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Effectiveness and safety of acupuncture for post-stroke spasticity: A systematic review and meta-analysis

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Objective: This systematic review and meta-analysis aimed to comprehensively evaluate the effectiveness and safety of acupuncture for post-stroke spasticity.

Methods: Nine electronic databases were searched from their inception to 6 June 2022, to identify randomized-controlled trials (RCTs) that investigated the effectiveness and safety of acupuncture for post-stroke spasticity. Two reviewers independently screened the studies, extracted the data, assessed the risk of bias. The reporting quality of interventions in controlled trials of acupuncture was evaluated using Revised Standards for Reporting Interventions in Clinical Trials of Acupuncture (STRICTA). The RevMan 5.4 and R 4.2.0 software were used for statistical analysis.

Results: A total of 88 eligible studies were included, involving 6,431 individuals. The pooled data demonstrated that acupuncture combined with conventional rehabilitation (CR) was superior to CR in reducing the Modified Ashworth Scale (MAS) score (standardized mean difference [SMD] = −0.73; 95% CI = −0.83 to −0.63; I^2 = 65%; low certainty of evidence). The favorable results were also observed in comparisons of acupuncture vs. CR (SMD = −0.22, 95% CI = −0.36 to −0.07; I^2 = 49%; moderate certainty of evidence). Subgroup analysis showed that acupuncture treatment with a frequency of once or twice a day was more effective than CR. In addition, the antispasmodic effect of acupuncture treatment increased with more sessions. Four studies explicitly reported slight acupuncture-related adverse events.

Conclusion: Acupuncture could be recommended as adjuvant therapy for spasticity after stroke. However, due to the high risk of bias and heterogeneity of the included studies, the effectiveness of acupuncture for post-stroke spasticity remains to be confirmed.

KEYWORDS

acupuncture, spasticity, stroke, systematic review, meta-analysis

Introduction

Spasticity is one of the most common complications after stroke with a prevalence of 30–80% (1). As a motor dysfunction after the central nervous system lesions, spasticity is characterized by a velocity-dependent increase in tonic stretch reflex with exaggerated tendon jerks (2). Spasticity often results in several clinical symptoms, including joint contractures, deformities, swelling, and pain, which severely limits the motor functions of patients with stroke (3). Moreover, the presence of spasticity may interfere with self-care ability of patients, reduce their quality of life and lead to depressive symptoms (4). More importantly, spasticity brings a heavy financial burden to families and society. According to statistics, approximately 50% family members have to reduce work hours or even stop working to take care of patients with spasticity after stroke (5). The direct cost for patients with spasticity is US$84,195 during the 1st year after stroke, which were four times higher than those without spasticity (6).

Currently, there are quite a few therapeutic strategies (e.g., physiotherapy, oral spasmolytics, injections of botulinum toxin) to treat post-stroke spasticity, while the therapeutic effect of spasticity is unsatisfactory. In terms of physiotherapy, the limited effect and long-term treatment course may lead to poor compliance (7). The effect of oral spasmolytics is not long-lasting, and prolonged use of these drugs might cause multiple side effects, such as hepatotoxicity and muscle weakness (8). Repetitive injections of botulinum toxin may result in the formation of neutralizing antibodies and attenuate the treatment efficacy (9). Therefore, there is a need for an effective and safe therapy for post-stroke spasticity.

Acupuncture, as a pragmatic and safe traditional Chinese medicine (TCM) treatment (10), has been used for the rehabilitation of patients with post-stroke spasticity (11). Several SRs have explored the effectiveness of acupuncture for spasticity in stroke survivors. Notwithstanding, they showed inconsistent results (12–19). With the emergence of new randomized-controlled trials (RCTs) in recent years, we plan to conduct this SR and meta-analysis to update the evidence of the effectiveness and safety of acupuncture for post-stroke spasticity.

Methods

The protocol of this SR has been registered on PROSPERO https://www.crd.york.ac.uk/PROSPERO/display_record.php?RecordID=129779 (registration ID: CRD42019129779) and published in advance (20). We conducted this study strictly in compliance with A Measurement Tool to Assess Systematic Reviews (AMSTAR 2.0) (21) and reported following the Preferred Reporting Items for Systematic reviews and Meta-Analysis 2020 (PRISMA) statement (22). The completed PRISMA checklist is shown in Supplementary File 1.

Literature search

We performed a literature search in the following databases from their inception to 6 June 2022: PubMed, Embase, the Cochrane Library, Web of Science, Epistemonikos Database, Chinese Biomedical Database, Chinese National Knowledge Infrastructure, Chinese Science and Technology Periodical Database, and Wangfang Database. Comprehensive search strategies applied to the above databases were developed by a professional library staff (DLZ), which used logical operators to link subject terms and free words together. The detailed search strategies of all databases are shown in Supplementary File 2. We also searched the Chinese Clinical Trial Registry and ClinicalTrials.gov to identify possible eligible trials. Potential articles were hand-searched from gray literature, reference lists of included studies, and relevant SRs. In addition, we also consulted the experts in this field.

Inclusion criteria

Types of studies

We included RCTs published in English or Chinese that evaluated the effectiveness and safety of acupuncture for post-stroke spasticity. The included studies should specify the randomization method in detail.

Types of participants

Patients with post-stroke spasticity were included. The stroke was diagnosed according to the acknowledged diagnostic criteria and confirmed by magnetic resonance imaging or computed tomography. The spasticity was defined as Brunnstrom stage II–V, the Modified Ashworth Scale (MAS) graded I–IV, or Composite Spasticity Scale (CSS)/Clinical Spasticity Index (CSI) >0 (23). There were no restrictions on age, gender, race, duration of stroke, type of stroke, and position of spasticity.

Types of interventions

The experimental group received acupuncture as a monotherapy or adjunctive therapy. We included manual acupuncture, electroacupuncture, body needling, abdominal acupuncture, scalp acupuncture, and eye acupuncture in accordance with definition of acupuncture [1].

1 Available online at: https://www.news-medical.net/health/What-is-Acupuncture.aspx.

Types of comparisons

Patients in the control group were treated with conventional rehabilitation (CR), sham acupuncture, or Western medicine (WM). CR mainly included general supportive care, kinesiotherapy, occupational therapy, and physical factor therapy. Sham acupuncture was designed using the method of "shallow needling to non-acupoints" (24).

Types of outcome measures

The primary outcome was the MAS score of affected limbs. The secondary outcomes included effective rate (ER) that refer to the reduction of MAS by more than one grade, Fugl–Myer Assessment (FMA), Barthel Index (BI), CSS, CSI, integral electromyography (iEMG), root mean square (RMS), a ratio of maximum H-reflex to maximum M response (H_{max}/M_{max} ratio), co-contraction rate (CCR), and acupuncture related adverse events.

Exclusion criteria

Studies were excluded if (1) they were quasi-RCT, crossover RCT, and cluster RCT; (2) patients had no clear diagnostic criteria or suffered from spasticity due to other reasons, such as traumatic brain injury, tumor, or poisoning; (3) studies explored the effect of different types of acupuncture; (4) other types of acupuncture (e.g., warm-needle moxibustion, acupoint injection, floating acupuncture, cutaneous needle, dry needling, and plum-blossom needle) were used as treatment for spasticity; (5) acupuncture combined with other TCM therapy (e.g., Chinese herb, massage, moxibustion, scraping, cupping, and bloodletting) to alleviate spasticity; and (6) data were unavailable by extensive searching.

Study selection

The retrieved records were imported into Endnote (X9). After removing duplicates, two researchers (WJT and JS) independently reviewed the titles and abstracts to eliminate irrelevant records, and then read the rest records in full text to identify eligible studies. Disagreements were settled through team discussion or consultation with the third reviewer (JL).

Data extraction

Two reviewers (CX and YXL) independently extracted data from the included studies using a predesigned extraction form. The following information was extracted: (1) the general characteristics of included studies, (2) demographic data of patients at study level, (3) characteristics of interventions and comparators, and (4) outcome measures. After extraction, two reviewers crosschecked to ensure accuracy. For multiarm RCTs, we extracted the eligible comparisons or extracted the comparison with inferior effect size. When the study reported indicators of spasticity more than one position, the recommended formula was used to merge the mean and standard deviation of multiple positions (25, 26). During this process, any ambiguities were resolved by the third author (RJJ).

Evaluation of reporting quality of interventions in controlled trials of acupuncture

We used Revised Standards for Reporting Interventions in Clinical Trials of Acupuncture (STRICTA) to appraise the reporting quality of interventions in controlled trials of acupuncture (27). The STRICTA consists of six items, including acupuncture rationale, details of needling, treatment regimen, co-interventions, practitioner background, and control or comparator interventions. Each study was assessed by two independent reviewers (CZJ and YYZ) using STRICTA. Discrepancies were resolved by the third reviewer (YF).

Assessment of risk of bias

The risk of bias was evaluated using the revised Cochrane risk-of-bias tool for randomized trials (ROB 2.0) (28). This tool contains five domains, namely, randomization process, deviations from intended interventions, missing outcome data, measurement of the outcome, and selection of the reported result. Each domain was judged as "low risk of bias," "some concerns," or "high risk of bias." Two trained reviewers (CZJ and YYZ) pre-assessed the five included studies with ROB 2.0. Then, the intraclass correlation coefficient (ICC) statistic was calculated to evaluate the inter-rater agreement. If consistency reached at least 80%, formal evaluations were performed. Any disagreements were arbitrated by discussion or consensus with a third reviewer (YF).

Statistical analysis

The ICC was calculated using Statistical Package for Social Sciences 25.0 to test consistency between reviewers. According to the ICC, the consistency was defined as poor 0.0–0.2, fair 0.21–0.4, moderate 0.41–0.6, good 0.61–0.8, and very good 0.81–1.00 (29). The Review Manager software (RevMan, version 5.4) and R software (version 4.2.0) were used for data synthesis. Mean difference (MD) or standardized mean difference (SMD) with 95% confidence intervals (CIs) was measured for continuous variables, and relative risk (RR) with 95% CI was calculated for dichotomous data. We defined p

< 0.05 as a statistically significant difference. If MAS was presented as rank variable, we transformed it into continuous data. Chi-square test and I^2 statistic were conducted to assess the heterogeneity among studies. When $I^2 \leq 50\%$, $p > 0.1$, we used fixed-effect model to pool data; otherwise, the random-effect model was used.

Subgroup analysis

We conducted subgroup analysis based on the following factors: (1) position of spasticity (upper limbs, lower limbs); (2) frequency of treatment (once a day, twice a day, once every other day); (3) total sessions of treatment (10–30, 30–60, >60 sessions); (4) needle stimulation (manual acupuncture, electroacupuncture); and (5) follow-up time (1 month after treatment, 3 months after treatment).

Sensitivity analysis

Sensitivity analysis was carried out to verify the robustness of the result by removing study one by one. Furthermore, we pooled data from the studies with unclear blinding of outcome assessors and explicit blinding of outcome assessors separately. We also explored the impact of risk of bias on the pooled estimate.

Publication bias

If the number of included trials over 10, funnel plots and *Egger*'s test were applied to detect publication bias.

Grading of recommendations assessment, development, and evaluation

We assessed the certainty of evidence by using the Grades of Recommendation, Assessment, Development, and Evaluation (GRADE) approach (30) and summarized the evidence profile using the GRADE profiler (version 3.6) software. Each outcome was evaluated from five considerations: limitations, inconsistency, indirectness, imprecision, and publication bias. Then, the certainty of evidence was rated in four grades, namely, high quality, moderate quality, low quality, or very low quality.

Results

Search results

A total of 25,096 records were identified, of which 7,523 duplicates were removed. By screening titles and abstracts, 17,076 irrelevant articles were eliminated. Among the remaining 497 articles, 88 studies (31–118) fulfilled the eligible criteria and were eventually included. The reasons for excluding the studies are listed in Supplementary File 3 (Supplementary Table S1). A detailed screening process is presented in Figure 1.

Studies characteristics

The characteristics of the included studies are presented in Supplementary File 3 (Supplementary Table S2). A total of 88 studies involving 6,431 patients were identified (3,347 in the intervention group and 3,084 in the control group). The average age of the patients ranged from 50 to 78. A total of 38 studies (31, 47, 48, 52, 55, 56, 59, 60, 62, 63, 66, 67, 69, 71–76, 79, 80, 82, 83, 88–90, 92–94, 99–101, 104, 107, 110, 112–114) included patients who suffered from stroke for the first time. The duration of stroke ranged from 2 weeks to 1 year. In addition, 19 studies (35, 40, 41, 44, 45, 47, 51, 52, 61, 65, 67, 68, 70, 77, 85, 100, 108, 109, 116) recruited patients with cerebral ischemia and 1 study (84) focused on cerebral hemorrhage; the rest studies included patients with ischemic stroke and hemorrhagic stroke. A total of 41 studies (33, 36, 38, 39, 41–43, 45, 49, 53–57, 59, 61, 65–67, 70–73, 78, 80, 82, 87, 88, 90, 96, 97, 100–102, 104–106, 108, 110, 116) observed spasticity of upper limbs, 25 studies (31, 32, 44, 47, 51, 62–64, 68, 77, 79, 81, 83, 84, 86, 89, 91, 93, 94, 98, 99, 107, 111–113) focused on lower limbs, and 22 studies (34, 35, 37, 40, 46, 48, 50, 52, 58, 60, 69, 74–76, 85, 95, 103, 109, 114, 115, 117, 118) reported both upper and lower limbs. The included studies involved the comparisons of acupuncture plus CR vs. CR, acupuncture vs. CR, acupuncture vs. WM and verum acupuncture vs. sham acupuncture.

Acupuncture protocols in included trials

A total of 61 studies (33, 35, 38, 39, 41–43, 45–48, 50, 52, 55–60, 63, 64, 66–73, 75, 78, 79, 81–90, 92, 94–96, 99, 100, 102, 103, 105–110, 112, 114–117) used manual acupuncture, and 27 studies (31, 32, 34, 36, 37, 40, 44, 49, 51, 53, 54, 61, 62, 65, 74, 76, 77, 80, 91, 93, 97, 98, 101, 104, 111, 113, 118) used electroacupuncture. All included studies described the choice of acupoints. As shown in Figure 2, the most frequent acupoints on upper limbs were *Hegu* (LI 4), *Jianyu* (LI 15), *Quchi* (LI 11), *Waiguan* (SJ 5), and *Shousanli* (LI 10). And *Zusanli* (ST 36), *Yanglinquan* (GB 34), *Sanyinjiao* (SP 6), *Taichong* (LR 3), and *Xuehai* (SP 10) in the lower limbs (see Figure 3). The retention time for the body acupuncture varied from 15 to 40 min. As for scalp acupuncture, the parietal median line (MS 5), parietal anterior temporal oblique line (MS 6), and parietal posterior temporal oblique line (MS 7) were commonly used. The retention time for scalp acupuncture ranged from 15 min to 6 h. Treatment frequency was once a day (31–37, 39–41, 44,

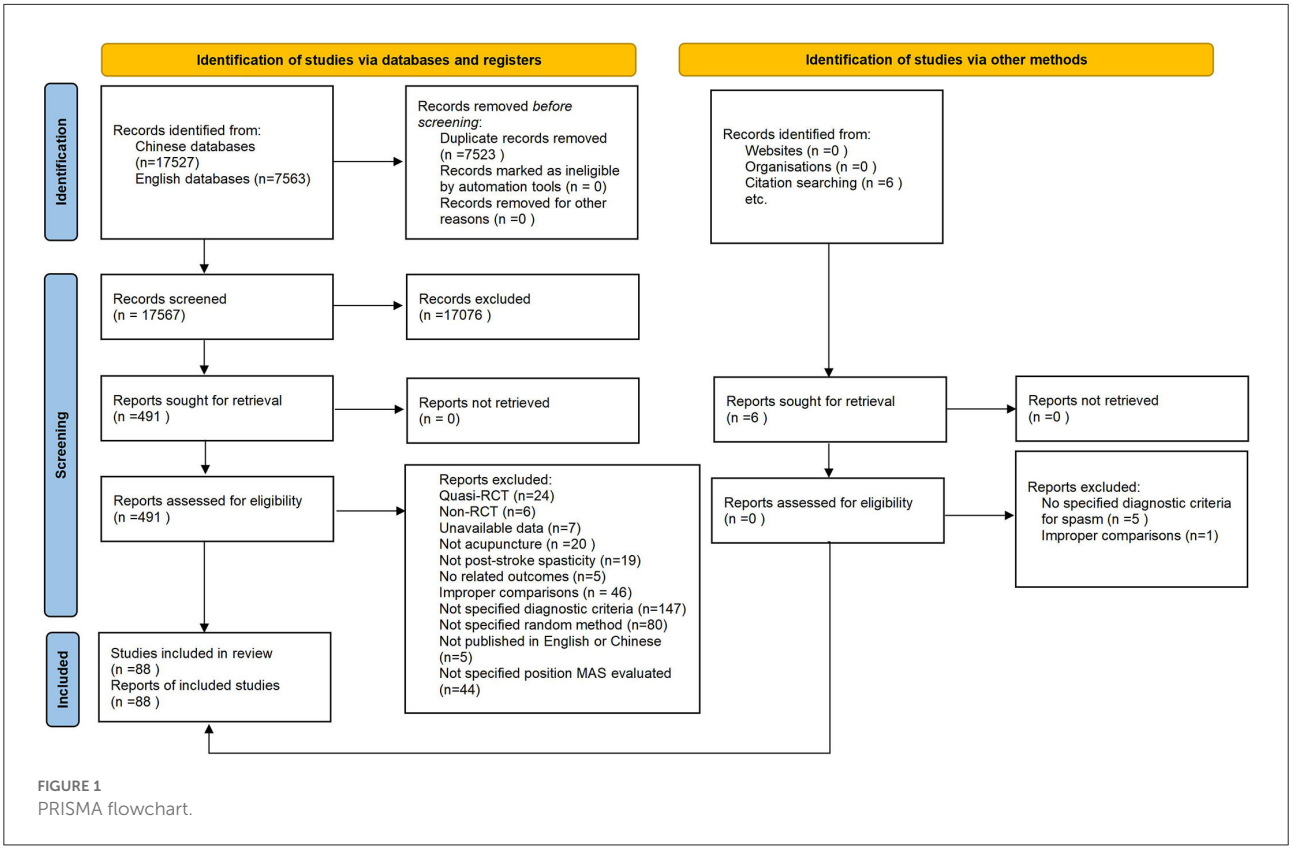

FIGURE 1
PRISMA flowchart.

45, 47–60, 63–67, 69–81, 83–110, 112–114, 116–118) twice a day (42, 43, 61, 62, 82, 111), and once every other day (38, 68, 115). Treatment period ranged from 2 weeks (52, 109) to 6 months (68, 70). The treatment positions were mostly located on affected limbs. Only one study (54) selected acupoints on the unaffected limb (opposing acupuncture). A total of 13 studies (31, 44, 50, 55, 73, 75, 81, 85, 87, 95, 109, 111, 115) used individualized acupoint protocol according to syndrome differentiation. The remaining studies applied fixed acupoint protocol. A total of 54 studies (31, 32, 34, 35, 37, 38, 40–45, 48, 49, 52, 54, 58, 59, 61–63, 66, 67, 71, 75, 78–80, 83–86, 88, 90, 92–98, 101–103, 105–109, 111, 113–116) emphasized *De qi*, which was a unique needling sensation and was essential for clinical efficacy (119).

STRICTA checklist for the included studies

The STRICTA checklist is shown in Supplementary File 3 (Supplementary Table S3). Almost all studies reported the style of acupuncture, needle stimulation, acupoint selection, needle retention time, frequency, and total sessions of treatment. More than half of the studies described unilateral or bilateral of acupoints, depth of insertion, *De qi*, and thickness of acupuncture. A total of 23 studies (41, 49, 53–55, 59, 60, 66–71, 75, 79, 83, 86, 87, 89, 92, 94, 95, 100) specified the rationale of acupoint protocol and 12 studies (36, 41, 53, 55, 60, 62, 69, 71, 74, 76, 79, 87) mentioned the number of needle insertions. Except for eight studies (45, 50, 55, 58, 106, 108, 114, 116), the remaining studies described the control in detail, but none of the studies elucidated the rationale of control group. A total of 80 studies (31–44, 46–49, 51–54, 56, 57, 59–105, 107, 109–113, 115, 117, 118) reported details of co-interventions. All included studies did not specify the setting and context of treatment. Among the included studies, merely eight studies (49, 54, 68, 70, 84, 102, 113, 118) provided information about the certification of acupuncturists.

Risk of bias assessment

The ICC value between the two reviewers for ROB 2.0 assessment was 0.917, which indicates very good agreement. The summary of risk of bias is presented in Figure 4, and the graph of risk of bias is provided in Supplementary File 3 (Supplementary Figure S1). Due to no blinding of outcome assessors, deviations from intended interventions, and missing outcome data, the overall risk of bias of 66 studies (31, 34, 35, 37, 39–46, 48–53, 55, 57–59, 61–65, 67–70, 73–79, 81, 83, 85, 86,

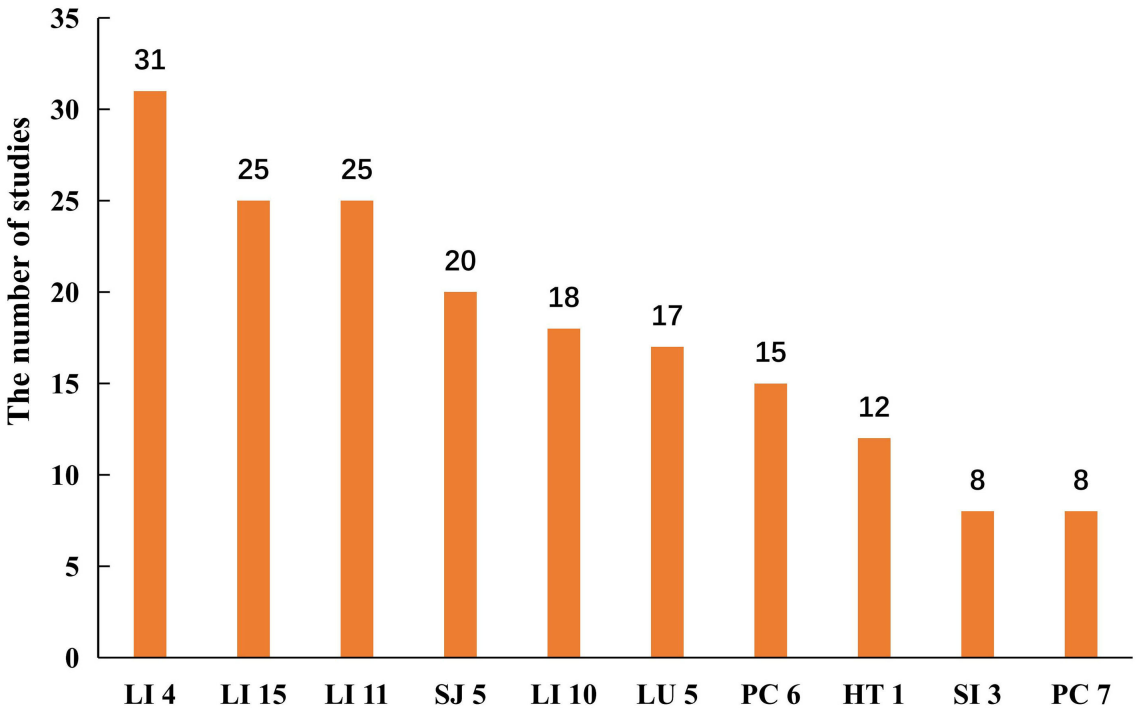

FIGURE 2
Acupoints selection on upper limbs.

89, 91–94, 96, 97, 99, 101–103, 105–112, 114–118) was evaluated as "high risk of bias," and because of selective reporting results (no protocol), 22 studies (32, 33, 36, 38, 47, 54, 56, 60, 66, 71, 72, 80, 82, 84, 87, 88, 90, 95, 98, 100, 104, 113) were categorized as "some concerns."

Primary outcome

Acupuncture plus CR vs. CR

A total of 70 trials (35–37, 40, 42–51, 53–60, 62, 63, 65, 67–71, 73–77, 79–89, 91, 93–100, 102–106, 108–112, 114–118) with 4,921 participants used the MAS score to evaluate the therapeutic effect of acupuncture for post-stroke spasticity. The results of meta-analysis revealed that acupuncture plus CR was superior to the CR in decreasing MAS score (SMD = −0.73; 95% CI = −0.83 to −0.63; $p < 0.00001$; $I^2 = 65\%$) (Figure 5). The funnel plot and *Egger*'s test ($p = 0.005$) indicated that potential publication bias might exist (Figure 6).

Acupuncture vs. CR

A total of 10 trials (33, 35, 41, 48, 56, 57, 73, 78, 96, 112) with 728 participants compared the effects of acupuncture with CR. The pooled data showed that acupuncture had a better effect than CR in ameliorating spasticity in patients with stroke (SMD = −0.22, 95% CI = −0.36 to −0.07; $p = 0.004$; $I^2 = 49\%$) (Figure 7). Funnel plot and *Egger*'s test ($p = 0.486$) showed no obvious publication bias (Figure 8).

Descriptive Analysis

Two trials (88, 90) reported that acupuncture was more effective than sham acupuncture in relieving spasticity. There was (92, 101) no significant difference between acupuncture and WM in reducing MAS score.

Subgroup analysis

The results of subgroup analysis (acupuncture plus CR vs. CR) are summarized in Table 1. With regard to sessions of acupuncture treatment, we found that acupuncture treatments of 10–30 sessions (SMD = −0.65, 95% CI −0.76 to −0.55), 30–60 sessions (SMD = −0.79, 95% CI −1.06 to −0.52), and >60 sessions (SMD = −0.97, 95% CI −1.25 to −0.69) were superior to CR in improving post-stroke spasticity. As for acupuncture frequency, acupuncture combined with CR with once a day (SMD = −0.75, 95% CI −0.86 to −0.64) or twice a day (SMD = −0.55, 95% CI −0.85 to −0.25) reduced more MAS score than CR. However, once every other day showed no significant difference in reducing MAS score compared

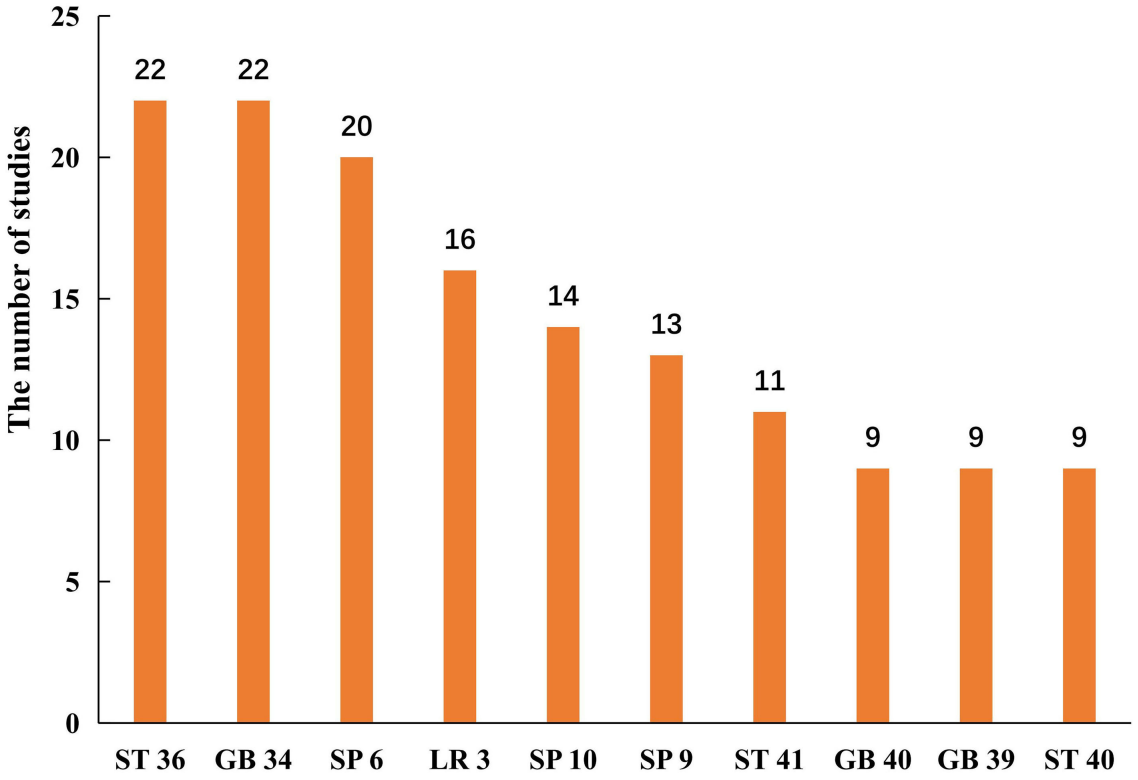

FIGURE 3
Acupoints selection on lower limbs.

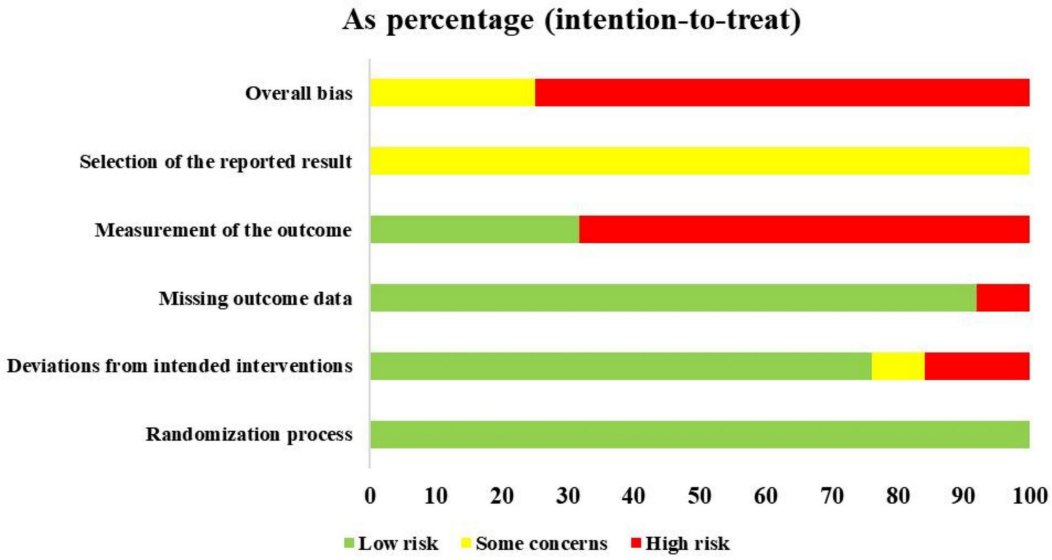

FIGURE 4
Risk of bias summary.

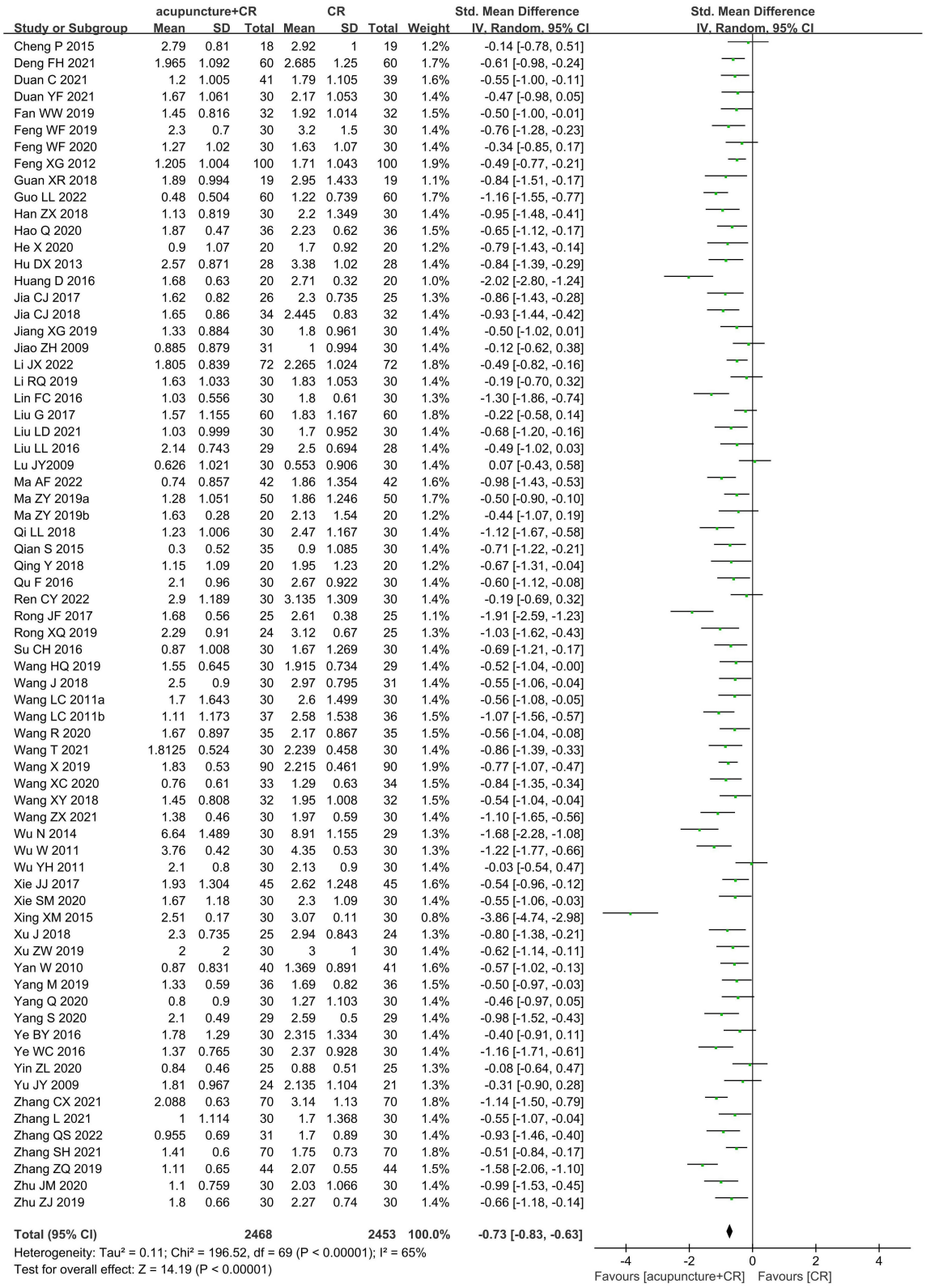

FIGURE 5
The forest plot of MAS score in comparison of acupuncture plus CR vs. CR.

with the CR (SMD = −0.56, 95% CI −1.31 to 0.18). Manual acupuncture (SMD = −0.74, 95% CI −0.84 to −0.64) and electroacupuncture (SMD = −0.71, 95% CI −0.96 to −0.46) combined with CR decreased greater MAS score than CR. For different positions of spasticity, acupuncture plus CR was better than CR in improving spasticity of both upper limbs (SMD = −0.74, 95% CI −0.87 to −0.61]) and lower limbs (SMD = −0.76, 95% CI −0.94 to −0.58). One study (54) reported that acupuncture treatment had long-term effect (3 months) in ameliorating spasticity.

Sensitivity analysis

As for primary outcome in the comparison of acupuncture plus CR vs. CR, we used three methods to verify the robustness of the result. By excluding studies one by one, we found that the pooled effect size of MAS score was stable (Figure 9). By synthesizing the data from studies with unclear and explicit blinding of outcome evaluators respectively, the results demonstrated that acupuncture plus CR was superior to CR in relieving post-stroke spasticity (Figure 10). Moreover, the result was stable *via* merging studies with "some concerns" and "high risk of bias" separately (Figure 11).

Regarding the MAS score in the comparison of acupuncture vs. CR, as shown in Figure 12, the result altered when excluding Wu NA 2014 (48). As shown in Figure 13, we pooled data from studies with blinding of outcome assessors and the result changed.

Secondary outcomes

The pooled data of secondary outcomes are shown in Table 2. Meta-analysis showed that patients receiving acupuncture plus CR achieved better improvements on FMA and BI than those receiving CR alone. In addition, relevant

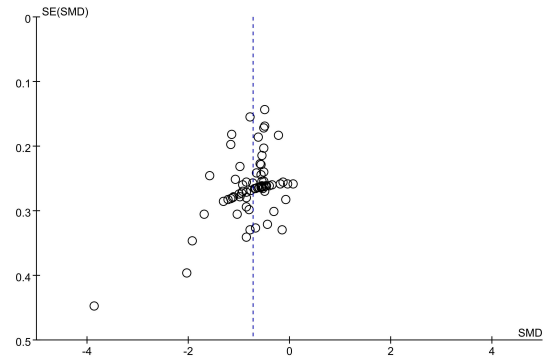

FIGURE 6
The funnel plot of MAS score in comparison of acupuncture plus CR vs. CR.

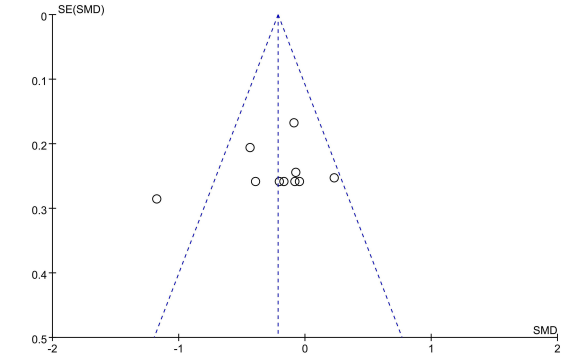

FIGURE 8
The funnel plot of MAS score in comparison of acupuncture vs. CR.

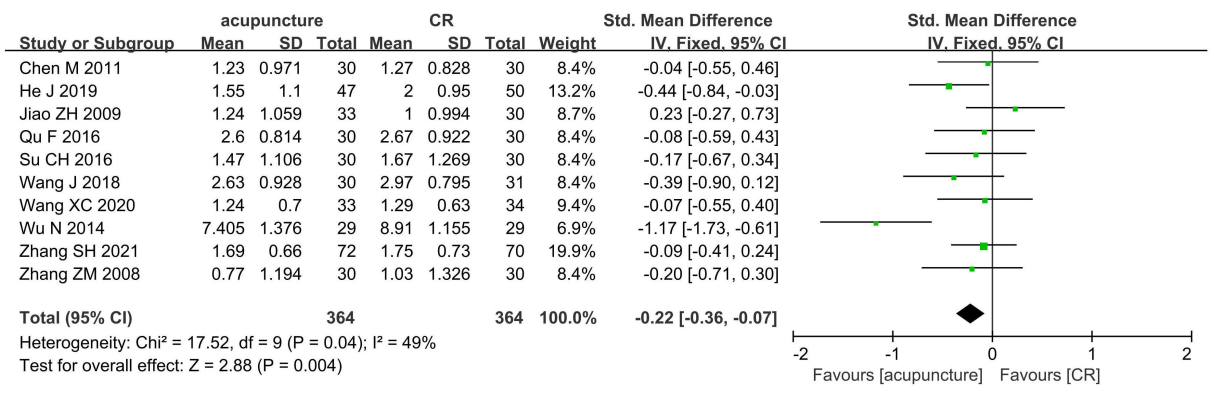

FIGURE 7
The forest plot of MAS score in comparison of acupuncture vs. CR.

TABLE 1 Subgroup analyses of MAS score.

Subgroups	No. of studies	MAS Effect size (95% Cl)	*P*-value	I^2
Positions of spasticity				
Upper limbs	50	−0.74[−0.87, −0.61]	<0.00001	72%
Lower limbs	39	−0.76[−0.94, −0.58]	<0.00001	81%
Frequency of treatment				
Once a day	62	−0.75[−0.86, −0.64]	<0.00001	66%
Twice a day	5	−0.55[−0.85, −0.25]	<0.001	46%
Once every other day	2	−0.56[−1.31, 0.18]	0.14	76%
Total sessions of treatment, session				
10–30	42	−0.65[−0.76, −0.55]	<0.00001	44%
30–60	17	−0.79[−1.06, −0.52]	<0.00001	82%
≥60	10	−0.97[−1.25, −0.69]	<0.00001	66%
Needle stimulation				
Manual acupuncture	49	−0.74[−0.84, −0.64]	<0.00001	50%
Electroacupuncture	21	−0.71[−0.96, −0.46]	<0.00001	79%
Follow-up time				
Immediately	70	−0.73[−0.83, −0.63]	<0.00001	65%
1 month after-treatment	2	−1.28[−1.98, −0.57]	<0.001	79%
3 months after-treatment	1	−1.17[−1.72, −0.62]	<0.00001	/

MAS, Modified Ashworth Scale; 95% CI: 95% confidence interval.

indicators of surface electromyogram such as CCR and H_{max}/M_{max} indicated that acupuncture plus CR was effective in relieving the post-stroke spasticity in patients. We also found that acupuncture was better than CR in improving BI and the upper limbs of FMA and ER.

Adverse events

A total of 12 studies (33, 48, 60, 69, 75, 87, 88, 92, 94, 95, 106, 117) reported no treatment-related adverse events occurred, whereas, four studies (52, 54, 78, 118) explicitly reported adverse events, such as punctate hemorrhage (118), subcutaneous hematoma (52), subcutaneous ecchymosis (54), and needle syncope (52, 78).

Certainty of evidence

The ER of upper limbs and MAS score in comparison of acupuncture vs. CR was rated as "moderate" certainty of evidence, while the rest outcomes were considered as "low" or "very low". The certainty of evidence was downgraded primarily because of the high risk of bias of the included studies and inconsistency of results. A summary of findings table from the GRADE profiler is provided in Supplementary File 3 (Supplementary Figures S2, S3).

Discussion

This SR and meta-analysis showed that acupuncture as an adjuvant therapy could effectively reduce MAS score, CCR, and H_{max}/M_{max}, and improve FMA and BI. Subgroup analysis demonstrated that once or twice a day acupuncture treatment and a greater total sessions of acupuncture treatment might be associated with better antispasmodic effects. Notably, 66 studies were evaluated as "high risk of bias," 22 studies were categorized as "some concerns," and publication bias might exist. Therefore, the above results should be treated with caution.

Our result showed that acupuncture exerted a better effect than CR in relieving post-stroke spasticity, which was consistent with the previous findings (13, 15, 16). As is known, the minimum clinically important difference (MCID) refers to the smallest change in the outcome measurements, which is considered to be clinically meaningful for patients (120). Chen et al. (120) reported the MCID of MAS with moderate clinical significance and high clinical significance were 0.48 and 0.76, respectively. The effect size of MAS (acupuncture plus CR vs. CR) in our study was 0.73, which indicated that acupuncture combined with CR had a moderate clinical effect to attenuate post-stroke spasticity.

The results of subgroup analysis demonstrated that acupuncture treatment one or two times a day was better than CR in alleviating spasticity after stroke, whereas acupuncture treatment once every other day showed no significant difference.

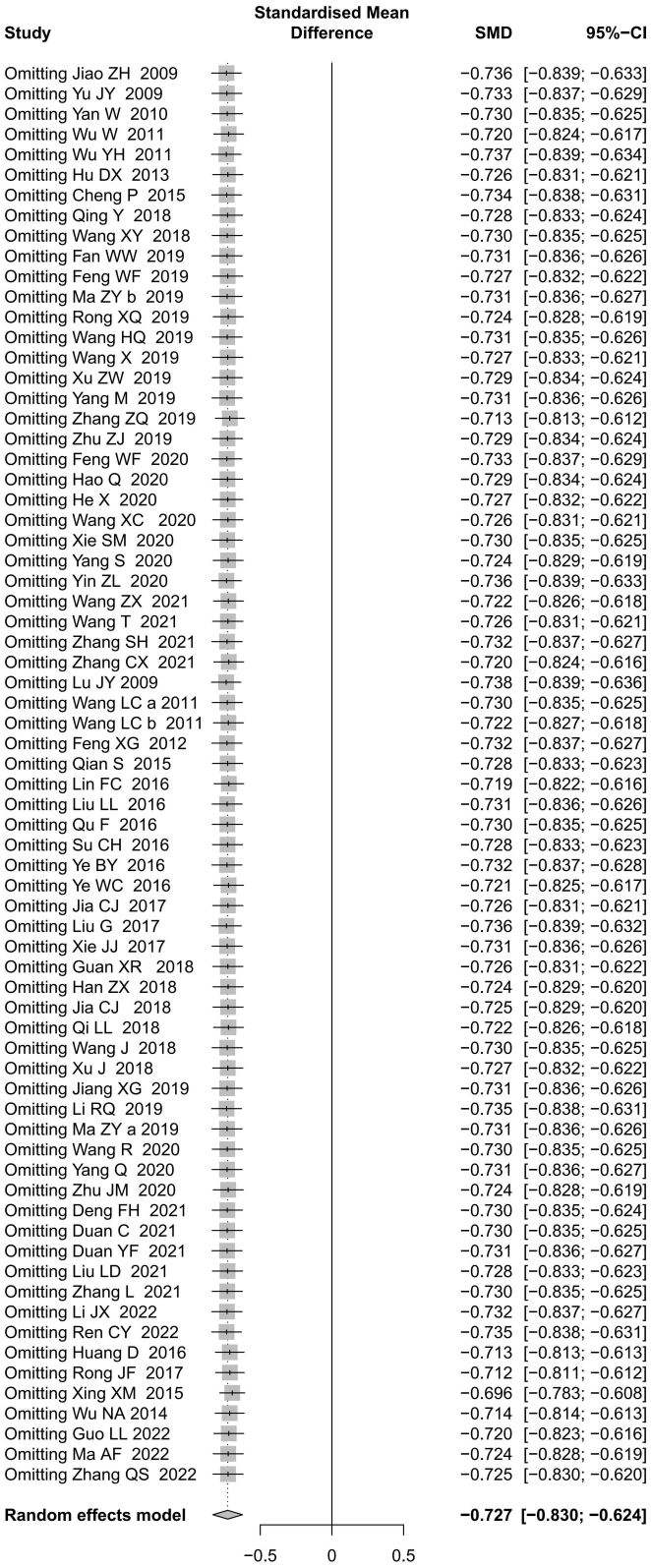

FIGURE 9
Sensitivity analysis by excluding studies one by one for MAS score (acupuncture plus CR vs. CR).

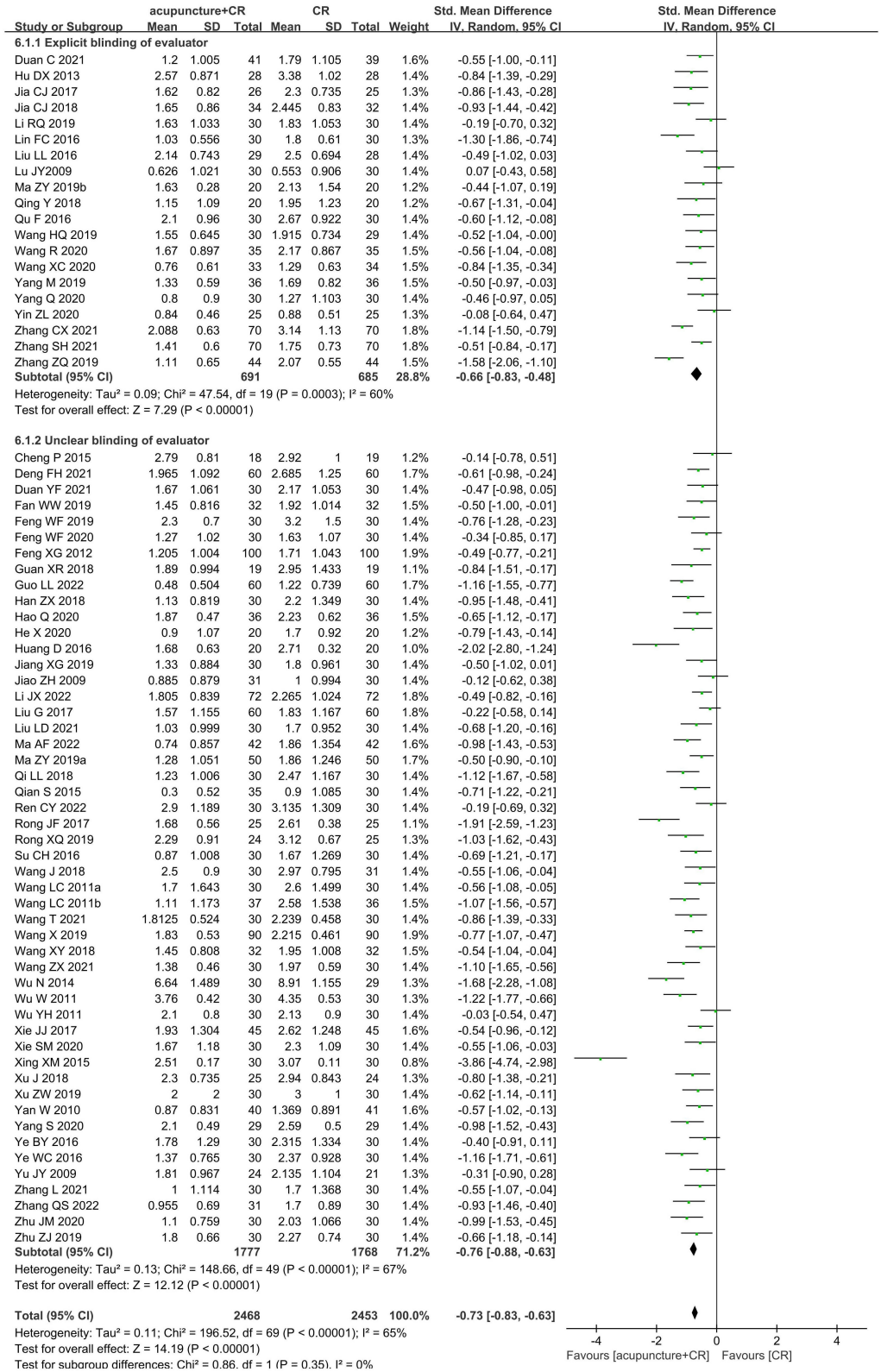

FIGURE 10
Sensitivity analysis based on blinding of outcome assessor (acupuncture plus CR vs. CR).

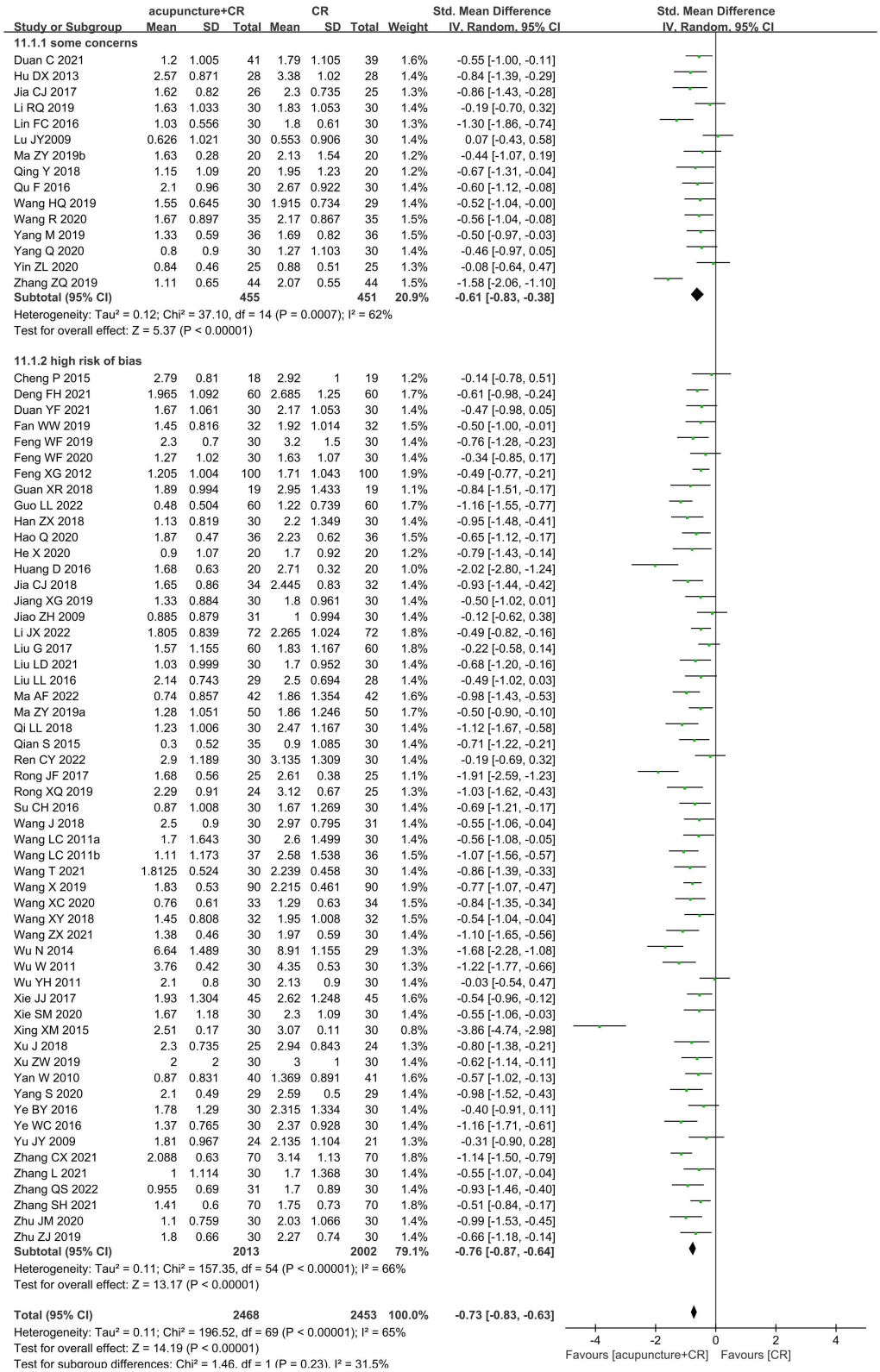

FIGURE 11
Sensitivity analysis by separately merging "high risk of bias" and "some concerns" studies (acupuncture plus CR vs. CR).

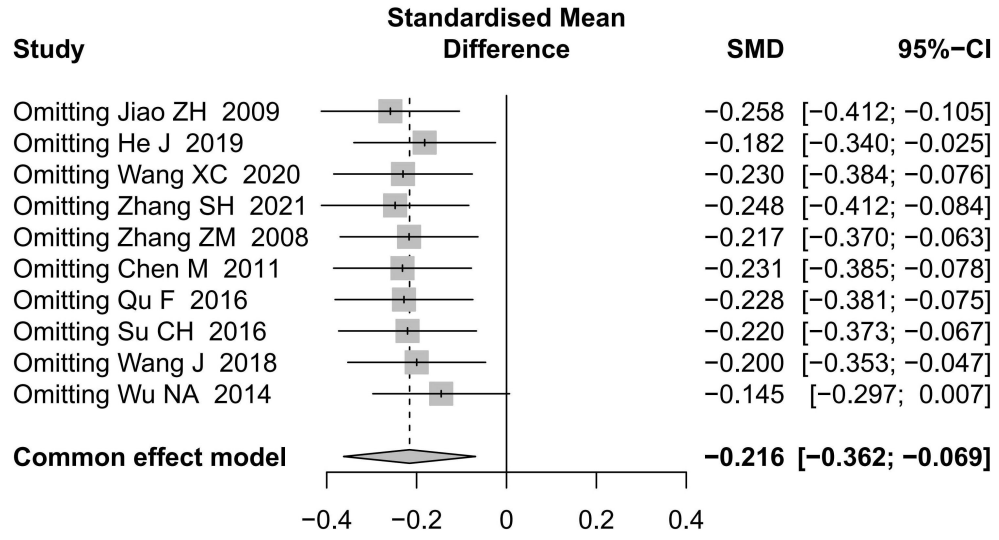

FIGURE 12
Sensitivity analysis by excluding studies one by one for MAS score (acupuncture vs. CR).

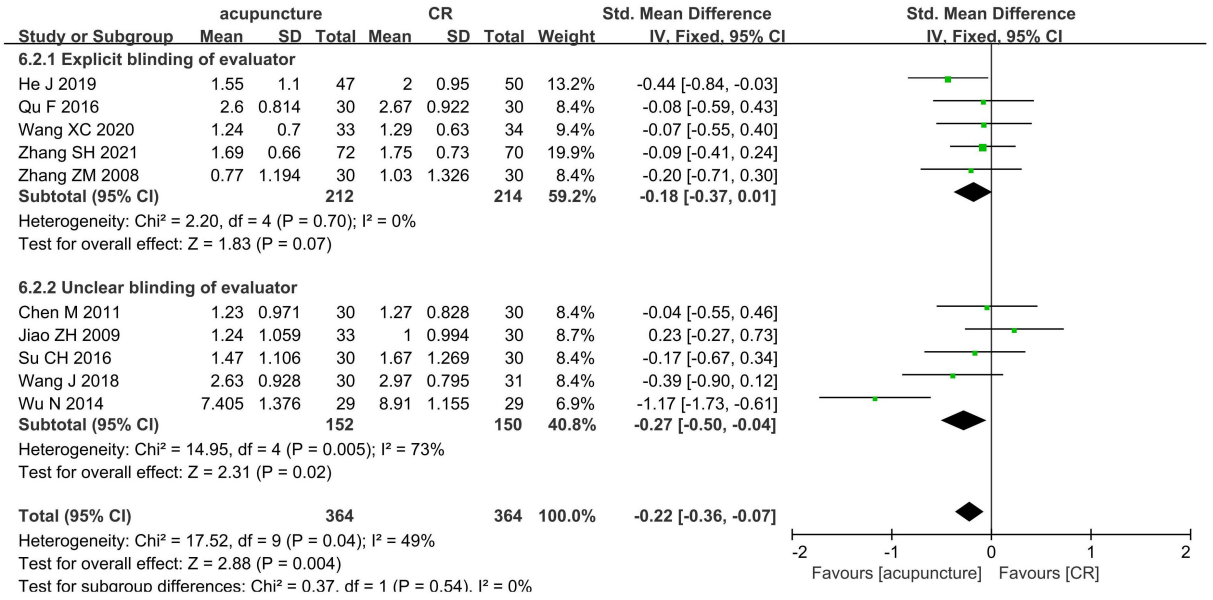

FIGURE 13
Sensitivity analysis based on blinding of outcome assessor (acupuncture vs. CR).

The possible explanation was that, as the prolongation of treatment interval, the effector substance gradually attenuated and the therapeutic effect was unsustainable (121). Besides, our result suggested that more sessions of acupuncture treatment might yield greater effect to relieve spasticity. This result might be attributed to the cumulative effect of acupuncture. Notwithstanding, considering apparent heterogeneity and high risk of bias, rigorous clinical trials are required to explore the optimal protocol of acupuncture treatment for spasticity in the future.

As the spasticity worsens, movement function and daily activities of patients would be unavoidably affected. Our results showed that acupuncture plus CR enhanced motor function and activities of daily living in patients with spasticity following stroke. The MCID of FMA of upper limbs and lower limbs were 4.48 and 3.31, separately, the MCID of

TABLE 2 Meta-analysis of secondary outcomes.

Outcomes	No. of studies	Effect size (95% CI)	*P*-value	I^2
Acupuncture plus CR vs. CR				
ER-U	18	RR 1.31[1.15, 1.50]	<0.0001	78%
ER-L	10	RR 1.15[1.01, 1.32]	<0.05	67%
FMA-U	36	MD 5.56[4.42, 6.71]	<0.00001	89%
FMA-L	23	MD 3.68[2.72, 4.65]	<0.00001	86%
BI	50	MD 8.61[6.76, 10.45]	<0.00001	90%
iEMG	6	SMD 1.49[−0.05, 3.02]	0.06	97%
CCR	3	SMD −2.42[−4.69, −0.15]	<0.05	97%
RMS	5	SMD 0.02[−1.31, 1.35]	0.97	97%
CSS	3	MD −0.15[−1.47, 1.16]	0.82	77%
CSI	10	MD −1.59[−2.17, −1.01]	<0.00001	92%
H_{max}/M_{max}	3	SMD −0.75[−1.01, −0.49]	<0.00001	9%
Acupuncture vs. CR				
ER-U	5	RR 1.08[0.97, 1.21]	0.16	0%
CSI	3	MD −0.97[−2.23, 0.3]	0.13	79%
FMA-U	9	MD 2.87[0.46, 5.28]	<0.05	84%
FMA-L	4	MD 0.14[−0.92, 1.19]	0.8	0%
BI	9	MD 4.27[0.67, 7.88]	<0.05	69%

No. of studies, number of studies; MD, mean difference; SMD, standardized mean difference; RR, relative risk; CR, conventional rehabilitation; 95% CI: 95% confidence interval; ER-U, effective rate of upper limb; ER-L, effective rate of lower limb; FMA-U: Fugl–Myer Assessment of upper limb; FMA-L, Fugl–Myer Assessment of lower limb; BI, Barthel Index; iEMG, integral electromyography; CCR, co-contraction rate; RMS: root mean square; CSS, composite spasticity scale; CSI, clinical spasticity index; H_{max}/M_{max}: ratio of maximum H reflex to maximum M response.

BI was 1.85 (122, 123). The effect size of FMA of upper limbs and lower limbs (acupuncture plus CR vs. CR) were 5.56 and 3.68, respectively, and the effect size of BI was 8.61 in our study, which demonstrated that the effects of acupuncture plus CR in improving FMA and BI were clinically meaningful.

Several problems existed in the RCTs of acupuncture for post-stroke spasticity, for example, no blinding of patients and outcome assessors, without objective outcome measures, lack of follow-up, and absence of detailed acupuncture protocol. Such problems hinder us from comprehensively and objectively evaluating the authentic efficacy of acupuncture for post-stroke spasticity. Hence, sham acupuncture should be set as comparison. Additionally, it is crucial to assess spasticity with objective indicators to obtain objective data. Future studies should also focus on the long-term effect of acupuncture for spasticity after stroke. To improve the reporting quality, researchers should report studies in accordance with the Consolidated Standards of Reporting Trials (124) and STRICTA (27).

This is the latest SR and meta-analysis that comprehensively evaluated the effectiveness and safety of acupuncture for post-stroke spasticity. The protocol of this SR and meta-analysis was registered in advance. This SR and meta-analysis was conducted strictly in accordance with AMSTAR 2.0 and reported complying with PRISMA 2020. However, some limitations should also be acknowledged. First, we used MAS score as the primary outcome measure, which is a subjective assessment scale, unclear blinding of outcome assessors and explicit blinding of outcome assessors separately, measurement bias was inevitable. Second, the published language of included RCTs in this SR and meta-analysis was limited to Chinese or English, hence, language bias might exist. Third, the overall risk of bias of the included studies was evaluated as "high risk of bias" and "some concerns."

Conclusion

Acupuncture could be recommended as adjuvant therapy for spasticity after stroke. However, due to the high risk of bias and heterogeneity of the included studies, the effectiveness of acupuncture for post-stroke spasticity remains to be confirmed.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary material, further inquiries can be directed to the corresponding author/s.

Author contributions

RJ, JL, and YF designed the study. DZ designed the search strategy. WT and JS selected the studies. CXu and YL extracted the data. CJ and YZ assessed the risk of bias and reporting quality. XL, HZ, and CXi analyzed the data. CXu, CJ, and YZ wrote and drafted the manuscript. All authors approved the manuscript.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fneur.2022.942597/full#supplementary-material

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