pain zone as a possible sign of the autonomic nervous system involvement in the referred pain/sensation phenomenon [16, 23]. Until now, this reaction has been confirmed for

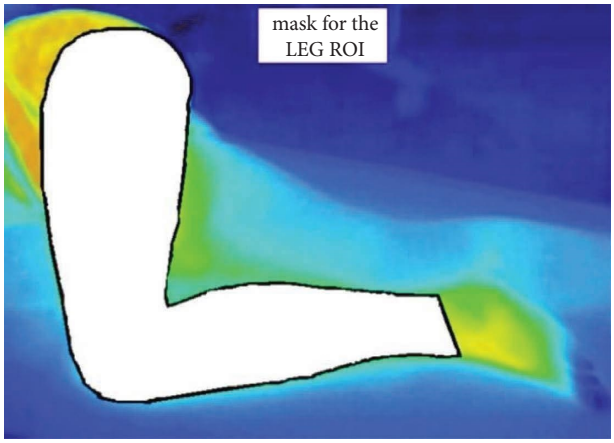


Figure 3: The mask applied for the ROI determination in a representative thermogram.

Table 1: The SP test® results of the healthy subjects depend on the latent trigger points presence.

The SP test® gluteus minimus muscle	Parameter description	The size of amplified vasodilatation, which covered lower leg (%)	
		LTrPs	Control
End of stimulation (10′ of the test)	Median (Q1, Q3)	5.8 (0.09, 24.6)*	0.6 (0.03, 3.1)*
	Average ± SD	6.9 ± 6.8*	1.1 ± 1.03*
End of observation at rest (16′ of the test)	Median (Q1, Q3)	8.4 (0.04, 31.62)*	0.5 (0.15, 1.61)*
	Average ± SD	11.1 ± 10.96*	0.8 ± 0.6*

LTrPs, latent trigger points; Q1 and Q3, first and third quartile; SD, standard deviation; * $p < 0.05$, Mann–Whitney U test.

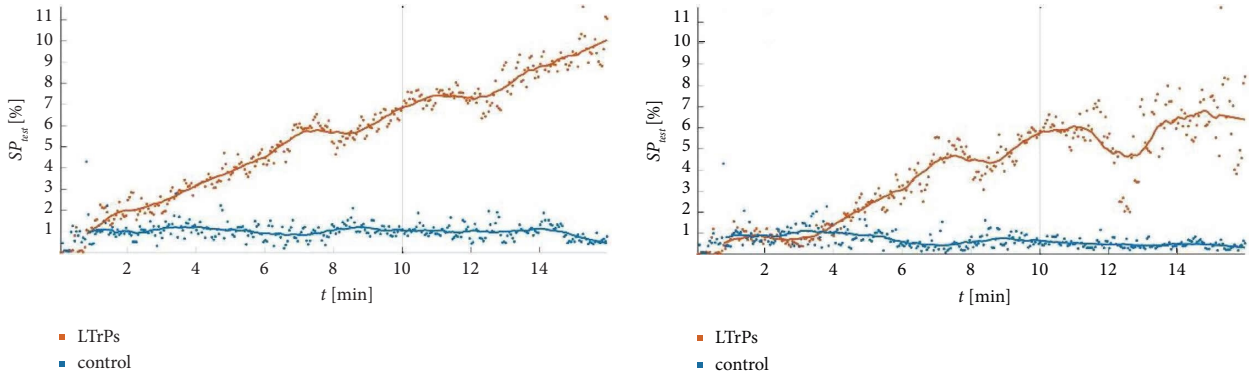
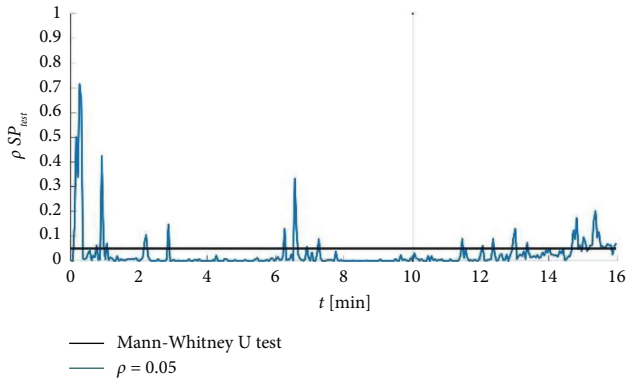
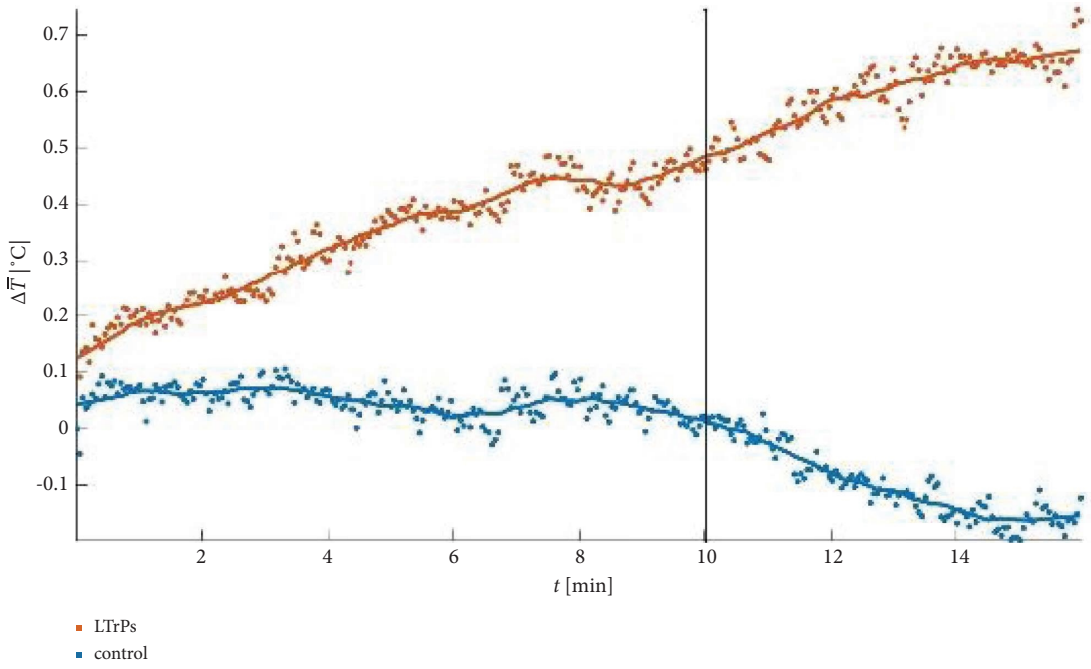


Figure 4: Continued.



(c)

Figure 4: MATLAB trends of the SP test® results depend on the latent trigger points presence and the SP test® phase: (a) median value, (b) average value, and (c) Mann–Whitney U test results. The LTrPs subjects presented abnormal autonomic activity that was confirmed by amplified vasodilatation. The MATLAB trends showed the development of the percentage size of amplified vasodilatation spreading in the lower leg in time. The significant difference between both groups stabilized around $2'$ of the noxious stimulation, but in $4'$ the size of the amplified vasodilatation had a tendency to an intensive increase. The control showed stable thermal fluctuations during the whole procedure.



(a)

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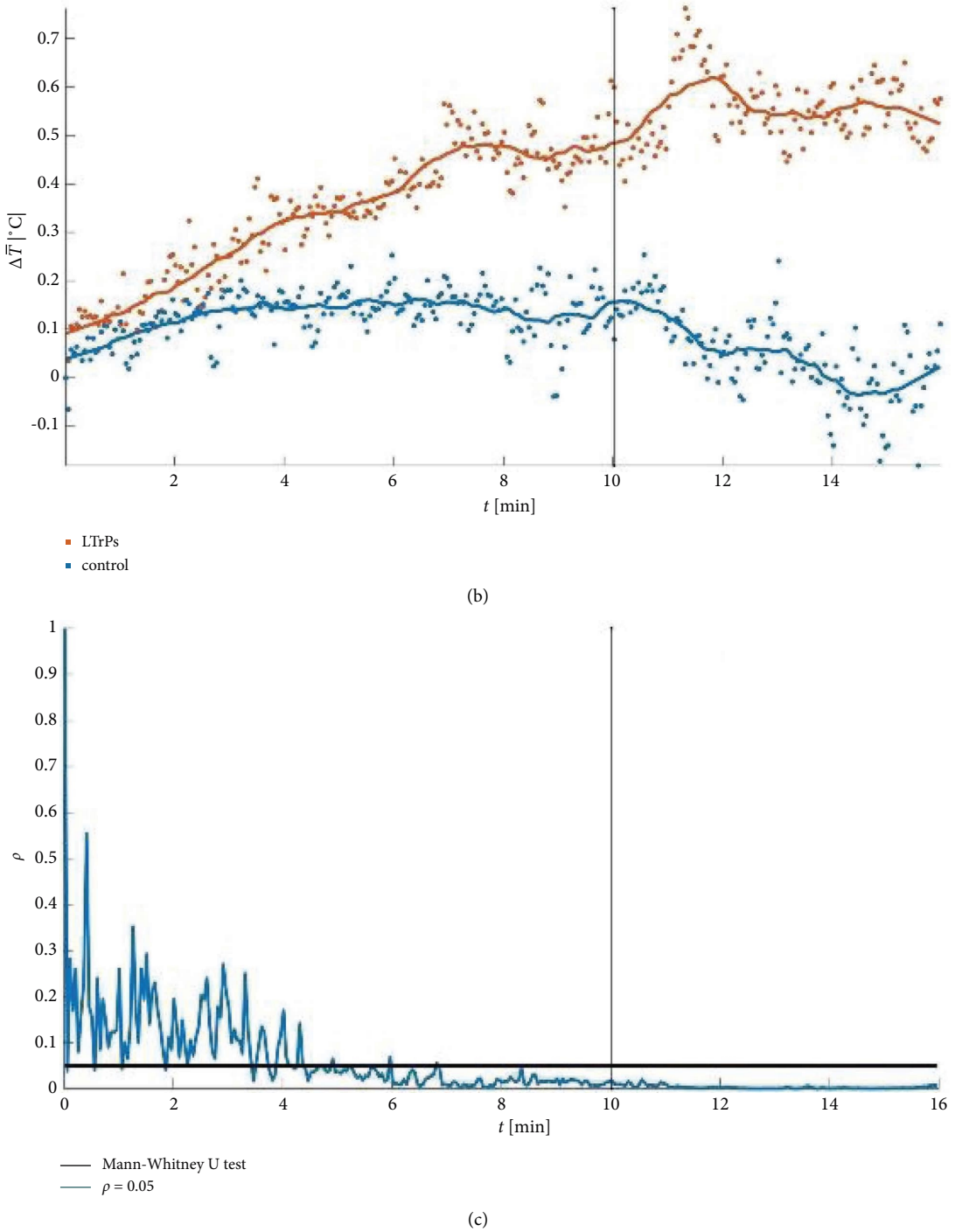

Figure 5: MATLAB trends of the development of the average temperature changes compared to the cutoff point as observed during the SP test® depend on the examined group and time of the procedure 4: (a) median value, (b) average value, and (c) Mann–Whitney *U* test results. The control group was characterized by the temperature decrease, which confirmed the lack of abnormal autonomic phenomenon* in this group (*the conditions of the positive the SP test® for vasodilatation: (i) development of a new thermal subarea above the cutoff; (ii) ΔT increase of more than 0.3°C as compared to the cutoff point).

patients with active trigger points characterized by amplified vasodilatation that is coincident with the referred pain zone.

The present study was aimed at examining whether gluteus minimus latent trigger points (LTrPs) can develop an abnormal autonomic response to the SP test®.

All subjects with referred pain that was provoked from gluteus minimus LTrPs were characterized by amplified vasodilatation. The SP test® revealed that the LTrPs subjects presented a constant increase in the amplified vasodilatation size from the first minute to the end of the test. Importantly,

the biggest size was reached during the poststimulation observation phase of the test. The majority of the control group revealed no signs of vasomotor reactivity. Three out of ten subjects presented small vasomotor reactivity during the test. Still, these values were significantly smaller compared to the ones presented by the LTrP subjects ($p < 0.05$). Moreover, control subjects presented a decrease in the average temperature of the observed area when compared to the cutoff point established for the SP test®. This indicated the lack of amplified vasodilatation. The analysis of the SP test® results depended on the anatomical parts, and it showed that only a few subjects from the LTrPs group presented amplified vasodilatation in the calf, which reflects intersubject variability in referred pain occurrence. The analysis of the average temperature changes in the observed region indicated that the poststimulation observation phase was characterized by a further temperature increase among the LTrPs subjects, contrary to the controls who presented the average temperature decrease.

The pathological autonomic reactivity of latent TrPs is similar to characteristic of active trigger points, which were previously examined using the SP test® [10, 16]. However, the phenomenon observed in case of latent TrPs analysis differed in size. The latent form was characterized by a smaller size of the observed amplified vasodilatation and a lower temperature increase within the referred pain zone that occurs due to noxious stimulation. For comparison, as a result of gluteus minimus active trigger points stimulation, sciatica patients with TrPs presented amplified vasodilatation with the size of more than 30% of the observed area and a $\Delta\overline{T}^{\circ}$ increase above 1°C [25]. Furthermore, the results of the present analysis are contrary to some of other available studies reporting attenuated vasoconstriction due to glutamate injection to trigger points or some vasomotor changes not detectable by infrared thermal (IRT) imaging [13, 14]. This discrepancy can be explained by a different type of noxious stimulus used during the SP test®, which involved direct long-lasting mechanical nociceptive muscle stimulation instead of the chemical one, achieved by glutamate injection [26, 27]. This hypothesis is consistent with Nickel et al. study [26], which showed that the autonomic nervous system reactivity depends on the time and intensity of the noxious stimulus, but not the clinical state or pain level. Additionally, we suggest that the local twitch response evoked by dry needling used as noxious stimulus during the SP test® probably may have essential meaning for provoked amplified vasomotor response into referred pain zone. As stated above, amplified vasodilatation within the lower leg due to nociceptive muscle stimulation demands the ANS activity at the level of the spinal cord and/or hypothalamus. Thus, the twitch response defined as a possible pathological spinal cord reflex that leads to autonomic and motor effects in the referred pain zone, can explain the changes observed evoked by the SP test® [2, 15, 28].

Though the most important result of the study is observation, we found that latent TrPs, similarly to active TrPs, provoked amplified vasomotor reactivity within the referred pain zone. The vasomotor reactivity provoked by the SP test® can be explained by the activation of the nonnoradrenergic vasodilator system, which affected the processes of reflex cutaneous vasoconstriction and vasodilatation and reflected a temporary autonomic nervous system (ANS) imbalance within the referred pain zone [29, 30]. Furthermore, the observed phenomenon is unique to TrPs-related referred pain [7, 21, 31]. The IRT-controlled needle stimulation of an acupoint has been shown to result in vasodilatation spreading a maximum of 5–10 centimeters from the stimulation point or has failed to visualize any reactions apart from technical artifacts [32, 33]. Ten-minute dry needle stimulation of soft tissue can explain the dynamic and extensive autonomic response observed in the present study.

The concept of nociplastic pain related to muscles is based on the link between the TrPs-referred pain mechanism and the central sensitization (CS) process that has been postulated in the literature [10, 21]. It has been hypothesized that the process of CS involvement in muscles is initiated by a brief burst of C-fiber activity followed by nociceptor activity that provokes the excitability of central nociceptive neurons in the cortex, brain stem, trigeminal nucleus, and spinal cord [34]. In this process, the ANS dysregulation is indicated as one of the main causes of the central sensitization phenomenon development and/or maintenance [13, 14]. Moreover, central sensitization is characterized by secondary hyperalgesia, allodynia, and/or the presence of increased temporal summation of pain [35]. Temporal summation manifests itself as an increasing response to repeated nociceptive stimulations within the same receptive field [6]. The analysis of both the SP test® diagnostic parameters (namely, the size of the amplified vasomotor reactivity and ΔT increase higher than >0.3°C) measured every 3 seconds revealed the fluctuating and increasing in time character of the observed phenomenon. Additionally, a further increase in the SP test® parameters seen during the observation phase can be a mark of the temporal summation characteristic of CS. This supports the hypothesis that TrPs more probably represent a central phenomenon not a peripheral sensation. However, the concept of central sensitization processes has some gaps, especially when both active and latent TrPs are considered. On the one hand, CS is characteristic of chronic pain patients. On the other hand, CS is associated with a family history of pain, high psychological comorbidity, increased sensitivity to nonpain sensory stimuli, and a high number of chronic overlapping pain conditions. It is worth noting that the beginning of the symptoms is associated with puberty [36].

In addition to mention above hypothesis, there is also a new concept by Harte et al. proposing that two types of CS should be distinguished, namely, top-down and bottom-up. The first one is characterized by a greater number of severe sensations typical, for example, fibromyalgia, where the primary problem likely originates from the supraspinal structures and which symptoms are irreversible. The second type is defined as a possibly to reverse the process. This bottom-up type of CS is characterized by pain due to an excess noxious peripheral input that eventually sensitizes the central nervous system to the point of perceiving pain. Harte et al. [36] stated, that over a time, pain is perceived even

when there is no peripheral drive. Generally, the bottom-up CS subtype is indicated as a lower burden. Based on that statement, it can be hypothesized that TrPs might be categorized as bottom-up. However, if we consider that CS is characteristic of patients with pain, the referred pain provoked by latent TrPs can be categorized as nociplastic one, which is a broader term than CS.

A potential role of the autonomic nervous system involvement in nociplastic pain (central sensitization) and TrPs development has been indicated by other authors [6, 28, 29]. Even though only gluteus minimus TrPs were examined using the SP test®, it can be assumed that other muscles with TrPs will react similarly. The fact that latent TrPs presented a pathological autonomic phenomenon just like active TrPs allows us to believe that the autonomic nervous system measurement can possibly play a crucial role in an objective diagnosis of nociplastic pain related to muscle. The idea that the SP test® can possibly become a new diagnostic method for the objective confirmation of nociplastic pain related to TrPs, understood as a subtype of central sensitization and probably categorized as bottom-up, seems worth addressing [36, 37]. Further studies considering the SP test® application to other muscles with both types of trigger points are recommended to support the concept that referred pain can be classified as the source of nociplastic pain related to trigger points.

4.1. The Clinical Implications of the Study. The SP test® allows the confirmation of both active and latent gluteus minimus TrPs. Thus, it might be presumed that the test can be used to objectively confirm referred pain in other muscles. This provides an opportunity for extensive clinical studies towards nociplastic pain involvement in patients with musculoskeletal pain disorders. However, further studies considering the SP test® response of other muscles that provoke referred pain are necessary.

4.2. Limitation of the Study. The main limitation of the study is the fact that the SP test® is a 10-minute painful protocol. The dry needling technique used as a noxious stimulus is widely applied as a therapeutic tool in clinical practice. The extended time of dry needling stimulation, above the clinical recommendation, was applied for diagnostic purposes only. All of the patients withstood the SP test® but they confirmed unpleasant sensations. Moreover, the therapist who performed dry needling in the present study was not blinded to the trigger point diagnosis, which could have biased the results to some extent.

5. Conclusions

Noxious stimulation of latent TrPs provoked abnormal autonomic nervous system activity within the referred pain zone. The observed phenomenon supports the concept of central sensitization related to trigger points. Further studies towards the autonomic response of other muscles with trigger points are recommended.

Abbreviations

TrPs: Trigger points
CS: Central sensitization
LTrPs: Latent trigger points
AURP: Autonomic referred pain
AURPT0: Autonomic referred pain with the temperature not registered for the patient before the stimulation
ROI: Region of interest
$\Delta\overline{T}^{\circ}$: Change in the mean temperature of the area
SD: Standard deviation
ANS: Autonomic nervous system
IRT: Infrared thermal camera/imaging.

Data Availability

The data used to support the findings of this study are available from the corresponding author upon request.

Conflicts of Interest

The authors declare that they have no conflicts of interest in this work.

Authors' Contributions

ES, TD, and DW conceived the original study idea and wrote the first draft of the manuscript. TD, ES, and DW provided input for the analysis and interpretation of data. ES, MR, and TD performed the investigation. MJ and PD conducted the data analysis. AJ and AS supervised and provided critical review, commentary, and revision. All authors have read and agreed to the published version of the manuscript.

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Research Article

Dry Needling Produces Mild Injuries Irrespective to Muscle Stiffness and Tension in Ex Vivo Mice Muscles

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Numerous studies have suggested that the myofascial trigger points are responsible for most of the myofascial pain syndrome, so it seems reasonable that its destruction is a good therapeutic solution. The effectiveness of dry needling (DN) has been confirmed in muscles with myofascial trigger points, hypertonicity, and spasticity. The objective of this study is to analyze the need of repetitive punctures on muscles in different situations. The levator auris longus (LAL) muscle and gastrocnemius muscle from adult male Swiss mice were dissected and maintained alive, while being submerged in an oxygenated Ringer's solution. DN was evaluated under four animal models, mimicking the human condition: normal healthy muscles, muscle fibers with contraction knots, muscles submerged in a depolarizing Ringer solution (KCl-$CaCl_2$), and muscles submerged in Ringer solution with formalin. Thereafter, samples were evaluated with optical microscopy (LAL) and scanning electron microscopy (gastrocnemius). Healthy muscles allowed the penetration of needles between fibers with minimal injuries. In muscles with contraction knots, the needle separated many muscle fibers, and several others were injured, while blood vessels and intramuscular nerves were mostly not injured. Muscles submerged in a depolarizing solution inducing sustained contraction showed more injured muscular fibers and several muscle fibers separated by the needle. Finally, the muscles submerged in Ringer solution with formalin showed a few number of injured muscular fibers and abundant muscle fibers separated by the needle. Scanning electron microscopy images confirm the optical analyses. In summary, dry needling is a technique that causes mild injury irrespective of the muscle tone.

1. Introduction

The most frequent cause of muscular pain is the myofascial pain syndrome (MPS) [1]. MPS is a collection of known sensory, motor, and autonomic symptoms caused by myofascial trigger points (MTrPs) [2, 3]. Myofascial trigger points are hyperirritable nodules within taut bands of skeletal muscle responsible for sensory, motor (stiffness, weakness, and restricted range of motion), and autonomic dysfunction [3]. Electromyography defines this as "spontaneous electrical activity" (SEA), also called "end plate noise." The irritability of the MTrP can be objectively assessed in rabbit alongside the changes in prevalence or amplitude of SEA that are recorded in this region [4]. Histologically, in the mouse myocyte, it appears as a contraction knot located close to a synaptic contact, constituting what is called "active loci" (a well-defined area of accumulation of dysfunctional motor plates) [5].

The most common therapeutic technique employed in the treatment of MTrPs is dry needling (DN) [6]. DN consists of using the mechanical stimuli of a needle to either eliminate or inactivate the MTrP. The DN technique requires multiple insertions [7–9]. The number of needle insertions is associated with postneedling soreness [10]. In our laboratory, we repeatedly needled the levator auris longus muscle of mice and described denervation and fiber muscular damage [11]. These repeated muscle punctures do not interfere with the different stages of normal muscle

regeneration and reinnervation. However, little is known about the local effects of repeated DN immediately after the puncture.

In subjects with MTrPs, DN has been reported to decrease pain [12]. The possible physiological effects of DN involve both mechanical stimulation and the consequences of local microtrauma. DN can influence the SEA by causing a local twitch reflex (LTR). LTR is an involuntary spinal reflex that results in a localized contraction of affected muscle fibers that are manually stretched with dry needles. Both Chen et al. [6] and Hsieh et al. [12] demonstrated in their studies with rabbit that DN to a MTrP region could effectively suppress SEA, when LTRs were elicited. They suggested that inserting a needle into the endplate region may lead to increased discharges and thus immediately reduce available ACh stores, leading to a decrease in the SEA. Another possible mechanism could be that sufficient mechanical activation of the puncture around the endplate area causes the muscle fibers to discharge, thereby producing a LTR. Baldry [13] mentioned that a LTR causes alterations in muscle fiber length and tension and stimulates mechanoreceptors such as Aβ fibers. On the other hand, microtrauma caused by needle insertion can increase blood flow and muscle oxygenation. Indeed, local microtrauma leads to the release of vasoactive substances, such as CGRP and SP, which are also increased after the activation of *C* fibers through the axon reflex, leading to vasodilation of small vessels [11]. The clinical and scientific evidence of the beneficial effects of DN has been on the increase over the years [14, 15]. But there is no consensus on how many inserts are needed. For example, Fernández-Carnero et al. [16] report that different numbers of DN (including not generating LTRs and generating six LTRs, or continuing until no more LTRs are obtained) in the upper trapezius produce similar improvements in patients with cervical myofascial pain. Moreover, the mechanisms of action of DN in managing other muscle tone abnormalities (such as hypertonia or spasticity) have been poorly studied. Nonpharmacological treatments like dry needling have been used for years to decrease hypertonia and spasticity (DNHS®, Dry Needling for Hypertonia and Spasticity) and improve the function of muscles [13]. Spasticity is a common disabling motor deficit after a stroke [17–19]. DN of the hypertonic and spastic muscles in individuals with stroke produces an immediate reduction in spasticity and an increase in active range of motion [8, 9]. Some studies have tried to objectively quantify the adverse effects of the DNHS technique on the contractile properties of spastic muscles [20], but there is still a dearth of knowledge regarding this subject.

Despite repeatedly inserting a solid needle into the muscles of patients, the role of DN in muscles with MTrPs, hypertonia, or spasticity is not well known. There are no biological foundations for multiple insertions. The working hypothesis of this study is that increased muscle stiffness and tension are associated with increased likelihood of muscle fiber injury from dry needling and, therefore, provide elements to decide the need for multiple insertions.

2. Materials and Methods

2.1. Animals and Muscles. Adult male Swiss mice (30 to 40 days of age; Charles River, L'Arbresle, France) were used for this study (15 animals). The animals were housed in plastic cages containing 2–5 individuals and allowed free access to food and water all through the period of experiment. The animals' room was maintained at a temperature of $22 \pm 2^{\circ}$C, a relative humidity of $50 \pm 10\%$, and a 12 h light/dark automatic light cycle. This study was approved by the Ethics Committee CEIm-IISPV (Ref. 178/2019). The mice were cared for in accordance with the guidelines of the European Community's Council Directive (2010/63/EU) for the humane treatment of laboratory animals.

Animals were sacrificed by exsanguination under anesthesia. Thereafter, the *levator auris longus* (LAL) muscle was dissected. This muscle was chosen because it is a thin and flat muscle with a well-known intramuscular nerve branching pattern and it is easy to handle, while applying specific techniques to obtain optical images that allow us to observe the whole fiber and the contraction knot [5]. Recently, in our laboratory, we created an animal model with myofascial trigger points produced by a single subcutaneous injection of neostigmine [5]. Neostigmine induces an increase in spontaneous ACh release, followed by a cascade of events that finally results in contraction knots.

2.2. Dry Needling. The animals were anesthetized with 2% tribromoethanol (0.15 ml/10 g of body weight, I.P.). The LAL and gastrocnemius muscles were extracted and pinned on Sylgard-coated Petri dish containing normal Ringer solution (containing (in mM): 135 NaCl, 5KCl, 2.5 $CaCl_2$, 1 MgSO4, 1 NaH_2PO_4, 15 $NaHCO_3$, and 11 glucose) continuously bubbled with 95% O_2/5% CO_2. Thereafter, repeated punctures on the muscles were performed. Muscles immersion in oxygenated normal Ringer is a conventional procedure when some aspects of muscle physiology are to be studied. Upon these conditions, the muscle maintains the ability to contract and react to the physical aggression of inserting a solid needle. In this study, we used a solid needle habitually used for acupuncture and dry needling (0.25 mm thick and 25 mm long; AguPunt, Barcelona, Spain). Punctures were made at different sites in the muscle. The LAL muscle is a flat muscle, so when a puncture is made, a hole remains. In this experimental condition, if that hole is punctured again, the rest of the muscle fibers remain unaffected. Furthermore, dry needling has also been performed in the gastrocnemius muscle since this muscle is thicker than the LAL. Under the conditions of performing dry needling (punctures in different sites of the muscle), not more than 15 punctures on the LAL muscle can be performed. In both the LAL and the gastrocnemius, all punctures were performed in the middle third of the muscle, where the synaptic contacts are concentrated. To mimic muscle conditions in human patients, four types of situations have been designed (from low to high muscle contraction): normal healthy muscles; muscles with contraction knots (mimicking human muscles with MTrPs; thirty minutes after a subcutaneous administration of

neostigmine; for more details, see Margalef et al. [5]); muscles submerged in a depolarizing Ringer solution (KCl, 20 mM) rich in calcium ($CaCl_2$, 5 mM) mimicking human muscles with hypertonia; and muscles submerged in a Ringer solution with formalin (4%) mimicking spastic muscles. Treatment with neostigmine causes the subsynaptic contraction knots to appear in muscle fibers. Muscle fibers with contraction knots cause shortening of the sarcomeres in the area where the knots are. However, it has been described that the rest of the fiber is tighter [21]. The depolarizing Ringer solution rich in calcium sustains contraction throughout the entire length of the muscle fiber. The action of formalin on living muscle fibers is to achieve the highest homogeneous contraction throughout their length (like that caused in spasticity). Muscle samples were studied with optical microscopy and scanning electron microscopy. Fifteen animals per group were used (total 60 animals). In almost all groups, the muscle has been dissected and immersed in different types of physiological solutions. The group treated with neostigmine was anesthetized and injected subcutaneously with neostigmine and 30 minutes after the muscle was extracted and immersed in Ringer to perform the punctures. Of the initial 15 animals in neostigmine group, 2 died. Something similar happened with the samples mimicking spasticity. Once extracted, the muscle was pinned and immersed in a formalin solution. The formalin-induced contraction was so significant that 6 muscles were torn from their pins and had to be discarded from the study.

2.3. Methylene Blue Staining. Only LAL muscles were processed for optical study and morphometric analyses. The LAL muscles were fixed in 10% neutral formalin for 3 to 10 days and exposed to a 1% methylene blue dissolved in 1% borax for two minutes. Subsequently, the samples were washed with distilled water for two minutes each during the three steps. Finally, we proceeded to dehydration and mounting with epoxy resin.

The samples were observed at 1000x with an optical microscope to evaluate the number of injured fibers per hole. An injured fiber is considered when it is seen to be cut and/or dilated. The LAL is an extremely flat muscle, so it was easy to visualize these fibers surrounded by a hole created by the insertion of the needle. The number of fibers injured per hole created by the insertion of the needle has been counted. The experimental unit is the muscle hole. Fifteen insertions were made, which are the maximum that the muscle admits. In this sense, there was no randomization.

2.4. Scanning Electron Microscopy (SEM). Only gastrocnemius muscles treated with neostigmine were processed for SEM observations. This muscle was chosen because of its thickness and the presence of abundant connective tissue surrounding its fibers. The connective tissue that surrounds the fibers of the LAL muscle is not very evident, unlike in the gastrocnemius muscle. The connective tissue contributes to the stability of muscle tissue. For this reason, the samples have been processed without using collagenase. All samples were dehydrated in sequence with increasing alcohol concentrations (50%, 70%, 80%, 90%, and 100%; V alcohol/V demineralized water) and then dried at room temperature. Samples were observed using an environmental scanning electron microscopy (FEI ESEM Quanta 600 FEG—Environmental Scanning Electron Microscope, Graz, Germany). In addition, needle tips (0.25 mm thick and 25 mm long; AguPunt, Barcelona Spain) were visualized with the SEM.

2.5. Statistical Procedure. Data were analyzed using SPSS version 21.0 (SPSS, Inc., Chicago, IL, USA). Results are expressed as means ± standard deviation (SD), considering the 95% CI. Normality was assessed by Shapiro–Wilk test, the Kolmogorov–Smirnov test was used for comparisons between groups not showing a normal distribution, and differences were considered significant at $P < 0.05$.

3. Results

3.1. DN in Healthy Muscles. As given in Table 1, the number of injured fibers was very low in healthy muscles (about 4). Figure 1 shows how there are almost no muscle fibers sectioned and most have been set aside. The punctures were made in the innervation band. In Figure 1(a), several intramuscular nerves can be seen to cross the image. Figure 1(b) shows a greater magnification and how some fibers were injured, and others were separated by the needle. Moreover, Figure 1(b) shows the use of a solid needle for insertions observed using the scanning electron microscopy. The magnifications of the methylene blue image and the needle are the same. Note that the hole in the puncture zone is smaller than the diameter of the needle. When the needle is removed, the muscle fibers return to their initial position, partially closing the hole created.

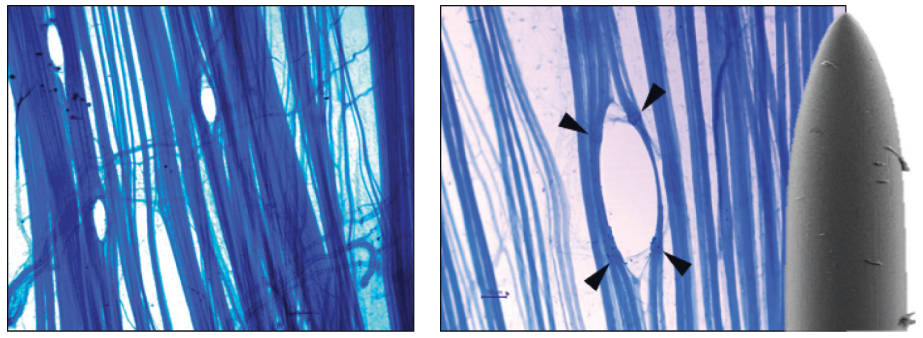
3.2. DN in Muscles with Fibers with Contraction Knots. Thirty minutes after a subcutaneous administration of neostigmine, several knots of contraction can be observed (Figure 2(a)). We observed that there are also lateral displacements and lower injuries than expected (Figure 2(b)). The number of fibers injured by the needle increases by 10% with increasing tension in these muscles and fibers with contraction knots (Table 1). Figure 2(c) shows how the needle separates some muscle fibers and some are injured in the process. In this kind of experiments, the punctures were also made in the innervation band. Surprisingly, in many cases, the tip of the needle also separates structures such as nerves or blood vessels (Figures 2(c) and 2(d)). In Figure 2(c), erythrocytes remain in the undamaged blood vessel. In areas of puncture, intact intramuscular nerves could also be seen (Figure 2(d)).

3.3. DN in Muscles Treated with KCl/$CaCl_2$. In order to achieve a sustained contraction, KCl has been used as a depolarizing agent and $CaCl_2$ has been used to increase extracellular calcium and facilitate the contraction. Few seconds after the

Table 1: Number of fibers injured by puncture (LAL muscle).

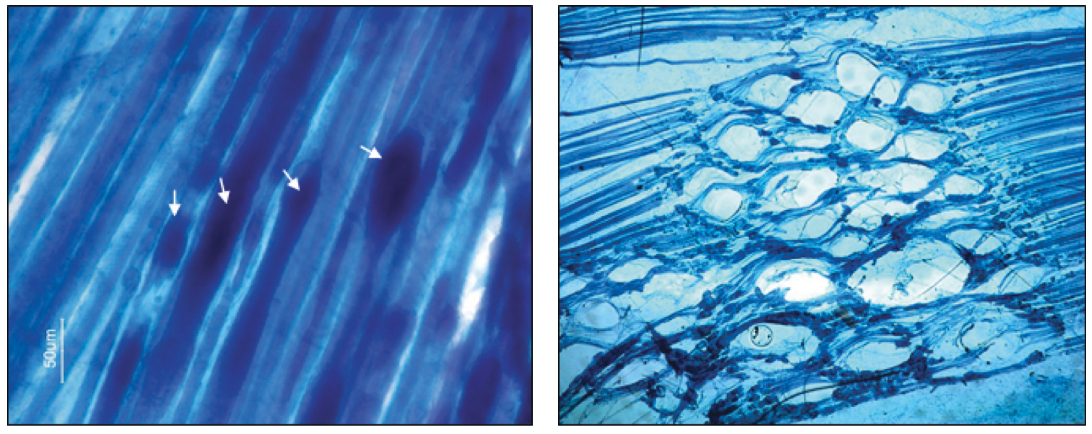
	Healthy muscles	Muscles with MTrPs	Mimicking hypertonic muscles	Mimicking spastic muscles
Mean ± SD	4.2 ± 2.9	4.7 ± 1.7	5.6 ± 2.3	3.0 ± 1.1
P		0.008	<0.001	<0.001
n of holes	225	195	225	135
95% intervals	3.9851 4.4238	4.4913 4.9959	5.3894 5.9440	2.8730 3.1714

Data expressed as the average number of fibers injured per hole created by the insertion of the needle ± SD. Fifteen insertions per LAL muscle and stained with methylene blue. In parentheses are the numbers of holes evaluated from 15 healthy muscles, 13 muscles with fibers with contraction knots, 15 hypertonic muscles, and 9 spastic muscles. Muscles submerged in a depolarizing Ringer solution (KCl, 20 mM) rich in calcium ($CaCl_2$, 5 mM) mimicking human muscles with hypertonia. Muscles submerged muscles in a Ringer solution with formalin (4%) mimicking spastic muscles. *P* values were obtained by the Kolmogorov–Smirnov test and corresponds to comparison with respect to healthy muscles values.



(a) (b)

Figure 1: Ex vivo dry needling with solid needle in normal healthy LAL muscle. (a) Three punctures were performed in the innervation area of the muscle. Note that few muscle fibers are injured, and the needle sets many of them a side (initial magnification: 100x). (b) Detail of a puncture. The SEM image is an example of a solid needle habitually used for acupuncture and dry needling (diameter of 250 μm). Arrowheads, muscle fiber injury points. Two images are on the same scale (scale bar: 50 μm).



(a) (b)

Figure 2: Continued.

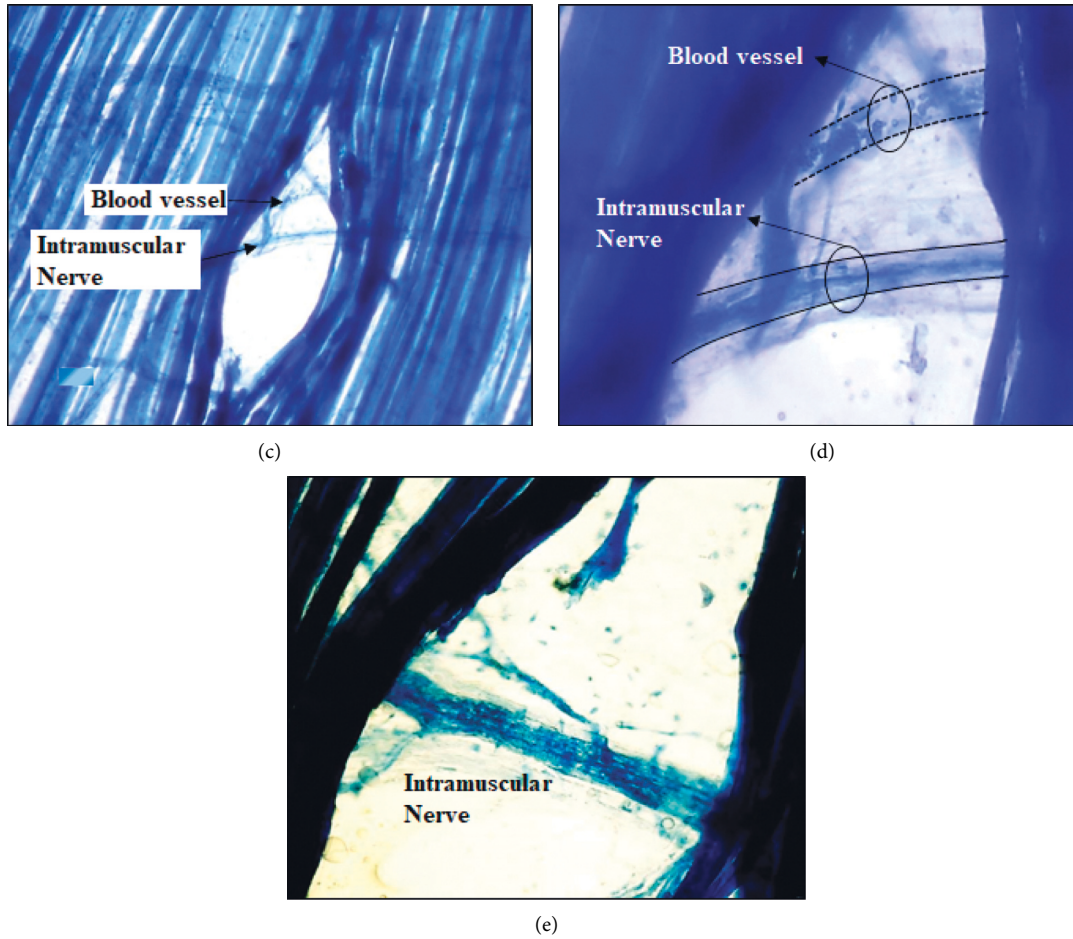


Figure 2: Ex vivo dry needling in LAL muscle with fibers with contraction knots. (a) Thirty minutes after a subcutaneous administration of neostigmine, the muscle shows several knots of contraction (arrows). (b) Several repeated punctures on the muscle were performed. Note that punctures were not performed at the same point. The needle separates many muscle fibers, and many others are injured (initial magnification: 100x). (c) Details of a puncture. Vessels and nerves in the puncture site can be seen without injury (initial magnification: 200x). Erythrocytes circulating through the vessel can be seen (d) (initial magnification: 400x). (e) Another example of puncture showing an intramuscular nerve without injury (initial magnification: 400x).

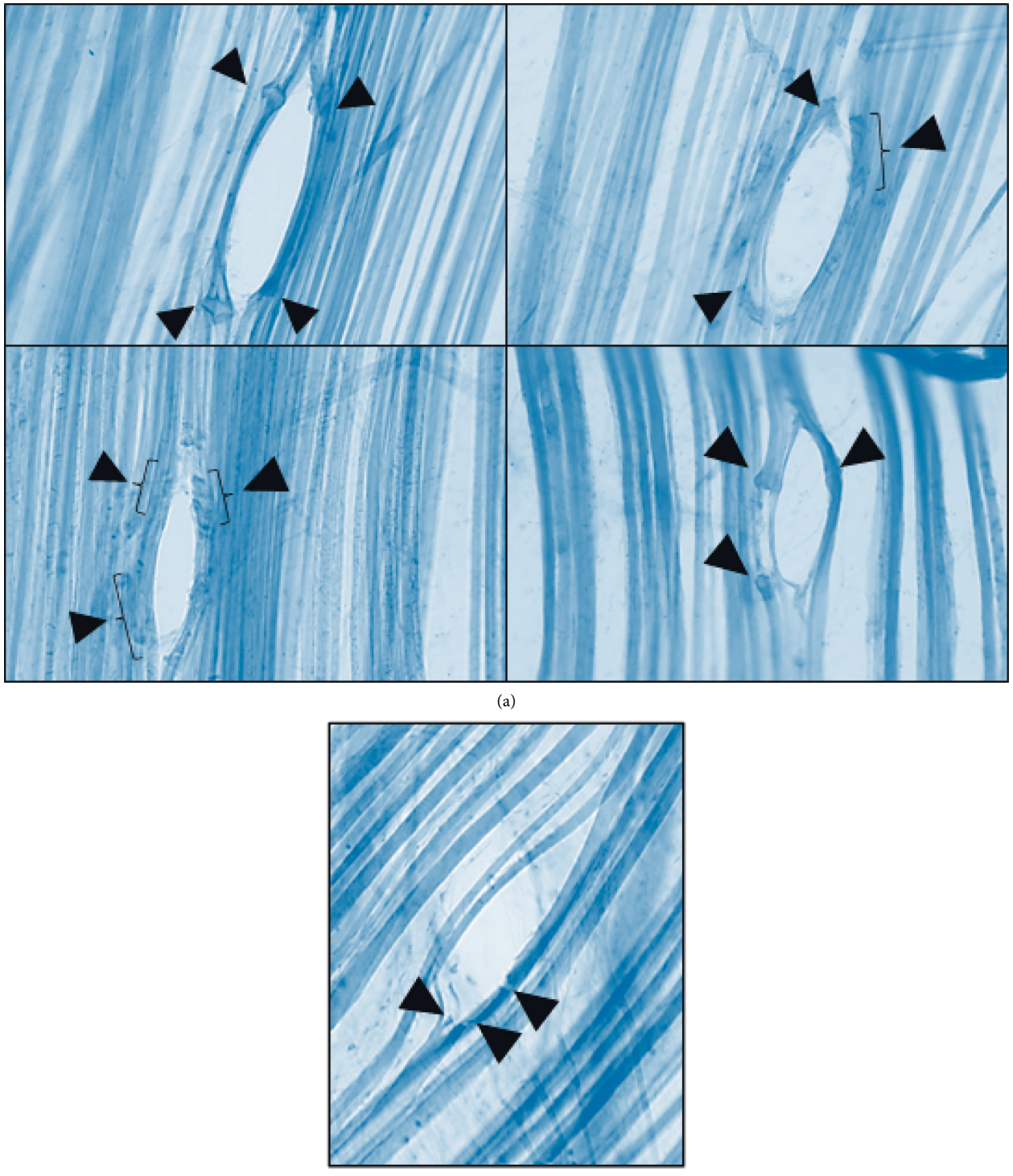
exposure of the muscle to this situation, a sustained muscle contraction is obtained. Those muscles are a model of human muscles with hypertonia. We observed more injured fibers in these muscles than in muscles where several contraction knots have been induced (Figure 3(a)). In this experimental situation, the highest number of fibers injured by the insertion of the needle was obtained (around 5; Table 1). However, the observed injury is less than expected.

3.4. DN in Muscles Treated with Formalin. Immersing the living muscles in formalin resulted in a powerful contraction. When DN was performed, most of the fibers were separated and few were sectioned (Figure 3(b)). Surprisingly, in muscles that mimic spastic muscles, the number of fibers injured by the needle was 30% less than in healthy muscles (Table 1).

3.5. Ex vivo Dry Needling Seen by Scanning Electron Microscopy (SEM). To confirm the observations made by optical study with methylene blue on the LAL muscle, gastrocnemius muscles with contraction knots were treated with DN and studied with SEM. The SEM technique enables us to observe the tissue as a whole, and the muscle fibers were almost completely (Figure 4(a)) covered by connective tissue (Figure 4(b)). As observed by optical microscopy in the LAL muscle, only some muscle fibers were injured (Figure 4(b)) in gastrocnemius. Moreover, when the needle is removed, muscle fibers return back, and the hole is almost closed (Figures 4(c) and 4(d)). The tips of the DN needles used in this study are neither sharp nor beveled (Figure 4(e)).

4. Discussion

In order to analyze the effect of the repetitive mechanical injury induced by puncture in the muscle fiber at different degrees of contraction, we studied structural changes after 15 repeated punctures in the LAL muscle. Four conditions, healthy normal muscles, muscles with fibers, and contraction knots as well as chemically contracted muscles ($CaCl_2$/



(a)

(b)

Figure 3: Ex vivo dry needling in contracted healthy LAL muscle. (a) Muscles were contracted with a calcium-rich depolarizing medium ($KCl/CaCl_2$). In the different examples, more injured fibers can be seen than in the muscles with fibers with contraction knots seen in Figure 2 (initial magnification: 200x). (b) After a more powerful contraction by immersing the muscles in formalin. The needle separates most of the fibers and only few of them are sectioned. Arrowheads, muscle fiber injury points. Bracket, area with various lesions (initial magnification: 200x).

KCl and formalin) have been studied. In most cases, the muscle fibers are not injured; instead, they are pushed away by the tip of the needle. The muscles manipulated in these experimental situations have preserved the ability to contract. It is known that injury to muscle fibers causes them to contract [22].

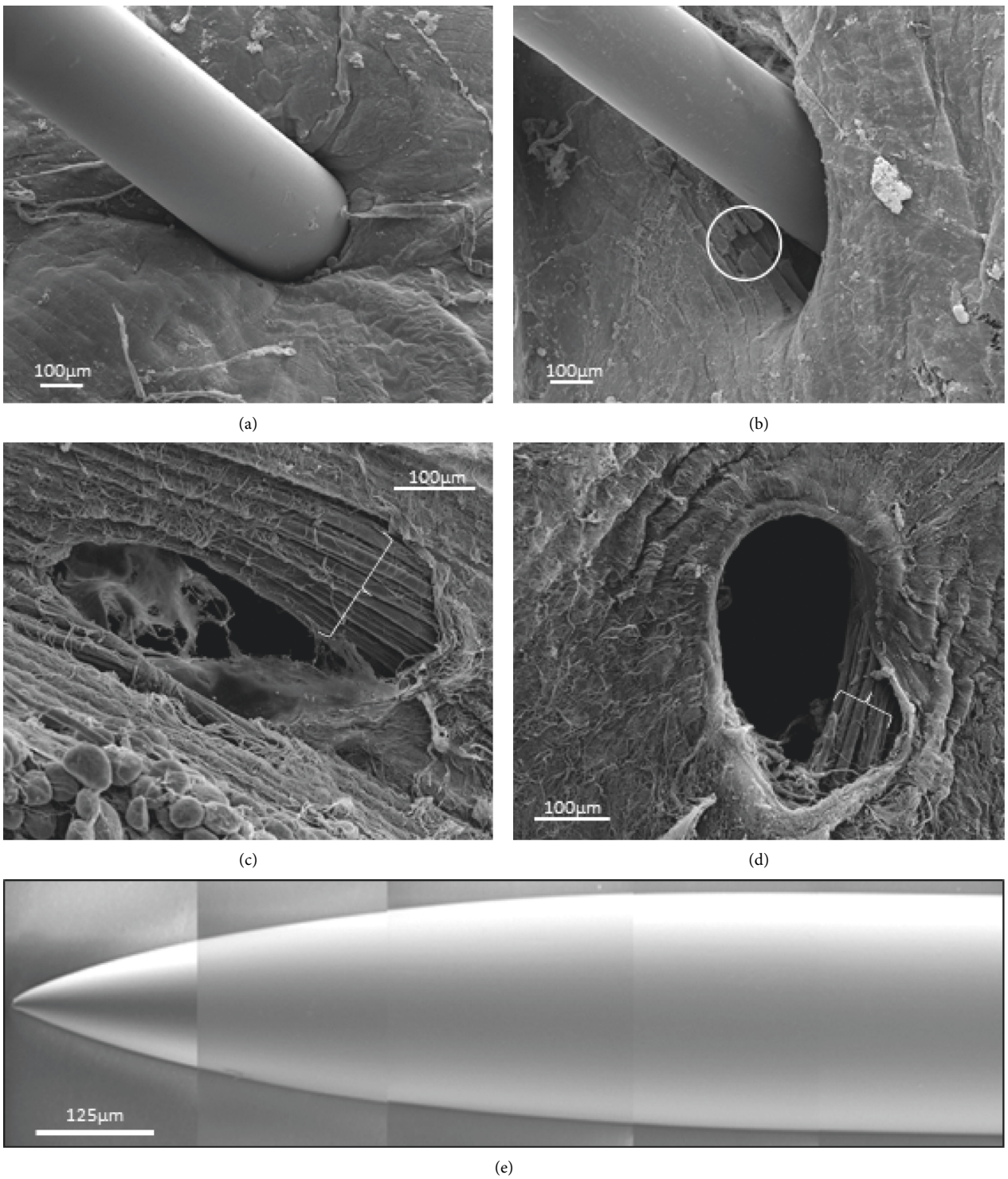


Figure 4: Scanning electron microscopy: examples of ex vivo dry needling in gastrocnemius muscle. The samples were processed without using collagenase. For this reason, the muscle fibers are mostly covered by endomysium and perimysium. This situation is especially evident in (a), where the needle punches the endomysium and perimysium. (b) A few injured muscle fibers are shown (white circle). Immediately below these, the fibers are unchanged. When the needle is removed, the muscle fibers return to its original position and the hole is almost closed (c), (d). Brackets, healthy muscle fibers. (e) Example of the tips of the needles used in DN.

DN consists of the insertion of a solid intramuscular needle to eliminate or inactivate the MTrP. This inactivation requires the muscular injury, inflammatory reaction, and muscle regeneration [10]. In addition, multiple insertions are necessary to obtain a clinical benefit [7, 23, 24]. The most common number of punctures in patients is 8 to 10 insertions per intervention [8, 9]. However, there is no consensus on how many insertions are necessary to obtain

clinical improvement. Some authors associate the success of DN with the generation of LTR. On the contrary, Fernández-Carnero et al. [16] in a randomized, double-blind clinical trial reported that different numbers of DN with and without RTL in the upper trapezius produce similar improvements in patients with cervical PG. A small lesion area will facilitate good muscle regeneration [23]. In the present study, we observed that the injury produced by the DN technique is small. In addition, to a small puncture hole, few fibers were injured, while the rest of fibers are only displaced by the passage of the tip of the needle. Healthy muscles are very elastic and upon the penetration of needles, fibers are displaced. In our laboratory, Domingo et al. have shown that there is complete recovery seven days after the injury by dry needling on mice skeletal muscle [25]. In the present study, we described that the damage caused by each insertion is limited to few muscle fibers. Furthermore, in the study by Domingo et al., repeated insertions (15 in total) were made to produce enough injured fibers in order to evaluate their regeneration. In such conditions, Domingo et al. also described that vascular injury occurs only sporadically [25]. The presence of vascular injury can imply poor irrigation of the injured area, which in turn makes difficult the muscular regeneration [26]. In the present study, we observed that the DN needle can frequently displace the blood vessels without damaging them. Thus, the vascular injury is minimal, which favors a good muscular regeneration in case of lesion.

Since MTrPs are placed in the innervation band [5], there is relevance to determine whether the DN technique could cause any damage to the intramuscular nerves. In the present study, similarly, as observed for blood vessels, intramuscular nerves are frequently displaced by the tip of the needle. Although Domingo et al. described that after DN distal nerve injury on normal muscles of mice can occur, no intramuscular nerve trunk lesions were evidenced [25]. To the best of our knowledge, there are no previous studies evaluating DN in muscle fibers with contraction knots.

Thirty minutes after a single subcutaneous injection of neostigmine (NTG), rodent muscles showed MTrPs [24]. In the present study, we provide evidence supporting the fact that the DN technique produced minimal lesions to healthy muscles. However, when the muscle tension is increased due to the presence of MTrPs, the lesion is greater. Treatment with neostigmine causes subsynaptic contraction knots to appear in the muscle fibers. It has been suggested that the shortening of the sarcomeres in contraction knots results in shortening of the muscle fiber and the generation of the taut band, therefore resulting in an increase in tension [22, 27, 28]. When the needle penetrates healthy areas of the muscle in the direction of the MTrPs, it does not cause a great injury as may be suggested. However, when the needle arrives in the area of the MTrPs, it is more effective in causing injury and affects the structure of the MTrPs. However, the level of injury is below expectation and more than one puncture is needed to achieve clinical results. In this regard, several years ago, Janet Travell developed a specific technique of DN that consisted of multiple insertions [7, 9, 21]. Dry needling is believed to damage or destroy the dysfunctional motor endplates of the MTrP [29]. The present work shows a low level of muscle and nerve injury produced by DN, indicating that the use of multiple insertions in the muscles of patients may be beneficial.

After a stroke, hypertonia or muscle spasticity is likely to appear [17]. DN is also performed in these muscles (DN for hypertonia and spasticity, DNHS®) [30]. Some studies tried to quantify the effects of the DNHS technique on the contractile properties of spastic muscles and a decrease in spasticity [20, 31] and an increase in active range of motion was reported [32, 33]. In order to increase muscle tone, we used normal Ringer rich in KCl and $CaCl_2$. The first depolarizes the muscular and axonal membranes and the calcium enabled the increase of the neurotransmission and the availability of calcium for the contraction, thereby creating an artificial chemical model of contraction that was maintained over time. Hodgkin and Horowicz [34, 35] have previously described the quantitative effects of sudden changes in potassium concentration in the membrane potential and the effects produced on the contraction of the individual muscle fibers. In addition, Luettgau [36], working with external calcium, described that the process that controls the development of the tone of the muscle is influenced by the addition of solutions with high potassium content. In this model of hypertonia, the muscle tension is stronger than in the two previous situations. Possibly due to the greater sustained contraction, the muscles are stiffer and less flexible and therefore do not move as easily. In this model of hypertonia, DN was more harmful than muscles with fibers with contraction knots. Most of the muscle fibers were separated and only some were injured. The solid needle used may have a point blunt enough to push back the hypertonic fibers.

Unlike expected, the fibers of the fixed muscles suffered less injury than the other studied conditions. Fixation with formaldehyde is a crucial step to preserve cellular architecture and composition of cells in the tissue; in this case, the proteins are preserved. Several mechanisms can intervene in proteins fixation. It consists of a physical-chemical change of the molecule without altering the percentage of its constituent elements. They have more facility to be decomposed or digested but, unlike what is expected, the fibers that compose are less injured by the mechanical effect of the needle. Prior to denaturation, the proteins undergo a specific coagulation [37]. This process does not occur in a local area but appears in the whole set of fibers that are affected by formaldehyde and enables the separation of these fibers jointly when the needle is introduced.

In the SEM images, it was observed how the connective tissue could preserve the muscle fibers from damage. The collagen fibrils in the endomysium change direction as the muscle fibers stretch [38]. During the stretching process, the circumferentially oriented collagen fibers are reoriented in the longitudinal direction, increasing the stiffness of the fiber. The endomysium is not capable of transmitting the tensile forces of the muscle fibers in the resting length of the sarcomere. However, it transmits contractile force between adjacent muscle fibers by translaminar shear through the thickness of the connective tissue [39, 40]. Thus, the connective tissue of the endomysium could increase the resistance of the muscle fibers

as their contractile tension increases under the different experimental conditions used in this study.

The tips of the DN needles used in this study (Figures 1(b) and 4(e)) are not sharp enough to justify a large injury. In a previous study, we evidenced with scanning electron microscopy that the tips of the needles commonly used in DN are dull [41]. These needles did not improve during repetitive insertions of either the skin only or the skin and muscle in patients. Thus, DN with these solid needles does not justify extensive muscle injury.

These results suggest that when puncturing deep muscles, the needle will not excessively injure healthy muscles when it passes through. In addition, the probability of injuring vessels and nerve trunks is low. In other words, it is a safe technique. In all the experimental situations used in this work, the probability of injuring muscle fibers is low. Therefore, if the intention of the dry needling is to inactivate all the contraction nodes of the patients' PGMs, there is need to perform several insertions. This is also true for patients with hypertonic or spastic muscles.

5. Limitations

As there are no previous studies similar to the present one, we have not calculated the sample size a priori; however the samples used have been enough to obtain significant differences compared to control.

DN has been performed on isolated muscles ex vivo. A muscle in these conditions does not have upper layers or skin that modify its response to DN. Also, due to their isolated condition, these muscles are denervated, so only passive responses of the tissue can be evaluated.

Isolated hypertonic and spastic muscles have been achieved by playing with the degree of contraction using local chemicals. In patients, these muscles would respond to a superior nervous problem.

6. Conclusion

Dry needling induces a lateral displacement of the muscle fibers and causes little damage. The present work shows a low level of muscle and nerve injury produced by DN, indicating that the use of multiple insertions in the muscles of patients may be beneficial.

Data Availability

All data used to support the findings of this study are included within the article (Table 1) and as supplementary material (Raw Date Table 1.xls).

Conflicts of Interest

The authors declare that there are no conflicts of interest.

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Supplementary Materials

Table 1. The number of muscles and number of fibers injured per orifice are shown for each type of experimental procedure and control. (*Supplementary Materials*)

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Review Article

A Critical Overview of Systematic Reviews and Meta-Analyses of Acupuncture for Female Stress Urinary Incontinence

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Objectives. As a urinary dysfunction disorder, stress urinary incontinence (SUI) is more common in women than in men. Acupuncture, a traditional minimally invasive technique, has potential efficacy in the treatment of SUI. The purpose of this overview is to critically assess the available evidence on acupuncture for the treatment of SUI in women. *Methods*. Two researchers searched seven databases for systematic reviews (SRs)/meta-analyses (MAs) of randomized controlled trials (RCTs) on acupuncture for SUI. Two researchers assessed the included SRs/MAs using the Assessment of Multiple Systematic Reviews 2 (AMSTAR-2), the Risk of Bias in Systematic (ROBIS) scale, the list of Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA), and the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) system. *Results*. Eight published SRs/MAs were included in our overview. According to the results of the AMSTAR-2 assessment, all SRs/MAs were of very low quality. According to the ROBIS evaluation results, no SR/MA was assessed as low risk of bias. According to the results of the PRISMA checklist assessment, no SR/MA was fully reported on the checklist. According to GRADE, a total of 27 outcomes extracted from the included SRs/MAs were evaluated, and only 1 was rated as high quality. *Conclusions*. Acupuncture may be an effective and safe complementary treatment for SUI in women. However, further standard and comprehensive SRs/MAs and RCTs are needed to provide an evidence-based medical rationale for this.

1. Introduction

As a form of dysfunction disorder, stress urinary incontinence (SUI) is the most common type of urinary incontinence. It is defined as the involuntary flow of urine due to physical exertion or effort, coughing, or sneezing [1]. SUI has a prevalence of up to 49% in physically active women and up to 15% in women aged 30–60 [2]. SUI can cause psychological burden, affect relationships, decrease physical productivity, and reduce a woman's quality of life [3], and its harm is even greater than that of major chronic diseases such as diabetes, hyperlipidemia, and chronic kidney diseases [4]. However, more than 80 percent of women received no treatment at all [5].

The main treatment modalities for SUI include lifestyle interventions, electrical stimulation, pelvic floor muscle training (PFMT), medication, and surgery [6]. The American Urological Association (AUA) currently recommends conservative treatment, such as PFMT, for patients with mild and moderate SUI [7]. However, this method has shortcomings such as poor compliance and difficulty in mastering training skills. Surgical treatment is effective in

patients with severe SUI, but it can cause potential complications, including pain, infection, and dysuria [8]. Therefore, there remains an urgent need for an effective and safe complementary treatment for SUI.

As a minimally invasive treatment method, acupuncture has a history of more than 2,500 years in China and is gaining more and more international attention in the field of healthcare [9]. With its unique advantages, acupuncture plays an irreplaceable role in the treatment of SUI. With the extensive use of acupuncture in the treatment of SUI, related systematic reviews (SRs) and meta-analyses (MAs) have also been published. Since the evidence provided by these SRs/MAs for acupuncture for SUI in women is sometimes inconsistent and varies in quality, a reevaluation is needed. An overview of SRs/MAs is a new method to comprehensively assess the methodological quality and certainty of quality across multiple SRs/MAs. Therefore, our research aimed to critically evaluate the quality of SRs/MAs regarding the acupuncture for female SUI through a comprehensive overview.

2. Materials and Methods

The methodology of this study follows the Cochrane manual, as well as the study methods of some high-quality SRs/MAs overviews [10–12].

2.1. Inclusion and Exclusion Criteria. The criteria for inclusion of SRs/MAs in this overview are as follows: (1) Study design: This overview includes SRs/MAs of randomized controlled trials (RCTs) of the acupuncture on SUI; (2) Type of participants: Female subjects diagnosed with SUI based on any authoritative national or international diagnostic criteria regardless of race, age, gender, time of onset, and source of cases; (3) Intervention: The control group received the following treatments: Conventional medication (CM), rehabilitation training (RT), sham acupuncture (SA), and placebo. The intervention group received acupuncture treatment, including plum blossom acupuncture, fire acupuncture, electro-acupuncture, body acupuncture, manual acupuncture, warm acupuncture, or acupuncture therapy in combination with the treatments received by the control group; (4) Outcome indicators: Outcomes assessed in this overview include: Effective rate, 1-hour pad test, international consultation on incontinence questionnaire short form (ICIQ-SF) score, visual analog scale (VAS) score, and adverse reactions.

The criteria for exclusion of SRs/MAs in this overview are as follows: (1) Animal studies; (2) Network MAs, research protocols, narrative reviews, overviews, dissertation, and conference abstracts.

2.2. Search Strategy. Literatures were retrieved from PubMed, Cochrane Library, EMBASE, Chongqing VIP, Wanfang Database, CNKI, and SinoMed on 1 January 2022. We adopted a search strategy combining keywords with free words, and the keywords include acupuncture, urinary incontinence, systematic review, and meta-analysis. The literature search strategy (shown in Table 1) of the PubMed database was reasonably tuned for each database. We also reviewed the references of the all retrieved literature to avoid missing topic-related SRs/MAs.

2.3. Literature Screening and Data Extraction. The literature screening (HS-S and LZ-Z) and information extraction (WB-L and ZC-W) were performed independently by two researchers. We firstly input the retrieved documents into Endnote X9 document management software, and then removed the duplicates. The literatures that potentially met the inclusion and exclusion criteria were then obtained by reading the titles and abstracts. Eventually, we finalized the included SRs/MAs by reading the full text. A standardized data extraction form was adopted to extract relevant information for the inclusion of SRs/MAs. The following information was extracted from each SR/MA: First author, year of publication, author nationality, number of RCTs included, sample size, intervention group measures, control group measures, tools used to assess the risk of bias, and main findings.

2.4. Quality Assessment for Inclusion in SRs/MAs. Two researchers (PL-L and D-W) independently assessed the methodological quality and certainty of quality of the included SRs/MAs.

2.4.1. Assessment of Methodological Quality. The methodological quality of the included SRs/MAs was assessed by the Assessment System for Evaluating Methodological Quality 2 (AMSTAR-2) [13]. Seven (2, 4, 7, 9, 11, 13, and 15) of the 16 items in the tool are critical areas.

2.4.2. Assessment of Risk of Bias. The Risk of Bias in Systematic Review (ROBIS) [14] scale was used in this overview to evaluate the risk of bias in the inclusion of SRs/MAs and the evaluation was carried out in three stages.

2.4.3. Assessment of Reporting Quality. The quality of each SR/MA report of the included SRs/MAs was evaluated by the list of PRISMA [15] which consists of 27 items focusing on the reporting methods and results that were incorporated into SRs/MAs.

2.4.4. Assessment of Certainty of Quality. The certainty of quality for each SR/MA outcome was evaluated by The Grading of Recommendations Assessment, Development, and Evaluation (GRADE) [16], and five aspects will lead to the degradation of certainty of quality, including limitations, inconsistencies, indirectness, imprecision, and publication bias.

3. Results

3.1. Literature Search and Screening Results. A total of 166 publications were retrieved from seven electronic databases. Nine publications were retrieved for full-text evaluation after

Table 1: Search strategy for the PubMed database.

Query	Search terms
#1	"Acupuncture" [mesh]
#2	"Pharmacopuncture" OR "acupuncture" OR "plum blossom needle" OR "fire needling" OR "warm needling" OR "electroacupuncture"
#3	#1 OR #2
#4	"Urinary Incontinence"[Mesh]
#5	"Incontinence, urinary", "urinary incontinence"
#6	#4 OR #5
#7	"Urinary incontinence, stress"[mesh]
#8	"Urinary stress incontinence" or "incontinence, urinary stress" or "stress incontinence, urinary" or "stress urinary incontinence"
#9	#7 OR #8
#10	#6 OR #9
#11	Meta-analysis as topic [mesh]
#12	"Systematic review" OR "meta-analysis" OR "meta analysis" OR "meta-analyses" OR "review, systematic" OR "systematic reviews"
#13	#12 OR #13
#14	#3 AND #10 AND #13

the duplicates removal and title/abstract screening. One paper [17] was excluded because it didn't focus on RCTs, and the remaining 8 SRs/MAs [18–25] were included in this overview. The flowchart of the screening process is shown in Figure 1. The exclusion list for the literature is in Table 2.

3.2. Inclusion of Characteristics of SRs/MAs. The characteristics of the 8 SRs/MAs included in our final evaluation were summarized, as shown in Table 3. These SRs/MAs were published between 2014 and 2021, with 6 [18–23] published after 2017. Three of the SRs/MAs [18–20] were in English, and the remaining five [21–25] were in Chinese. The number of RCTs included in the SRs/MAs ranged from 9 to 15, and the total number of subjects included in each SR/MA ranged from 579 to 1,577. The interventions for the control group were CM, SA, RT, and placebo, and the treatments for the intervention group were electroacupuncture (EA) and manual acupuncture (MA) or EA or MA in combination with the treatments received by the control group. In terms of the quality assessment for inclusion in RCTs, the Cochrane criteria was used for four SRs/MAs [18–20, 23] and the Jadad scale was used for four SRs/MAs [21, 22, 24, 25].

3.3. Results on SRs/MAs Quality Assessment

3.3.1. Results of the Methodological Quality. Regarding the methodological quality of the included SRs/MAs, all were considered to be of very low quality because more than one key item was missing from the SRs/MAs included in the quality assessment. Methodological quality limitations come from the following items: Items 2 (Only 2 SRs/MAs [19, 20] registered the research protocol), Item 4 (None of the SR/MA performed a comprehensive literature search), Item 7 (None of the SR/MA provided studies excluded from the list), and Item 10 (None of the SR/MA reported the funding of RCTs included in SRs/MAs). The evaluation details of the included SRs/MAs on the AMSTAR-2 are shown in Table 4.

3.3.2. Results of the Risk of Bias Assessment. Regarding the results of the ROBIS assessment, Phase 1 assessed the relevance of the study topic and Domain 1, with all SRs/MAs rated as low risk of bias in both items. Domain 2 assessed the identification and selection of studies, and none of the SR/MAs had a low risk of bias. In Domain 3, 6 SRs/MAs [18–22, 25] were rated as low risk of bias. Domain 4 assessed the synthesis and findings, and only 2 SRs/MAs [19, 23] were rated as low risk of bias. Phase 3 considered the overall risk of bias in the reviews, and none of the SR/MA had a low risk of bias. The evaluation details of the included SRs/MAs on the ROBIS scale are shown in Table 5.

3.3.3. Report Quality of the Included SRs/MAs. The results of the PRISMA inventory evaluation were shown in Table 6. 22 out of 27 items have a "yes OR partially yes" response rate of more than 60%, and this shows that the report is relatively complete. However, there are some reporting deficiencies in other items. The reports of Items 7 (search strategy), Item 15 (certainty assessment), Item 22 (competing interests), Item 23 (certainty of evidence), and Item 24 (registration and protocol) are incomplete (the "yes OR partially yes" response rate is less than 50%).

3.3.4. Results of the Certainty of Quality. The 8 SRs/MAs included 27 outcomes related to the effectiveness of acupuncture for SUI. For all the outcome indicators, 1 was rated as high quality, 10 moderate, 6 low and 10 very low by means of the GRADE evaluation. Publication bias ($n = 24$) was the most common downgrading factor, followed by risk of bias ($n = 13$), inconsistency ($n = 13$), imprecision ($n = 9$), and indirectness ($n = 0$). GRADE specific assessment details are shown in Table 7.

3.4. Description of Efficacy and Safety. Details of outcomes included in SRs/MAs are shown in Table 8, and 2 SRs/MAs [19, 20] provide narrative reviews that regard acupuncture as a safe treatment option. It can be seen that acupuncture is effective and safe for the treatment of female SUI.

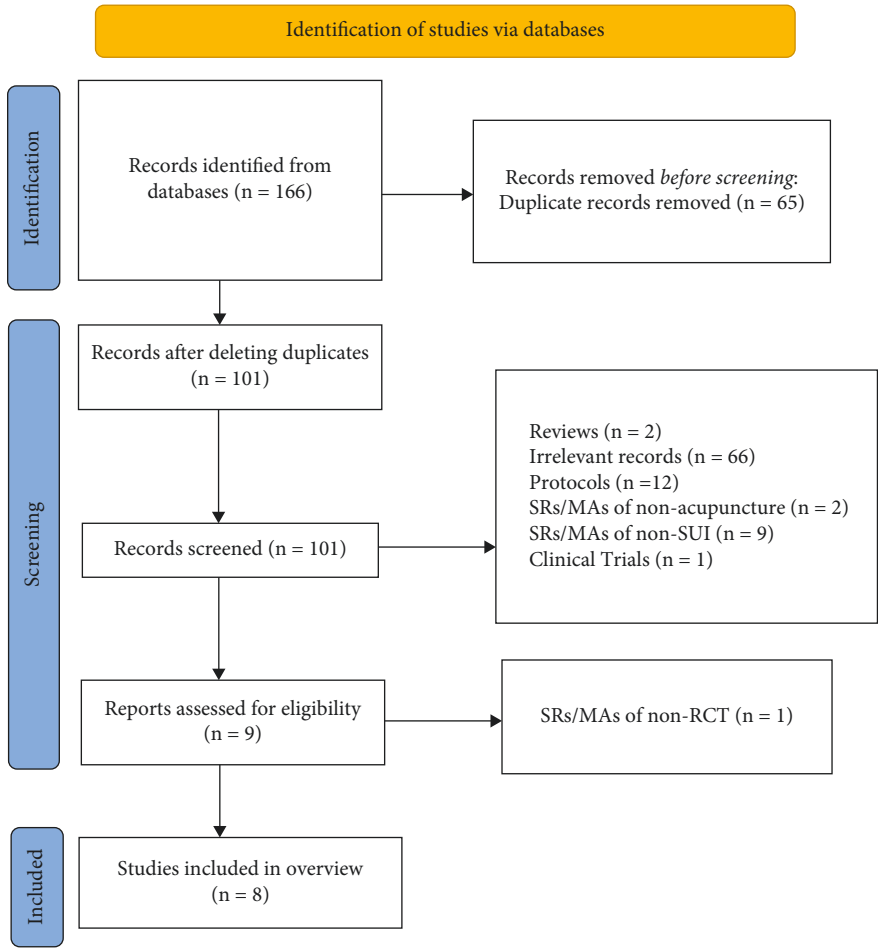

Figure 1: The flowchart of the screening process.

Table 2

Report excluded	Reason for Exclusion
Cheng, P., Chi, Z., Xiao, Y., Xie, W., Zhu, D., Yu, T., Jiao, L. (2020). The acupuncture-related therapy for post-stroke urinary incontinence: A protocol for systematic review and network meta-analysis. Medicine (Baltimore), 99(44), e22865. doi:10.1097/md.0000000000022865	Research Protocol
Huang, W., Li, X., Wang, Y., Yan, X., & Wu, S. (2017). Electroacupuncture for women with stress urinary incontinence: Protocol for a systematic review and meta-analysis. Medicine (Baltimore), 96(49), e9110. doi: 10.1097/md.0000000000009110	Research Protocol
Lin, Q., Ren, Y., Chen, K., Duan, H., Chen, M., & Liu, C. (2021). Efficacy and safety of heat-sensitive moxibustion in the treatment of neurogenic bladder after spinal cord injury: A protocol for systematic review and meta-analysis. Medicine (Baltimore), 100(24), e26424. doi:10.1097/md.0000000000026424	Research Protocol
Mo, Q., Wang, Y., Ye, Y., Yu, J., & Liu, Z. (2015). Acupuncture for adults with overactive bladder: a systematic review protocol. BMJ Open, 5(1), e006756. doi:10.1136/bmjopen-2014-006756	Research Protocol
Su, T., Zhou, J., Liu, Z., Chen, Y., Zhang, W., Chu, H., Liu, B. (2015). The efficacy of electroacupuncture for the treatment of simple female stress urinary incontinence - comparison with pelvic floor muscle training: study protocol for a multicenter randomized controlled trial. Trials, 16, 45. doi:10.1186/s13063-015-0560-1	Research Protocol
Sun, Z., Yu, N., Yue, J., & Zhang, Q. (2016). Acupuncture for urinary incontinence after stroke: a protocol for systematic review. BMJ Open, 6(2), e008062. doi:10.1136/bmjopen-2015-008062	Research Protocol
Wang, P., Shi, J., Zhao, L., Li, M., Jiao, J., Li, L., Zhang, S. (2020). The efficacy and safety of electroacupuncture against urinary incontinence after stroke: A protocol for systematic review and meta analysis. Medicine (Baltimore), 99(38), e22275. doi:10.1097/md.0000000000022275	Research Protocol
Wang, T. S., Wang, Z. M., Zhao, Y., Tang, Z. C., Song, W. D., & Wang, G. K. (2020). Effectiveness of electroacupuncture (EA) for the treatment of urinary incontinence (UI) in patients with spinal cord injury (SCI): A protocol of systematic review of randomized controlled trials. Medicine (Baltimore), 99(30), e21077. doi:10.1097/md.0000000000021077	Research Protocol

Table 2: Continued.

Report excluded	Reason for Exclusion
Wang, Y., Li, H., Wang, J., Hao, Q., Tu, Y., Chen, Y., Zhu, T. (2020). A network meta-analysis protocol of conservative interventions for urinary incontinence in postpartum women. Medicine (Baltimore), 99(33), e21772. doi:10.1097/md.0000000000021772	Research Protocol
Yang, J., Cheng, Y., Zhao, L., Chen, J., Zheng, Q., Guo, Y., & Liang, F. (2020). Acupuncture and related therapies for stress urinary incontinence: A protocol for systematic review and network meta-analysis. Medicine (Baltimore), 99(28), e21033. doi:10.1097/md.0000000000021033	Research Protocol
Zhong, D., Tang, W., Geng, D., & He, C. (2019). Efficacy and safety of acupuncture therapy for urinary incontinence in women: A systematic review and meta- analysis. Medicine (Baltimore), 98(40), e17320. doi: 10.1097/md.000000000001732	Research Protocol
Zhu, Z., Zhuo, Y., Jin, H., Wu, B., & Li, Z. (2021). Chinese medicine therapies for neurogenic bladder after spinal cord injury A protocol for systematic review and network meta-Analysis. Medicine (United States), 100(37). doi:10.1097/MD.0000000000027215	Research Protocol
Li Na. Meta-analysis of the effect of electroacupuncture combined with pelvic floor muscle exercise in the treatment of female stress urinary incontinence [J]. New Chinese Medicine, 2019, 51(08): 208-211. DOI: 10.13457/j.cnki.jncm.2019.08.062.	SRs/MAs of non-RCT
Fu Linhui, An Junming, Zhang Ding, Yang Pengcheng. Meta-analysis of electroacupuncture for neurogenic bladder after spinal cord injury [J]. Journal of Yunnan University of Traditional Chinese Medicine, 2019, 42(03): 61-68. DOI: 10.19288/j.cnki.issn.1000-2723.2019.03.011.	SRs/MAs of non-SUI
Liu Zhishun, Liu Baoyan, Yang Tao, Ye Yongming, Zhao Hong, Zhang Wei, Liu Jun, Liu Yuanshi, Guo Yufeng, Li Yisong, Huang Man, Yang Zhiqiang, Long Shuping, Huang Shixi. Clinical study of electroacupuncture in the treatment of senile urge urinary incontinence[1] J]. Chinese Acupuncture, 2001(10):5-8.	SRs/MAs of non-SUI
Tan Zhigao, Zhang Wei, Gong Houwu, Qin Zuoai, Zhong Feng, Cao Yue. Meta-analysis of the clinical efficacy of electroacupuncture in the treatment of post-stroke urinary incontinence [J]. Clinical Journal of Acupuncture and Moxibustion, 2015, 31(02): 74-77.	SRs/MAs of non-SUI
Wang Chaoran, Li Xiaojiang, Yang Peiying, Zhang Yao, Guo Shanqi, Jia Yingjie. Quality evaluation of literature reports on randomized controlled trials of acupuncture for postoperative urinary incontinence after prostate cancer [J]. Journal of Traditional Chinese Medicine Oncology, 2021, 3(04): 82-87.DOI:10.19811/ j.cnki.ISSN2096-6628.2021.04.015.	SRs/MAs of non-SUI
Wang Jiaqi, Liu Zhishun, Yu Jinna, Zhang Wei. A systematic review on the treatment of neurogenic bladder dysfunction after spinal cord injury with acupuncture and moxibustion [J]. Henan Traditional Chinese Medicine, 2018, 38(03): 467-472. DOI: 10.16367/j.issn.1003-5028.2018.03.0124.	SRs/MAs of non-SUI
Wang Qiong, Cao Zhengliang, Sun Jiaqi, Li Saiqun, Zhou Youjun, Zhang Wei. A systematic review of the efficacy of acupuncture in the treatment of urge urinary incontinence [J]. Clinical Journal of Acupuncture and Moxibustion, 2015, 31(08): 50-52.	SRs/MAs of non-SUI
Wang Zailing, Fu Lixin, Xiong Jun, Qi Yingzhou, Li Sheng. A systematic review of the efficacy of acupuncture in the treatment of urinary incontinence after stroke [J]. Clinical Journal of Acupuncture and Moxibustion, 2010, 26(01): 39-43.	SRs/MAs of non-SUI
Xu Hairong, Liu Zhishun, Zhao Hong. A systematic review of acupuncture in the treatment of overactive bladder [J]. Journal of Modern Integrative Medicine, 2011, 20(04): 393-399.	SRs/MAs of non-SUI
Zhang Jiapeng, Chen Peiyi, Zhao Ziyu. Meta-analysis of clinical research on electroacupuncture for senile urinary incontinence [J]. Nursing Research, 2018, 32(07):1082-1087.	SRs/MAs of non-SUI
Guo Guangming, Yuan Baofeng, Zhu Shina, Li Jun. Meta-analysis of the efficacy of moxibustion combined with pelvic floor muscle training in the treatment of mild to moderate stress urinary incontinence [J]. Journal of Xiangnan University (Medical Edition), 2021, 23(03):13-18.DOI:10.16500/j.cnki.1673-498x.2021.03.003.	SRs/MAs of non-acupuncture
Liu Qinyu, Huang Huirong, Liu Fang, Han Xueqi, Miao Shaofang. Meta-analysis of the efficacy and quality of life of moxibustion on female stress urinary incontinence [J]. Massage and Rehabilitation Medicine, 2021, 12(04):8-14.DOI:10.19787/j.issn.1008-1879.2021.04.003.	SRs/MAs of non-acupuncture
Li Xiaoning, Yao Suyuan, Li Xiaowei, Ni Jinxia, Sheng Guobin. A clinical study of electroacupuncture on 120 cases of non-inhibitory neurogenic bladder [J]. Clinical Journal of Acupuncture and Moxibustion, 2005(05): 40-41.	Clinical Trials

4. Discussion

SUI can severely impair a patient's ability to perform daily activities, leading to embarrassment, insomnia, and social isolation [26], and acupuncture is a minimally invasive technique with the potential treatment of SUI. This research aimed to systematically and comprehensively collate, evaluate and summarize the published evidence on acupuncture for SUI in recent years.

4.1. Summary of the Main Findings. This overview incorporated 8 SRs/MAs on acupuncture for SUI. These publications were based on the RCT and were published from 2014 to 2021. Six (6/8, 75%) SRs/MAs were published in the last five years, indicating that acupuncture had received increasing attention as an important intervention modality for SUI in women.

Based on the results of the AMSTAR-2, ROBIS, and PRISMA evaluation in this overview, the methodological

Table 3: Characteristics of the included SRs/MAs.

Author, year (Country)	Trials (subjects)	Intervention group	Control group	Risk of bias assessment tool	Main results
Na Yang, 2021 (China) [18]	8 (607)	MA, EA, MA + control group, EA + control group	CM, SA, RT	Cochrane criteria	Based on this study, acupuncture intervention on SUI in middle-aged and elderly women can improve clinical efficacy, reduce urine leakage and decrease ICIQ-SF score in the urine pad test.
Xiuhua Lai, 2020 (China) [19]	15 (1,577)	EA	CM, SA, RT	Cochrane criteria	Electroacupuncture for women with SUI demonstrates significant efficacy and safety across key outcomes.
Yajing Zhong, 2020 (China) [20]	10 (1,200)	EA, EA + control group	CM, SA, RT	Cochrane criteria	In conclusion, our findings suggest that there is weak evidence for the use of EA to improve response rates, reduce urine leakage, and decrease incontinence episodes in patients with SUI.
Chen, et al. 2018 (China) [21]	14 (1,172)	EA, MA, MA + control group	RT, CM	Jadad scale	The acupuncture therapy was compared with other treatments, and the data analysis shows that the total effective rate of acupuncture in the treatment of female SUI is higher than that of the control group.
Chen, 2020 (China) [22]	11 (1,005)	EA, MA, MA + control group	RT, CM	Jadad scale	The clinical efficacy of acupuncture in the treatment of female SUI is significantly better than that of pelvic floor muscle exercises.
Ma, et al. 2021 (China) [23]	16 (985)	MA, EA, MA + control Group, EA + control Group	RT	Cochrane Criteria	Compared with Kegel exercise, acupuncture in the treatment of female SUI showed statistically significant differences in four commonly used indicators: Effective rate, ICI-Q-SF score, 1-hour urine pad test and 24-hour urine diary.
Wang, et al. 2014 (China) [24]	9 (579)	MA, EA, MA + control group, EA + control group	RT, CM, placebo	Jadad scale	The results show that acupuncture is effective in treating stress urinary incontinence, and is superior to western medicine and pelvic floor muscle training. It has no toxic side effects and is easy for patients to adhere to.
Zhang,et al. 2016 (China) [25]	10 (785)	EA, MA, EA + control group	RT, CM, placebo	Jadad scale	In conclusion, the analysis results show that the acupuncture prescription has some advantages in treating female SUI, but the limitations of inclusion in the study reduce the reliability of the above results.

Table 4: Result of the AMSTAR-2 assessments.

Author, year (Country)	Q1	**Q2**	Q3	**Q4**	Q5	Q6	**Q7**	Q8	**Q9**	Q10	**Q11**	Q12	**Q13**	Q14	**Q15**	Q16	Quality
Na Yang, 2021 (China) [18]	Y	PY	Y	PY	Y	Y	N	Y	Y	N	Y	Y	Y	N	Y	Y	VL
Xiuhua Lai, 2020 (China) [19]	Y	Y	Y	PY	Y	Y	N	Y	Y	N	Y	Y	Y	Y	Y	Y	VL
Yajing Zhong, 2020 (China) [20]	Y	Y	Y	PY	Y	Y	N	Y	Y	N	Y	Y	Y	Y	N	Y	VL
Chen, et al. 2018 (China) [21]	Y	PY	Y	PY	Y	Y	N	Y	Y	N	Y	Y	N	N	Y	N	VL
Chen, 2020 (China) [22]	Y	PY	Y	PY	Y	Y	N	Y	Y	N	Y	N	N	Y	N	N	VL
Ma, et al. 2021 (China) [23]	Y	PY	Y	PY	Y	N	N	Y	Y	N	Y	Y	Y	Y	Y	Y	VL
Wang, et al. 2014 (China) [24]	Y	PY	Y	PY	Y	N	N	Y	Y	N	Y	Y	Y	Y	Y	Y	VL
Zhang, and Xie 2016 (China) [25]	Y	PY	Y	PY	Y	N	N	Y	Y	N	Y	Y	Y	N	Y	N	VL

Note: Y, Yes; PY, partial Yes; N, No; VL, Very low; H, High. Note: Key areas are marked in bold.

and reporting quality of the SRs/MAs were unsatisfactory. Only two SRs/MAs contained initial research protocol registrations, the lack of which could lead to non-standardization of the research process, increase the risk of bias and impact the rigor and credibility of the final SRs/MAs results. All of the included SRs/MAs lacked a search of the gray literature, which made it difficult to ensure the comprehensiveness of the literature search and tended to generate publication bias. None of the SR/MA provided a complete list of exclusions for each study, which may affect the reliability of the results and assessment of publication bias. The provision of a list of exclusion researches can be a stronger demonstration of the rigor of the literature screening process. No SR/MA reporting was included in the RCT's funding resources, which may increase the bias in clinical trials as the results of corporate-funded studies may be biased in favor of the funder. None of the SR/MA provides comprehensive search strategies, which reduced the

Table 5: Results of the ROBIS assessments.

Author, year (Country)	Phase 1	Phase 2				Phase 3
	Assessing relevance	Domain 1: Study eligibility criteria	Domain 2: Identification and selection of studies	Domain 3: Collection and study appraisal	Domain 4: Synthesis and findings	Risk of bias in the review
Na Yang, 2021 (China) [18]	√	√	×	√	×	×
Xiuhua Lai, 2020 (China) [19]	√	√	×	√	√	×
Yajing Zhong, 2020 (China) [20]	√	√	×	√	×	×
Chen, et al. 2018 (China) [21]	√	√	×	√	×	×
Chen, 2020 (China) [22]	√	√	×	√	×	×
Ma, et al. 2021 (China) [23]	√	√	×	×	√	×
Wang, et al. 2014 (China) [24]	√	√	×	×	×	×
Zhang and Xie, 2016 (China) [25]	√	√	×	√	×	×

Note: √, low risk; ×, high risk.

Table 6: Results of the PRISMA checklist.

Section/topic		Items	Na Yang, 2021 (China) [18]	Xiuhua Lai, 2020 (China) [19]	Yajing Zhong, 2020 (China) [20]	Chen, et al. 2018 (China) [21]	Chen, 2020 (China) [22]	Ma, et al. 2021 (China) [23]	Wang, et al. 2014 (China) [24]	Zhang and Xie 2016 (China) [25]	Number of yes or partially yes (%)
Title	Title	Item 1	Y	Y	Y	Y	Y	Y	Y	Y	100%
Abstract	Abstract	Item 2	PY	PY	PY	PY	PY	PY	PY	PY	100%
Introduction	Rationale	Item 3	Y	Y	Y	Y	Y	Y	Y	Y	100%
	Objectives	Item 4	Y	Y	Y	Y	Y	Y	Y	Y	100%
Methods	Eligibility criteria	Item 5	Y	Y	Y	Y	Y	Y	Y	Y	100%
	Information sources	Item 6	Y	Y	Y	Y	Y	Y	Y	Y	100%
	Search strategy	Item 7	N	N	N	N	N	N	N	N	0%
	Selection process	Item 8	Y	Y	Y	Y	Y	Y	Y	Y	100%
	Data collection process	Item 9	Y	Y	Y	Y	Y	N	N	N	62.50%
	Data items	Item 10 (a)	Y	Y	Y	Y	Y	Y	Y	Y	100%
		Item 10 (b)	PY	PY	PY	PY	PY	PY	PY	PY	100%
	Study risk of bias assessment	Item 11	Y	Y	Y	Y	Y	PY	PY	Y	100%
	Effect measures	Item 12	Y	Y	Y	Y	Y	Y	Y	Y	100%

Table 6: Continued.

Section/topic		Items	Na Yang, 2021 (China) [18]	Xiuhua Lai, 2020 (China) [19]	Yajing Zhong, 2020 (China) [20]	Chen, et al. 2018 (China) [21]	Chen, 2020 (China) [22]	Ma, et al. 2021 (China) [23]	Wang, et al. 2014 (China) [24]	Zhang and Xie 2016 (China) [25]	Number of yes or partially yes (%)
		Item 13 (a)	Y	Y	Y	Y	Y	Y	Y	Y	100%
		Item 13 (a)	Y	Y	Y	Y	Y	Y	Y	Y	100%
	Synthesis methods	Item 13 (c)	Y	Y	Y	Y	Y	Y	Y	Y	100%
		Item 13 (d)	Y	Y	Y	Y	Y	Y	Y	Y	100%
		Item 13 (e)	N	Y	Y	N	Y	Y	Y	N	62.50%
		Item 13 (f)	N	Y	Y	N	Y	Y	N	Y	62.50%
	Reporting bias assessment	Item 14	Y	Y	N	Y	N	Y	N	Y	62.50%
	Certainty assessment	Item 15	N	N	N	N	N	N	N	N	0%
Results		Item 16 (a)	Y	Y	Y	Y	Y	Y	Y	Y	100%
	Study selection	Item 16 (b)	Y	Y	Y	Y	Y	N	Y	Y	87.50%
	Study characteristics	Item 17	Y	Y	Y	Y	Y	Y	Y	Y	100%
	Risk of bias in studies	Item 18	Y	Y	Y	Y	Y	Y	Y	Y	100%
	Results of individual studies	Item 19 (a)	Y	Y	Y	Y	Y	Y	Y	Y	100%
		Item 19 (b)	Y	Y	Y	Y	Y	Y	Y	Y	100%
	Results of syntheses	Item 20 (a)	Y	Y	Y	Y	Y	Y	Y	Y	100%
		Item 20 (b)	Y	Y	Y	Y	Y	Y	Y	Y	100%
		Item 20 (c)	N	Y	Y	N	Y	Y	Y	N	62.50%
		Item 20 (d)	N	Y	Y	N	Y	Y	N	Y	62.50%
	Reporting biases	Item 21	Y	Y	N	Y	N	Y	Y	Y	75%
	Certainty of evidence	Item 22	N	N	N	N	N	N	N	N	0%
Discussion		Item 23 (a)	Y	Y	Y	Y	Y	Y	Y	Y	100%
	Discussion	Item 23 (b)	Y	Y	Y	Y	Y	Y	Y	Y	100%
		Item 23 (c)	Y	Y	Y	Y	Y	Y	Y	Y	100%
		Item 23 (d)	Y	Y	Y	Y	Y	Y	Y	Y	100%

Table 6: Continued.

Section/topic		Items	Na Yang, 2021 (China) [18]	Xiuhua Lai, 2020 (China) [19]	Yajing Zhong, 2020 (China) [20]	Chen, et al. 2018 (China) [21]	Chen, 2020 (China) [22]	Ma, et al. 2021 (China) [23]	Wang, et al. 2014 (China) [24]	Zhang and Xie 2016 (China) [25]	Number of yes or partially yes (%)
Other information		Item 24 (a)	N	Y	Y	N	N	N	N	N	25%
	Registration and protocol	Item 24 (b)	N	Y	Y	N	N	N	N	N	25%
		Item 24 (c)	N	N	N	N	N	N	N	N	0%
	Support	Item 25	Y	Y	Y	N	N	Y	Y	N	62.50%
	Competing interests	Item 26	Y	Y	Y	N	N	N	N	N	37.50%
	Availability of data, code, and other materials	Item 27	Y	Y	Y	Y	Y	Y	Y	Y	100%

Note: Y, yes; N, no; PY, partially yes.

Table 7: Results of certainty of quality.

Author, year (Country)	Outcomes	Studies (participants)	Limitations	Inconsistency	Indirectness	Imprecision	Publication bias	Quality
Na Yang, 2021 (China) [18]	Effective rate	7 (523)	0	0	0	0	0	High
	1-hour pad test	5 (417)	0	−1②	0	0	−1④	Low
	ICIQ-SF score	4 (366)	0	−1②	0	−1③	−1④⑤	Low
Xiuhua Lai, 2020 (China) [19]	Effective rate	13 (1,333)	0	0	0	0	−1④	Moderate
	ICIQ-SF score	6 (763)	0	−1②	0	0	−1④	Low
	1-hour pad test	5 (900)	0	−1②	0	0	−1④	Low
Yajing Zhong, 2020 (China) [20]	Effective rate	7 (1,010)	0	−1②	0	0	−1④	Low
	1-hour pad test	9 (1,157)	0	−1②	0	0	−1④	Low
	ICIQ-SF score	9 (1,157)	0	−1②	0	0	−1④	Moderate
	72-hour incontinence episodes	3 (654)	0	0	0	0	−1④	Moderate
	Follow-up of the effective rate	2 (584)	0	0	0	0	−1④⑤	Moderate
	Follow-up of the ICIQ-SF score	3 (644)	0	−1②	0	0	−1④⑤	Moderate
	Follow-up of the 72-hour incontinence episodes	2 (584)	0	0	0	0	−1④⑤	Moderate
Chen, et al. 2018 (China) [21]	Effective rate (acupuncture and RT)	8 (558)	−1①	0	0	0	0	Moderate
	Effective rate (acupuncture and CM)	3 (220)	−1①	0	0	−1③	−1④	Low
	ICIQ-SF score (acupuncture and RT)	5 (323)	−1①	−1②	0	−1③	−1④	Very low
Chen, 2020 (China) [22]	Effective rate	7 (577)	−1①	0	0	0	−1④	Low

Table 7: Continued.

Author, year (Country)	Outcomes	Studies (participants)	Limitations	Inconsistency	Indirectness	Imprecision	Publication bias	Quality
Ma, et al. 2021 (China) [23]	Effective rate	13 (812)	−1①	0	0	0	−1④	Low
	ICIQ-SF score	6 (377)	−1①	−1②	0	−1③	−1④	Very low
	1-hour pad test	9 (504)	−1①	−1②	0	0	−1④	Very low
	24-hour urination diary	9 (143)	−1①	0	0	−1③	−1④	Low
Wang, et al. 2014 (China) [24]	Effective rate (acupuncture and RT)	5 (461)	−1①	0	0	0	0	Moderate
	Effective rate (acupuncture and CM)	3 (220)	−1①	0	0	−1③	−1⑤	Moderate
	Effective rate (acupuncture and placebo)	2 (198)	−1①	0	0	−1③	−1⑤	Moderate
Zhang and Xie, 2016 (China) [25]	Effective rate	10 (607)	−1①	−1②	0	0	−1④	Low
	ICIQ-SF score	4 (257)	−1①	−1②	0	−1③	−1④	Very low
	VAS	2 (206)	0	0	0	−1③	−1④⑤	Moderate

Note: ① The included studies have a large bias in methodology such as randomization, allocation concealment, and blinding. ② The confidence interval overlaps less or the I2 value of the combined results was larger. ③ The sample size from the included studies does not meet the optimal sample size or the 95% confidence interval crosses the invalid line. ④ The funnel chart is asymmetry. ⑤ Fewer studies were included, and their results were all positive, which may result in a large publication bias.

Table 8: Summary of evidence.

Author, year (country)	Outcomes	Studies (participants, intervention group/control group)	Relative effect (95% CI)	Heterogeneity	p value
Na Yang, 2021 (China) [18]	Effective rate	7 (523, 264/259)	OR = 5.52 (3.13, 9.73)*	$I^2 = 0\%$	$p < 0.00001$
	1-hour pad test	5 (417, 210/207)	SMD = −2.67 (−4.05, −1.29)*	$I^2 = 96\%$	$p = 0.0001$
	ICIQ-SF score	4 (366, 183/183)	MD = −3.46, (−3.69, −3.22)*	$I^2 = 87\%$	$p < 0.00001$
Xiuhua Lai, 2020 (China) [19]	Effective rate	13 (1,333, 667/666)	OR = 5.64 (4.19, 7.59)*	$I^2 = 22\%$	$p < 0.00001$
	ICIQ-SF score	6 (763, 381/382)	SMD = −0.61 (−0.74, −0.48)*	$I^2 = 80\%$	$p < 0.00001$
	1-hour pad test	5 (900, 450/450)	MD = −4.14 (−4.96, −3.33)*	$I^2 = 78\%$	$p < 0.00001$
Yajing Zhong, 2020 (China) [20]	Effective rate	7 (1,010, 503/507)	RR = 2.03 (1.40, 2.95)*	$I^2 = 89\%$	$p = 0.0002$
	1-hour pad test	9 (1,157, 578/579)	MD = 3.33 (0.89, 5.77)*	$I^2 = 98\%$	$p = 0.008$
	ICIQ-SF score	9 (1,157, 578/579)	MD = 3.14 (2.42, 3.85)*	$I^2 = 63\%$	$p < 0.00001$
	72-hour incontinence episodes	3 (654, 327/327)	MD = 1.17 (0.56, 1.78)*	$I^2 = 0\%$	$p = 0.0002$
	Follow-up of the effective rate	2 (584, 292/292)	MD = 2.10 (1.28, 2.92)*	$I^2 = 0\%$	$p < 0.00001$
	Follow-up of the ICIQ-SF score	3 (644, 322/322)	MD = 2.89 (1.96, 3.82)*	$I^2 = 54\%$	$p < 0.00001$
	Follow-up of the 72-hour incontinence episodes	2 (584, 292/292)	MD = 2.10 (1.28, 2.92)*	$I^2 = 0\%$	$p < 0.00001$
Chen, et al. 2018 (China) [21]	Effective rate (acupuncture and RT)	8 (558, 281/277)	RR = 1.33 (1.22, 1.46)*	$I^2 = 0\%$	$p < 0.00001$

Table 8: Continued.

Author, year (country)	Outcomes	Studies (participants, intervention group/control group)	Relative effect (95% CI)	Heterogeneity	p value
	Effective rate (acupuncture and CM)	3 (220, 110/110)	RR = 2.15 (1.64, 2.83)*	$I^2 = 0\%$	$p < 0.00001$
	ICIQ-SF score (acupuncture and RT)	5 (323, 162/161)	MD = −1.29 (−2.88, 0.31)	$I^2 = 80\%$	$p = 0.11$
Chen, 2020 (China) [22]	Effective rate	7 (577, 289/287)	OR = 4.10 (1.85, 9.10)*	$I^2 = 62\%$	$p = 0.0005$
Ma, et al. 2021 (China) [23]	Effective rate	13 (812, 408/404)	OR = 6.04 (3.84, 9.49)*	$I^2 = 0\%$	$p < 0.00001$
	ICIQ-SF score	6 (377, 189/188)	MD = −3.03 (−4.17, −1.90)*	$I^2 = 80\%$	$p < 0.00001$
	1-hour pad test	9 (504, 252/252)	MD = −2.95 (−3.86, −2.04)*	$I^2 = 88\%$	$p < 0.00001$
	24-hour urination diary	9 (143, 71/72)	MD = −0.97 (−1.61, −0.33)*	$I^2 = 65\%$	$p < 0.00001$
Wang, et al. 2014 (China) [24]	Effective rate (acupuncture and RT)	5 (461, 231/230)	OR = 4.00 (2.51, 6.39)*	$I^2 = 0\%$	$p = 0.003$
	Effective rate (acupuncture and CM)	3 (220, 110/110)	OR = 9.14 (4.77, 17.53)*	$I^2 = 47\%$	$p < 0.00001$
	Effective rate (acupuncture and placebo)	2 (198, 99/99)	OR = 3.05 (1.59, 5.84)*	$I^2 = 0\%$	$p = 0.0008$
Zhang and Xie 2016 (China) [25]	Effective rate	10 (785, 394/391)	OR = 4.27 (2.42, 7.56)*	$I^2 = 50\%$	$p < 0.00001$
	ICIQ-SF score	4 (257, 129/128)	SMD = −0.41 (−1.00, 0.18)	$I^2 = 82\%$	$p = 0.17$
	VAS	2 (206, 103/103)	SMD = −2.16 (−2.51, −1.81)*	$I^2 = 0\%$	$p < 0.00001$

Note: * The 95% confidence interval does not cross the invalid line.

reproducibility and credibility of the study. In addition, the lack of reporting of conflicts of interest also potentially affected the credibility of the article.

Based on the GRADE assessment, publication bias was deemed as the most significant downgrading factor. Further analysis revealed a risk of publication bias for the outcome indicators included in the SRs/MAs, which may be related to incomplete searches and the insufficient number of RCTs included in the relevant outcomes. In addition, other reasons for the downgrading risk of bias included: Most of these RCTs mentioned randomization without giving the randomization method; most didn't conceal allocation; and most didn't use blinding method or just used single blinding. Declining certainty of quality due to inconsistency may stem from substantial clinical and methodological differences in the included RCTs, which could be avoided by standardizing the inclusion and exclusion criteria as well as the literature screening process.

Descriptive analysis suggested that acupuncture was an effective treatment for SUI in women with a high safety profile. However, due to the low methodological quality and certainty of quality of the included studies, these findings may deviate from the actual results. Therefore, caution should be exercised when recommending acupuncture as a complementary intervention for SUI in women.

4.2. Implications for Practice and Research. Featuring unique advantages, acupuncture therapy plays an integral role in the treatment of urinary incontinence. Acupuncture works by repeatedly stimulating the points within the body by needling the control points of the bladder and sphincter muscles, thus effectively repairing and improving the body's various control functions [27].

This paper gave a comprehensive assessment of all aspects of the included SRs/MAs using AMSTAR-2, PRISMA, ROBIS, and GRADE, and the methodological quality and certainty of quality were found unsatisfactory. As implied, there is still considerable scope for addressing the quality issues in the process of conducting SRs/MAs. When selecting topics for SRs/MAs, investigators should register or publish study protocols in advance to minimize the risk of bias and ensure the standardization of SRs/MAs. The search for gray literature, complete search strategy and the list of excluded literature need to be supplemented in SRs/MAs, which can reduce publication bias and improve the certainty of quality. A list of funding for RCTs and declarations of conflicts of interest need to be provided to increase the credibility of SRs/MAs. In addition to this, the specific nature of acupuncture treatment makes it difficult to perform a blinded acupuncture-related RCT. However, patients, care providers, and outcome evaluators should be

blinded whenever possible to minimize the risk of bias. A well-designed and rigorously executed RCT is believed to be the gold standard for evaluating interventions to minimize or avoid bias [28]. Acupuncture has its origins in TCM theory, and there exist a diverse and individualized selection of acupuncture points, and future research protocols on acupuncture should be fully standardized to improve the quality of research. In addition, the currently published SRs/MAs neglect the assessment of indicators related to urodynamic indices, and it is expected that future studies should help us to better understand the potential mechanism of acupuncture for SUI by increasing the assessment of related indicators.

4.3. Strength and Limitations. Our overview is the first to use AMSTAR2, ROBIS, PRISMA, and GRADE to evaluate SRs/MAs regarding acupuncture for the treatment of female SUI. The evaluation process revealed clear limitations of the current relevant SRs/MAs and RCTs, which may help boost the quality of future clinical studies. However, the overview may have some limitations due to the subjectivity of the evaluation. Although our evaluation had been assessed and reviewed by two independent reviewers, different reviewers may have their own judgments about each factor, so the results may vary. In addition, for different SRs/MAs included in this overview, the definition of effective rate is not mentioned.

5. Conclusion

In conclusion, acupuncture is a beneficial and safe way to treat SUI in women. However, due to the generally low methodological quality and certainty of quality in the included SRs/MAs, clinicians should approach these findings with caution in their practice.

Data Availability

The datasets analyzed during the current study are available from the corresponding author upon reasonable request.

Disclosure

Hongshuo Shi and Leizuo Zhao are the co-first authors.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Authors' Contributions

LWB and ZLZ participated in the research design. SHS, WZC, LWB, and ZLZ conducted a literature search and screened data extraction. SHS, LPL and WD analyzed the data, did a statistical analysis, and wrote a manuscript. DCD, LPL, and SHH participated in the correction of the manuscript. GD and CLR helped with manuscript revision. All authors reviewed the manuscript. All authors read and approved the final version of the manuscript.

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Supplementary Materials

Supplementary file 1: List of articles excluded from this study. (*Supplementary Materials*)

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Review Article

Efficacy and Safety of Transcutaneous Electrical Acupoint Stimulation for Postoperative Pain: A Meta-Analysis of Randomized Controlled Trials

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Objective. This meta-analysis aims to evaluate the effectiveness and safety of transcutaneous electrical acupoint stimulation (TEAS) in treating post-operative pain. *Methods*. This meta-analysis was registered in PROSPERO (CRD42021286753). We searched PubMed, Embase, and the Cochrane Library for relevant randomized controlled trials (RCTs) about TEAS in treating postoperative pain that were published before November 2021. The primary outcome was visual analogue scale (VAS) within 24 h after surgery. The secondary outcomes included postoperative opioid analgesic drug consumption and the occurrence of adverse reactions within the postoperative 24–72 h. Adverse reactions included dizziness, nausea, and vomiting. Continuous variables were analyzed using mean difference (MDs) or standardized mean difference (SMDs) and 95% CIs. Relative risk (RR) and 95% CI were used for dichotomous data. The data were pooled and analyzed by RevMan 5.4 and STATA15.0 software. *Results*. Seventeen trials with 1375 participants were included. The current results suggested that application of TEAS showed obvious superiority in reducing VAS scores (SMD = −1.51, 95% CI = −2.20~−0.82, I2 = 96%). Subgroup analysis was performed according to open surgery and minimally invasive surgery. VAS scores were decreased after surgery at 24 h (SMD = −0.84, 95% CI = −1.07~−0.6, I2 = 96%; SMD = −0.88, 95% CI = −1.02~−0.75, I2 = 96%). The incidence of postoperative dizziness and nausea and vomiting was significantly lower in the TEAS group within postoperative 24–72 h (RR = 0.48, 95% CI = 0.34~0.68, I2 = 0%; RR = 0.66, 95% CI = 0.44~1.01, I2 = 69%; and RR = 0.49, 95% CI = 0.24~1.00, I2 = 51%). Postoperative opioid analgesics were also reduced in the TEAS group within 72 h after surgery (SMD = −2.10, 95% CI = −3.37~−0.82, I2 = 96%). *Conclusions*. TEAS can reduce post-operative pain as well as the incidence of dizziness, nausea, and vomiting and the number of analgesics used after surgery. TEAS is a reasonable modality to incorporate into a multimodal management approach for postoperative pain.

1. Introduction

Postoperative pain, including acute postoperative pain and persistent chronic postoperative pain, remains a main clinical problem [1]. In 2020, the current International Association for the Study of Pain (IASP) defined pain as "an unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damages" [2]. A 2011 report from the US National Institutes of Health states that more than 80% of patients suffer postoperative pain, with fewer than 50% receiving adequate pain relief [3]. US surveys from 1993, 2003, and 2012 have shown that postoperative pain is common and remains undertreated, and that the distribution and quality of perceived pain have remained largely unchanged [3]. Evidence suggests that less than half of patients who undergo

surgery report adequate postoperative pain relief and about 10% of postoperative pain develops into chronic pain [4]. In addition to impairing the patient's comfort, inadequately controlled pain negatively affects quality of life, function, and functional recovery, increases the risk of postsurgical complications. Postoperative pain not only reduces patients' satisfaction about the healthcare system but also prolongs the length of hospital stay and healthcare costs. Postoperative pain management is still based on the use of traditional opioids such as paracetamol, nonsteroidal anti-inflammatory drugs (NSAIDs), and local anesthetics [5]. A recent retrospective review based on more than 300 000 patients across 380 US hospitals showed that about 95% of surgical patients were treated with opioids [3]. However, opioids have many side-effects that range from bothersome to life-threatening, including nausea, vomiting, constipation, oversedation, somnolence, and respiratory depression [6]. NSAIDs can be responsible for several well-known side effects, comprising upper gastrointestinal bleeding and cardiovascular disease [7]. Local anesthetics are widely used in various fields, but the long-term effects of local anesthetics can lead to adverse conditions, such as inhibition of central and respiratory circulation, and even death of patients [8]. Therefore, it is particularly urgent to find a more efficient way to manage postoperative pain.

Transcutaneous electrical acupoint stimulation (TEAS) is a noninvasive form of electrical acupoint stimulation. Instead of traditional acupuncture intervention, which involves inserting a needle into an acupoint and applying manual stimulation including acupuncture and electroacupuncture, the stimulation on the acupoint is delivered through electricity which is delivered through the surface electrodes [9]. Modern medical research has proved that acupuncture treatment can inhibit the body's pain conduction [10], promote local blood circulation [11], improve the immunity of the patients [12], and enhance the body's anti-inflammatory and metabolic ability [13]. All of these mechanisms can have a rapid analgesic effect. However, there is still a lack of strong clinical evidence to confirm its effectiveness and safety in treating patients with postoperative pain. Therefore, we performed this meta-analysis to assess the effectiveness and safety of TEAS in the treatment of postoperative pain. The primary outcome is the visual analogue scale (VAS) within 24 h after surgery. While the secondary outcomes include postoperative analgesic drug consumption and the occurrence of adverse reactions within postoperative 24–72 h. Adverse reactions included dizziness, nausea, and vomiting.

2. Materials and Methods

2.1. Compliance with Ethics Guidelines. This article is based on previously conducted studies and does not contain any studies with human participants or animals performed by any of the authors.

2.2. Inclusion and Exclusion Criteria. Two authors independently identified the eligibilities of articles for in-depth examination by using the following inclusion: (1) The type of research should be a randomized controlled trial (RCT), and the language is limited to English. (2) Patients of any age and gender with postoperative pain, and if there are other causes of pain will be excluded. (3) The intervention in the experimental group was TEAS (patients in this group received electrical stimulation on the target acupoints. The stimulation was provided by an electrical stimulator through electrode tabs on the target acupoints. The electrical stimulator was set at certain modes, frequency, and intensity accordingly), and the control group was treated with sham-TEAS, blank control, or the same intervention as the treatment group other than TEAS will also be included. (4) Articles involved in evaluating the effectiveness of TEAS on postoperative pain. The exclusion criteria were as follows: (1) article types of comments, case reports, crossover studies, letters, editorials, review articles, meta-analysis, and retrospective studies; (2) studies of animal experiments; and (3) studies involving data that cannot be extracted or lacking adequate data. If discrepancies existed, final decisions were reached via consensus of all authors.

Table 1: Embase search terms.

Number	Search terms
#1	"Postoperative pain"/exp
#2	"Postoperative pain":ab, ti
#3	"Postoperative analgesi*":ab, ti
#4	"Pain management":ab, ti
#5	ache*:ab, ti
#6	#1 OR #2 OR #3 OR #4 OR #5
#7	"Transcutaneous electrical acupoint stimulation":ab, ti
#8	"Transcutaneous acupoint electrical stimulation":ab, ti
#9	electroacupuncture*:ab, ti
#10	"Electro acupuncture":ab, ti
#11	teas: ab, ti
#12	#7 OR #8 OR #9 OR #10 OR #11
#13	#6 AND #12

2.3. Search Strategy. The meta-analysis was performed in accordance with the Cochrane Handbook for Systematic Reviews of Interventions [14] and is reported in compliance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement [15]. This meta-analysis was prospectively registered in PROSPERO (CRD42021286753). We searched PubMed, Embase, and the Cochrane Library from inception to November 2021, without any restrictions. The search terms included terms related to TEAS (e.g., " transcutaneous electrical acupoint stimulation " OR " TEAS " OR " transcutaneous acupoint electrical stimulation " OR′ " acustimulation ") and terms related to postoperative pain (e.g., ' post-operative analgesi*" OR " pain, post-operative " OR " pain management " OR′ " ache*") (Table 1). There were no restrictions on dates, sex, or age, or type of surgery. We searched for these terms in the titles and abstracts of potentially relevant papers. The references of the retrieved papers were also reviewed for further relevant studies. The lists of references of retrieved articles will be searched for identifying potentially eligible trials.

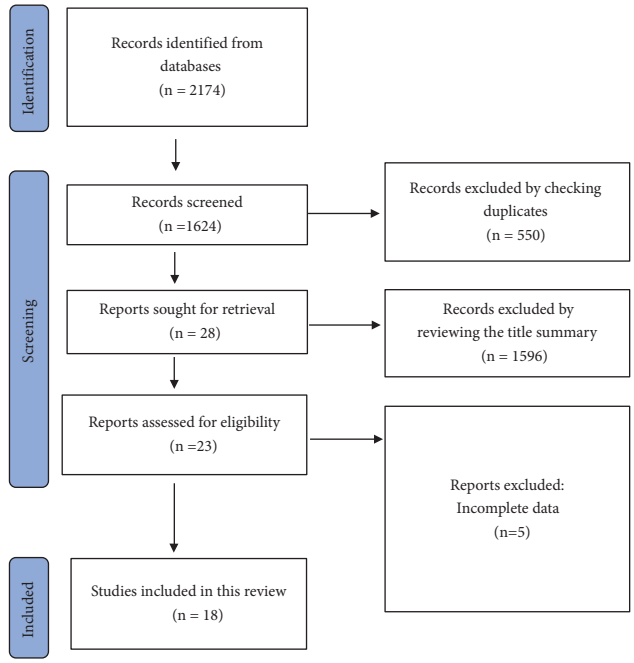

Figure 1: Flow diagram of study selection.

Table 2: Characteristic of the included studies.

Trial	Year	Sample size		Interventions		Acupoint selections	Target outcomes	Type of surgery
		TEAS group	Control group	TEAS group	Control group			
AoLi [14]	2020	35	35	TEAS	Shame teas	Hegu (LI4),Neiguan (PC6), Zusanli (ST36)	5/3/1	Breast cancer surgery
JihengChen [15]	2020	40	40	TEAS	Shame teas	Hegu (LI4), Neiguan (PC6), Houxi (SI3), Zhigou (TE6)	5/3/4	Lung cancer surgery
MiaoMiaoLi [16]	2020	54	54	TEAS	Shame teas	Zusanli (ST36)	2/3	Cesarean section
XingLiu [17]	2015	44	44	TEAS	Shame teas	Hegu (LI4), Waiguan (TE5), Jinmen (BL63), Taichong (LR3), Zusanli (ST36), Qiuxu (GB40), Fengchi (GB20), Tianzhu (BL10), Cuanzhu (BL2), Yuyao (EXHN4)	2/3/4	Infratentorial craniotomy
YuanyuanChang [18]	2020	42	43	TEAS	Shame teas	Shenmen (HT7), Neiguan (PC6), Zusanli (ST36), Hegu (LI4)	3	Thoracoscopic surgery
YanMin [19]	2016	89	90	TEAS	Shame teas	Hegu (LI4), Neiguan (P6)	3	Laparoscopic surgery
MateuszSzmit [20]	2021	24	24	TEAS + PCA	Shame teas + PCA	Hegu (LI4), ashi points	5/2/3	Laparoscopic inguinal hernia surgery
JianhuiGan [21]	2018	60	60	TEAS	Conventional treatment	Shenyu (BL23), Yinlingquan (SP9)	5/3	Ureteroscopic surgery
BaoguoWang [22]	1997	25	25	TEAS + PCA	Shame teas + PCA	Hegu (LI4)	5/2/3/4	Lower abdominal surgery
YushengYao [23]	2015	35	36	TEAS	Shame teas	Hegu (LI4), Neiguan (PC6), Zusanli (ST36), Sanyinjiao (SP6)	2/3/1/4	Gynecological Laparoscopic surgery
YehMeiLing [24]	2010	30	30	TEAS	Shame teas	Weizhong (BL40), Yanglingquan (GB34), Shenmen (HT7), Neiguan (P6)	5	Gynecological Laparoscopic surgery

Table 2: Continued.

Trial	Year	Sample size		Interventions		Acupoint selections	Target outcomes	Type of surgery
		TEAS group	Control group	TEAS group	Control group			
YehMeiLing [25]	2017	39	41	TEAS	Conventional treatment	Chengshan (BL57), Erbai (EX-UE2)	3	Hemorrhoid resection
XiangdiYu [26]	2020	30	30	TEAS	Shame teas	Baihui(GV20), Yingtang(EX-HN3), Zusanli (ST36), Neiguan (PC6)	3	
Gaoz [27]	2014	33	32	TEAS	Shame teas	Hegu (LI4), Neiguan (PC6), Zusanli (ST36)	2/1/4	Ambulatory breast surgery
XinZhou [28]	2021	41	40	TEAS	Conventional treatment	Hegu (LI4), Neiguan (PC6), Weishu (BL21), Xiaochangshu (BL27), Zusanli (ST36), Shangjuxu (ST37)	2/4	Laparoscopic surgery for gastric cancer
Wzhan [29]	2019	30	30	TEAS + TAP	TAP	Zusanli (ST36), Neiguan (PC6)	3/1	Abdominal surgery

Note. TEAS, transcutaneous electrical acupoint stimulation; VAS, visual analogue scale; 1. postoperative dizzy; 2. postoperative nausea; 3.VAS; 4. postoperative vomiting; 5. postoperative analgesic dosage.

Table 3: Details of interventions.

Trial	Year	Time point	Postoperative opioid analgesics
AoLi [14]	2020	30 min before induction of anesthesia at 4 and 12 h postoperation	PCA:150 ml Sufentanil 1.5 μg/kg if needed
JihengChen [15]	2020	30 min before induction, throughout the surgical, and 6, 24, and 48 h; sufentanil 1.5 μg/kg if needed postoperation	PCIA : sufentanil 1.5 μg/mL if needed
MiaoMiaoLi [16]	2020	60 min postoperative and twice times on the next 24, 48, and 72 h after surgery	Not mentioned
XingLiu [17]	2015	30 min before induction	Not mentioned
YuanyuanChang [18]	2020	30 min preoperative, the end of surgery and 24 and 48 h after surgery	Not mentioned
YanMin [19]	2016	30 min before induction	Not mentioned
MateuszSzmit [20]	2021	30 min at intervals of 2 h within 24 hours after surgery	PCA: morphine 15 ml if needed
JianhuiGan [21]	2018	30 min at 4, 8, and 12 h postoperatively and three times on the next 2 days after surgery	Tramadol hydrochloride tablets if needed
Baoguo Wang [22]	1997	30 min every 2 h on the next 2 days after surgery	PCA: hydromorphone 1 or 2 mL if needed
YushengYao [23]	2015	30 min before the induction of anesthesia	Not mentioned
YehMeiLing [24]	2010	20 min at 2 and 4 h after surgery	PCA: morphine 1 mg if needed
YehMeiLing [25]	2017	20 min at 4, 6 h and at 7 a.m. and 11 a.m. on the next day after surgery, 4 times in total	Not mentioned
XiangdiYu [26]	2020	30 min before induction	Not mentioned
Gaoz [27]	2014	30 min before induction	Not mentioned
XinZhou [28]	2021	30 min at 8 : 00 a.m. and 4 : 00 p.m. on the next 3 days after surgery	Not mentioned
Wzhan [29]	2019	30 min preoperative and postoperative	Not mentioned

Note. TEAS, transcutaneous electrical acupoint stimulation.

2.4. Data Extraction and Outcomes Assessment. All data extraction was independently undertaken by 2 reviewers using predesigned forms. Clinical features (participants, interventions, and outcome measurements), details of the treatments, methodological characteristics, and the results of each outcome were extracted for each study. Discrepancies were handled by discussion. The following information was extracted from each trial: author, year, population, sample size, drug regimen (pathway and dose), and outcome. The primary efficacy outcome was VAS within 24 h after surgery. A VAS score of 0 indicated no pain, and a VAS score of 10 indicated the most severe pain. The secondary efficacy outcomes included postoperative opioid analgesic drug consumption and the occurrence of adverse reactions within postoperative 24–72 h. Adverse reactions included dizziness, nausea, and vomiting.

2.5. Quality Assessment and Certainty of Evidence. The Cochrane Collaboration's tool was used to evaluate the risk of bias [16] in the methodology of the included literature. We reviewed each trial and classified the risks as high, low, or unclear, including the following domains: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessments, incomplete outcome data, selective reporting, and other biases, such as sample size. Trials rated a high risk of bias in 1 or more areas will be rated high risk, while trials rated a low risk of bias in all aspects will be rated low risk. Two researchers independently performed the quality evaluation of the included articles.

2.6. Statistical Analysis. RevMan 5.4 and STATA14.0 software provided by the Cochrane Collaboration were used for data analysis. Continuous variables were analyzed using mean difference (MDs) or standardized mean difference (SMDs) and 95% CIs. Relative risk (RR) and 95%CI were used for dichotomous data. The heterogeneity between the results of the study was examined using the Q test (test level is $\alpha = 0.1$), and the magnitude of heterogeneity was judged by combining the findings with the I2 test. Heterogeneity is expressed as p and I2; if $p > 0.10$ and I2 $< 50\%$, a fixed effects model was adopted; otherwise, a random effects model was chosen. Sensitivity analysis and subgroup analyses were conducted to assess the stability of results and detect the potential source of heterogeneity. Publication bias was analyzed by performing funnel plots qualitatively and estimated by Egger's test quantitatively.

3. Results

3.1. Trial Selection. Based on our search strategy, a total of 1277 articles were extracted from the above databases. We first excluded 404 repetitive articles, and then we excluded 852 articles according to the title and abstract. Then, 21 articles were identified for full-text review. Of these, 5 articles were excluded for lack of complete data. Finally, 16 studies [17–32] were included (Figure 1).

3.2. Trial Characteristics. The characteristics of the included trials are presented in Tables 2 and 3. The trials were published between 1997 and 2021. Among the 16 RCTs included, 11 papers were published in the last 5 years (64.7%). Sample sizes ranged from 24 to 90 patients, and a total of 1305 patients were included, with 651 (49.8%) in the TEAS group and 654 (50.1%) in the control group. The population mainly involved patients with pain after surgery. All trials reported efficacy and safety outcomes. The details of the risk of bias assessment for each included trial are summarized in Figure 2. Overall, 7 trials were classified as low risk of bias, 8 as unclear risk of bias, and 1 as high risk.

3.3. Efficacy and Safety of TEAS for the Treatment of Postoperative Pain VAS. The meta-analysis combined data from 1019 participants (control group = 511 and intervention = 508). We used a standardized mean difference model to complete a meta-analysis of the pain degree at 24 h after the TEAS intervention in these twelve RCTs. Through meta-analysis, we found that TEAS can significantly reduce VAS scores of patients (SMD = −1.51, 95% CI = −2.20∼−0.82, I2 = 96%) (Figure 3(a)). Then, we stratified the study according to the type of open surgery and minimally invasive surgery (Figure 3(b)). SMD shows that

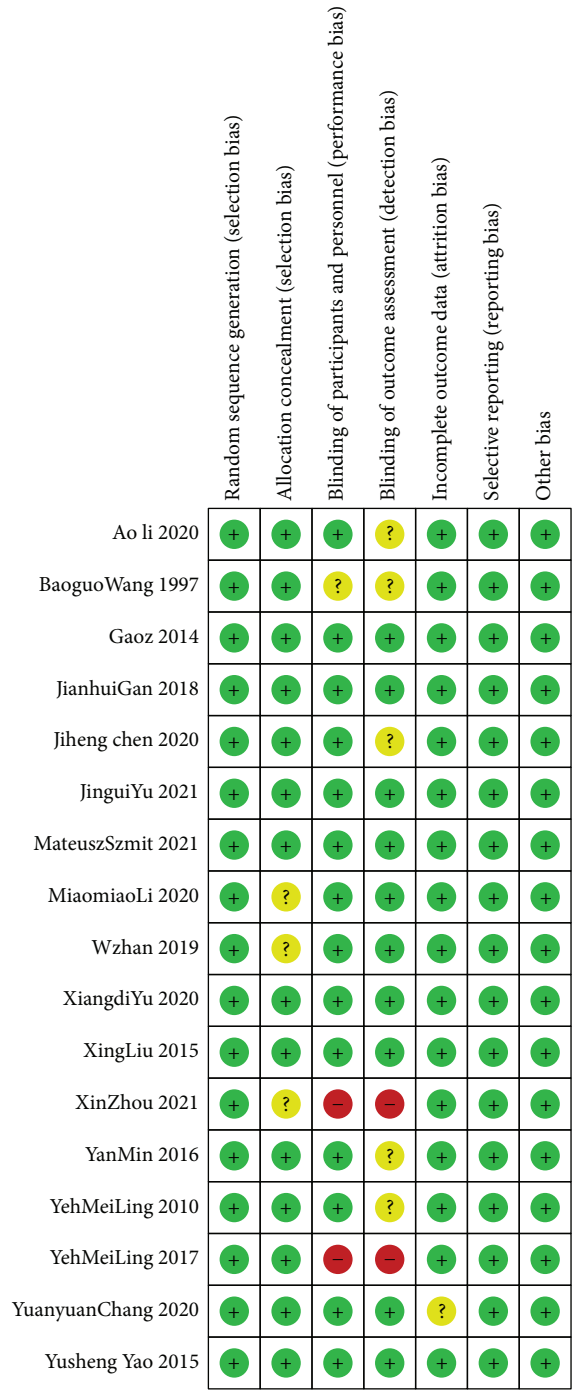

Figure 2: Potential risk of bias of each included study. *Note.* "+" represents low risk; "?" represents unclear risk; and "-" represents high risk.

Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight (%)	Std. Mean Difference IV, Random, 95% CI
Aoli 2020	2.4	0.5	35	2.9	0.6	35	8.5	−0.90 [−1.39, −0.40]
BaoguoWang1997	4.4	2.3	25	4.8	2.2	25	8.4	−0.17 [−0.73, 0.38]
JianhuiGan 2018	2.2	0.9	60	3.4	0.8	60	8.6	−1.40 [−1.80, −1.00]
Jiheng Chen2020	2.9	0.2	40	6	0.6	40	7.1	−6.86 [−8.04, −5.69]
MateuszSzmit 2021	1.3	1	24	2.9	1.5	24	8.3	−1.23 [−1.86, −0.61]
Miaomiao LI2020	2	0.1	54	2.6	0.1	54	7.7	−5.96 [−6.85, −5.06]
Wzhan 2019	1.7	2.2	30	2	3	30	8.5	−0.11 [−0.62, 0.39]
Xingliu 2015	2.6	1.3	44	3.7	2.6	44	8.6	−0.53 [−0.96, −0.10]
YanMin2016	3.5	0.9	89	4.1	1	90	8.7	−0.63 [−0.93, −0.33]
YuanyuanChang 2020	2.8	1.1	42	3.2	1.1	43	8.6	−0.36 [−0.79, 0.07]
YushengYao2015	1.5	1.8	35	2.5	1.2	36	8.5	−0.65 [−1.13, −0.17]
YuXiangdi 2020	3.7	1.5	30	4.7	1.5	30	8.5	−0.66 [−1.18, −0.14]
Total (95% CI)			*508*			*511*	*100.0*	*−1.51 [−2.20, −0.82]*

Heterogeneity: Tau² = 1.39; Chi² = 259.03, df = 11 (P < 0.00001); I^2 = 96%
Test for overall effect: Z = 4.29 (P < 0.0001)

Std. Mean Difference IV, Random, 95% CI
−4 −2 0 2 4
Favours [experimental] Favours [control]

(a)

Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight (%)	Std. Mean Difference IV, Fixed, 95% CI
1.1.1 Open surgery								
Aoli 2020	2.4	0.5	35	2.9	0.6	35	7.9	−0.90 [−1.39, −0.40]
BaoguoWang 1997	4.4	2.3	25	4.8	2.2	25	6.2	−0.17 [−0.73, 0.38]
Miaomiao LI2020	2	0.1	54	2.6	0.1	54	2.4	−5.96 [−6.85, −5.06]
Wzhan 2019	1.7	2.2	30	2	3	30	7.5	−0.11 [−0.62, 0.39]
Xingliu 2015	2.6	1.3	44	3.7	2.6	44	10.6	−0.53 [−0.96, −0.10]
Subtotal (95% CI)			*188*			*188*	*34.6*	*−0.84 [−1.07, −0.60]*

Heterogeneity: Chi² = 141.68, df = 4 (P < 0.00001); I^2 = 97%
Test for overall effect: Z = 6.97 (P < 0.00001)

1.1.2 Minimally invasive surgery								
JianhuiGan 2018	2.2	0.9	60	3.4	0.8	60	11.9	−1.40 [−1.80, −1.00]
JihengChen2020	2.9	0.2	40	6	0.6	40	1.4	−6.86 [−8.04, −5.69]
MateuszSzmit 2021	1.3	1	24	2.9	1.5	24	5.0	−1.23 [−1.86, −0.61]
YanMin2016	3.5	0.9	89	4.1	1	90	21.3	−0.63 [−0.93, −0.33]
YuanyuanChang 2020	2.8	1.1	42	3.2	1.1	43	10.4	−0.36 [−0.79, 0.07]
YushengYao2015	1.5	1.8	35	2.5	1.2	36	8.4	−0.65 [−1.13, −0.17]
YuXiangdi 2020	3.7	1.5	30	4.7	1.5	30	7.1	−0.66 [−1.18, −0.14]
Subtotal (95% CI)			*320*			*323*	*65.4*	*−0.91 [−1.08, −0.74]*

Heterogeneity: Chi² = 117.11, df = 6 (P < 0.00001); I^2 = 95%
Test for overall effect: Z = 10.42 (P < 0.00001)

Total (95% CI)			*508*			*511*	*100.0*	*−0.88 [−1.02, −0.75]*

Heterogeneity: Chi² = 259.03, df = 11 (P < 0.00001); I^2 = 96%
Test for overall effect: Z = 12.53 (P < 0.00001)
Test for subgroup differences: Chi² = 0.24, df = 1 (P = 0.62), I^2 = 0%

Std. Mean Difference IV, Fixed, 95% CI
−4 −2 0 2 4
Favours [experimental] Favours [control]

(b)

Figure 3: (a) Forest plots comparing the VAS at 24 h between the TEAS and control groups; (b) subgroup analysis of the effect of TEAS for open surgery and minimally invasive surgery.

Study or Subgroup	Experimental Events	Total	Control Events	Total	Weight (%)	Risk Ratio M-H, Fixed, 95% CI
AoLi2020	7	35	9	35	14.2	0.78 [0.33, 1.86]
Gaoz2014	7	32	17	33	26.4	0.42 [0.20, 0.88]
Wzhan2019	2	30	10	30	15.8	0.20 [0.05, 0.84]
YushengYao2015	14	35	28	36	43.6	0.51 [0.33, 0.80]
Total (95% CI)		*132*		*134*	*100.0*	*0.48 [0.34, 0.68]*
Total events	30		64			

Heterogeneity: Chi² = 2.83, df = 3 (P = 0.42); I^2 = 0%
Test for overall effect: Z = 4.18 (P < 0.0001)

Risk Ratio M-H, Fixed, 95% CI
0.01 0.1 1 10 100
Favours [experimental] Favours [control]

Figure 4: Forest plots comparing the incidence of postoperative dizziness between the TEAS and control groups.

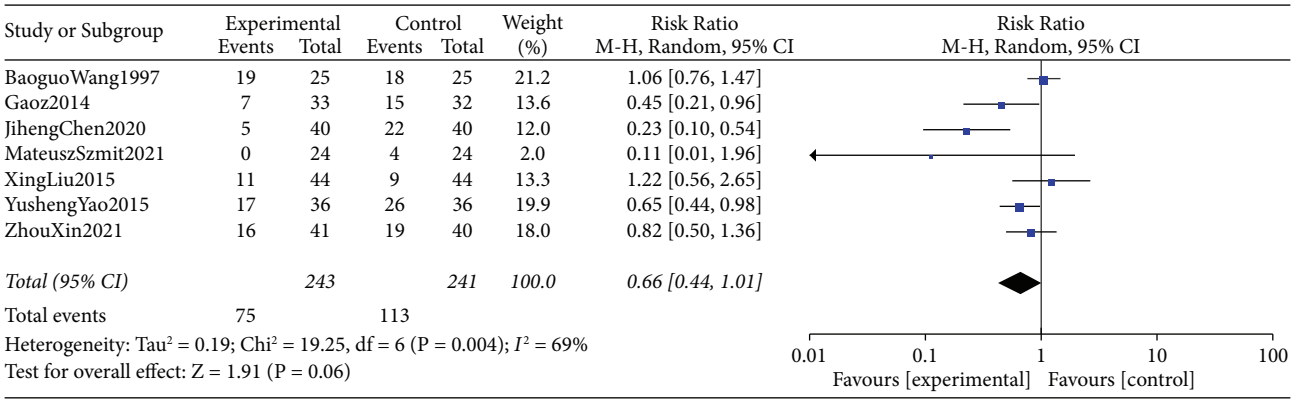

Figure 5: Forest plots comparing the incidence of postoperative nausea between the TEAS and control groups.

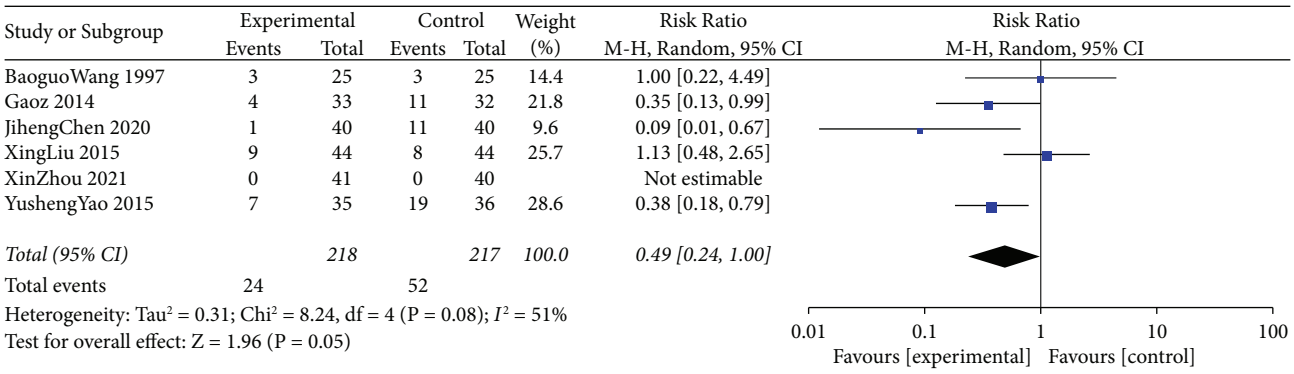

Figure 6: Forest plots comparing the incidence of postoperative vomiting between the TEAS and control groups.

TEAS can significantly reduce the VAS scores when open surgery is performed (SMD = −0.84, 95% CI = −1.07~−0.6, I2 = 96%). We found that VAS scores also decreased significantly after minimally invasive surgery (SMD = −0.88, 95%CI = −1.02~−0.75, I2 = 96%).

3.4. Incidences of Postoperative Dizziness. The meta-analysis combined data from 266 participants (control group = 134 and intervention = 132). Four studies compared the incidence of postoperative dizziness within postoperative 24–72 h. The incidence of dizziness was significantly lower in the TEAS group than in the control group (RR = 0.48, 95% CI 0.34~0.68, I2 = 0%) (Figure 4).

3.5. Incidences of Postoperative Nausea. The meta-analysis combined data from 484 participants (control group = 241 and intervention = 243). Seven studies compared the incidence of postoperative nausea within postoperative 24–72 h. The incidence of postoperative nausea was lower in the TEAS group than in the control group, but this was not statistically significant (RR = 0.66, 95% CI 0.44~1.01, I2 = 69%) (Figure 5).

3.6. Incidence of Postoperative Vomiting. The meta-analysis combined data from 435 participants (control group = 217 and intervention = 218). Six studies compared the incidence of postoperative vomiting within postoperative 24–72 h. Among them, the article XinZhou 2021 did not have the occurrence of vomiting. Compared with the control group, the TEAS group significantly reduced the incidence of postoperative vomiting (RR = 0.49, 95% CI = 0.24~1.00, I2 = 51%) (Figure 6). We then conducted a sensitivity analysis to further explore the heterogeneity of included studies, which showed that the results of studies were relatively stable and reliable.

3.7. Postoperative Opioid Analgesic Consumption. The meta-analysis combined data from 428 participants (control group = 214 and intervention = 214). Six studies compared postoperative opioid analgesic consumption. Compared with the control group, the TEAS group significantly reduced postoperative analgesic consumption (SMD = −2.10, 95% CI = −3.37~−0.82, I2 = 96%) (Figure 7). The sensitivity analysis findings indicated that the results were robust and reliable.

3.8. Publication Bias Analysis and Sensitivity Analysis. There are more than 10 studies on the VAS score after surgery. Sensitivity analyses were performed by removing one study each time to assess the influence of an individual study on the overall outcomes. No significant changes were observed after combining the results, indicating that the results of the study were relatively stable. Then, Egger's test

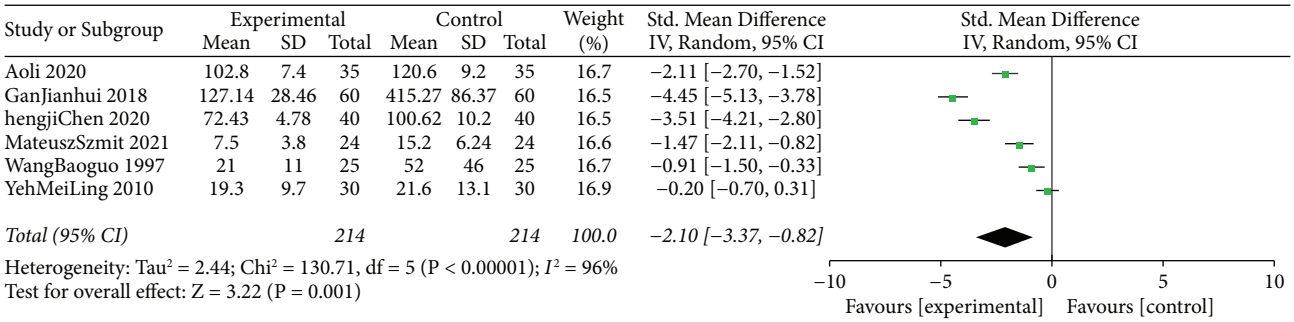

Figure 7: Forest plots comparing the incidence of postoperative analgesic consumption between the TEAS and control groups.

($p = 0.32$) was used to detect publication bias and showed that there was no possibility of publication bias, besides, there was no publication bias by observing the funnel chart (Figure 8).

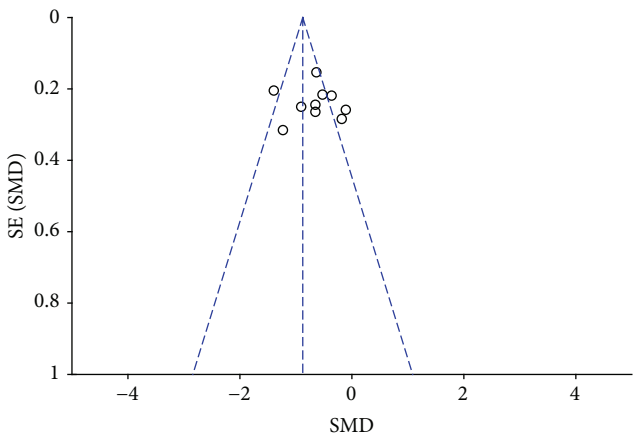

Figure 8: Funnel plot of 24 h VAS score.

4. Discussion

TEAS has been widely accepted and used worldwide. To our knowledge, our meta-analysis is the first to research the efficacy and safety of TEAS in treating postoperative pain. Our research shows that TEAS can significantly decrease VAS scores of patients. According to subgroup analysis, we found that VAS scores decreased significantly after minimally invasive surgery and open surgery. Minimally invasive surgery is the direction of surgery [30]. TEAS selections need to be considered to improve the efficacy and clinical quality of patients. In addition, our study revealed that TEAS provides broadly generalizable benefits during the postoperative recovery period and helps to accelerate the progress of enhanced recovery after surgery.

According to the theory of traditional Chinese medicine, acupuncture meridians represent "channels" through which energy called "meridian qi" flows [31]. Acupuncture has been utilized in Chinese health care for at least 2500 years, which is a technique for balancing the flow of energy [32]. The underlying mechanisms of TEAS's analgesic effects have not been clearly clarified. Basic studies have shown that TEAS can achieve the intervention effect on pain sensation and can be exerted via multiple mechanisms. (1) TEAS may produce analgesia by promoting the release of endogenous opioid peptides [33]. (2) TEAS inhibit the production of endogenous pain-causing substances [33]. (3) TEAS to intervene in the MAPK signal transduction pathway to play analgesic effect [34]. (4) TEAS inhibit pain sensitization. The early peripheral sensitization of neuropathic pain may be interfered by downregulating TRPV1 phosphorylation level and calcitonin gene-related peptide expression level of injured DRG [35].

Postoperative pain contributes to increased morbidity, impaired physical function and quality of life, slowed recovery, and increased cost of care [36]. Given the unclear formation mechanism of postoperative pain, it remains one of the most challenging problems in clinical pain therapeutics. Studies have shown that TEAS could regulate the function of the hypothalamic pituitary-adrenal (HPA) axis and antagonize the hyperfunction of the HPA axis [37]. The HPA axis has many functions including regulation of appetite, sleep, sexual desires, and adaptation to stress [38]. Dysfunction of the HPA axis is thought to be primarily responsible for psychological/behavioral symptoms (pain sensitivity, depression, and fatigue) [38]. An RCT showed that TAES treatment can increase the serum levels of IL-2 and IFN-γ, and decreased IL-4 secretion and return the aforementioned cellular immune factors to the preoperative control value at a faster rate [39]. These results suggest that TAES can reduce postoperative immune dysfunction by changing the expression of Th1/Th2 cell-associated cytokines [39]. Simultaneously, some preclinical studies have also shown that TEAS can attenuate cognitive deficits by inhibiting neuronal peroxide reactions in hippocampus tissue and inflammation of the central and peripheral nervous systems [40]. The major pathway is the cholinergic anti-inflammatory pathway (CAP). TEAS can stimulate the vagus nerve to activate CAP so as to inhibit the production of proinflammatory cytokines [41]. Studies have revealed that low-frequency electrical stimulation can release enkephalins and endorphins from the central nervous system [42]. High frequency electrical stimulation induces the release of endorphins from the spinal cord. Low frequency/high frequency alternating density waves can simultaneously stimulate these three peptides to produce a synergistic analgesic effect [43]. TEAS may affect 5-HT transmission by

activating 5-HT and norepinephrine fibers to promote gastrointestinal motility and reduce the incidence of nausea and vomiting [44]. Meanwhile, there is a dose-response relationship between opioid dosage and associated side effects [45]. Opioid analgesics are commonly used postoperative analgesics in clinics, but they easily cause dose-dependent respiratory depression, gastrointestinal reaction, urinary retention, skin itching, and other adverse reactions [46]. Our study revealed that the application of TEAS was associated with lower opioid analgesic consumption. Therefore, TEAS provides a nondrug alternative for multimodal analgesia for postoperative pain.

5. Conclusions

TEAS is a reasonable modality to incorporate into a multimodal management approach for postoperative pain. TEAS can reduce postoperative pain as well as the incidence of dizziness, nausea, and vomiting and the number of analgesics used after surgery. Owing to the limitations, further large-scale and well-designed studies are required to verify and expand on our conclusion.

Data Availability

The datasets analyzed during the current study are available from the corresponding author on reasonable request.

Disclosure

Dan Wang and Hongshuo Shi are the co-first authors.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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Review Article

Dry Needling and Antithrombotic Drugs

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Many clinicians increasingly use dry needling in clinical practice. However, whether patients' intake of antithrombotic drugs should be considered as a contraindication for dry needling has not been investigated to date. As far as we know, there are no publications in analyzing the intake of antiplatelet or anticoagulant agents in the context of dry needling techniques. A thorough analysis of existing medications and how they may impact various needling approaches may contribute to improved evidence-informed clinical practice. The primary purpose of this paper is to review the current knowledge of antithrombotic therapy in the context of dry needling. In addition, reviewing guidelines of other needling approaches, such as electromyography, acupuncture, botulinum toxin infiltration, and neck ultrasound-guided fine-needle aspiration biopsy, may provide specific insights relevant for dry needling. Based on published data, taking antithrombotic medication should not be considered an absolute contraindication for dry needling techniques. As long as specific dry needling and individual risks are properly considered, it does not change the risk and safety profile of dry needling. Under specific circumstances, the use of ultrasound guidance is recommended when available.

1. Introduction

Worldwide, clinicians are using dry needling (DN) to reduce pain [1, 2], increase range of motion and flexibility [3], enhance performance [4], reduce spasticity [5], or improve fascial and scar tissue mobility [6, 7]. Dry needling is a safe and cost-effective treatment approach [8–11], but there is no literature informing clinicians whether DN can be applied safely in patients with altered coagulation. Potentially, patients taking antithrombotic drugs may have an increased risk of suffering bleeding complications when being treated with DN. The American Physical Therapy Association recommends that "patients with an abnormal bleeding tendency must be needled with caution. Dry needling of deep muscles that cannot be approached with direct pressure to create hemostasis may need to be avoided to prevent excessive bleeding" [12]. The most common target of DN is trigger points, which are located in close proximity to endplate zones [13]. Dry needling may also target fascia and fascial adhesions [6, 13, 14], but since veins and arteries are never the therapeutic targets, the risk of bleeding is significantly reduced. During DN, the needle may inadvertently penetrate blood vessels before reaching its therapeutic target, which may be relevant to patients taking antithrombotic agents. Some caution is warranted, especially when DN is targeting deeper muscles in close proximity of major arteries and veins, such as the maxillary artery when needling the lateral pterygoid muscle [15].

In an Irish study of the possible adverse events of DN, 39 physiotherapists used trigger point DN 20 times per month within a 9-month time frame for a total of 7,629 treatments. Mild adverse events, including bleeding, bruising, and pain during and after treatment, were reported in 19.18% of the treatments. While no significant adverse events occurred, the risk of significant adverse events for 10,000 treatments was estimated to be less than 0.04% [8]. Boyce et al., using a

similar research design to Brady et al., reported 7,531 minor adverse events and 20 major adverse events out of a total of 20,494 DN treatments by 420 physiotherapists over a period of 6 weeks [10], which corresponded to 36.7% of the treatments resulting in a minor adverse event. The top three minor adverse events were bleeding (16%), bruising (7.7%), and pain during DN (5.9%) [10]. Comparing the two studies, it is not clear why the adverse event rate in Boyce et al.'s study was nearly twice as high as in Brady et al.'s study, but in both studies, bleeding was a common minor adverse event. There is no universally accepted system for reporting adverse events of DN, and therefore, the actual incidence of dry needling-related adverse events is unknown [16].

There are many specific factors to consider before using DN, such as the actual needling procedures, the area to be needled, and the characteristics of the needles. Specific factors to be considered are the diameter and type of needle, the technical procedure, the target of the intervention, and the anatomical structures in proximity of the needling site. Much can be learned from studies of electromyography (EMG), acupuncture, botulinum toxin (BTX) infiltration, and neck ultrasound-guided fine-needle aspiration biopsy (USGFNAB), realizing the obvious differences between these procedures and DN with respect to clinical practice or the type of needles used.

Dry needling is used mostly by physiotherapists, but other disciplines have also started to use DN, such as occupational therapy, athletic training, chiropractic, and acupuncture. Since these clinicians may not have a solid working knowledge of antithrombotic drugs and their specific risk factors, it is imperative to review the different kinds of antithrombotic drugs before reviewing guidelines from other procedures that use needles.

2. Antithrombotic Medications

There are two classes of antithrombotic drugs: antiplatelet agents and anticoagulants. The main antiplatelet agents are aspirin and P2Y12 receptor blockers. Anticoagulants include vitamin K antagonists (VKAs) and direct oral anticoagulants (DOACs), which are administered orally, and heparins, which are administered subcutaneously or intravenously.

Aspirin, the first-line antiplatelet, prevents the formation of blood clots and is used in patients with angina, previous heart attack or stroke, coronary artery stents, after coronary artery bypass graft surgery, and in patients undergoing surgery for hip fracture [17]. Other antiplatelet agents are the P2Y12 receptor blockers, such as clopidogrel, prasugrel, and ticagrelor. It is very frequently used as dual antiplatelet therapy (DAPT) with aspirin plus a P2Y12 receptor inhibitor to avoid thrombosis following balloon angioplasty or angioplasty with stent implantation. The main risk of DAPT is bleeding [18].

The main types of oral anticoagulant agents are VKAs and DOACs. Warfarin is the most widely used VKA worldwide, while in Europe acenocoumarol and phenprocoumon are the most frequently prescribed VKAs [19]. They are prescribed for the prevention and treatment of patients suffering from venous thromboembolism (VTE) or the prevention of systemic embolism or stroke in patients with prosthetic heart valves or atrial fibrillation (AF) [20]. In recent years, DOACs have been developed to overcome some of the limitations of VKAs, and they are expected to be used more widely in the coming years [20]. Currently, the US Food and Drug Administration (FDA) has approved five DOACs: dabigatran, rivaroxaban, apixaban, edoxaban, and betrixaban [21].

Finally, unfractionated heparins (UFH) and low molecular weight heparins (LMWH) have been used for decades. UFH are administered subcutaneously or intravenously. LMWH, derived from UFH, are administered subcutaneously and have gradually replaced UFH for most clinical indications. UFH and LMWH are prescribed, along with dual antiplatelet therapy in patients with acute coronary syndrome (ACS) and they reduce VTE complications of high-risk medical conditions, such as heart failure or prolonged immobilization in bed, or in knee or hip arthroplasty [22]. Table 1 summarizes the different types of antithrombotic drugs, their generic and brand names, their mechanism of action, and other specific information.

3. Bleeding Risks Related to Drugs

During VKA therapy, the risk of bleeding is assessed with the International Normalized Ratio (INR), which is a standardized method for reporting results of the prothrombin time (PT assay) [31]. Typically, an INR range of 2.0–3.0 is recognized as the therapeutic range and recommended by international guidelines [32]. Some reports assumed a lower risk of stroke with an INR range between 2.0 and 3.5 and an increased risk with INR values below 2.0 or above 3.5 [33–35]. An optimal time in the therapeutic range (TTR >75%) is associated with a lower risk of adverse events [36, 37]. VKAs are effective and widely used, but their use can be problematic because of several drawbacks (see Table 1). The risk of major bleeding is significantly lower in patients with a stable INR control. However, even optimal maintenance therapy within the therapeutic range does not necessarily avoid all possible bleeding complications. Many individual factors can influence the INR. Therefore, routine monitoring of the INR, appropriate clinical control, and continuous patient education are required [19].

DOACs have equivalent or improved therapeutic profiles compared to warfarin, and they are associated with significant reductions in stroke, intracranial haemorrhage, and mortality [30]. As the mechanism of action of DOACs differs from that of VKAs, the results of INR tests are unreliable in patients treated with these new agents [38]. Currently, there are several available tests to assess the anticoagulant effects of DOACs, but they have poor sensitivity and specificity, providing limited information [39]. DOACs do have predictable pharmacological profiles, which implies that they can be given in fixed doses without the need for routine therapeutic monitoring [29]. Despite their benefits, DOACs do have some drawbacks, such as certain drug-drug interactions [40].

Factors influencing blood clotting must also be considered (see Table 2). The FDA-approved reversal agent

Table 1: Summary of antithrombotic drugs characteristics.

Type of drug		Generic names	Brand names*	Observations	Mechanism of action
Antiplatelets	Nonselective inhibitor of COX [23]	Aspirin	*Ascriptin, Ecotrin, Ecpirin*	Causes gastrointestinal irritation and bleeding that can be reduced by the intake of a proton pump inhibitor (e.g., omeprazol) [17]	Nonselective inhibitor of COX [23]
	P2Y12 receptor blockers	Clopidogrel	*Plavix*	High interindividual variability, delayed onset of action, and bleeding episodes in certain cases [17]	Irreversible inhibitors of P2Y12 receptors in platelets [24, 25]
		Prasugrel	*Effient*	Faster onset of action, less interindividual variability but higher risk of bleeding vs. clopidogrel [25, 26]	
		Ticagrelor	*Brilinta*	More benefits vs. clopidogrel and prasugrel [27]	Reversible inhibitor of P2Y12 receptors [27]
Anticoagulants	VKAs	Warfarin	*Coumadin, Jantoven*	Used for decades for patients that need long-term oral anticoagulation [28]	Indirect mechanism of action by inhibiting the synthesis of coagulation factors [29]
		Acenocoumarol	*Sinthrome, Sintrom*	Slow onset of action, narrow therapeutic window, genetically determined inter- and intrapatient variability, and multiple possible interactions with various foods and drugs [19]	
		Phenprocoumon	*Falithrom, Marcoumar*		
	DOACs	Rivaroxaban	*Xarelto*	Faster onset and offset of action vs. VKAs [28], lower bleeding risk vs. warfarin in younger patients but not in those >75 years [30]	Direct inhibition of factor Xa [28]
		Apixaban	*Eliquis*		
		Dabigatran	*Pradaxa, Pradax*		
		Edoxaban	*Savaysa, Lixiana*	Much more expensive vs. VKAs, but lower resource consumption vs. cost of VKAs and the required therapeutic monitoring [19]	
		Betrixaban	*Bevyxxa*	Betrixaban is not indicated for treatment. It is used as a prophylactic agent for prevention of deep vein thrombosis and pulmonary embolism in adults hospitalized for an acute medical illness [21]	

Abbreviations: COX: cyclooxygenase enzyme; VKAs: vitamin K antagonists; DOACs: direct oral anticoagulants. *There are many other brand names for some of the medications.

specific for VKAs is 4-Factor Prothrombin Complex Concentrate (4F-PCC) [50]. The FDA-approved antidotes readily available for DOACs are idarucizumab for dabigatran, and andexanet alfa for rivaroxaban and apixaban. However, Prothrombin Complex Concentrate (PCC) may be used off-label for reversing DOACs. Ciraparantag is a universal reversal agent, which is in development [39].

In case of major bleeding, it is recommended to withhold antithrombotic drugs and provide mechanical hemostasis and hemodynamic support [51]. Numerous studies have compared bleeding rates between different anticoagulant agents, as well as for different pathologies, but any comparison remains difficult due to different bleeding definitions, differences in individual trials, and various populations with different bleeding risks [52]. If there is a high thromboembolic risk, concomitant therapy is administered with an oral anticoagulant and an antiplatelet agent. It is more effective in reducing the risk of death and thromboembolism than a VKA alone, but it increases the risk of major bleeding, especially with long-term use, and in some cases may outweigh the benefits [25, 53, 54]. Concomitant therapy may also include the administration of aspirin and a P2Y12 blocker. Regarding the bleeding risk associated with antiplatelet agents, each agent needs to be considered individually due to different profiles (Table 2).

4. Other Factors Affecting Bleeding Risks

Moreover, other factors such as age [41], gender [42], interactions with food and drugs [40, 43, 44, 55], renal function [37, 41], and possibly exercise [56, 57] have to be considered. More specific details are shown in Table 2. Being 75 years or older is considered a risk factor in stroke risk-stratification schemes, as the prevalence of arterial and venous thromboembolic diseases and other risk factors, such as hypertension or diabetes mellitus, is higher in elderly adults [41]. Regarding gender, a review assessing the evidence of increased thromboembolic risk in women with AF suggests that the female gender is an independent stroke risk factor, but the causes of increased thromboembolic risk in women have not yet been fully determined [42].

Table 2: Specific details of factors affecting bleeding.

Factor	How it affects
Age	Conventional risk factors, comorbidities, and malignant disease in elderly adults increase the risk of bleeding and VTE [41]. In younger patients, DOACs were associated with lower bleeding risk compared with warfarin but there were no statistically significant differences in >75 years [30].
Gender	Factors proposed to explain the increased thromboembolic risk in women: increased hypertension, renal dysfunction, hyperthyroidism, increased hypercoagulability, cardiovascular remodeling, and estrogen hormone replacement therapy, as well as specific gender influences on the quality of the anticoagulant treatment (i.e., lower quality of warfarin anticoagulation in females with AF, which requires higher rates of anticoagulation prescription that increases the risk of bleeding [42].
Food interactions	Warfarin is affected by a wide range of targets in blood hemostasis, including inhibition of COX, the presence of coumarins and other substances, or high amounts of vitamin K. Herbs with the greatest potential to interact with warfarin include ginseng, garlic, ginkgo, St. John's wort, and ginger, but even menthol cough drops may reduce the INR [43].
Drug-drug interactions	Some examples of medication affecting VKAs: (a) Drugs, including ciprofloxacin, cotrimoxazole, cephalosporins, fluconazole, and metronidazole, can increase the warfarin effect. (b) Several cardiovascular drugs can potentiate the metabolism of warfarin and increase the INR, including aspirin, amiodarone, antihyperlipidemic agents, and statins, such as fluvastatin, lovastatin, and simvastatin. (c) Analgesics, including phenybutazone, piroxicam, acetaminophen, and NSAIDs, can increase the anticoagulation effects. (d) Central nervous system drugs, such as antidepressants, citalopram, fluoxetine, paroxetine, and tricyclics antidepressant can increase the INR and the risk of bleeding. (e) Alcohol is a risk factor with concomitant liver disease. (f) Gastrointestinal drugs, such as cimetidine and omeprazole, can increase the INR [44]. Some examples of medication affecting DOACs: (a) Dabigatran interacts with antacids, which decrease the effect of dabigratan; (b) Antiarrhythmic agents, such as amiodarone, verapamil, quinidine, as well as antiplatelet agents, LMWH, and nonsteroidal anti-inflammatory drugs (NSAIDs), increase the anticoagulant effects [40]. (c) Rivaroxaban interacts with antiacids, antifungical medications, such as itraconazole, voriconazole, and posaconazole, antiplatelet agents, NSAIDs, such as naproxen, and LMWH among others increasing the anticoagulant effects [40].
Renal impairments	In mild renal insufficiency (eGFR: 50–79 mL/min), the major bleeding risk was lower with any DOACs than with warfarin. In moderate renal insufficiency (eGFR: 30–49 mL/min), the risk was higher, with rates of major bleeding of 6.8% versus 4.8% in patients with mild insufficiency and a trend toward less major bleeding with the DOACs [41].
Exercise	A study carried out on three patients taking warfarin showed an inverse relationship with increased physical activity and decreased INR. Thus, it may be possible that an increase in physical activity puts patients at greater risk of thromboembolism [45–47]. Ryan et al.'s study showed that taking aspirin before running 60 minutes increased both the intestinal and gastroduodenal permeability of aspirin compared with taking a placebo and running or placebo plus rest but not aspirin plus rest. Nevertheless, the clinical significance of this study is highly questionable [48]. In a study by Sawrymowicz et al., 20 healthy patients took an oral dose of aspirin 1 g and then walked on a treadmill at 4.8 km/h for 20 minutes per half hour for 3 hours. Blood samples taken during the exercise did not show changes in plasma concentration, clearance, or half-life compared with a 3-hour rest [49].

Abbreviations: COX: cyclooxygenase enzyme; DOACs: direct oral anticoagulants.

In relation to the interaction between food and anticoagulants, Violi et al. concluded that the available evidence does not support current advice to restrict dietary vitamin K intake while taking VKAs. However, they recommended maintaining a stable diet avoiding wide variations in vitamin K [55].

Leite et al. analyzed the interferences of medicinal plants with blood hemostasis and warfarin anticoagulation and found a total of 58 different plants that may alter blood clotting and anticoagulation with warfarin [43]. Regarding drug interactions of VKAs, many medications influence their anticoagulant effect, such as anti-infectious and cardiovascular drugs, analgesics, anti-inflammatories, immunologic, central nervous system drugs, and gastrointestinal drugs. DOACs also interact with several drugs [40, 44]. In relation to renal insufficiency, Szummer et al. concluded that severe chronic kidney disease patients with an estimated glomerular filtration rate (eGFR) of less than 30 mL/min have a worsened INR control while taking warfarin. However, an optimal time in the therapeutic range (TTR >75%) is associated with a lower risk of adverse events, independently of underlying renal function [37]. When comparing DOACs with VKAs/warfarin, LMWH, aspirin, and placebo in patients with renal insufficiency, the recommended doses were noninferior and relatively safe compared with conventional anticoagulants, and all had a comparable efficiency [41].

Further research is needed to assess the influence of physical activity on the pharmacokinetics of antithrombotic drugs. Shendre et al. demonstrated that regular physical

activity in patients on chronic anticoagulation therapy with warfarin is associated with higher dose requirements and a lower risk of haemorrhage [57], which was confirmed by Rouleau-Mailloux et al. [56].

5. Specific Risks of Other Needling Therapies and Interventions

Considering the type of needle, the degree of potential tissue damage is dependent on whether the needle is bevelled. The potential for tissue damage and bleeding is greater with a hypodermic needle than with a solid filament needle used with DN. Other needling approaches use different types of needles. For example, the needle diameter used with DN is smaller than the typical gauge of needles used for diagnostic EMG or hypodermic needles, ranging from 35 G to 28 G or 0.14 mm to 0.35 mm, respectively, compared to gauges of 30 G (0.30 mm), 26 G (0.45 mm), or 23 G (0.60 mm) with EMGs [58]. Interestingly, EMGs usually do not produce significant bleeding or hematomas [59]. Factors that may influence the patient's bleeding risk with these other needling procedures may be applied cautiously to the context of DN.

Another factor is the technical procedure itself. Typically, DN involves manipulating the needle within a muscle and fascia to elicit the so-called local twitch responses [1]. Theoretically, the risk of injury and bleeding may increase when multiple insertions are performed or when the needle is moved back and forth within the muscle. However, the small diameter and shape of the needle usually do not cause much concern. Of course, clinicians may opt to use needles with smaller diameters and limit the number of passes through a muscle. Another factor is the target of the intervention, which requires thorough anatomical knowledge of the location and the common distribution of blood vessels and nerves.

6. Electromyography

Several EMG studies have evaluated the incidence of hematoma and the risk of bleeding after the procedure in patients taking antithrombotic medication [59]. Two cases of symptomatic bleeding while performing an EMG were reported with patients who had abnormal blood coagulation and who were taking antithrombotic medication. Rosioreanu et al. reported a case of a pseudoaneurysm of the calf after an EMG in a patient with AF who was taking warfarin [60]. Butler et al. reported a case of a significant subcutaneous haemorrhage in a patient on chronic anticoagulant therapy, which required a two-unit blood transfusion [61]. Lynch et al. evaluated the risk of hematoma formation in patients taking antithrombotic medication compared to controls after standard needle EMG of the tibialis anterior muscle followed by ultrasound. There were no hematomas in the control group (51 patients). Of 101 patients taking warfarin, two had small, subclinical hematomas, and one out of 57 patients taking clopidogrel or aspirin had a small, subclinical hematoma. None of the patients had symptomatic bleeding. Therefore, there were no statistically significant differences between groups [62].

Gertken et al. established the incidence of Magnetic Resonance Imaging- (MRI-) detectable hematomas after EMG of the paraspinal muscles. The sample included patients taking antithrombotic agents and controls. A total of 431 spine segments and a total of 370 patients were reviewed with 139 patients taking aspirin, eight taking clopidogrel, ten taking warfarin, two taking heparin, and two taking LMWH. In this study, no paraspinal hematomas were observed in any group, which suggests that EMG of paraspinal muscles is a relatively safe procedure [63]. These results do vary from those obtained by London et al. in which possible hematomas were found in patients undergoing MRI after EMG. In this study, the risk of paraspinal hematoma formation was assessed by MRI scans after performing extensive EMG of the lumbar paraspinal muscles using the paraspinal mapping technique, which involves inserting the needle at multiple levels on both sides of the back. Of 29 patients who underwent MRI after EMG, six had possible hematomas, but they were not clinically relevant, and there were no significant bleeding complications [64]. Lee and Kushlaf assessed the risk of bleeding after needle EMG in patients taking DOACs. A 19-item survey questionnaire was sent to 3,959 members of the American Association of Neuromuscular and Electrodiagnostic Medicine (AANEM) and 58 responded. Fifty-four (93%) responders performed needle EMG on patients taking DOACs, 13 (22%) responders had written laboratory guidelines specific to perform EMG on patients taking anticoagulants, and 4 (7%) responders had written laboratory guidelines including DOACs. Seven (12%) responders asked patients to withhold DOACs before performing EMG. One responder mentioned that the period for withholding DOACs depended on the medication. Two (3%) responders had known patients with thrombotic complications when discontinuing DOACs. A single (2%) responder reported a case of a small asymptomatic hematoma in the paraspinal muscle region detected by post-EMG MRI [65].

7. Acupuncture

Lee et al. found that increasing the diameter of acupuncture needles significantly increased the incidence of bleeding-related adverse events in patients taking anticoagulants or antiplatelet therapy, especially more in the head, face, and feet regions [66]. A prospective adverse effects acupuncture study by Witt et al. showed that the most common adverse effects were bleedings or hematoma [67]. McCulloch et al. reported that acupuncture appears safe in patients taking anticoagulants citing a 0.003% complication rate, assuming adequate needling location and depth. Bleeding events with acupuncture were limited to asymptomatic bruises or minor drops of blood after removing the needle. The only serious reported bleeding events were due to inappropriately deep needling (acute carpal tunnel syndrome induced by haemorrhage and cecal intramural hematoma in a patient taking anticoagulant agent) or by aggressive concomitant anticoagulant therapy itself (intracranial haemorrhage) [68].

A retrospective chart review of 242 patients and 4,891 acupuncture treatments concluded that acupuncture appeared safe for patients taking warfarin or antiplatelet medications [69]. The World Health Organization (WHO) published a systematic review of the Chinese-language literature on acupuncture-related adverse events based on 115 articles (98 case reports and 17 case series). One of the most common acupuncture-related adverse events was subarachnoid haemorrhage, which was reported in 35 patients of the 296 cases [70]. As with DN, there is no universally accepted system for reporting adverse events of acupuncture [16, 71]. Lee et al. evaluated the risk of bleeding-related adverse events (microbleeding, hematoma, and ecchymosis) after acupuncture treatment in patients taking anticoagulant or antiplatelet therapy; 169 patients taking anticoagulants or antiplatelet therapy (exposure group) and 259 patients taking no medication (nonexposure group) were assessed immediately after acupuncture treatment and before acupuncture treatment the following day. Mild bleeding-related adverse events occurred in 38.5% of patients in the exposure group and 44.4% of patients in the nonexposure group. Microbleeding was most common in both groups (70.0% and 59.1% in the exposure and nonexposure group, respectively). Results showed that the use of such medication did not increase the incidence of bleeding-related adverse events in acupuncture treatment, and most of the adverse events related to bleeding were mild [66]. Kwon et al.'s study also demonstrated that acupuncture is safe in patients taking DOACs. Recorded medical data about bleeding-related side effects immediately after needle removal in patients taking DOACs versus those patients taking antiplatelet agents and no anticoagulant therapy were retrospectively reviewed. One hundred-sixteen patients received 10,177 acupuncture sessions during a 9-month period, and the incidence of microbleeding was 3.9% in the DOAC group compared with 5.6% and 5.1% in the antiplatelet and the control group, respectively [72].

8. Botulinum Toxin Injections

Studies of botulinum toxin (BTX) injections and potential bleeding complications must be considered with some caution as the infiltrations are generally made with larger and bevelled-edged needles compared to the smaller solid filament needles used with DN. Nevertheless, a review of possible BTX bleeding complications may help as injections are commonly used for the management of spasticity in patients taking antithrombotic agents. Only a few studies have attempted to determine the rates of bleeding complications, the particular physicians' practice of performing the injections, and common preferences to control the risk of bleeding prior to the injections. For example, a Korean survey of physiatrists found a high variability between physicians with respect to injecting patients on anticoagulant therapy, and generally, there was a tendency to avoid BTX injections all together. Seventy percent of the respondents considered the INR value prior to performing the injections in patients taking anticoagulants. The majority of respondents thought that INR values between 2 and 3 were optimal. However, many others replied that an INR value lower than 2 was the preferred range. Most respondents used an INR value measured 2–7 days prior to the injection and acknowledged that they did not have access to standardized prevention protocols for performing BTX injections. Thirty-one percent of the respondents used some preventive measures, such as applying prolonged compression at the injection site and observing signs of swelling or bruising after the injection [73].

In a 2012 study by Schrader et al., 20 patients on the oral anticoagulant phenprocoumon with optimal INR values received BTX therapy using a 27 G (0.40 mm) needle without producing an increase in hematoma formation [74]. In relation to the previous study and after a follow-up period of four years, Schrader et al. published an article in 2017 concluding that none of the hematomas were surgically relevant and that the risk of minor hematoma after BTX therapy in patients taking anticoagulants is slight and only occurs in periocular injections [75]. Phadke et al. conducted a retrospective review of medical charts of patients with spasticity who received BTX injections with 26 G (0.45 mm) needles in their leg compartment muscles. Patients were taking anticoagulants, antiplatelet medications, or no medication. INR values were below 2.5. The authors found no evidence of compartment syndrome or bleeding events in the superficial or deep compartment locations [76].

In summary, there are no established and validated criteria, recommendations, or consensus for BTX injections for patients taking anticoagulants [73, 77]. With an INR $\leq$2.6 and 27 G (0.40 mm) or thinner needles, BTX injections do not pose a risk in patients [74, 76].

9. Ultrasound-Guided Fine-Needle Aspiration Biopsy

USGFNAB is the most accurate technique to evaluate thyroid nodules, and many patients who are candidates for this procedure are on anticoagulant treatment [78]. The needle used in this technique is a thin, fine-gauge needle, usually 25 G (0.50 mm) or 27 G (0.40 mm), which is smaller in diameter than typical hypodermic needles, but bigger than the needles used for DN. A study of USGFNAB bleeding risks concluded that the aspiration did not increase the formation of hematomas, nor did it pose an increased risk of major bleeding. Discontinuing anticoagulant therapy with VKAs before the procedure was not necessary. There are no specific published studies of patients taking DOACs who undergo USGFNAB but continuing the medication prior to this procedure is safe [78].

10. Recommendations

There are no studies comparing the incidence and prevalence of adverse events associated with DN in subjects taking antithrombotics and subjects who do not take these medications. It is also not known whether some of the relatively mild adverse effects in general populations may become more severe for patients taking anticoagulants.

Clinicians must always be cautious when applying DN techniques, considering the use of medications that affect coagulation. Besides, it is necessary to have other competencies, especially excellent anatomical knowledge. It is mandatory to complete a thorough clinical evaluation, which should include an inspection of the skin prior to DN looking for signs of excessive bruising [59]. According to the "Analysis of Competencies for Dry Needling by Physical Therapists," published by the Federation of State Boards of Physical Therapy in the US, of the 116 entry-level and 22 dry needling-specific knowledge requirements, 117 were identified as important for competency in DN [79].

Although not directly related to DN, some professional associations have recommended specific considerations that may be considered for DN. For example, AANEM has advised that an EMG evaluation should start with small superficial muscles before proceeding to deeper ones, although according to Boon et al., standard needle EMG of potentially high-risk muscles in patients taking antithrombotic drugs does not imply an increased risk of hematoma formation [58, 80]. Currently, as in EMG procedures, there is no evidence to support postposing DN routinely because of antithrombotics use, and medications should not be discontinued before the procedure [59]. Other examples are the recommendations of the AANEM [80] and the WHO guidelines on drawing blood [81]. In patients who are at higher risk of bleeding, the AANEM recommends to control hemostasis throughout the procedure by applying prolonged direct compression after removing the needle over the insertion site to minimize the risk of bleeding and bruising [80]. The WHO Guidelines recommend using a gauge of 19–23 and a length of 1–1.5 inches (except for a 19–20 gauge for which this is not applicable) for drawing blood in adults. After withdrawing the needle and syringe, firm and sustained pressure must be applied to stop any bleeding for as much as 2–3 minutes or 5 minutes or more for patients on anticoagulants. Moreover, to reduce the risk of extensive bleeding the WHO also recommends using a needle gauge smaller than the actual vein [81]. Considering drawing blood versus DN, it is important to consider that with DN techniques, veins are not purposely punctured. Besides, needles used with DN do not have a cutting bevelled edge like those used for blood draws or BTX infiltration, so they will cause less tissue damage. Moreover, the small diameter of the needles minimizes the likelihood of bleeding [15].

In conclusion, with DN, the pressure is usually maintained for about 5 seconds for nonanticoagulated patients; for patients taking anticoagulants the pressure should be applied for about 10–15 seconds. Despite the low risk of bleeding and bruising with DN in patients who are taking medications that affect coagulation, it is important to be cautious when needling close to major blood vessels, or when applying hemostasis is not an option. The patient's individual risks must be considered as previously described, similar to EMGs and other needling procedures [59].

The use of sonography in Doppler mode is recommended, but not essential, with DN of particular muscles such as the tibialis posterior, lateral pterygoid, or psoas major muscle, which not only reduces the chance of penetration major vessels but also increases the accuracy of the technique. Although sonography is increasingly used in clinical practice, most clinicians do not have access to sonography.

11. Conclusions

Clinicians must always inform patients about the possible risks of DN and obtain at least an oral informed consent prior to DN. When specific information about the patient's coagulation status, such as the INR, is not readily available, clinicians should determine the potential risk factors by including specific questions during the clinical interview, such as the patient's experience with bleeding following venipuncture. When a given patient presents with diminished coagulation, clinicians may consider initially reducing the intensity of the DN techniques. Although the bleeding response for every patient may vary between days or even on the same day, it is recommended to observe the patient's bleeding response and initially avoid DN in deeper muscles until its safety has been established with more superficial muscles, especially with patients on anticoagulant therapy. Applying prolonged hemostasis following DN is recommended.

Venipuncture and other invasive procedures, such as USGFNAB and botulinum injections, are performed regularly in patients who are taking anticoagulants, and they have been proven to be safe. They do not cause a major bleeding event. Therefore, taking antithrombotic medication should not be considered an absolute contraindication for DN techniques. If specific dry needling and individual risks are properly considered, antithrombotic medications do not change the risk and safety profile of dry needling. For improving the safety of DN practice in these patients, the use of ultrasound guidance is recommended, but not essential, for DN in locations close to major blood vessels or in deeper muscles where hemostasis cannot be applied.

Conflicts of Interest

Sandra Calvo, Jan Dommerholt, and Pablo Herrero disclose that they teach dry needling courses, which may be considered a potential conflict of interest in the subject matter or materials discussed in the article. Jan Dommerholt received royalties from published books on dry needling.

Authors' Contributions

M.M. and P.H. conceptualized the study; M.M, S.P, and P.H. developed methodology; M.M., S.P, S.C, and P.H. investigated the study; P.H., M.M., J.D, and S.C. wrote the original draft; P.H., S.C., S.P., and J.D. reviewed and edited the manuscript; P.H. and J.D supervised the study. All authors read and agreed to the published version of the manuscript.

Supplementary Materials

Supplementary File 1. Dry needling of the abductor digiti minimus muscle. (*Supplementary Materials*)

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Research Article

Quality of Evidence Supporting the Role of Acupuncture for the Treatment of Irritable Bowel Syndrome

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Objectives. To systematically collate, appraise, and synthesize the current evidence on acupuncture for irritable bowel syndrome (IBS). *Methods*. Systematic reviews (SRs)/meta-analyses (MAs) of acupuncture for IBS were searched in eight databases. For quality evaluation of the enrolled studies, Assessment of Multiple Systematic Reviews 2 (AMSTAR-2) was used for methodological quality, Preferred Reporting Item for Systematic Reviews and Meta-Analyses (PRISMA) for reporting quality, and Grading of Recommendations Assessment, Development, and Evaluation (GRADE) for evidence quality. *Results*. Ten studies were included in our review. According to AMSTAR-2, only one study met all the criteria and was rated as high methodological quality, and the rest were rated as low or very low methodological quality. According to the PRISMA checklist, most of the items were fully reported, with the exception of Q5 (protocol and registration), Q8 (search), and Q27 (funding). With the GRADE system, no outcome measure was rated as high quality. *Conclusions*. Acupuncture may be a promising therapy for IBS. However, this conclusion must be treated with caution since the quality of SRs/MAs providing evidence is generally low.

1. Introduction

Irritable bowel syndrome (IBS) is a functional gastrointestinal disorder characterized by recurrent abdominal pain accompanied by abnormal or altered defecation habits [1]. From country to country, the prevalence of IBS ranges from 1.1% to 45.0% [2], with global estimates of 11.2% [3] in Rome, 5.9% in China [4], and 7.1% in the United States [3]. This disorder not only has a marked negative impact on quality of life (QOL) and work productivity but also increases medical healthcare costs and imposes a huge socioeconomic burden [5, 6]. It is reported that the annual direct cost per patient due to IBS is estimated to be $348 to $8,750 and the indirect cost is $355 to $3,344 [7].

The pathophysiology of IBS is poorly understood and is currently thought to represent a complex interplay among the gut microbiota, mucosal immune system, impaired mucosal barrier function, visceral hypersensitivity, gut motility, and alterations in the gut-brain axis [8–10]. The conventional medication (CM) recommended to alleviate the symptoms include antispasmodics, fiber supplementation antidepressants, and probiotics [2, 8]. However, the effects are limited and accompanied by various side effects [11]. As a nonpharmacological treatment technique, acupuncture is believed to be beneficial to IBS based on the theory of the visceral hyperalgesia theory of the central nervous system.

Acupuncture is becoming more widely used, and the number of published systematic reviews (SRs) and meta-analyses (MAs) has increased, but the evidence they provide for acupuncture for IBS is not always consistent. SR/MA is considered the gold standard for assessing the effectiveness of clinical interventions; however, high-quality SRs/MAs can provide reliable evidence, while low-quality SRs/MAs might

instead mislead clinical decision-making [12]. Thus, there may be a gap between evidence-based clinical implementation of acupuncture and its actual implementation in real-world dynamics. Clinical decision-making requires a comprehensive overview of the available evidence in order to identify potential benefits and harms of the intervention [13]. Within this framework, the overview of SRs/MAs is a relatively new approach, which aims to summarize and evaluate the strength of the evidence provided in multiple SRs/MAs [14]. By mapping the evidence in the real-world implementation field of acupuncture, an umbrella review will help draw a clear link between the need to address uncertainty and advancing clinical knowledge a priori [15]. Therefore, we conducted this study.

2. Methods

The Cochrane criteria and the statements of Preferred Reporting Item for Systematic Reviews and Meta-Analyses (PRISMA) [16] were followed to carry out this overview. The protocol was registered in PROSPERO (CRD42021228185).

2.1. Strategy for Search. PubMed, Cochrane Library, Web of Science, Embase, Chinese Scientific Journal Database, CNKI, VIP, and Wanfang were systematically searched from inception to July, 2021. Irritable bowel syndrome, acupuncture, systematic review, and meta-analyses were used as search key terms. A search strategy used for PubMed is shown in Table 1.

2.2. Criteria Used to Consider Studies. The studies that met the following criteria were included: (1) SRs/MAs based on randomized controlled trials; (2) the Rome I–IV criteria were adopted as diagnostic criteria for IBS; (3) the experimental intervention was acupuncture or a combination of acupuncture plus medications and the control intervention was Sham acupuncture or CM; and (4) outcome measures should be effective rate, recurrence rate, IBS symptom scores, IBS-QOL, and Symptom Severity Scale of IBS (IBS-SSS). The studies that met the following criteria were excluded: (1) duplicate publications; (2) updated SRs/MAs; (3) dissertations without peer review; and (4) the control intervention that included acupuncture.

2.3. Literature Selection and Data Extraction. Literature selection and data extraction were carried out by two independent authors, respectively. For literature selection, titles and abstracts were first screened and then, the full text of potentially relevant studies was further reviewed to determine eligibility. In addition to the outcomes of meta-analyses, data regarding the characteristics of the studies and subjects, details of the treatments, and methods of the SRs/MAs were extracted. Any discrepancies were resolved by discussion.

2.4. Quality Assessment. Quality assessment was carried out by two independent authors. The Assessment of Multiple Systematic Reviews 2 (AMSTAR-2) [17], PRISMA tool, and Grading of Recommendations Assessment, Development, and Evaluation (GRADE) [18] were used to evaluate the methodological quality, reporting quality, and evidence quality, respectively. Any discrepancies were resolved by discussion.

3. Results

3.1. Included Studies. As shown in Figure 1, the literature search identified 243 citations, and after removing the duplicates, 173 citations were further eliminated, 167 of which were excluded. Finally, 10 studies [19–28] met the inclusion criteria.

3.2. Study Characteristics. As shown in Table 2, 10 MAs published from 2010 to 2020 were enrolled in this overview. Half of these studies were published in English, with the number of trails ranging from 6 to 41 and the subjects ranging from 664 to 3440. The experimental intervention was mainly acupuncture or a combination of acupuncture plus medications, and the control intervention was mainly Sham acupuncture or CM characteristics.

3.3. Quality Assessment

3.3.1. Methodological Appraisal. According to AMSTAR-2, only one review met all items and was rated as high methodological quality, and the rest were rated as low or critically low methodological quality. Key items affecting the methodological quality were item 2 (established protocol), item 4 (comprehensive search strategy), and item 7 (a list of excluded trails). Further details are shown in Figures 2 and 3.

3.3.2. Reporting Quality Appraisal. According to PRISMA checklists, most of the items were fully reported in these included reviews, with the exception of Q5 (protocol and registration), Q8 (search), and Q27 (funding). Further details are given in Table 3.

3.3.3. Evidence Quality Classification. 25 outcome indicators regarding the effects of acupuncture for IBS were extracted from the included studies. With GRADE, 12 outcome indicators were rated as moderate quality and the rest were rated as low or critically low quality. The risk of bias, imprecision, inconsistency, and publication bias were the main reasons for evidence degradation (Table 4).

3.4. Description of Efficacy

3.4.1. Effect of the Interventions. Relative effects of the outcome indicators regarding the effectiveness of acupuncture for IBS are shown in Table 4. Two studies [20, 23] compared the effects of acupuncture and Sham acupuncture, and reportedly no statistically significant difference was found in effective rate, IBS-QOL, or IBS-SSS. Nine studies [19, 20, 22–28] compared the effects of acupuncture and CM, and results revealed that patients receiving acupuncture

Table 1: Search strategy for the PubMed database.

Query	Search term
#1	Irritable bowel syndrome [Mesh]
#2	Irritable bowel syndrome [Title/abstract] OR irritable colon syndrome [Title/abstract] OR irritable colon [Title/abstract] OR gastrointestinal syndrome [Title/abstract] OR colon spasm [Title/abstract] OR allergic colitis [Title/abstract] OR colon allergy [Title/abstract] OR IBS [Title/abstract]
#3	#1 OR #2
#4	Acupuncture [Mesh]
#5	Acupuncture [title/abstract] OR pharmacoacupuncture [title/abstract] OR acupotomy [title/abstract] OR acupotomies [title/abstract] OR pharmacopuncture [title/abstract] OR needle [title/abstract] OR needling [title/abstract] OR dry-needling [title/abstract] OR body-acupuncture [title/abstract] OR electroacupuncture [title/abstract] OR electro-acupuncture [title/abstract] OR auricular acupuncture [title/abstract] OR warm needle [title/abstract]
#6	#4 OR #5
#7	Meta-analysis as topic [mesh]
#8	Systematic review [title/abstract] OR meta-analysis [title/abstract] OR meta-analyses [title/abstract]
#9	#7 OR #8
#10	#3 AND #6 AND #9

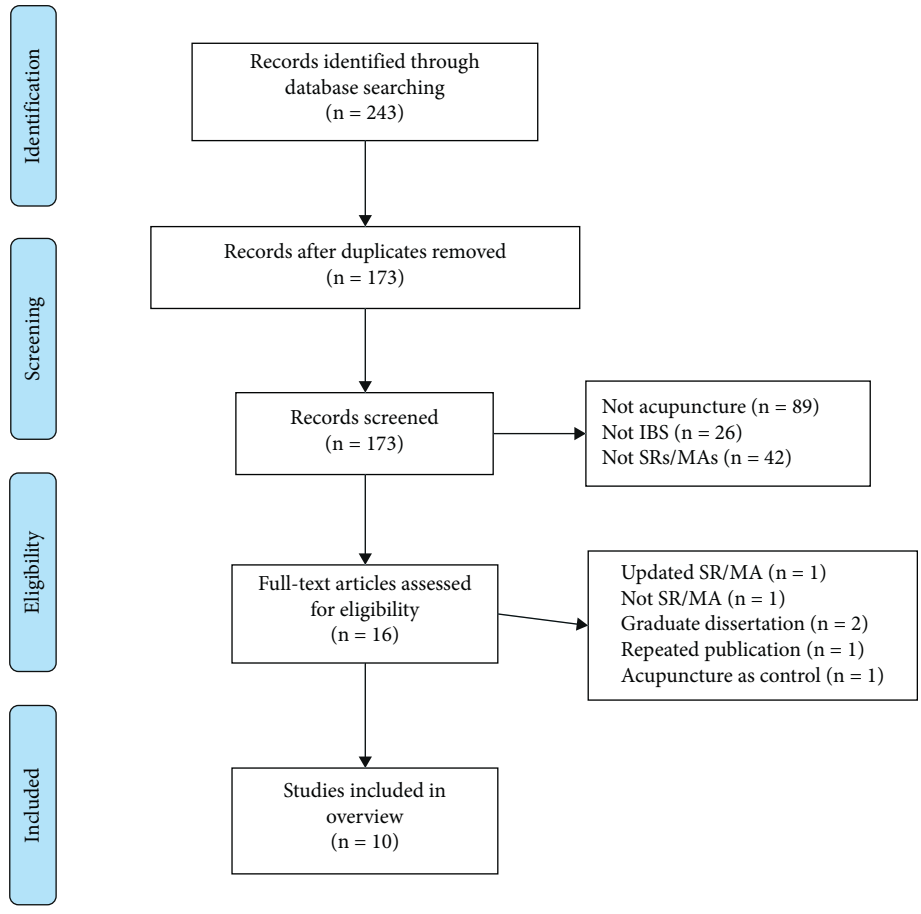

Figure 1: Literature screening flow chart.

therapy showed a greater improvement in effective rate, recurrence rate, weekly defecation, IBS symptom scores, IBS-QOL, and IBS-SSS than patients receiving CM. One study [21] compared the effects of acupuncture plus Chinese herbal medicine and CM, and results revealed that patients receiving combination therapy reported a significantly greater improvement in effective rate and abdominal pain than patients receiving CM.

Table 2: Baseline characteristics of included reviews.

Studies	Country	Trials (subjects)	Experimental Intervention	Control Intervention	Quality assessment	Meta-analyses	Results summary
Guo et al. [19]	China	31 (3234)	AT	CM	Cochrane criteria	Yes	Acupuncture was an effective and safe therapy for IBS.
Zheng et al. [20]	China	41 (3440)	AT, AT + CM	Sham AT, CM	Cochrane criteria	Yes	The effect of acupuncture on IBS was better than that of CM, which could be used as an adjuvant therapy in clinical practice.
Yan et al. [21]	China	21 (1834)	AT + CHM	CM; CHM	Cochrane criteria	Yes	The combination of acupuncture and Chinese herbal medicine was effective and safe in the treatment of IBS.
Chao and Zhang [22]	China	6 (664)	AT	Sham AT, CM	Jadad	Yes	Acupuncture was significant in relieving the symptoms of IBS.
Manheimer et al. [23]	United States	17 (1806)	AT	Sham AT, CM	Cochrane criteria	Yes	The effect of acupuncture on IBS was better than that of CM, which could be used as an adjuvant therapy in clinical practice.
Fu and Jiang [24]	China	23 (1685)	AT	CM; AT + CM	Jadad	Yes	Acupuncture therapy was superior to conventional CM in the treatment of IBS.
Deng et al. [25]	China	17 (1333)	AT; AT + CM	CM; Sham AT + CM	Jadad	Yes	Acupuncture for IBS was superior to conventional treatment, which could improve the clinical symptoms and reduce the recurrence rate of patients.
Li et al. [26]	China	12 (715)	AT	CM	Cochrane criteria	Yes	The evidence of this study was not sufficient to prove that the efficacy of acupuncture was better than CM.
Pei et al. [27]	China	11 (969)	AT; AT + CM	CM; Sham AT + CM	Cochrane criteria	Yes	Acupuncture for IBS was better than the CM treatment.
Zhao et al. [28]	China	10 (810)	AT	CM	Jadad	Yes	The effect of acupuncture on IBS was superior to that of western medicine.

AT: acupuncture therapy; CHM: Chinese herbal medicine.

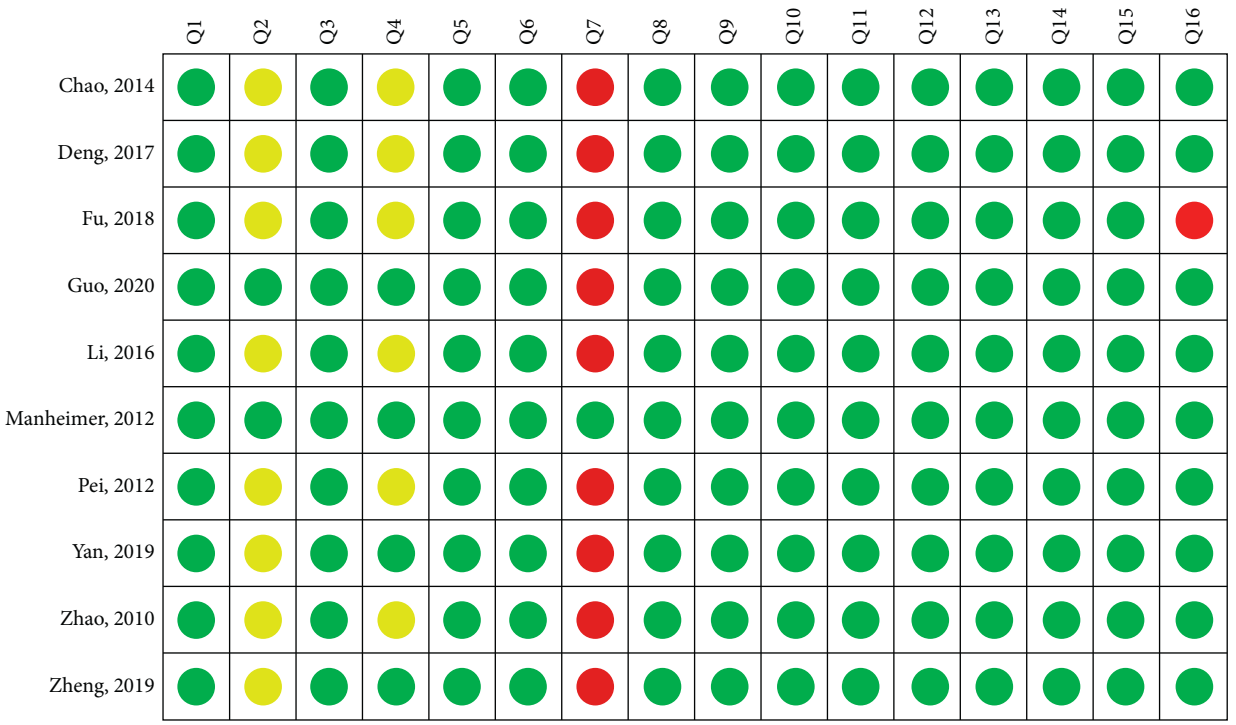

Figure 2: Summary of the AMSTAR-2 assessments.

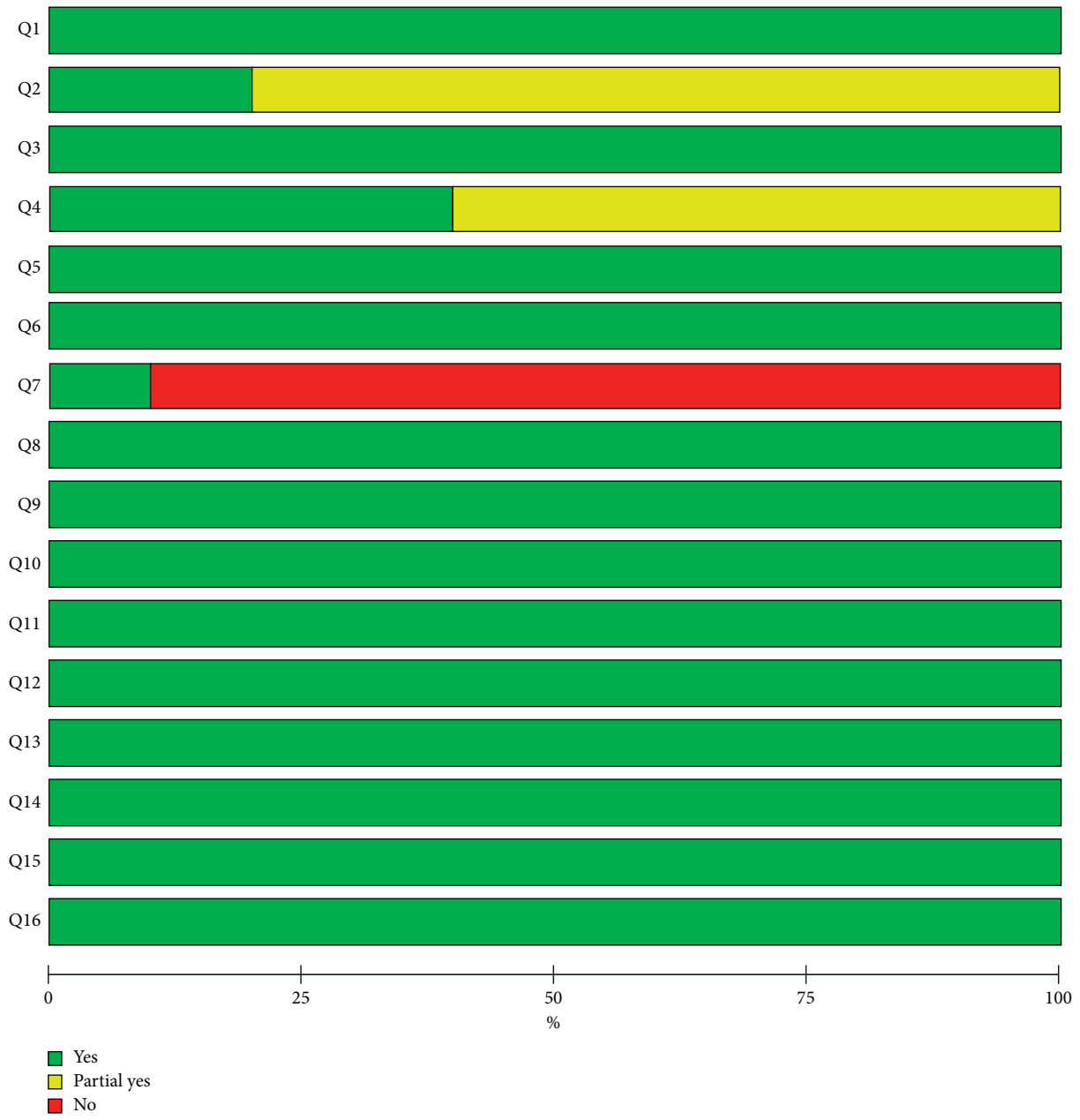

Figure 3: Graphical representation of the AMSTAR-2 assessments.

3.4.2. Safety of the Interventions. One study [19] reported the meta-analysis results in adverse effects, and no statistically significant difference was found between patients treated with acupuncture and CM.

4. Discussion

Treatment of IBS focuses on symptom management to maintain daily functioning and improve QOL. However, due to significant side effects of prescribed medications, some sufferers do not take multiple CM but instead turn to complementary and alternative therapies for remedy [11, 29]. A number of SRs/MAs have investigated the efficacy of acupuncture for IBS patients. The purpose of this study was to systematically collate, appraise, and synthesize the evidence published in recent years.

Ten SRs/MAs regarding to the efficacy of acupuncture for IBS were finally included. From the meta-analysis results of these studies, patients reported that acupuncture had a greater benefit on IBS symptoms than CM. However, these findings must be considered cautiously, given the limitations on methodological quality, reporting quality, and evidence quality of the included studies. According to AMSTAR-2 and PRISMA checklists, most of (80%) the included studies did not establish a protocol, which could undermine the rigor of the study and increase the risk of bias. For literature search, 60% studies only provided the search keywords but no specific search strategies, which could lead to publication

Table 3: Results of the PRISMA checklists.

Section/ topic	Items	Guo, 2020	Zheng, 2019	Yan, 2019	Chao, 2014	Manheimer, 2012	Fu, 2018	Deng, 2017	Li, 2016	Pei, 2012	Zhao, 2010	Compliance (%)
Title	Q1. Title	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	100
Abstract	Q2. Structured summary	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	100
Introduction	Q3. Rationale	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	100
	Q4. Objectives	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	100
Methods	Q5. Protocol and registration	Y	N	N	N	Y	N	N	N	N	N	20
	Q6. Eligibility criteria	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	100
	Q7. Information sources	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	100
	Q8. Search	Y	Y	Y	PY	Y	PY	PY	PY	PY	PY	40
	Q9. Study selection	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	100
	Q10. Data collection process	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	100
	Q11. Data items	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	100
	Q12. Risk of bias in individual studies	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	100
	Q13. Summary measures	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	100
	Q14. Synthesis of results	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	100
	Q15. Risk of bias across studies	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	100
	Q16. Additional analyses	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	100
Results	Q17. Study selection	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	100
	Q18. Study characteristics	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	100
	Q19. Risk of bias within studies	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	100
	Q20. Results of individual studies	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	100
	Q21. Synthesis of results	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	100
	Q22 Risk of bias across studies	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	100
	Q23. Additional analysis	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	100
Discussion	Q24. Summary of evidence	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	100
	Q25. Limitations	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	100
	Q26. Conclusions	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	100
Funding	Q27. Funding	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	90

bias and undermined the credibility of the results. Moreover, 90% studies did not provide the lists of excluded trails, which may undermine the transparency of the study process. According to the GRADE tool, no outcome indicators provided high-quality evidence, indicating that the meta-analyses results of the included studies may differ from the true results. The risk of bias for the enrolled trails of the included studies was the main reason for evidence degradation. Further analyses found common limitations of the enrolled trails as follows: only randomization was mentioned without the randomization method; the allocation was not concealed; and only single blinding was implemented. Therefore, the basic factor leading to the decline in the quality of evidence was the low methodological quality of the enrolled trails. It was believed that well-designed and implemented randomized controlled trials were considered to be the gold standard to avoid the risk of bias [30]. Furthermore, almost all of the included SRs/MAs indicated that acupuncture seemed to have a significant clinical efficacy for IBS; however, most authors did not wish to draw clear conclusions due to low methodological quality or the small size of the enrolled trails.

Table 4: Certainty of evidence quality.

Studies	Treatments	Outcomes	Limitations	Inconsistency	Indirectness	Imprecision	Publication bias	Relative effect (95% CI)	Quality
Guo et al. [19]	AT versus CM	Weekly defecation	−1	0	0	0	0	SMD, −0.29 (−0.49, −0.08)	M
		IBS symptom scores	−1	0	0	0	0	SMD, −1.17 (−1.42, −0.93)	M
		IBS-QOL	−1	0	0	−1	0	SMD 2.37 (1.94, 2.80)	L
		IBS-SSS	−1	0	0	0	0	SMD −0.75 (−1.04, −0.47)	M
Zheng et al. [20]	AT versus Sham AT	Effective rate	−1	0	0	0	0	RR 1.25 (1.18, 1.32)	M
		Recurrence rate	−1	0	0	−1	0	RR 0.43 (0.28, 0.66)	L
		Adverse effects	−1	0	0	−1	0	RR 0.59 (0.12, 2.90)	L
		Effective rate	−1	0	0	0	0	RR 1.22 (1.01, 1.47)	M
		IBS-QOL	−1	0	0	0	0	SMD −0.10 (−0.31, 0.11)	M
	AT versus CM	Effective rate	−1	0	0	0	0	RR 1.17 (1.12, 1.23)	M
		IBS symptom scores	−1	−1	0	0	0	SMD −1.16 (−1.61, −0.71)	L
		IBS-QOL	−1	0	0	−1	0	SMD 0.75 (0.34, 1.16)	L
Yan et al. [21]	AT + CHM versus CM	Effective rate	−1	0	0	0	0	RR 1.29 (1.24, 1.35)	M
		Abdominal pain	−1	−1	0	0	0	SMD −0.45 (−0.72, −0.17)	L
Chao and Zhang [22]	AT versus CM	Effective rate	−1	0	0	0	0	RR 1.75 (1.24, 2.46)	M
Manheimer et al. [23]	AT versus Sham AT	IBS-SSS	−1	0	0	−1	0	SMD −0.11 (−0.35, 0.13)	L
		IBS-QOL	−1	0	0	−1	0	SMD −0.03 (−0.27, 0.22)	L
Fu and Jiang [24]	AT versus CM	Effective rate	−1	0	0	0	0	RR 1.28 (1.12, 1.45)	M
	AT versus CM	Effective rate	−1	0	0	0	0	RR 1.20 (1.15, 1.25)	M
Deng et al. [25]	AT versus CM	Effective rate	−1	0	0	0	0	OR 3.92 (2.83, 5.43)	M
		Recurrence rate	−1	0	0	−1	0	OR 0.22 (0.12, 0.41)	L
Li et al. [26]	AT versus CM	Recurrence rate	−1	0	0	−1	−1	RR 0.49 (0.35, 0.68)	CL
		Effective rate	−1	0	0	0	−1	RR 1.17 (1.08, 1.26)	L
Pei et al. [27]	AT versus CM	Effective rate	−1	−1	0	0	0	RR 1.27 (1.09, 1.49)	L
Zhao [28]	AT versus CM	Effective rate	−1	0	0	0	−1	RR 1.28 (1.20, 1.38)	L

The action mechanism of acupuncture for IBS includes regulating the gastrointestinal motility, reducing visceral hypersensitivity, regulating the brain-intestine axis, reducing low-level intestinal mucosal inflammation, promoting intestinal microflora balance, and adjusting psycho-psychological status [31]. IBS is a gastrointestinal disorder in which intestinal spasm causes abdominal pain, hypermotility leads to diarrhea, and hypomotility leads to constipation. Thus, for the purpose of treatment, IBS can be divided into three types: constipation-predominant, diarrhea-predominant, or mixed [32]. Animal experiments revealed that acupuncture stimulation of IBS-D model rats effectively improved diarrhea symptoms in rats, and it was found that the mRNA and protein expression of APQ8 in the rat colon tissue was reduced, while the protein expression of VIP was increased [33]. For patients with IBS-C, electroacupuncture stimulation of Zusanli can promote contraction of the patient's colon ends and accelerate colonic transit, which in turn improves constipation symptoms [34]. These results suggest that acupuncture has a bidirectional regulatory effect on intestinal motility in IBS patients. Furthermore, EA intervention can ameliorate the fecal property in IBS-C rats, which may be associated with its function in inhibiting the expression of colonic CGRP and SP proteins [35]. Visceral hypersensitivity is considered an important pathological mechanism in the development of IBS. It is reported that EA can alleviate visceral hypersensitivity in IBS-D and IBS-C rats by regulating the expression level of TRPV1 in the colon [35, 36]. The brain-gut axis was a complex, bidirectional signaling system between the central nervous system and the gastrointestinal system. It is reported that acupuncture could improve intestinal motility and visceral sensitivity by modulating brain-gut peptide levels in the central nervous system, gut, and blood [31]. Furthermore, electroacupuncture decreases 5-HT and CGRP, increases NPY in the brain-gut axis in rat models of IBS-D [37], and increases the number of neurons in the myenteric plexus of IBS-C rats [38]. Posttraumatic stress disorder (PTSD) is thought to be associated with IBS and is a common comorbidity [39]. It is reported that acupuncture can affect the autonomic nervous system, and the prefrontal as well as limbic brain structures, enabling it to relieve the symptoms of PTSD [40]. Activation of the immune system was strongly associated with IBS, and acupuncture could downregulate the expression of serum IL-18, TNF-α, and IL-23 in IBS patients, thus playing an immunoregulatory role [41]. The overgrowth of intestinal flora may be an important factor in the induction of IBS [42]. It is reported that acupuncture treatment may modulate intestinal bacteria and the psychological state tends to balance to relieve the symptoms of IBS [31, 43]. However, there is still a lack of evidence on the regulation of intestinal microbiota in IBS through the use of acupuncture.

This overview would provide some useful information on unique treatments in clinical practice for physicians in the management of IBS, thus providing more treatment options for IBS patients. However, we found that the majority of the included reviews were of poor quality, which could result in them having low credibility. Furthermore, the AMSTAR-2 tool, PRISMA checklist, and the GRADE system are highly subjective. Thus, different reviewers may have their own independent judgments on the evaluation results. Even with two independent reviewers in this study, subjective factors or errors cannot be completely eliminated. Finally, there is limited evidence for the efficacy of acupuncture for IBS subtypes, especially IBS-C. Further clinical and mechanistic studies of acupuncture for IBS subtypes are still necessary.

5. Conclusion

Acupuncture may be a promising treatment for IBS, and it could be used as an adjunct in clinical settings to improve efficacy. However, this conclusion must be treated with caution since the quality of SRs/MAs providing evidence is generally low.

Abbreviations

IBS: Irritable bowel syndrome
SR: Systematic review
MA: Meta-analysis
AMSTAR-2: Assessment of Multiple Systematic Reviews 2
PRISMA: Preferred Reporting Item for Systematic Reviews and Meta-Analyses
GRADE: Grading of Recommendations, Assessment, Development, and Evaluation
QOL: Quality of life
SSS: Symptom Severity Scale
CM: Conventional medication.

Data Availability

All analyses were based on previously published studies.

Consent

No informed consent was required.

Disclosure

Jinke Huang and Mengxiong Lu are the co-first authors.

Conflicts of Interest

The authors declare that there are no conflicts of interest.

Authors' Contributions

Jinke Huang and Mengxiong Lu initiated the study design and drafted the manuscript. Both these authors have contributed equally to this work. Jinxin Ma, Jing Ma, Xiangxue Ma, Yitian Wang, Yijun Zheng, and Kunli Zhang helped with implementation to this work. All authors read and approved the final manuscript. Fengyun Wang and Xudong Tang contributed to the methodology, review, and editing of the manuscript. All authors read and approved the final manuscript.

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Research Article

Effect of Electroacupuncture on Shoulder Subluxation in Poststroke Patients with Hemiplegic Shoulder Pain: A Sham-Controlled Study Using Multidimensional Musculoskeletal Ultrasound Assessment

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Objective. This study aimed to use multidimensional musculoskeletal ultrasound imaging technique to investigate the effect of electroacupuncture (EA) on shoulder subluxation in poststroke patients with hemiplegic shoulder pain. *Methods*. In this prospective single-blind, randomized, sham-controlled study, thirty-four patients with shoulder subluxation and hemiplegic shoulder pain were recruited and randomly assigned into the EA group or the sham EA (SEA) group. In the EA group, EA was applied to the Jian yu (LI15), Bi nao (LI14), Jian zhen (SI9), and Jian liao (TE14) acupoints. In the SEA group, the EA was applied 15 mm away from the Lou gu (SP7), Di ji (SP8), Jiao xin (KI8), and Zhu bin (KI9) acupoints. Both groups underwent treatment 30 minutes/day, five days a week, for two weeks using dense waves with a frequency of 2/100 Hz. A Visual Analogue Scale (VAS) was used to evaluate the effectiveness of treatment in reducing shoulder pain. Musculoskeletal ultrasound was used to evaluate the changes of measures of shoulder subluxation in multidimensions (i.e., the acromiohumeral distance, AHD; acromion-greater tuberosity, AGT; and acromion-lesser tuberosity, ALT). Both the within- and between-groups treatment effects were assessed. *Results*. The pain intensity measured by VAS and shoulder subluxation measured by musculoskeletal ultrasound (i.e., AHD, AGT, and ALT) showed significant ($p < 0.05$) within-group difference in both groups. The between-group difference appeared in the pain intensity ($p < 0.05$), while it disappeared in the three measures of shoulder subluxation ($p > 0.05$). *Conclusions*. Using VAS for measuring pain intensity and multidimensional musculoskeletal ultrasound imaging technique for measuring shoulder subluxation, this study finds that the hemiplegic shoulder pain can be improved significantly by the EA while the shoulder subluxation cannot be. Our findings further reveal the analgesic mechanism of EA on hemiplegic shoulder pain following stroke.

1. Introduction

Stroke is a common neurological disease noted for its high morbidity, residual disability, and mortality rate [1, 2]. It places a significant burden on families and society [3]. Subluxation of the shoulder joint is a common complication of stroke [4]. Its incidence is as high as 81%, and it usually occurs within three months of the onset of stroke [4]. Subluxation of the shoulder joint is a possible cause for hemiplegic shoulder pain, which seriously affect the recovery of upper limb function [5]. This, in turn, aggravates the economic burden of stroke on family and society and brings immense pain to hemiplegic stroke survivors [6].

Commonly used treatments for shoulder subluxation include electrical stimulation, strapping, and/or orthosis [7–9]. However, there is insufficient evidence to confirm that these treatments definitely reduce shoulder subluxation and promote functional recovery of the upper limbs [7–9]. Thus, it is necessary to find other effective methods for treating shoulder subluxation. Electroacupuncture (EA), as a complementary and alternative therapy, is a form of acupuncture which involves a small pulsed electric current delivered to single or pairs of acupuncture needles [10]. It combines electrical stimulation with traditional acupuncture. Studies have found that EA has significant analgesic effects [11], improves limb muscle strength [12], and improves limb function [13]. Research also indicates that EA applied to the scapula and arm may effectively treat shoulder subluxation [14]. Thus, EA is a potential effective therapy to improve the shoulder subluxation in the stroke patients with hemiplegic shoulder pain.

The analgesic mechanism of EA is still being investigating. It has been studied at peripheral, spinal, and supraspinal levels which involve a series of bioactive molecules [15]. These molecules can be regulated and modified by EA and the relevant nociceptive neurons can also be impacted [16]. It is indicated that EA can relieve shoulder pain effectively through neural-immune-endocrine interactions [16, 17]. Because many clinical factors including physiological and psychological factors are highly correlated to the pain symptom [17, 18], it is also significant to investigate the analgesic mechanism of EA by measuring these clinical factors. Taking these factors into consideration, the relationship between the occurrence of shoulder subluxation and the development of hemiplegic shoulder pain is not consistent in the literature of stroke [19, 20]. By analyzing the alteration of hemiplegic shoulder pain and shoulder subluxation following EA, it will help to explore the relationship between the shoulder subluxation and the EA as well as the hemiplegic shoulder pain.

In order to assess the alteration of shoulder subluxation following EA and explore the possible analgesic mechanism of EA, an appropriate evaluation tool should be applied. The musculoskeletal ultrasound imaging is a noninvasive objective tool to diagnose the shoulder subluxation [21, 22]. Compared to other radiological examinations, it shows advantages including excellent visualization of shoulder structure, lack of ionizing radiation, dynamic assessment, uncomplicated operation, and cost-effectiveness [23]. By measuring the distance between two osseous landmarks, including acromiohumeral distance (AHD) [24], acromion-greater tuberosity (AGT) [22], and acromion-lesser tuberosity (ALT) [24, 25], musculoskeletal ultrasonography can accurately compute the degree of subluxation in multidimensions [25]. This enables objective evaluation of treatment effect and exploration of its mechanism.

Thus, this study aimed to use multidimensional musculoskeletal ultrasound imaging technique to objectively evaluate the effect of electroacupuncture on shoulder subluxation in stroke patients. The findings may help to further understand the treatment mechanism of EA in stroke.

2. Materials and Methods

2.1. Participants. Patients hospitalized with shoulder subluxation and hemiplegic shoulder pain after stroke were recruited from the Huazhong University of Science and Technology Union Shenzhen Hospital (China) from October 2018 to September 2019. The sample size in this study was computed according to previous literature on EA treatment for hemiplegic shoulder pain [26]. By using GPower 3.1.9.2 software, the sample size was estimated to be 34 in this study, while the effect size is 1.11, α is 0.05 with a power of 80%, and patient shedding rate is 20%. This study's protocol was approved by the institution's ethics committee (IRB no. 032502). It was also registered with the Chinese Clinical Trial Registry (no. ChiCTR2000029051). All patients (and/or their families) provided informed written consent prior to study participation.

To be included in the study, patients were required to meet the diagnostic criteria for stroke as defined by the Chinese Guidelines for the Prevention and Treatment of Cerebrovascular Diseases [27], be diagnosed using computerized tomography (CT) or magnetic resonance imaging (MRI), and meet the diagnostic criteria for fingerbreadth palpation of shoulder subluxation [28, 29]. This third criterion required that the degree of subluxation be more than half a fingerbreadth gap [28]. Other inclusion criteria were aged 30–75 years; first stroke or previous stroke without sequelae; subluxation that appeared within one year of the stroke; limb dysfunction on only one side of the body; stable vital signs; no severe heart, lung, liver, or kidney dysfunction; no coagulation dysfunction; and visual analogue scale (VAS) pain score $\geq$4 points. The exclusion criteria were any history of rotator cuff injury; periarthritis, shoulder surgery, or shoulder trauma; malignant tumor; quadriplegia; severe speech or cognitive dysfunction; mental illness; pain caused by cancer, menopause, or fracture; and poststroke depression. We also excluded individuals with severe dizziness or a pacemaker.

2.2. Experimental Design. The study is a prospective single-blind, randomized, sham-controlled study. The recruited patients were assigned to EA group or sham EA (SEA) group randomly. All patients enrolled in the study were grouped using a simple randomization method and table of random numbers. Patients were randomly assigned envelopes with

randomization number by physicians not participating in the study. If the selected numbers were even, the patients were assigned to the EA group; if the selected numbers were odd, the patients were assigned to the SEA group; if the two groups were not balanced, a random number table was further used to evenly distribute them (ratio: 1 : 1).

In addition to EA treatment, both groups of patients also received conventional drug and rehabilitation treatment. Conventional drug treatment followed the Chinese Cerebrovascular Disease Prevention and Treatment Guidelines [27]. In order to avoid the bias between EA group and SEA group, we recruited the patients who received the identical series of conventional rehabilitation treatments including good limb positioning, passive shoulder movement, active shoulder strapping, rood therapy, weight training of the affected limb, and electrical stimulation therapy. All recruited patients underwent conventional rehabilitation treatments once a day, five days a week, for two weeks. If the type of the patient's rehabilitation treatment changed, this patient would be excluded from this study. By this means, the baseline conventional rehabilitation treatments of both groups can be consistent.

The details of all conventional rehabilitation treatments are as follows:

(i) Good limb positioning

Lying on the uninjured side: Shoulder joint was bent as much as possible; then the joints of the elbow, wrist, and fingers were stretched, respectively, on a cushion.

Lying on the affected side: put a cushion to support the back, the body torso was bent slightly backward so that the shoulder of the affected side was extended, the forearm and fingers of the affected side were naturally stretched, and the palm of the hand was upward.

Lateral decubitus position: A cushion was placed behind the shoulder joint on the affected side so as to make the shoulder blades maintain extended forward, and upper extremity was naturally stretched, and the palm of the hand was upward.

(ii) Passive shoulder movement

Making gentle, slow passive movement for joints of the shoulder, elbow, wrist, and fingers of the affected side to avoid excessive strain on the shoulder tissue.

(iii) Active shoulder strapping

The patient was lying on the uninjured side, the therapist placed one hand in the acromion of the affected side, and one hand passed through the affected side armpit and placed the palm of the hand in the medial lower angle of the scapula. Both hands were used to lift the shoulder and drop and retract the scapula.

(iv) Rood therapy

The therapist held up the affected side of the upper arm to ensure shoulder abduction, parallel to the long axis of the upper limb repeatedly stimulate the shoulder joint capsule, and told the patient to try to maintain confrontation with the treatment, while stimulating the shoulder muscles such as the deltoid muscle and supraspinatus muscle. Finally, the therapist will be relative to the palms of both hands, gently squeeze the affected shoulder joint.

(v) Weight training of the affected limb

The therapist instructed the patients to straighten their upper arm and forearm of the affected side and bend the wrist back after sitting down and then put the palm down on the hard plane on one side of the body. The therapist helped the patient to slowly tilt their upper body to the affected side, and make the shoulder joint of the affected side bear weight of the upper body.

(vi) Electrical stimulation therapy

The low-frequency neuromuscular electrical stimulation (NMES) was applied to patients. The frequency of stimulation was 1 Hz, while the intensity of stimulation was 20 mA–30 mA depending on the patients' tolerance.

2.3. Electroacupuncture (EA) Treatment. In the EA group, EA was applied to the jian yu (LI15), bi nao (LI14), jian zhen (SI9), and jian liao (TE14) acupoints. The positioning and depth were as recommended by Gao Shuzhong in his textbook Acupuncture and Moxibustion therapy [30]. During treatment, the patient was in a side-lying position, and the local skin was disinfected with 75% alcohol. The Hua tuo acupuncture needles were inserted 1–1.5 inches vertically into the skin. The needles were lifted and twisted to produce a feeling of deqi (i.e., sensation of soreness, numbness, distention, or radiating, which is considered to indicate effective needling). The acupuncture was followed by 30 minutes of electroacupuncture performed with a HANS-200A instrument (Suzhou Medical Supplies Ltd., China) using dense waves at 2/100 Hz. Patients underwent treatment once a day, five days a week, for two weeks.

2.4. Sham Electroacupuncture (SEA) Treatment. The SEA group received the same treatment as the EA group except for the location of needle insertions—the needles were applied 15 mm from the lou gu (SP7), di ji (SP8), jiao xin (KI8), and zhu bin (KI9) points [31, 32]. Specifically, after disinfection, Hua tuo acupuncture needles 1–1.5 inches long were inserted vertically into the skin of the side-lying participant, to a depth of five millimeters. Following the acupuncture, EA was applied using the same stimulation parameters as for the EA group.

2.5. Clinical Outcome Measurements. Outcome measurements were conducted before and after two weeks of treatment. Measures of shoulder subluxation were obtained by the same rehabilitation physician using a uSmart 3300 musculoskeletal ultrasound system (Terason Ultrasound Imaging System Version 5.11.4, frequency 3–17 Hz, USA).

Measure of pain intensity was conducted by using Visual Analogue Scale (VAS).

2.5.1. Acromiohumeral Distance (AHD). The musculoskeletal ultrasound probe was placed at the anterior border of the acromion. When both the acromion and humerus head appeared on the screen, the image was frozen, and the shortest distance between the acromion and humerus head was measured. We calculated the difference in AHD values before and after treatment (Figure 1).

2.5.2. Acromion-Greater Tuberosity (AGT). A musculoskeletal ultrasonic probe was placed on the lateral edge of the acromion and the lateral edge of the long head of the biceps tendon. When the lateral edge of the acromion and the upper edge of the greater tuberosity appeared on the screen at the same time, the image was frozen, and the AGT was measured. We calculated the difference in AGT values before and after treatment (Figure 2).

2.5.3. Acromion-Lesser Tuberosity (ALT). The musculoskeletal ultrasonic probe was placed on the lateral edge of the acromion and the medial edge of the long head of the biceps tendon. When the lateral edge of the acromion and the upper edge of the lesser tuberosity appeared on the screen at the same time, the image was frozen, and the ALT was measured. We calculated the difference in ALT values before and after treatment (Figure 3).

2.5.4. Visual Analogue Scale (VAS) for Shoulder Pain. Shoulder pain was evaluated using a VAS. Specifically, the patient graded their degree of pain on a 10 cm scale with 1 cm marked intervals (where 0 = not painful at all, 10 = unbearable pain, and the interval between represented a gradual increase in pain).

2.6. Statistical Analysis. IBM SPSS Statistics for Windows, version 23.0 (IBM Corp., Armonk, NY, USA) was used for statistical analysis. The Shapiro–Wilk test was used to determine whether the data were normally distributed. Descriptive statistics were presented using the mean ± standard deviation (normally distributed data) or median (%25, %75) (nonnormally distributed data) for continuous variables, or numbers for categorical variables. Independent sample t-test and χ^2 test were used to compare the baseline characteristics between groups. When data followed normal distribution, paired t-test was used for within-group comparison and independent sample t-test was used for between-group comparison. Otherwise, Mann–Whitney U tests were used to compare nonnormally distributed data. The threshold of statistical significance was set to $p < 0.05$.

3. Results

3.1. Demographic and Clinical Baseline Characteristics. Two patients in the SEA group dropped out of the study due to being unable to tolerate the pain associated with acupuncture.

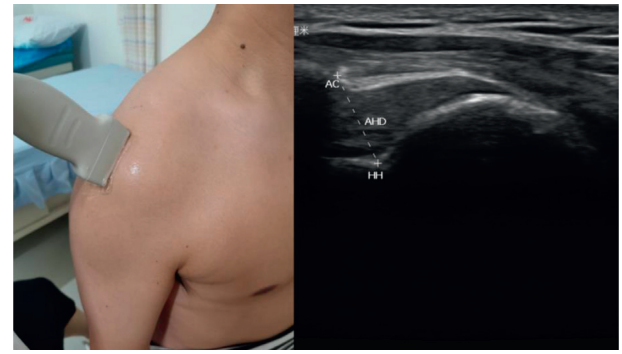

Figure 1: Measurement of acromiohumeral distance (AHD) for shoulder subluxation by using musculoskeletal ultrasound imaging technique. AC indicates acromion; HH indicates humerus head.

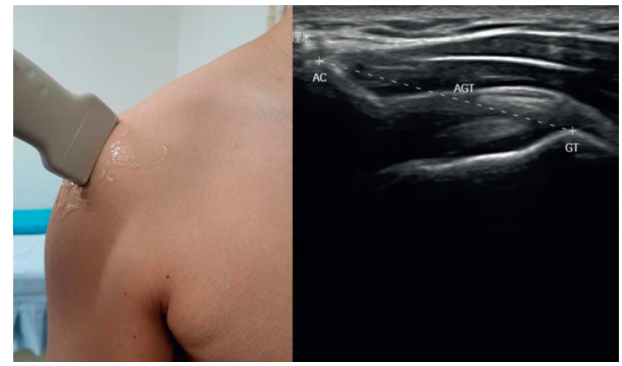

Figure 2: Measurement of acromion-greater tuberosity (AGT) for shoulder subluxation by using musculoskeletal ultrasound imaging technique. AC indicates acromion; GT indicates greater tuberosity.

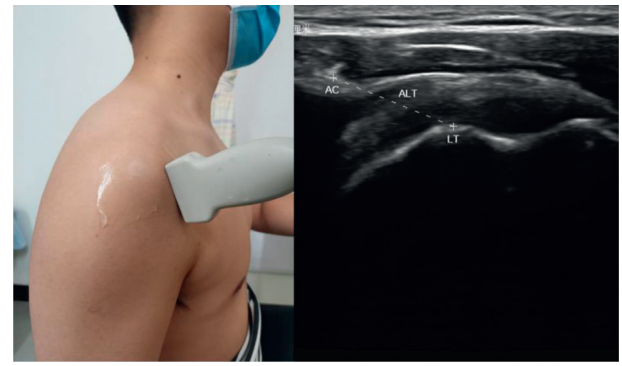

Figure 3: Measurement of acromion-lesser tuberosity (ALT) for shoulder subluxation by using musculoskeletal ultrasound imaging technique. AC indicates acromion; LT indicates lesser tuberosity.

Thus, 32 individuals (17 in the EA group and 15 in the SEA group) were included in the analyses. Participants included 22 men and 10 women. The mean ages of the EA and SEA groups were 51.00 ± 12.44 years (range = 32–68 years) and 54.40 ± 8.16 years (range = 41–68 years), respectively. The median hemiplegia duration was 64 (range = 14–188) days in the EA group and 65 (range = 12–183) days in the SEA group. There were no statistically significant differences between the EA and SEA groups in gender, age, disease course, or stroke type (Table 1).

Table 1: Participants' demographic characteristics.

Group	Gender		Age	Course of disease	Stroke type	
	Male	Female	Years, mean ± SD	Days, median (25%, 75%)	Hemorrhage	Infarction
EA group	12	5	51.00 ± 12.44	33.00 (23.00, 114.00)	7	10
SEA group	10	5	54.40 ± 8.16	44.00 (25.00, 112.00)	5	10
P value	0.811*		0.363#	0.961#	0.647*	

* indicates χ^2 test; # indicates independent t-test. SD indicates standard deviation.

3.2. Comparison of Pain Intensity. Before treatment, there were no significant differences in average VAS scores between the two groups. After two weeks of treatment, the average VAS scores of both groups were significantly lower than before treatment ($p < 0.05$). Moreover, the EA group's average VAS score was lower than the SEA's group. There were significant differences in the average VAS scores of both groups ($p < 0.05$) (Table 2 and Figure 4). By using independent t-test to compare the change of VAS, it showed a significant difference between EA and SEA groups (change of VAS: 3.29 ± 1.04 vs. 2.53 ± 0.83, $p = 0.03$).

3.3. Comparison of Ultrasound-Based Measures of Shoulder Subluxation. Before treatment, there were no significant differences in the average AHD, AGT, and ALT values between the two groups. After treatment, the average AHD, AGT, and ALT values were lower in both groups than before the treatment ($p < 0.05$). However, there were no significant between-group differences in the reductions in AHD, AGT, or ALT values (Table 3 and Figure 4). By using independent t-test to compare the change of ultrasound-based measures, it showed no significant difference between EA and SEA groups in all measures (change of AHD: 1.74 ± 2.30 vs. 0.87 ± 1.43, $p = 0.21$; change of AGT: 2.02 ± 3.34 vs. 1.43 ± 1.49, $p = 0.52$; and change of ALT: 1.99 ± 2.72 vs. 1.41 ± 1.26, $p = 0.44$).

4. Discussion

In this study, we compared EA with SEA so as to provide further clinical evidence for the effectiveness of EA in the treatment of shoulder subluxation as well as hemiplegic shoulder pain following stroke. Findings from the VAS indicated that, combining with conventional drug and rehabilitation therapy, the EA treatment could reduce more shoulder pain than SEA treatment. Specifically, the EA group showed statistically significant improvement in shoulder pain as compared with the SEA group. However, there were no significant between-group differences in changes of measures of shoulder subluxation via musculoskeletal ultrasound examination.

This study found that after two weeks of treatment, the analgesic effect of the EA group was significantly better than that of the SEA group, indicating that EA can effectively relieve shoulder pain. However, it is unclear whether this treatment produces long-term analgesic effects. Electroacupuncture is widely used in the clinical treatment of pain. As a form of acupuncture, EA's analgesic effects have been widely established in various conditions such as inflammatory pain, postoperative pain, and pathological neuralgia [33–35]. Many studies have proved that EA has analgesic effect, but the analgesic mechanism of EA is not completely clear. Studies have shown that EA may promote local blood circulation, accelerate the absorption of local inflammatory substances, nourish nerves, repair damaged tissues, stimulate the brain to release endogenous morphine substances, and improve the pain threshold [36]. Wang et al. [37] used traditional acupuncture in the treatment of poststroke shoulder pain and found that traditional acupuncture may treat poststroke shoulder pain by promoting the release of endorphins, nourishing muscle fiber repair, and breaking the pain-immobilization-pain cycle. A study by Li et al. [38] used EA combined with massage to treat poststroke shoulder pain. Their results suggested that EA combined with massage may reduce abnormal shoulder movement patterns, promote local blood circulation, reduce local tissue adhesion, and have analgesic effects. Multiple studies have also shown that EA may have a significant analgesic effect in the treatment of shoulder subluxation and hemiplegic shoulder pain after stroke [39–41]. Proposed mechanisms include improvements in shoulder joint adhesions, muscle strength improvements, and relief in the pull on the shoulder capsule (and thus shoulder pain) [39–41]. Some researchers discussed the possible mechanisms of acupuncture analgesia from three aspects (nerve, body fluid and enzyme) and found the pain is mainly due to the nerve mediation [10, 42]. These papers mainly verify the analgesic mechanisms of electroacupuncture from the aspect of the neuromuscular system.

Although previous studies showed that EA treatment may minimize shoulder joint subluxation [39, 40], there is no concrete evidence to support this assertion. In this study, musculoskeletal ultrasound was used to evaluate the effect of EA treatment on shoulder subluxation in stroke patients with hemiplegic shoulder pain. The findings show that there is no significant difference in reducing the distance of shoulder joint subluxation between EA and SEA groups. It indicates the decrease of pain intensity can be due to different modulating mechanisms and lead to increased function without a need of structural changes, as this has widely been demonstrated in many other areas of research [42, 43]. The EA can sustain local muscle relaxation and contraction. In this study, the EA point of the shoulder was just around the deltoid and the supraspinatus muscle. This was chosen to stimulate the corresponding acupoints and increase muscle strength, as well as potentially strengthen the traction and contraction of the deltoid and supraspinatus muscles on the humeral head. Watson [44] also demonstrated that electrical stimulation may accelerate the

Table 2: Scores of VAS before and after treatment.

Observation indicator	Group	Pretreatment	Posttreatment
VAS	EA group	5.29 ± 1.26	2.00 ± 0.94*●
	SEA group	5.47 ± 1.30	2.93 ± 1.28*

* indicates a significant improvement compared with before treatment, $p < 0.05$. ● indicates a significant between-group difference after 2 weeks of treatment, $p < 0.05$. Data are expressed as mean ± standard deviation (SD).

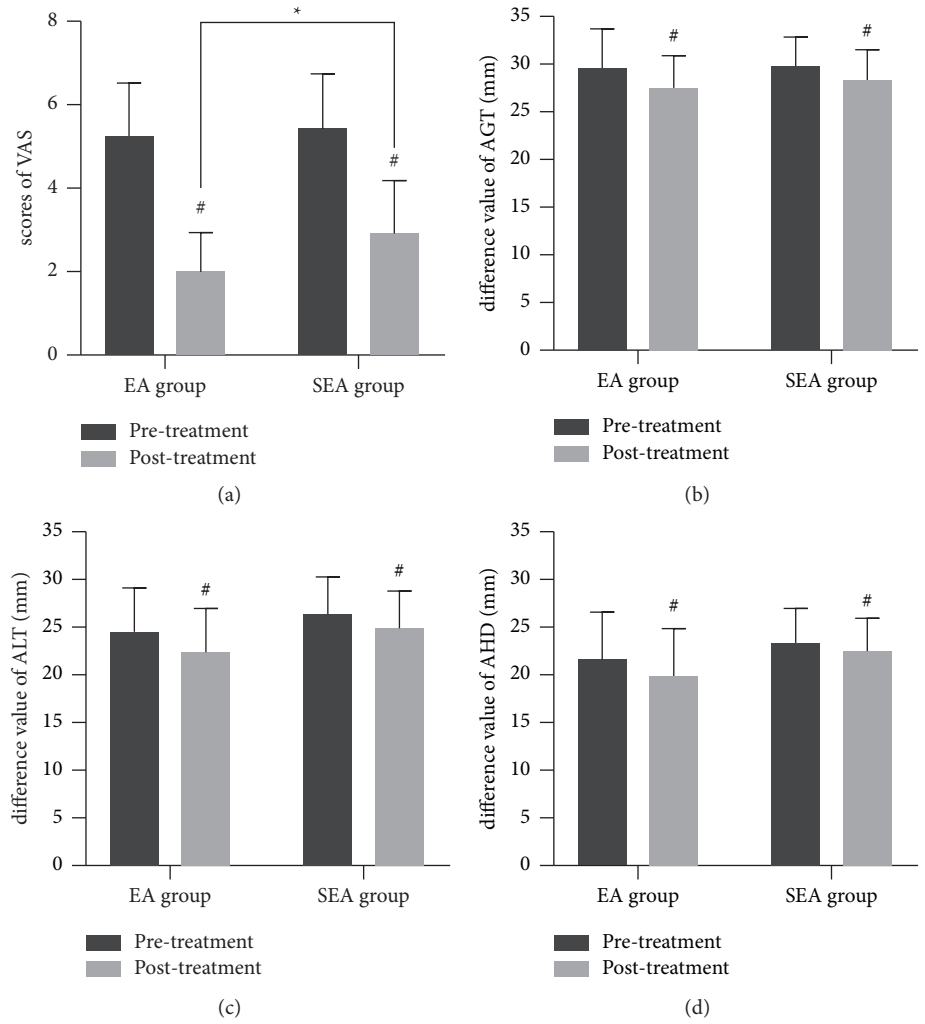

Figure 4: Comparison of VAS scores and measures of shoulder subluxation distances between the two groups before and after treatment. Comparison within groups: $^{\#}p < 0.05$. Comparison between groups: $^{*}p < 0.05$.

recovery of related muscle functions, while Zhou et al. [45] determined that electrical stimulation may improve the upper limb function.

The results of this study showed that there was no correlation between hemiplegic shoulder pain and shoulder subluxation. This finding was also displayed in some previous studies [43, 46]; there was no clear causal relationship between pain and structural changes. Hemiplegic shoulder pain is a complex phenomenon whose pathophysiological mechanism is not fully clear [47]. Shoulder subluxation is considered to be the most significant risk factor for shoulder pain [4]. It is caused by the dislocation of the humeral head from the glenoid, and its clinical manifestation is usually marked by a depression between the acromion and the humeral head [5]. Common causes of shoulder subluxation are reduced strength of the muscles around the shoulder (especially the medial and lateral parts of the deltoid and supraspinatus muscles) [48], the shoulder capsule and surrounding soft tissue being pulled and relaxed under the effect of gravity, uneven tension, and changes in the brachial-lump rhythm, poor limb placement, and improper stretching of the upper limbs [49, 50]. Since pain sensors in the shoulder joint capsule are more susceptible to damage in shoulder subluxation, most patients experience shoulder

Table 3: Measures of shoulder subluxation distances before and after treatment.

Observation indicators	Group	Pretreatment	Posttreatment
AHD (millimeter)	EA group	21.74 ± 4.71	20.00 ± 4.88*
	SEA group	23.36 ± 3.58	22.49 ± 3.46*
AGT (millimeter)	EA group	29.71 ± 4.08	27.69 ± 3.27*
	SEA group	29.98 ± 2.94	28.55 ± 3.12*
ALT (millimeter)	EA group	24.62 ± 4.60	22.62 ± 4.44*
	SEA group	26.52 ± 3.86	25.10 ± 3.96*

* indicates a significant difference as compared with before treatment by using paired t-test, $p < 0.05$. Data are expressed as mean ± standard deviation (SD).

pain [51]. Nonetheless, currently, more and more researchers believe that the occurrence of hemiplegic shoulder pain is multifactor. It can be classified according to three aspects: impaired motor control (altered muscle tone) [51], soft tissue injury (shoulder subluxation [20, 52], biceps longhead tendinopathy [52], supraspinatus tendinopathy [19]), and changes in peripheral and central nervous activity [46, 47]. The relationship between the shoulder subluxation and pain needs a larger sample size study.

This study still has some limitations. Unlike the majority of other studies, ours only included Chinese stroke survivors. Participants' conventional treatment programs could not be completely standardized, but every effort was made to reduce heterogeneity between patients. Use of musculoskeletal ultrasonic evaluation could have reduced the error, including obtaining as many ultrasonic results as possible to take the average value of multiple evaluations. Finally, future studies should use larger sample sizes and contain longer follow-up periods. We plan to address these limitations and further clarify the therapeutic effects of EA on shoulder subluxation and hemiplegic shoulder pain following stroke in future work.

5. Conclusions

Using the VAS for measuring pain intensity and multidimensional musculoskeletal ultrasound imaging technique for measuring shoulder subluxation, this study finds that the hemiplegic shoulder pain can be improved significantly by the EA while the shoulder subluxation cannot be. Our findings further reveal the analgesic mechanism of EA on hemiplegic shoulder pain following stroke.

Data Availability

The data used to support the findings of this study are available from Dr. Minghong Sui (e-mail: meekoo@163.com) upon request.

Disclosure

The funders had no role in the design of this study and did not have any role during its execution, analyses, interpretation of the data, or decision to submit results.

Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of this paper.

Authors' Contributions

Minghong Sui, Yun Xiang, Tiebin Yan, and Guanglin Li designed the study. Luhui Yan, Bin Luo, and Chenxi Zhang conducted the study. Minghong Sui, Naifu Jiang, and Bin Luo carried out the data analysis. Minghong Sui, Luhui Yan, Jiaqing Liu, Chenxi Zhang, and Bin Luo wrote the manuscript. Naifu Jiang, Yun Xiang, Tiebin Yan, and Guanglin Li helped revise the manuscript. Minghong Sui, Naifu Jiang, and Luhui Yan have contributed equally to this work and share first authorship.

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