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Electroacupuncture Add-on Therapy for Improving Post-stroke Motor Dysfunction: A Systematic Review and Meta-analysis

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ABSTRACT

Objectives: To assess the efficacy and safety of electroacupuncture (EA) combined with rehabilitation therapy (RT) and/or conventional drugs (CD) for improving post-stroke motor dysfunction (PSMD) .

Design: Systematic review and meta-analysis.

Methods: The China National Knowledge Infrastructure, Chinese Biological Medicine Database, Chinese Scientific Journal Database, Cochrane Library, Medline, and Embase were electronically searched from inception to December 2016. The methodological quality of the included trials was assessed using the Cochrane risk of bias assessment tool. Statistical analyses were conducted by RevMan Version 5.3.

Results: Nineteen trials with 1,434 participants were included for qualitative synthesis and meta-analysis. The methodological quality of the included trials was generally poor. The meta-analysis indicated that the EA group might be benefitting more than the non-EA group in terms of the changes in the Fugel-Meyer Assessment Scale (FMA) (weighted mean difference [WMD] 10.79, 95% confidence interval [CI] 6.39 to 15.20, P < 0.00001), FMA for upper extremity (WMD 3.43, 95% CI 1.27 to 5.59, P = 0.002), FMA for lower extremity (WMD 5.16, 95% CI 3.78 to 6.54, P < 0.00001), Barthel Index (WMD 12.73, 95% CI 9.78 to 15.69, P < 0.00001), and Berg Balance Scale (WMD 7.00, 95% CI 4.29 to 9.71, P < 0.00001), respectively. There was no difference between the EA and non-EA groups in the effective rate (RR 1.13, 95% CI 1.00 to 1.27, P = 0.05) and the change of Functional Independence Measure (WMD 5.50, 95% CI -1.62 to 12.62, P = 0.13), respectively. There were no side effects due to EA combined with RT and/or CD in the included trials.

Conclusions: This review provides new evidence for the effectiveness of EA combined with RT and/or CD for PSMD. However, its efficacy and safety should be used with caution due to methodological weakness and publication bias. Further rigorously designed trials with multiple centres and large sample sizes are warranted.

Keywords: motor function; post-stroke; electroacupuncture; RCT; systematic review

PROSPERO registration number: CRD42016037597

Strengths and limitations of this study:

- The scientific team and the standard operation may facilitate the high quality of this systematic review in assessing the efficacy and safety of EA combined with RT and/or CD for improving motor function after stroke.
- Currently, EA is more and more widely used in clinical practices because of its repeatability and standardization of frequency, intensity and duration. However, no clear evidence that EA can improve PSMD has been found.
- The main limitations to this review are the methodological defects in the included trials and potential publication bias.

INTRODUCTION

Stroke is one of the world's leading causes of death and disability, [1-2] causing heavy burdens to patients' families, communities and healthcare systems.[3] Motor dysfunction is a frequent and widely recognised complication that often follows strokes. Approximately 85% of stroke patients suffer from hemiparesis immediately after their stroke, and between 55% and 75% of stroke survivors may experience incomplete recovery with lingering motor dysfunction.[4] Post-stroke motor dysfunction (PSMD), which has a negative impact on the independence of functional activities, can reduce quality of life (QoL) and limit activities of daily living (ADL). Therefore, effective treatment of PSMD is needed to promote neurological function recovery and to alleviate the social and familial burdens of stroke.

Motor function recovery after stroke not only requires multi-disciplinary treatment team, but also involves various approaches such as conventional drugs (CD), rehabilitation therapy (RT), and nursing care. RTs play an important role in comprehensive stroke rehabilitation programs aimed at recovering function so as to reduce disabilities. Previous studies have demonstrated that the rehabilitation of neurological deficits due to stroke can benefit from RT.[5] However, the effects of current RT for motor dysfunction caused by stroke are still limited.[6] Over the last decade, an increasing number of researchers have focused on alternative therapies for stroke rehabilitation such as acupuncture.

For more than 3, 000 years, acupuncture has been used in China to treat different diseases including complications following strokes. In recent years, acupuncture, as one of the best known complementary and alternative medicines, has also been increasingly applied in other countries and regions of the world.[7] Electroacupuncture (EA), derived from the integration of traditional acupuncture and modern electrical stimulation, is a new kind of acupuncture. EA is widely accepted because it is a relatively simple, safe and cheap therapy, compared with other conventional therapies.[8] Additionally, EA has become more and more widely used in clinical practice because of its repeatability and standardization of frequency, intensity and duration.[9-10] EA may improve functional recovery after stroke by inhibiting cell apoptosis, regulating miR-9-mediated NF-κB downstream pathway and miR-181b/PirB/RhoA/GAP43 axis, and dynamically maintaining the balance of MMP-9 and TIMP-1.[11-13] However, no clear evidence has been found that EA is more effective in improving PSMD. Therefore, this study was conducted to assess the efficacy and safety of EA combined with RT for PSMD, and to provide the best available evidence for clinical practice. The study was registered on PROSPERO (No. CRD42016037597) as an acupuncture study, and then revised as a literature search and analysis, expected to focus on EA combined with RT and/or CD for PSMD.

METHODS

Types of studies

We included all randomized controlled trials (RCTs) assessing the efficacy and safety of EA combined with RT for PSMD. The comparators or controls in the trials were any other therapy modalities. Also, we only included trails with outcomes measuring changes in motor function. All eligible trials, regardless of publication status, and language were included.

Types of participants

We considered trials that included patients in acute stage following the onset of their first stroke, with motor dysfunction measured by validated instruments or by a decrease in the level of movement activity. Patients were required to be more than 18 years old, and from any ethnicity. Stroke diagnosis had to meet the WHO criteria or the corresponding diagnostic criteria adopted in China, [14-17] and had to be confirmable by computerized tomography (CT) or magnetic resonance imaging (MRI). Trials involving participants with subarachnoid hemorrhages or cerebrovascular tumors, as well as those in which patients were not in acute phases, were excluded.

Types of interventions

Patients in the experimental groups of the included trials had been treated with EA combined with RT and/or CD, at any frequency, intensity or duration. Patients in the control group of the trials had been treated by other therapies such as CD, RT, sham acupuncture, or by no treatments. However, trials which did not provide a detailed description or explanation of intervention, or those that compared different acupoint prescriptions or acupuncture types, were excluded.

Primary outcome assessments

The primary outcome for the system review was motor function. There are many types of motor function scales including but not limited to: the Fugel-Meyer Motor Assessment Scale (FMA);[18] the modified Rankin Scale (mRS);[19] the Motor Assessment Scale (MAS);[20] and Brunnstrom Stages.[21]

Secondary outcome assessments

Secondary outcomes included measures of ADL, such as the Barthel Index (BI),[22] the Functional Independence Measure (FIM),[23] and the response or effective rate (ER). Adverse events reported in included trials were also recorded.

Electronic searches

We electronically searched databases from their respective inceptions to December 2016. The databases included China National Knowledge Infrastructure (CNKI), Chinese Biological Medicine Database (CBM), Chinese Scientific Journal Database (VIP), Cochrane Library, Medline and Embase. We combined the PubMed search with the Cochrane highly sensitive search strategy for identifying randomized trials, and adapted the search strategy for searching the other databases.

We also searched other resources in order to identify potentially relevant trials. For example, we screened reference lists of included trials, and contacted trial authors. The detailed search steps are illustrated in supplementary *appendix 1*.

Data extraction and quality evaluation

Two review authors (J Zhan and M Zhou) independently scanned the titles and abstracts of articles obtained from the search and kept all potentially relevant articles. Then, they retrieved the full texts of these articles, and another two authors (Z Huang and R Pan) independently examined them to confirm that the trials met the inclusion criteria. We also recorded the reasons for exclusion of trials. If the same trail had more than one report, we only kept one originally published version. If necessary, we acquired further information from trial authors by e-mail or telephone. Moreover, we discussed any disagreements to decide whether a trial should be included or excluded, and if necessary, we consulted with another author (Z Wen).

Two authors (J Zhan and M Zhou) independently extracted information from included trials and created a database. The information was entered into an Excel formatted table (J Zhan) and the accuracy of the information entered was also checked (R Pan). The information extracted was as follows: trial design (e.g. sample size,

randomization method, blinding method); participants (e.g. gender, age); the details of intervention; outcomes (primary and secondary outcomes); adverse events; the name of the author, publication year, and so on. The trial selection details are shown in a PRISMA flow chart (*Figure 1*).

Risk of bias assessment in included studies

Two review authors (J Zhan and R Pan) independently used the risk of bias assessment tool in the *Cochrane Handbook for Systematic Reviews of Interventions* [24] to assess the methodological quality of each included trial. The specific domains were evaluated as follows: random sequence generation, concealment of allocation, blinding, incomplete outcome data, selective outcome reporting, and other sources of bias. We graded the risk of bias for each domain as follows: low risk of bias, high risk of bias, or unclear. We settled quality assessment disagreements by discussion with a third reviewer (Z Wen).

Data analysis

We tested clinical and statistical heterogeneity between trials by comparing the characteristics of the trials, and we used the I-squared statistic to test heterogeneity. If heterogeneity was not significant, we chose a fixed effects model to pool the data; otherwise, we used a random effects model after considering clinical homogeneity. When heterogeneity was substantial, we examined trials for potential explanations, or else conducted a qualitative summary rather than a meta-analysis. A meta-regression analysis was used to explain the potential trial-level covariates such as the duration of treatment. For continuous data, we calculated weighted mean difference (WMD) with a corresponding 95% confidence interval (CI). Considering outcomes may have been measured by different scales in different trials, we calculated standardized mean difference (SMD) with 95% CIs instead of WMD. For dichotomous data, we calculated relative risk (RR) with 95% CIs.

Subgroup analyses were performed as follows: 1) EA and CD plus RT compared to CD plus RT; 2) EA plus RT compared to RT alone; and 3) EA plus CD compared to CD alone. Sensitivity analysis was conducted to explore the robustness of our analysis, excluding studies from the overall analysis of high risk of bias due to lack of allocation concealment and blinding of assessors for primary outcome. If the number of included trials was over ten, funnel plots were performed for publication bias. For all statistical analyses, we used RevMan Version 5.3.[25]

RESULTS

Trial description

We initially identified 892 relevant articles according to the search strategy while 219 were excluded due to being duplicates from different databases. In total, nineteen trials met the eligibility criteria after being screened by title, abstract or full-text, and were included for meta-analysis (*Figure 1*). We did not find further trials for this review by examining the reference lists of the included trials. All trials were published between 2004 and 2016. One trial [26] was published in English, while the others were all published in Chinese. A total of 1,434 participants were included in these trials. All trials were performed in China. Sixteen trials [26-41] compared EA plus CD and RT with CD plus RT. Three trials [42-44] gave EA and RT to the experimental groups, while the control groups only received RT. The RCT characteristics included in this review are shown in *Table 1*.

Assessing risk of bias in the included trials

In adequate sequence generation, seven trials [26, 28-29, 32, 38, 42, 44] used proper generation methods with a low risk of bias, and the random number sequences were

produced by either a random number table, computer software or drawing lots. One trial used an incorrect sequence generation method.[43] Eleven trials [27, 30, 31, 33-37, 39-41] did not describe the randomization procedure clearly. Two trials [26, 28] used concealed envelopes, and the other trials did not report allocation concealment. Two trials [26, 28] reported that assessors were blind to group allocation. Two trials [26, 28] mentioned that investigators were unknown for allocation. One trial [26] reported drop-outs and conducted intention-to-treat analyses. In other sources of bias, eleven trials [30-31, 33-35, 37, 39-42, 44] had a high risk because of poor statistical methods. In general, the methodological quality in the included trials was poor. The results of the assessments are shown in *Figure 2*.

Primary outcomes

1. Fugel-Meyer Assessment scale (FMA)

The primary outcome, FMA score, was mentioned in thirteen trials with 1,010 patients.[26-35, 42-44] The effect of EA on FMA between the EA and non-EA groups was evaluated by a random effects model, owing to significant heterogeneity. A meta-regression analysis was used to explain the potential covariates. The treatment duration was included as a potential covariable in the meta-regression model because the duration was from 2 to 12 weeks. However, the treatment duration was not significant in the meta-regression model (adjusted R^2: 0.124, t = -1.57, P = 0.144, see *Figure 3a*). The FMA scores in the EA group increased more than those in the non-EA group, and there was a significant difference (WMD 10.79, 95% CI 6.39 to 15.20, P < 0.00001) (*Figure 4*).

2. FMA for upper extremity (FMA-U)

One trial [41] with 98 participants used FMA-U to evaluate the function of upper extremity, and the difference between the EA group and the non-EA group was obvious (WMD 3.43, 95% CI 1.27 to 5.59, P = 0.002) (*Table 2*).

3. *FMA for lower extremity (FMA-L)*

The function of lower extremity was assessed by FMA-L in four trials [36-39] with 234 participants. The effect on FMA-L was analyzed by using a fixed effects model, and there was a significant difference between the EA group and the non-EA group in the FMA-L (WMD 5.16, 95% CI 3.78 to 6.54, P < 0.00001) (*Table 2*). A meta-regression analysis was also conducted to explain the potential impact of the treatment duration. Treatment duration was not significant (adjusted R^2: -0.198, t = -0.86, P = 0.482, see *Figure 3 b*).

Secondary outcomes

1. Barthel Index (BI)

The effect on the BI was analyzed by using a random effects model, due to significant heterogeneity in eleven trials [27-29, 31, 33-34, 39, 40, 42-44] with 907 participants. The BI score of the EA group was better than that of the non-EA group (WMD 12.73, 95% CI 9.78 to 15.69, P < 0.00001) (*Figure 5*).

2. Response or effective rate (ER)

Two trials [28, 43] with a total of 171 participants showed that there was no significant difference between EA and non-EA groups on the ER (RR 1.13, 95% CI 1.00 to 1.27, P = 0.05; fixed effects model) (*Table 2*).

3. Berg Balance Scale (BBS)

BBS was assessed in one trial [29] with 120 participants. The BBS improvement in the EA group was better than that of the non-EA group (WMD 7.00, 95% CI 4.29 to 9.71, P < 0.00001) (*Table 2*).

4. Functional Independence Measure (FIM)

The changes in the FIM score were observed in one trial [26] with 63 participants.

The difference in the EA group versus the non-EA group was not significant (WMD 5.50, 95% CI -1.62 to 12.62, P = 0.13) (*Table 2*).

Adverse events

There were no adverse events reports due to EA combined with RT in any of the included trials.

Subgroup analysis

1. EA plus CD and RT versus CD plus RT

Ten trials [26-35] used FMA to assess the motor function of 796 participants with PSMD. A random effects model was used to analyze the effect on FMA and ADL in this subgroup analysis due to significant heterogeneity. There was a significant difference between EA combined with CD and RT versus CD plus RT (WMD 8.03, 95% CI 5.17 to 10.90, P < 0.00001) (*Figure 4*). Eight trials [27-29, 31, 33-34, 39-40] used BI to assess the ADL of 693 patients following PSMD. EA plus CD and RT for the improvement of ADL was better than that of CD plus RT (WMD 11.99, 95% CI 8.47 to 15.50, P < 0.00001) (*Figure 5*).

2. EA plus RT versus RT alone

Three trials [42-44] with 214 participants applied FMA to compare the efficacy of EA plus RT against RT alone. Meta-analyses with a random effects model were performed to evaluate the effect on FMA and ADL in this subgroup analysis due to statistical heterogeneity. There was a significant difference in these three trials (WMD 20.90, 95% CI 18.61 to 23.19, P < 0.00001) (*Figure 4*). In the comparison of EA plus RT versus RT alone, the difference in BI was obvious in the three trials [42-44] (WMD 15.06, 95% CI 7.33 to 22.79, P = 0.0001) (*Figure 5*).

Sensitivity analysis

We used the method of remove item-by-item to test the stability of meta-analysis, and the results showed that there had been no obvious change of any of the outcomes. The difference between the random and fixed effects models may have influenced the outcomes. Therefore, we used different statistical models to pool the data for the FMA, FMA-L, BI and ER. No obvious change in any of the outcomes was found (*Table 3*).

Furthermore, sensitivity analysis was conducted to explore the robustness of our analysis, excluding trials from the overall analysis of high risk of bias due to lack of adequate sequence generation, allocation concealment and blinding of assessors for primary outcomes (*Table 3*). The effects on FMA, BI and ER were robust, with random and fixed effects models with adequate sequence generation, with the exception of the comparison of EA plus RT versus RT alone and the trial subgroups (*Table 3*).

Publication bias

Thirteen trials [26-35, 42-44] and eleven trials [27-29, 31, 33-34, 39-40, 42-44] respectively showed a difference in FMA and BI between the EA and the non-EA groups. Therefore, we used funnel plots to assess publication bias based on FMA and BI. However, some trials did not lie inside the 95% CI and the distribution was in unbalance. This indicated potential publication bias (*Figure 6* and *Figure 7).*

DISCUSSION

This systematic review of nineteen RCTs with 1,434 participants comparing the effectiveness and safety of EA therapy and non-EA therapy showed that EA was better at improving the function of the lower and upper extremities as well as overall motor function. It was also better at promoting ADL recovery. There was no difference between EA and non-EA for the ER. However, it should be noted that the

review included add-on designed trials of EA plus RT and/or CD, which suggests that EA is a complementary therapy for PSMD. Meanwhile, there was insufficient data to assess the safety for EA plus RT, EA plus CD, and EA plus both CD and RT because most of the included trials did not report adverse events. Considering the pool effects on FMA and FMA-L with significant heterogeneity, meta-regression analysis was conducted to explain the impact of treatment duration as a covariable. The result showed that the treatment duration was not significant in the meta-regression model. This means the heterogeneity could not be explained by the trial-level's treatment duration.

Several experimental studies may at least partially explain the clinical benefits of EA as a complementary therapy for PSMD. Previous evidence has shown that the damaged structure and function of the central nervous system (CNS) make major contributions to motor dysfunction following stroke.[45] Fortunately, numerous studies have indicated that the brain has a property of plasticity, namely, CNS cells stimulated by the external world can modify their structure and function.[46-47] Moreover, several studies of stroke patients and animal models have demonstrated that the spontaneous rehabilitation of PSMD may benefit from brain plasticity.[48-49] EA combined with RT is able to promote the recovery of PSMD, and may be associated with the above mechanisms.

In this review, most of the included trials had small sample sizes. 63% of the included trials used a high risk of bias method or did not describe the generation of random sequence. 89% of the trials did not report allocation concealment and had inadequate blinding of outcome assessments. 58% of the trials used poorly designed statistical methods or did not fully describe the statistical methods. Only two trials [26, 28] were well-designed so as to assess the effect of EA combined with RT for PSMD. Additionally, all trials included in this review were conducted in China and most were published in Chinese, which likely lead to a selection bias, and therefore limits their representativeness.

The main limitations of this review are the methodological defects in the included trials and potential publication bias. These issues potentially lead to low quality of evidence, overreporting of positive results, and underreporting of adverse events. Also, the use of diverse CD and RT as add-on basis in the included trials makes it difficult to pool data by using a fixed effect model to interpret the clinical significance of EA. Therefore, the potential benefits of EA as an add-on therapy for PSMD evident in this review need to be further appraised through well-designed RCTs. Future RCTs should use large-scale sample size and be conducted in different countries.

Conclusions

EA as a complementary therapy that appears to have clinical benefits in terms of improving the function of extremities, ADL and balance function. However, these apparent benefits require further evaluation through well-designed multi-centre trials with large sample sizes. The safety of EA combined with RT and/or CD is still uncertain.

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Contributors

J Zhan and Z Wen are responsible for conception and design of this systematic review.

The manuscript of this article was drafted by J Zhan, and revised by Z Wen and F Tan. The search strategies were designed by Z Wen and J Zhan. The electronic search was conducted by J Zhan, M Zhou and J Dong. Z Huang manually searched key journals. J Zhan and M Zhou extracted data. The risk of bias was assessed by J Zhan and R Pan, independently. J Zhan and Z Wen analyzed and interpreted the data. Z Wen arbitrated any disagreements in the process of systematic review. All authors approved this manuscript.

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Figure Legends

Figure 1 Study flow diagram
Figure 2 Risk of bias assessments of included studies
Figure 3 Meta-regression analysis for potential covariates (a: For FMA, I-squared = 92.97%, Adjusted R-squared = 12.37%, Exp(beta) = 0.7113, t = -1.57, P = 0.144; b: For FMA for lower extremity (FMA-L), I-squared = 54.58%, adjusted R-squared = -19.78%, Exp(beta) = 0.9401, t = -0.86, P = 0.482)
Figure 4 Forest plot and meta-analysis of FMA. (CD, conventional drugs; EA, electroacupuncture; FMA, Fugel-Meyer Assessment Scale; RT, rehabilitation therapy)
Figure 5 Forest plot and meta-analysis of BI. (BI, Barthel Index; CD, conventional drugs; EA, electroacupuncture; RT, rehabilitation therapy)
Figure 6 Funnel plots illustrating meta-analysis of FMA. (CD, conventional drugs; EA, electroacupuncture; FMA, Fugel-Meyer Assessment Scale; RT, rehabilitation therapy; SE, standard error; MD, mean difference)
Figure 7 Funnel plots illustrating meta-analysis of BI. (BI, Barthel Index; CD, conventional drugs; EA, electroacupuncture; RT, rehabilitation therapy; SE, standard error; MD, mean difference)
Table 1 Characteristics of randomised controlled trials included in this review. (Notes. BI, Barthel Index; BBS, Berg Balance Scale; CD, conventional drugs; C, control group; EA, electroacupuncture; ER, effective rate; FMA, Fugel-Meyer Assessment Scale; FMA-U, FMA for upper extremity; FMA-L, FMA for lower extremity; FIM, Functional Independence Measure; RT, rehabilitation therapy; T, treatment group)
Table 2 Results of meta-analysis comparison for EA and non-EA. (Notes. FMA, Fugel-Meyer Assessment Scale; WMD/RR, weighted mean difference/Risk ratio; df, degrees of freedom; CI, confidence interval)
Table 3 Results of sensitivity analysis. (Notes: CD, conventional drugs; CI, confidence interval; df, degrees of freedom; EA, electroacupuncture; RT, rehabilitation therapy; WMD, weighted mean difference)

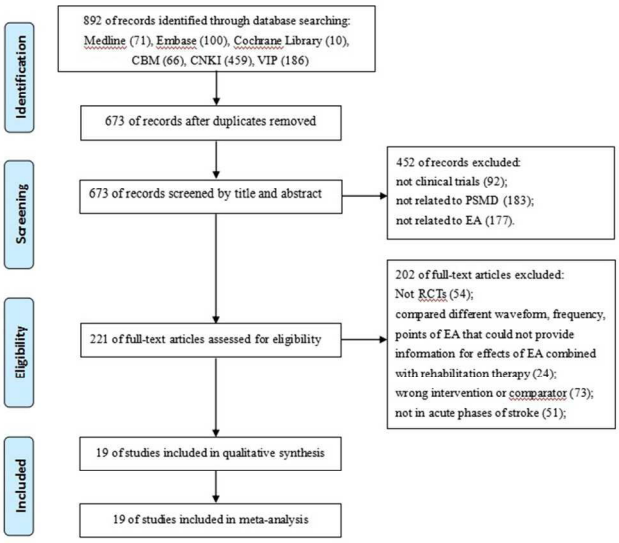

Figure 1 Study flow diagram

280x158mm (96 x 96 DPI)

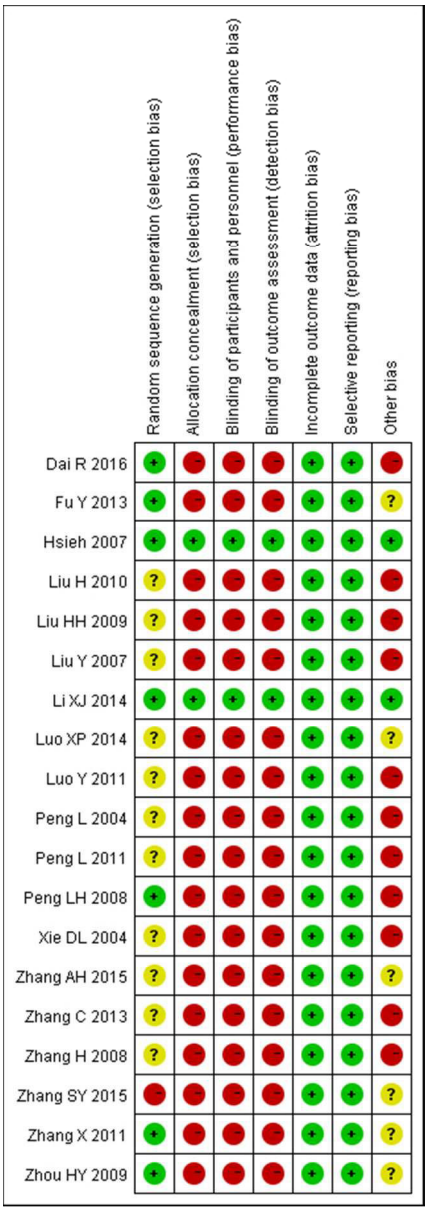

Figure 2 Risk of bias assessments of included studies

112x321mm (72 x 72 DPI)

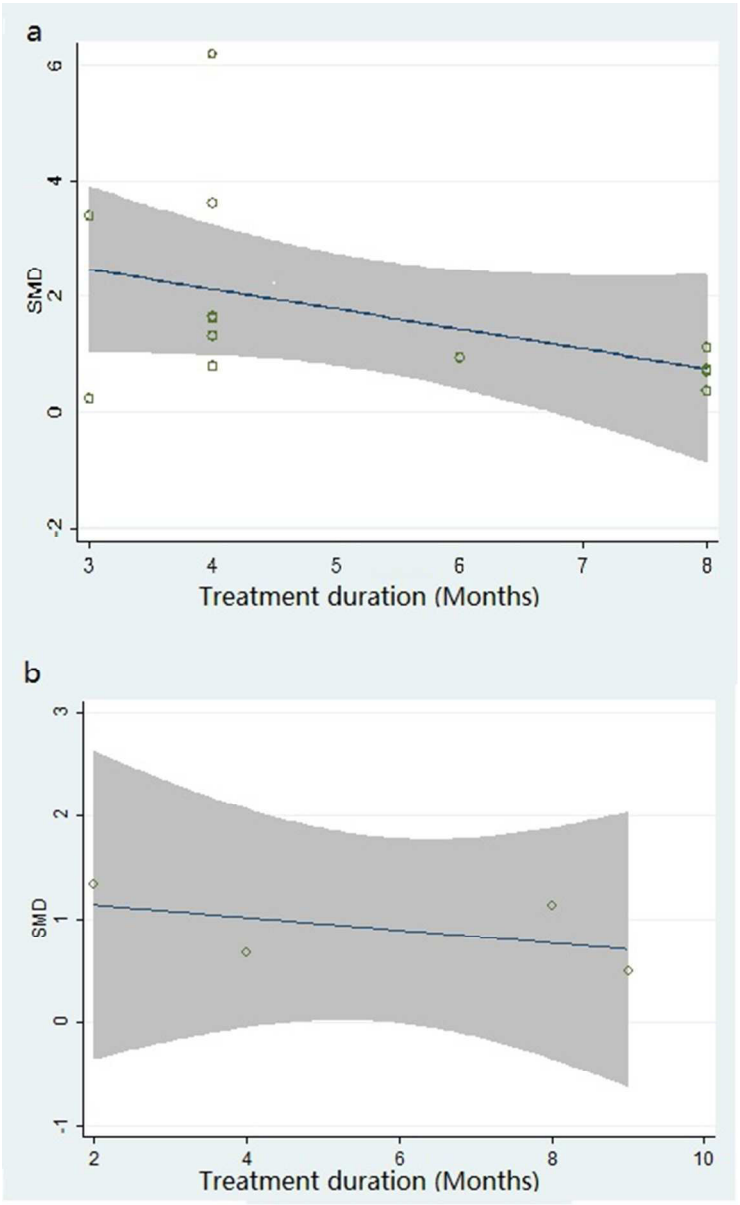

Figure 3 Meta-regression analysis for potential covariates (a: For FMA, I-squared = 92.97%, Adiusted R-squred = 12.37%, Exp(beta) = 0.7113, t = -1.57, P = 0.144; b: For FMA for lower extremity (FMA-L), I-squared = 54.58%, adjusted R-squared = -19.78%, Exp(beta) = 0.9401, t = -0.86, P = 0.482)

127x207mm (96 x 96 DPI)

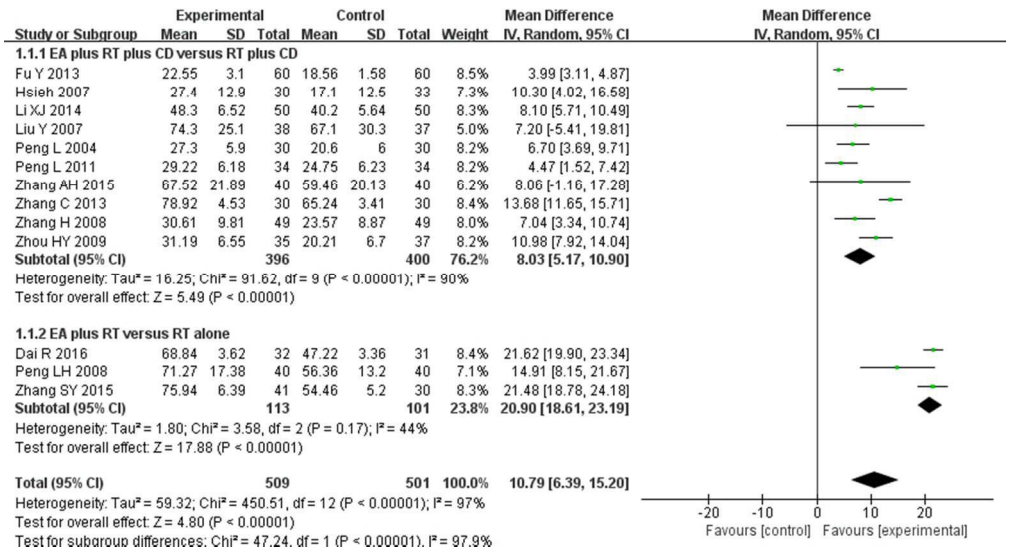

Figure 4 Forest plot and meta-analysis of FMA. (CD, conventional drugs; EA, electroacupuncture; FMA, Fugel-Meyer Assessment Scale; RT, rehabilitation therapy)

301x163mm (72 x 72 DPI)

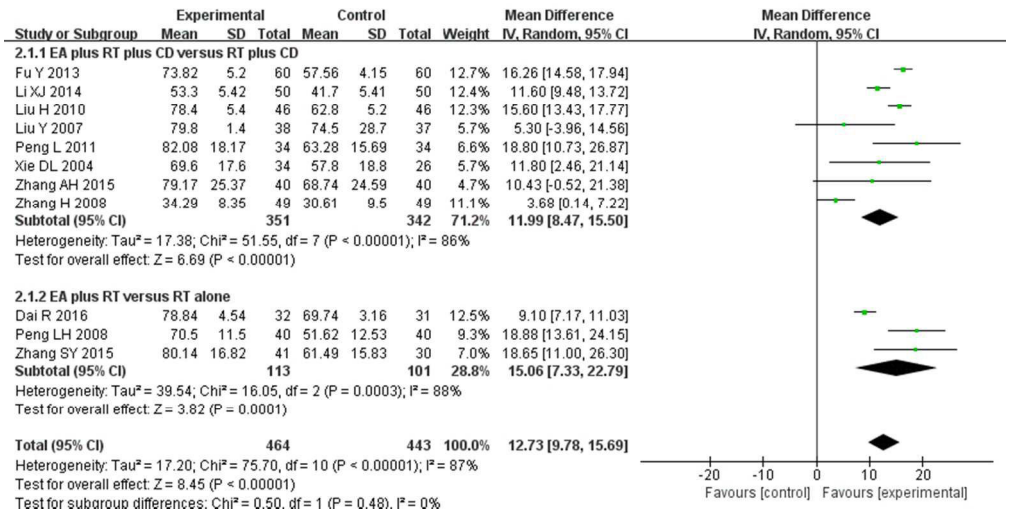

Figure 5 Forest plot and meta-analysis of BI. (BI, Barthel Index; CD, conventional drugs; EA, electroacupuncture; RT, rehabilitation therapy)

301x152mm (72 x 72 DPI)

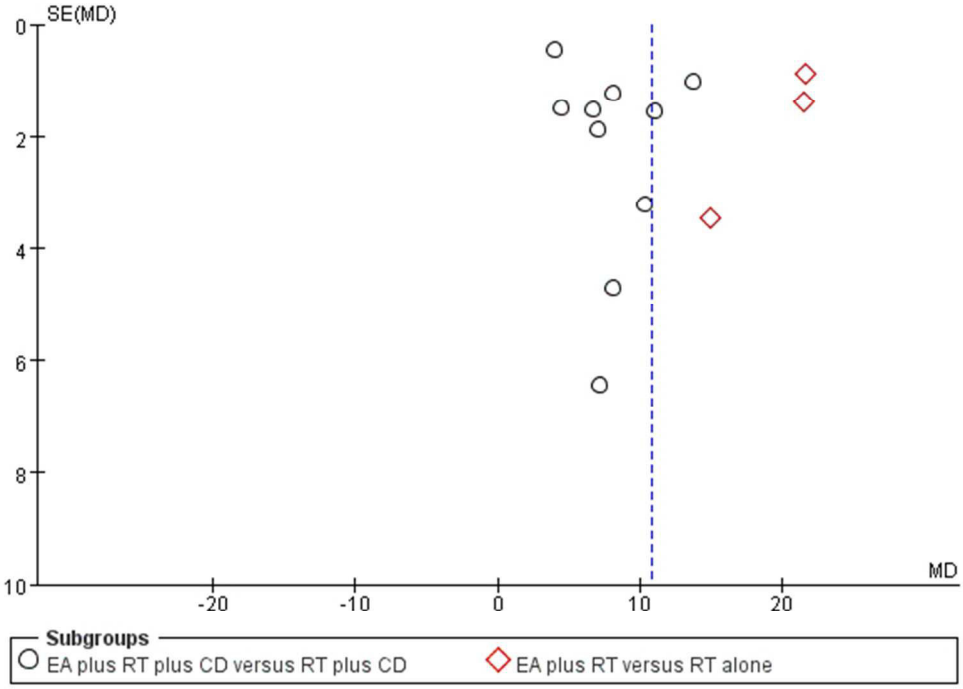

Figure 6 Funnel plots illustrating meta-analysis of FMA. (CD, conventional drugs; EA, electroacupuncture; FMA, Fugel-Meyer Assessment Scale; RT, rehabilitation therapy; SE, standard error; MD, mean difference)

211x150mm (72 x 72 DPI)

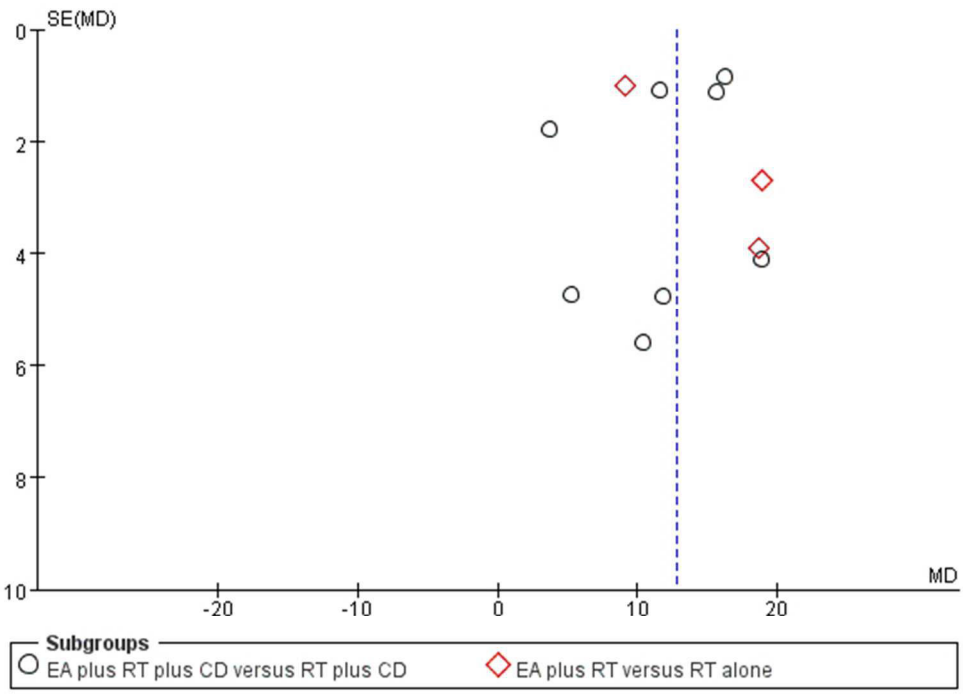

Figure 7 Funnel plots illustrating meta-analysis of BI. (BI, Barthel Index; CD, conventional drugs; EA, electroacupuncture; RT, rehabilitation therapy; SE, standard error; MD, mean difference)

211x150mm (72 x 72 DPI)

Table 1 Characteristics of the included trials in this review

Study	Sample size	Age (year)	Sex (male/female)	Treatment group regimen	Control group regimen	Treatment duration	Main outcomes
Dai R 2016	T:32; C:31	T:66.4±3.2; C:65.7±4.1	T:18/14; C:17/14	EA+RT	RT	4 weeks	FMA, BI
Zhang AH 2015	T:40; C:40	T:60.5(51-69); C:58.75(47-72)	T:22/18; C:24/16	EA+RT+CD	RT+CD	4-12 weeks	FMA ,BI
Zhang SY 2015	T:41; C:30	T:58.5±12.27; C:52.43±12.24	T:24/17; C:17/13	EA+RT	RT	4 weeks	FMA, BI, ER
Li XJ 2014	T:50; C:50	T:64±5; C:65±4	T:27/23; C:29/21	EA+RT+CD	RT+CD	4 weeks	FMA, BI ,ER
Luo XP 2014	T:30; C:26	T:60.83±9.58; C:62.47±8.72	T:21/9; C:19/7	EA+RT+CD	RT+CD	4 weeks	FMA-L
Fu Y 2013	T:60; C:60	T:62.05±6.25; C:63.07±5.1	T:37/23; C:36/24	EA+RT+CD	RT+CD	4 weeks	FMA, BI, BBS
Zhang C 2013	T:30; C:30	60.7±8.6	36/24	EA+RT+CD	RT+CD	20 days	FMA
Peng L 2011	T:34; C:34	55(37-77)	41/27	EA+RT+CD	RT+CD	8 weeks	FMA, BI
Luo Y 2011	T:30; C:30	55(37-78)	39/21	EA+RT+CD	RT+CD	8 weeks	FMA-L
Zhang X 2011	T:29; C:29	T:67.14±10.17; C:68.14±10.93	T:16/13; C:14/15	EA+RT+CD	RT+CD	2 weeks	FMA-L
Liu H 2010	T:46; C:46	T:65; C:62	T:29/17; C:30/16	EA+RT+CD	RT+CD	4 weeks	BI
Zhou HY 2009	T:35; C:37	T:63.7±10.5; C:64.5±10.6	T:17/18; C:20/17	EA+RT+CD	RT+CD	4 weeks	FMA
Liu HH 2009	T:49; C:49	55±0.24	T:26/23; C:24/25	EA+RT+CD	RT+CD	8 weeks	FMA-U
Peng LH 2008	T:40; C:40	58.5(35-78)	48/32	EA+RT	RT	6 weeks	FMA, BI

Zhang H 2008	T:49; C:49	T:51.49±8.35; C:54.73±6.75	T:26/23; C:24/25	EA+RT+CD	RT+CD	8 weeks	FMA, BI
Hsieh 2007	T:30; C:33	T:68.8; C:70.7	T:12/18; C:23/10	EA+RT+CD	RT+CD	4 weeks	FMA, FIM
Liu Y 2007	T:38; C:37	T:59.4±10.2; C:56.4±10.5	T:25/13; C:14/23	EA+RT+CD	RT+CD	20 days	FMA, BI
Peng L 2004	T:30; C:30	55(37-78)	39/21	EA+RT+CD	RT+CD	8 weeks	FMA
Xie DL 2004	T:34; C:26	T:53±9.3; C:56.5±6.4	T:22/12; C:17/9	EA+RT+CD	RT+CD	30-40 days	FMA-L, BI

Notes. T, treatment group; C, control group; EA, electroacupuncture; RT, rehabilitation therapy; CD, conventional drugs; BI, Barthel Index; BBS, Berg Balance Scale; ER, effective rate; FMA, Fugel-Meyer Assessment Scale; FMA-U, Fugel-Meyer Assessment Scale for upper extremity; FMA-L, Fugel-Meyer Assessment Scale for lower extremity; FIM, Functional Independence Measure

Table 2 Results of meta-analysis comparison of EA and non EA

Outcomes of interest	Studies, no.	Participants, no		WMD (95% CI)	*p* value	Study heterogeneity			
		EA group	non EA group			Chi^2	df	I^2, %	*p* value
Primary outcomes									
FMA for upper extremity	1	49	49	3.43 (1.27, 5.59)	0.002				
FMA for lower extremity	4	123	111	5.16 (3.78, 6.54)	<0.00001	1.76	3	0	0.62
Secondary outcomes									
Effective rate	2	91	80	1.13 (1.00, 1.27)*	0.05	2.8	1	64	0.09
Berg Balance Scale	1	60	60	7.00 (4.29, 9.71)	<0.00001				
Functional Independence Measure	1	30	33	5.50 (-1.62, 12.62)	0.13				

Notes. EA, electroacupuncture; FMA, Fugel-Meyer Assessment Scale; WMD/RR, weighted mean difference/Risk ratio; df, degrees of freedom; CI, confidence interval.

* Presented as relative risk (RR)

Table 3 Results of sensitivity analysis

Study type	Studies, no.	Participants, no		Study heterogeneity				Analysis model	WMD (95% CI)	*p* value
		Experiment group	Control group	Chi^2	df	I^2, %	*p* value			
Fugel-Meyer Assessment scale (FMA)										
EA versus non EA	13	509	501	450.51	12	97	<0.00001	random	10.79 (6.39, 15.20)	<0.00001
								fixed	8.97 (8.35, 9.58)	<0.00001
EA plus RT plus CD versus RT plus CD	10	396	400	91.62	9	90	<0.00001	random	8.03 (5.17, 10.90)	<0.00001
								fixed	6.13 (5.45, 6.82)	<0.00001
EA plus RT versus RT alone	3	113	101	3.58	2	44	0.17	random	20.90 (18.61, 23.19)	<0.00001
								fixed	21.29 (19.86, 22.71)	<0.00001
FMA for lower extremity (FMA-L)										
EA versus non EA	4	123	111	1.76	3	0	0.62	random	5.16 (3.78, 6.54)	<0.00001
								fixed	5.16 (3.78, 6.54)	<0.00001
Barthel Index (BI)										
EA versus non EA	11	464	443	75.70	10	87	<0.00001	random	12.73 (9.78, 15.69)	<0.00001

								fixed	12.90(12.00, 13.80)	<0.00001
EA plus RT plus CD versus RT plus CD	8	351	342	51.55	7	86	<0.00001	random	11.99 (8.47, 15.50)	<0.00001
								fixed	13.67 (12.63, 14.72)	<0.00001
EA plus RT versus RT alone	3	113	101	16.05	2	88	0.0003	random	15.06 (7.33, 22.79)	0.0001
								fixed	10.70 (8.94, 12.46)	<0.00001
Response or effective rate (ER)										
EA versus non EA	2	91	80	2.80	1	64	0.09	random	1.13 (0.90, 1.42)*	0.29
								fixed	1.13 (1.00, 1.27)*	0.05
Trials with adequate sequence generation: FMA										
EA versus non EA	6	247	251	327.63	5	98	<0.00001	random	11.61 (4.17, 19.04)	0.002
								fixed	7.98 (7.26, 8.69)	<0.00001
Trials with adequate concealed allocation and blinding of assessors: FMA										
EA versus non EA	2	80	83	0.41	1	0	0.52	random	8.38 (6.14, 10.61)	<0.00001
								fixed	8.38 (6.14, 10.61)	<0.00001

Notes. CD, conventional drugs; CI, confidence interval; df, degrees of freedom; EA, electroacupuncture; RT, rehabilitation therapy; WMD, weighted mean difference.

* Presented as relative risk (RR)

Appendix 1：search in different databases

Embase (Ovid)

1 exp basal ganglia cerebrovascular disease/ (589)
2 cerebrovascular disorders/ (28457)
3 exp intracranial arterial diseases/ (4033)
4 exp intracranial arteriovenous malformations/ (7627)
5 exp intracranial embolism/ and thrombosis/ (341)
6 exp intracranial hemorrhages/ (112672)
7 stroke/ (142289)
8 exp brain infarction/ (63904)
9 exp brain ischemia/ (146312)
10 exp carotid artery diseases/ (58463)
11 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 (435950)
12 (stroke$ or cva or poststroke or post-stroke tw).af. (377113)
13 (cerebrovasc$ or cerebral vascular tw).af. (258529)
14 (cerebral or cerebellar or brain$ or vertebrobasilar tw).af. (2073620)
15 (infarct$ or ish?emi$ or thrombo$ or emboli$ or apoplexy tw).af. (1331966)
16 14 and 15 (190335)
17 (cerebral or brain tw).af. (427090)
18 (haemorrhage or hemorrhage or haematoma or hematoma or bleed$ tw).af. (419811)
19 17 and 18 (51165)
20 exp hemiplegia/ or exp paresis/ (25724)
21 (hempar$ or paretic or paresis or hemipleg$).tw. (27554)
22 Gait Disorders, Neurologic/ (186)
23 11 or 12 or 13 or 16 or 19 or 20 or 21 or 22 (736569)
24 exp Upper Extremity/ (298321)
25 (upper limb$ or upper extremit$ or arm or shoulder or hand or axilla or elbow$ or forearm$ or finger$ or wrist$).tw. (815222)
26 exp Lower Extremity/ (340988)
27 (lower lib$ or lower extremit$ or buttock$ or foot or feet or hip or hips or knee or knees or leg or legs or thigh$ or ankle$ or heel$ or toe or toes).tw. (587073)
28 24 or 25 or 26 or 27 (1454564)
29 acupuncture.mp. or acupuncture/ or auricular acupuncture/ or acupuncture needle/ (39351)
30 electroacupuncture.mp. or electroacupuncture/ (5962)
31 29 or 30 (41050)
32 23 and 28 and 31 (352)
33 controlled clinical trial/ or randomized control.mp. (463239）
34 human/ (18118592)
35 32 and 33 and 34 (100)

Medline (Ovid)

1 ((cerebrovascular disorders/ or exp basal ganglia cerebrovascular disease/ or exp brain ischemia/ or exp carotid artery diseases/ or exp intracranial arterial diseases/ or exp intracranial arteriovenous malformations/ or exp intracranial

embolism/) and thrombosis/) or exp intracranial hemorrhages/ or stroke/ or exp brain infarction/ (174619)
2 (stroke$ or cva or poststroke or post-stroke).tw. (184045)
3 (cerebrovasc$ or cerebral vascular).tw. (48126)
4 (cerebral or cerebellar or brain$ or vertebrobasilar).tw. (1080871)
5 (infarct$ or isch?emi$ or thrombo$ or emboli$ or apoplexy).tw. (802321)
6 4 and 5 (112916)
7 (cerebral or brain).tw. (1000104)
8 (haemorrhage or hemorrhage or haematoma or hematoma or bleed$).tw. (299810)
9 7 and 8 (38074)
10 exp hemiplegia/ or exp paresis/ (18750)
11 (hempar$ or paretic or paresis or hemipleg$).tw. (19881)
12 Gait Disorders, Neurologic/ (5535)
13 1 or 2 or 3 or 6 or 9 or 10 or 11 or 12 (394414)
14 exp Upper Extremity/ (155762)
15 (upper limb$ or upper extremit$ or arm or shoulder or hand or axilla or elbow$ or forearm$ or finger$ or wrist$).tw. (603271)
16 exp Lower Extremity/ (156126)
17 (lower limb$ or lower extremit$ or buttock$ or foot or feet or hip or hips or knee or knees or leg or legs or thigh$ or ankle$ or heel$ or toe or toes).tw. (459027)
18 14 or 15 or 16 or 17 (1120852)
19 Acupuncture Therapy/ or Acupuncture/ or Acupuncture Points/ or Acupuncture, Ear/ or acupuncture.mp. (25001)
20 electroacupuncture.mp. or Electroacupuncture/ (4748)
21 19 or 20 (26152)
22 13 and 18 and 21 (183)
23 Random Allocation/ or Treatment Outcome/ or randomized control.mp. or Clinical Trials as Topic/ (1070629)
24 Humans/ (17431024)
25 22 and 23 and 24 (71)

Cochrane Library

1 "Cerebrovascular Disorders" or "Brain Ischemia" or "Cerebral Hemorrhage" or "Stroke" "Cerebrovascular" or "Cerebrovascular Disorder" or "cva"
2 MeSH descriptor: [Cerebrovascular Disorders] this term only
3 MeSH descriptor: [Brain Ischemia] this term only
4 MeSH descriptor: [Cerebral Hemorrhage] explode all trees
5 MeSH descriptor: [Stroke] explode all trees
6 1 or 2 or 3 or 4 or 5
7 "acupuncture" or "electroacupuncture" or "electroacupuncture":ti,ab,kw (Word variations have been searched)
8 MeSH descriptor: [Acupuncture] explode all trees
9 MeSH descriptor: [Acupuncture Therapy] this term only
10 MeSH descriptor: [Electroacupuncture] explode all trees
11 7 or 8 or 9 or 10
12 6 and 11
13 Upper Extremity:ti,ab,kw (Word variations have been searched)
14 Lower Extremity:ti,ab,kw (Word variations have been searched)
15 MeSH descriptor: [Motor Activity] explode all trees

16 13 or 14 or 15
17 12 and 16
18 human
19 17 and 18
20 randomized control
21 19 and 20

CNKI

主题=脑卒中 or 主题=中风 or 主题=脑梗死 or 主题=脑出血 or 主题=脑血管病 or 主题=脑血管障碍 and 主题=运动障碍 or 主题=运动功能 or 主题=偏瘫 and 主题=电针 and 主题=随机 or 主题=对照 and (模糊匹配)

VIP

(K=卒中 OR K=中风 OR K=脑梗死 OR K=脑出血 OR K=脑血管病 OR K=脑血管障碍) AND K=电针 AND (K=运动功能 OR K=运动障碍 OR K=偏瘫)

CBM

(((((((("卒中"[不加权:扩展]) OR "中风"[不加权:扩展]) OR "脑梗死"[不加权:扩展]) OR "脑出血"[不加权:扩展]) OR "脑血管障碍"[不加权:扩展]) AND "运动障碍"[不加权:扩展]) OR "偏瘫"[不加权:扩展]) AND "电针"[不加权:扩展] AND "随机对照试验"[不加权:扩展]

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	1-2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	3
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	3
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	3
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	3-4
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	4
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	4
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	4
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	4-5
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	5
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	5
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	5
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	5

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	5
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	5
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	5
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	5
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	5-6
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	6
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	6
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	7
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	7
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	7
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	8
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	8
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	9

BMJ Open

Electroacupuncture as an adjunctive therapy for motor dysfunction in acute stroke survivors: a systematic review and meta-analyses

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Electroacupuncture as an adjunctive therapy for motor dysfunction in acute stroke survivors: a systematic review and meta-analyses

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ABSTRACT

Objectives: To assess the effectiveness and safety of electroacupuncture (EA) combined with rehabilitation therapy (RT) and/or conventional drugs (CD) for improving post-stroke motor dysfunction (PSMD) .

Design: Systematic review and meta-analysis.

Methods: The China National Knowledge Infrastructure, Chinese Biological Medicine Database, Chinese Scientific Journal Database, Cochrane Library, Medline, and Embase were electronically searched from inception to December 2016. The methodological quality of the included trials was assessed using the Cochrane risk of bias assessment tool. Statistical analyses were conducted by RevMan Version 5.3.

Results: Nineteen trials with 1,434 participants were included for qualitative synthesis and meta-analysis. The methodological quality of the included trials was generally poor. The meta-analysis indicated that the EA group might be benefitting more than the non-EA group in terms of the changes in the Fugl-Meyer Assessment Scale (FMA) (weighted mean difference [WMD]: 10.79, 95% confidence interval

[CI]: 6.39 to 15.20, P < 0.001), FMA for lower extremity (WMD: 5.16, 95% CI: 3.78 to 6.54, P < 0.001), and activities of daily living (standardized mean difference [SMD]: 1.37, 95% CI: 0.79 to 1.96, P < 0.001), respectively. However, there was no difference between the EA and non-EA groups in the effective rate (relative risk [RR]: 1.13, 95% CI: 1.00 to 1.27, P = 0.050). Moreover, there was no reports of side effects due to EA combined with RT and/or CD in the included trials.

Conclusions: This review provides new evidence for the effectiveness of EA combined with RT and/or CD for PSMD. However, its effectiveness and safety should be used with caution due to methodological weakness and publication bias. Further rigorously designed trials with multiple centres and large sample sizes are warranted.

Keywords: motor function; post-stroke; electroacupuncture; RCT; systematic review

PROSPERO registration number: CRD42016037597

Strengths and limitations of this study:

- This systematic review with a comprehensive searching of 3 English and 3 Chinese databases and up to December 2016 was focussed especially on assessing the adjunctive effects of EA for motor dysfunction in acute stroke survivors within 14 days.
- Although the included trials in this review have methodological weakness, meta-regression analyses used to explain the potential influence of the duration of treatment was performed and sensitivity analyses with different risk of bias showed that the results were robust.
- Build on the low quality of included trials, we anticipate considerable difficulties in identifying the effectiveness of EA for motor dysfunction in acute stroke.

INTRODUCTION

Stroke is one of the world's leading causes of death and disability, [1-2] causing heavy burdens to patients' families, communities and healthcare systems. [3] Motor dysfunction is a frequent and widely recognised complication that often follows strokes. Approximately 85% of stroke patients suffer from hemiparesis immediately after their stroke, and between 55% and 75% of stroke survivors may experience incomplete recovery with lingering motor dysfunction. [4] Post-stroke motor dysfunction (PSMD), which has a negative effect on the independence of functional activities, can reduce quality of life (QoL) and limit activities of daily living (ADL). Therefore, effective treatment of PSMD is needed in order to promote neurological function recovery and to alleviate the social and familial burdens of stroke.

Motor function recovery after stroke not only requires multi-disciplinary treatment team, but also involves various approaches such as conventional drugs (CD), rehabilitation therapy (RT), and nursing care. RT play an important role in comprehensive stroke rehabilitation programs aimed at recovering the function so as to reduce disabilities. Previous studies have demonstrated that the rehabilitation of neurological deficits due to stroke can benefit from RT. [5] However, the effects of current RT for motor dysfunction caused by stroke are not a lotted. [6] Over the last decade, an increasing number of researchers have focused on alternative therapies for stroke rehabilitation such as acupuncture.

In recent years, acupuncture, as one of the best known complementary and alternative medicines, has also been increasingly applied in China and other regions of the world. [7] Electroacupuncture (EA), derived from the integration of traditional acupuncture and modern electrical stimulation, is another kind of acupuncture. EA is widely accepted because it is a relatively straightforward, safe and cheap therapy, compared with other conventional therapies. [8] Additionally, EA has become more and more commonly used in clinical practice because of its repeatability and standardization of frequency, intensity and duration. [9,10] After the needles inserting into the acupuncture points, the electrodes are attached to the pairs of needles, then a small electric current, usually pulse frequency of 1-100 Hz and pulse amplitude of 2-3 mA, is passed through the needles into the subject for 15 - 60 min. [11,12] The efficacy of EA with strongly continued stimulation to treat stroke is better than manual acupuncture. [12] Furthermore, EA has been commonly recommended for use

in clinic and research on acupuncture in China and the other countries. [10,13] EA may improve functional recovery after stroke by inhibiting cell apoptosis, regulating miR-9-mediated nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB) downstream pathway and miR-181b / paired-immunoglobulin-like receptor B (PirB) / ras homolog family member A (RhoA) / growth associated protein 43 (GAP43) axis, and dynamically maintaining the balance of matrix metallopeptidase-9 (MMP-9) and tissue inhibitor of metalloproteinase-1 (TIMP-1). [14-16]

A systematic review had suggested that EA was effective for the treatment of acute ischemic stroke, but its search time was up to June 2013 and not focus on PSMD. [17] Another newly published systematic review had revealed that EA had the potential of reducing spasticity within 180 days poststroke. [18] However, these systematic reviews did not focus specifically on the effects of EA as an adjunctive therapy for motor dysfunction of acute stroke (within 14 days of onset [19]). Up to now, no clear evidence has been found that EA is more effective than non-EA in improving motor dysfunction within 14 days after stroke. Therefore, this study was conducted to assess the effectiveness and safety of EA combined with RT for PSMD in acute period, and to provide the best available evidence for clinical practice. The systematic review was registered on PROSPERO (https://www.crd.york.ac.uk /PROSPERO/) (No. CRD42016037597).

METHODS

Types of studies

We included all randomized controlled trials (RCTs) evaluating the effectiveness and safety of EA combined with RT for PSMD. The comparators or controls in the trials were any other therapy modalities. Also, we only included trials with outcomes measuring changes in motor function. All eligible trials published in Chinese or English, regardless of publication status were included.

Types of participants

We considered trials that included patients in the acute stage following the onset of their first stroke, with motor dysfunction measured by validated instruments or by a decrease in the level of movement activity. Patients were to be more than 18 years old, and from any ethnicity. Stroke diagnosis had to meet the WHO criteria or the

corresponding diagnostic criteria adopted in China, [20-23] and had to be confirmed by computerized tomography (CT) or magnetic resonance imaging (MRI). Trials involving participants with subarachnoid hemorrhages or cerebrovascular tumors, as well as those in which patients were not acute stroke (within 14 days of onset [19]), were excluded.

Types of interventions

Patients in the experimental groups of the included trials had been treated with EA combined with RT and/or CD, at any frequency, intensity or duration. Patients in the control group of the trials had been treated by other therapies such as CD, RT, sham acupuncture, or no treatments. However, trials which did not provide a detailed description or explanation of intervention, or those that compared different acupoint prescriptions or acupuncture types, were excluded.

Primary outcome assessments

The primary outcome for the system review was motor function. There are many types of motor function scales including but not limited to: the Fugl-Meyer Motor Assessment Scale (FMA); [24] the modified Rankin Scale (mRS); [25] the Motor Assessment Scale (MAS); [26] and Brunnstrom Stages. [27]

Secondary outcome assessments

Secondary outcomes included measures of ADL, such as the Barthel Index (BI), [28] the Functional Independence Measure (FIM), [29] and the response or effective rate (ER). The ER was a standard of therapeutic effect recommended by the Fourth National Cerebrovascular Diseases Conference in China. And the ER classified disability of stroke into five grades: cure (the scores of functional deficit were decreased up to 91-100%), significant improvement (the scores of functional deficit were decreased at 46-90%), improvement (the scores of functional deficit were decreased at 18-45%), no improvement (the scores of functional deficit were decreased less than 18%), and deterioration (the scores of functional deficit were increased over 18%). [17] Adverse events as reported in the included trials were also recorded. The time of the outcome assessments was at the end of the intervention phase.

Electronic searches

We electronically searched databases from their respective inceptions up to December 2016. The databases included China National Knowledge Infrastructure (CNKI), Chinese Biological Medicine Database (CBM), Chinese Scientific Journal Database

(VIP), Cochrane Library, Medline and Embase. We combined the PubMed search with the Cochrane highly sensitive search strategy for identifying randomized trials, and adapted the search strategy for searching the other databases.

We also searched other resources in order to identify potentially relevant trials. For example, we screened reference lists of included trials, and contacted trial authors. The detailed search steps are illustrated in supplementary *appendix 1*.

Data extraction and quality assessment

Two review authors (J Zhan and M Zhou) independently scanned the titles and abstracts of articles obtained from the search and kept all potentially relevant articles. Then, they retrieved the full texts of these articles, and another two authors (Z Huang and R Pan) independently examined them to confirm that the trials met the inclusion criteria. We also recorded the reasons for exclusion of trials. If the same trial had more than one report, we only kept one originally published version. If necessary, we acquired additional information from trial authors by e-mail or telephone. Moreover, we discussed any disagreements to decide whether a trial should be included or excluded, and if necessary, we consulted with another author (Z Wen).

Two authors (J Zhan and M Zhou) independently extracted information from the included trials. The information was entered into an Excel formatted table (J Zhan) and the accuracy of the information entered was also checked (R Pan). The information extracted was as follows: trial design (e.g. sample size, randomization method, blinding method); participants (e.g. gender, age); the details of intervention; outcomes (primary and secondary outcomes); adverse events; the name of the author, publication year, and so on. The trial selection details are shown in a PRISMA-complied flow chart (*Figure 1*).

Risk of bias assessment in the included studies

Two review authors (J Zhan and R Pan) independently used the risk of bias assessment tool in the *Cochrane Handbook for Systematic Reviews of Interventions* [30] to assess the methodological quality of each included trial. The specific domains were evaluated as follows: random sequence generation, concealment of allocation, blinding, incomplete outcome data, selective outcome reporting, and other sources of bias. We graded the risk of bias for each domain as follows: low risk of bias, high risk of bias, or unclear. We settled quality assessment disagreements by discussion with a third reviewer (Z Wen).

Data analysis

We performed all statistical analyses by using RevMan Version 5.3 software. [31] For continuous data, we calculated weighted mean difference (WMD) with corresponding 95% confidence interval (CI). If the outcomes were measured by different scales in the included trials, we calculated standardized mean difference (SMD) with 95% CI instead of WMD. For dichotomous data, we calculated the relative risk (RR) with 95% CI. We tested clinical and statistical heterogeneity among trials by comparing the characteristics of the trials, and used the I-squared statistic to test heterogeneity. If heterogeneity was not significant, we chose a fixed effects model to pool the data; otherwise, we used a random effects model after considering clinical homogeneity. When heterogeneity was substantial, we examined trials for potential explanations, or else conducted a qualitative summary rather than a meta-analysis.

A meta-regression analysis was used to explain the potential trial-level covariates such as the duration of treatment. Subgroup analyses were carried out as follows: EA and RT plus CD compared to RT plus CD; and EA plus RT compared to RT alone. Sensitivity analysis was conducted to explore the robustness of our analysis, excluding studies from the overall analysis of high risk of bias due to lack of allocation concealment and blinding of assessors for the primary outcome. If the number of included trials was over ten, funnel plots and Egger's test were employed for publication bias analysis.

RESULTS

Trial description

We initially identified 892 relevant articles according to the search strategy while 219 were excluded due to being duplicates from different databases. In total, nineteen trials met the eligibility criteria after being screened by title, abstract or full-text, and were included for meta-analysis (*Figure 1*). We did not find further trials for this review by examining the reference lists of included trials. All trials were published between 2004 and 2016. One trial [32] was published in English, while the others were all published in Chinese. A total of 1,434 participants were enrolled in these trials. All trials were conducted in China. Sixteen trials [32-47] compared EA plus CD and RT with CD plus RT. Three trials [48-50] gave EA and RT to the experimental groups, while the control groups only received RT. CD were used according to the China national guidelines, including general supportive care and specialized care such

as antiplatelet agents, anticoagulants, fibrinogen-depleting agents, volume expansion and vasodilators. Because the patients enrolled in the trials were all within 14 days after stroke, CD were used similarly in each included trial. Trial characteristics included in this review are shown in *Table 1*.

Table 1 Characteristics of included trials

Study	Sample size	Age (year)	Sex (male/female)	T regimen vs C regimen	Electrical stimulation frequency	Power	Needle retention duration	Treatment duration	Main outcomes
[48] Dai R 2016	T:32 C:31	T:66.4 ± 3.2 C:65.7 ± 4.1	T:18/14 C:17/14	EA+RT vs RT	NR	2 mA	30 min	4 w	FMA, BI
[33] Zhang AH 2015	T:40 C:40	T:60.50 (51 - 69) C:58.75 (47 - 72)	T:22/18 C:24/16	EA+RT+CD vs RT+CD	NR	PCT	30 min	4 - 12 w	FMA ,BI
[49] Zhang SY 2015	T:41 C:30	T:58.5 ± 12.27 C:52.43 ± 12.24	T:24/17 C:17/13	EA+RT vs RT	NR	PCT	20 min	4 w	FMA, BI, ER
[34] Li XJ 2014	T:50 C:50	T:64 ± 5 C:65 ± 4	T:27/23 C:29/21	EA+RT+CD vs RT+CD	15 - 30 Hz	1 - 2 mA	30 min	4 w	FMA, BI , ER
[42] Luo XP 2014	T:30 C:26	T:60.83 ± 9.58 C:62.47 ± 8.72	T:21/9 C:19/7	EA+RT+CD vs RT+CD	NR	PCT	30 min	4 w	FMA-L
[35] Fu Y 2013	T:60 C:60	T:62.05 ± 6.25 C:63.07 ± 5.10	T:37/23 C:36/24	EA+RT+CD vs RT+CD	NR	PCT	30 min	4 w	FMA, BI, BBS
[36] Zhang C 2013	T:30 C:30	60.7 ± 8.6	36/24	EA+RT+CD vs RT+CD	NR	MSC	20 min	20 d	FMA
[37] Peng L 2011	T:34 C:34	55 (37 - 77)	41/27	EA+RT+CD vs RT+CD	NR	PCT	30 min	8 w	FMA, BI
[43] Luo Y 2011	T:30 C:30	55 (37 - 78)	39/21	EA+RT+CD vs RT+CD	NR	PCT	25 min	8 w	FMA-L
[44] Zhang X 2011	T:29 C:29	T:67.14 ± 10.17 C:68.14 ± 10.93	T:16/13 C:14/15	EA+RT+CD vs RT+CD	20 Hz	PCT	30 min	2 w	FMA-L

Table 1 Characteristics of included trials (Continued)

Study	Sample size	Age (year)	Sex (male/female)	T regimen vs C regimen	Electrical stimulation frequency	Power	Needle retention duration	Treatment duration	Main outcomes
[46] Liu H 2010	T:46 C:46	T:65 C:62	T:29/17 C:30/16	EA+RT+CD vs RT+CD	100 Hz	PCT	30 min	4 w	BI
[38] Zhou HY 2009	T:35 C:37	T:63.7 ± 10.5 C:64.5 ± 10.6	T:17/18 C:20/17	EA+RT+CD vs RT+CD	2.7 Hz	PCT	30 min	4 w	FMA
[47] Liu HH 2009	T:49 C:49	55 ± 0.24	T:26/23 C:24/25	EA+RT+CD vs RT+CD	10 - 15Hz	PCT	20 min	8 w	FMA-U
[50] Peng LH 2008	T:40 C:40	58.5 (35 - 78)	48/32	EA+RT vs RT	1.0 - 2.0 Hz	PCT	30 min	6 w	FMA, BI
[39] Zhang H 2008	T:49 C:49	T:51.49 ± 8.35 C:54.73 ± 6.75	T:26/23 C:24/25	EA+RT+CD vs RT+CD	10 - 15 Hz	PCT	20 min	8 w	FMA, BI
[32] Hsieh 2007	T:30 C:33	T:68.8 C:70.7	T:12/18 C:23/10	EA+RT+CD vs RT+CD	3 - 15 Hz	1 - 10 mA	20 min	4 w	FMA, FIM
[40] Liu Y 2007	T:38 C:37	T:59.4 ± 10.2 C:56.4 ± 10.5	T:25/13 C:14/23	EA+RT+CD vs RT+CD	3.3 Hz,	PCT	30 min	20 d	FMA, BI
[41] Peng L 2004	T:30 C:30	55 (37 - 78)	39/21	EA+RT+CD vs RT+CD	NR	PCT	25 min	8 w	FMA
[45] Xie DL 2004	T:34 C:26	T:53.0 ± 9.3 C:56.5 ± 6.4	T:22/12 C:17/9	EA+RT+CD vs RT+CD	2.7 Hz	MCS	20 min	30 - 40 d	FMA-L, BI

Notes. BI, Barthel Index; BBS, Berg Balance Scale; C, control group; CD, conventional drugs; d, day; EA, electroacupuncture; ER, effective rate; FMA, Fugl-Meyer Assessment Scale; FMA-U, Fugl-Meyer Assessment Scale for upper extremity; FMA-L, Fugl-Meyer Assessment Scale for lower extremity; FIM, Functional Independence Measure; MCS, muscles contract slightly; NR, not referred; PCT, patient can tolerate; RT, rehabilitation therapy; T, treatment group; w, week.

Assessing risk of bias in the included trials

In general, the methodological quality of the included trials was poor. In random sequence generation, seven trials [32, 34, 35, 38, 44, 48, 50] used proper generation methods with a low risk of bias, and the random number sequences were produced by either a random number table, computer software or drawing lots. One trial used an incorrect sequence generation method. [49] Eleven trials [33, 36, 37, 39-43, 45-47] did not describe the randomization procedure clearly. Two trials [32, 34] used concealed envelopes, and the other trials did not report allocation concealment. Two trials [32, 34] reported that outcome assessors were blind to group allocation. Two trials [32, 34] mentioned that investigators were unknown for allocation. One trial [32] reported drop-outs and conducted intention-to-treat analyses. In other sources of bias, eleven trials [36, 37, 39-41, 43, 45-48, 50] had a high risk because of inadequate statistical methods. These trials had not described the specific steps and methods of statistical analysis. The results of the assessments are presented in *Figure 2*.

Primary outcomes

1. Fugl-Meyer Assessment Scale (FMA)

The primary outcome, FMA score, was mentioned in thirteen trials with 1,010 patients. [32-41, 48-50] The effect of EA on FMA between the EA and non-EA groups was evaluated by a random effects model, owing to significant heterogeneity. A meta-regression analysis was used to explain the potential covariates. The treatment duration was included as a potential covariable in the meta-regression model because the duration was from 2 to 12 weeks. However, there was no significant difference for the treatment duration in the meta-regression model (adjusted R^2: 0.124, t = -1.57, P = 0.144). The FMA scores in the EA group increased more than those in the non-EA group, and there was a significant difference (WMD 10.79, 95% CI 6.39 to 15.20, P < 0.001) (*Figure 3*).

2. FMA for upper extremity (FMA-U)

One trial [47] with 98 participants used FMA-U to evaluate the function of upper extremity, and the difference between the EA group and the non-EA group was obvious (P < 0.050) .

3. FMA for lower extremity (FMA-L)

The function of the lower extremity was assessed by FMA-L in four trials [42-45] with 234 participants. The effect on FMA-L was analyzed by using a fixed effects model, and there was a significant difference between the EA group and the non-EA

group in the FMA-L (WMD 5.16, 95% CI 3.78 to 6.54, P < 0.001) (*Table 2*). A meta-regression analysis was also conducted to explain the potential impact of the treatment duration. And there was no significance for the treatment duration in the meta-regression model (adjusted R^2: -0.198, t = -0.86, P = 0.482).

Table 2 Results of sensitivity analysis

Study type	Studies, no.	Participants, no		Study heterogeneity				Analysis model	WMD (95% CI)	*p* value
		Experiment group	Control group	Chi^2	df	I^2, %	*p* value			
Fugl-Meyer Assessment scale (FMA)										
EA versus non EA	13	509	501	450.51	12	97	<0.001	random	10.79 (6.39, 15.20)	<0.001
								fixed[+]	8.97 (8.35, 9.58)	<0.001
EA plus RT plus CD versus RT plus CD	10	396	400	91.62	9	90	<0.001	random	8.03 (5.17, 10.90)	<0.001
								fixed[+]	6.13 (5.45, 6.82)	<0.001
EA plus RT versus RT alone	3	113	101	3.58	2	44	0.170	random	20.90 (18.61, 23.19)	<0.001
								fixed[+]	21.29 (19.86, 22.71)	<0.001
FMA for lower extremity (FMA-L)										
EA versus non EA	4	123	111	1.76	3	0	0.620	random[+]	5.16 (3.78, 6.54)	<0.001
								fixed	5.16 (3.78, 6.54)	<0.001
Activities of daily living (ADL)										
EA versus non EA	12	494	476	176.60	11	94	<0.001	random	1.37 (0.79, 1.96)[*]	<0.001
								fixed[+]	1.20 (1.06, 1.35)[*]	<0.001
EA plus RT plus CD versus RT plus CD	9	381	375	162.20	8	95	<0.001	random	1.29 (0.55, 2.02)[*]	<0.001
								fixed[+]	1.10 (0.94, 1.27)[*]	<0.001
EA plus RT versus RT alone	3	113	101	7.78	2	74	0.020	random	1.63 (1.01, 2.25)[*]	<0.001
								fixed[+]	1.57 (1.25, 1.88)[*]	<0.001

Table 2 Results of sensitivity analysis (Continued)

Study type	Studies, no.	Participants, no		Study heterogeneity				Analysis model	WMD (95% CI)	*p* value
		Experiment group	Control group	Chi^2	df	I^2, %	*p* value			
Response or effective rate (ER)										
EA versus non EA	2	91	80	2.80	1	64	0.090	random+	1.13 (0.90, 1.42)#	0.290
								fixed+	1.13 (1.00, 1.27)#	0.050
Trials with adequate sequence generation: FMA										
EA versus non EA	6	247	251	327.63	5	98	<0.001	random+	11.61 (4.17, 19.04)	0.002
								fixed+	7.98 (7.26, 8.69)	<0.001
Trials with adequate concealed allocation and blinding of assessors: FMA										
EA versus non EA	2	80	83	0.41	1	0	0.520	random+	8.38 (6.14, 10.61)	<0.001
								fixed+	8.38 (6.14, 10.61)	<0.001

Notes. CD, conventional drugs; CI, confidence interval; df, degrees of freedom; EA, electroacupuncture; RT, rehabilitation therapy; WMD, weighted mean difference.

Presented as relative risk (RR); * Presented as standardized mean difference (SMD); + Represents the meta-analysis results was not shown in the figures.

Secondary outcomes

1. Activities of daily living (ADL)

The effect of EA on the ADL was analyzed by using a random effects model, due to significant heterogeneity in twelve trials [32-35, 37, 39, 40, 45, 46, 48-50] with 970 participants. We calculated SMD with 95% CI as the outcomes were measured by different scales (FIM and BI) in the included trials. The improvement of ADL in the EA group was better than that in the non-EA group (SMD 1.37, 95% CI 0.79 to 1.96, P < 0.001) (*Figure 4*).

2. Response or effective rate (ER)

Two trials [34, 49] with a total of 171 participants showed that there was no significant difference between EA and non-EA groups on the ER (RR 1.13, 95% CI 1.00 to 1.27, P = 0.050; fixed effects model) (*Table 2*).

3. Berg Balance Scale (BBS)

BBS was assessed in one trial [35] with 120 participants. The improvement of BBS in the EA group was better than that in the non-EA group (P < 0.050) .

Adverse events

None of included trials mentioned adverse events due to EA combined with RT and/or CD.

Subgroup analysis

1. EA plus RT and CD versus RT plus CD

Ten trials [32-41] used FMA to assess the motor function of 796 participants with PSMD. A random effects model was utilized to analyze the effect on FMA and ADL in this subgroup analysis due to significant heterogeneity. There was a significant difference between EA combined with RT and CD versus RT plus CD (WMD 8.03, 95% CI 5.17 to 10.90, P < 0.001) (*Figure 3*). Nine trials [32-35, 37, 39-40, 45-46] used BI or FIM to assess the ADL of 756 patients following PSMD. EA plus RT and CD for the improvement of ADL was better than that of RT plus CD (SMD 1.29, 95% CI 0.55 to 2.02, P < 0.001) (*Figure 4*).

2. EA plus RT versus RT alone

Three trials [48-50] with 214 participants applied FMA to compare the effectiveness of EA plus RT against RT alone. Meta-analyses with a random effects model were performed to evaluate the effect on FMA and ADL in this subgroup analysis owing to statistical heterogeneity. There was a significant difference in these three trials (WMD 20.90, 95% CI 18.61 to 23.19, P < 0.001) (*Figure 3*). In the comparison of EA plus

RT versus RT alone in the three trials, the difference in ADL was obvious (SMD 1.63, 95% CI 1.01 to 2.25, P < 0.001) (*Figure 4*).

Sensitivity analysis

We used the method of removing item-by-item to test the stability of meta-analysis, and the results showed that there had been no obvious change of any of the outcomes. The difference between the random and fixed effects models may have influenced the outcomes. Therefore, we used different statistical models to pool the data for the FMA, FMA-L, ADL and ER. No obvious change in any of the outcomes was found (*Table 2*).

Furthermore, sensitivity analysis was conducted to explore the robustness of our analysis, excluding trials from the overall analysis of high risk of bias due to lack of adequate sequence generation, allocation concealment and blinding of assessors for primary outcomes (*Table 2*). The effects on FMA, ADL and ER were robust, with random and fixed effects models with adequate sequence generation, with the exception of the comparison of EA plus RT versus RT alone and the trial subgroups (*Table 2*).

Publication bias

Thirteen trials [32-41, 48-50] and twelve trials [32-35, 37, 39, 40, 45, 46, 48-50] respectively showed a difference in FMA and ADL between the EA and the non-EA groups. Egger's tests showed that there was publication biases for included trials of FMA (t = 5.21, P < 0.001) or ADL (t = 3.61, P= 0.005). The funnel plots showed that some trials did not lie inside the 95% CI and the distribution was located in unbalance. This may indicate potential publication bias (*Figure 5* and *Figure 6)*.

DISCUSSION

This systematic review included nineteen RCTs with 1,434 participants comparing the effectiveness and safety of EA therapy and non-EA therapy. The meta-analysis of 4 RCTs with 234 patients showed that adjunctive EA was better for improving the motor function of the lower extremity. One RCT with 98 patients demonstrated that added EA was benefit for upper extremity motor control. The meta-analysis of 13 RCTs with 1010 patients indicated that adjunctive EA had more advantage in the recovery of overall motor function. And the pooled results of 12 RCTs with 970 patients revealed that adjunctive EA was benefit for the improvement of ADL. There was not any difference between EA and non-EA for the ER. However, it should be

pointed out that the review included add-on designed trials of EA plus RT and/or CD, which suggests that EA is a complementary therapy for PSMD. Meanwhile, there was insufficient data to assess the safety for EA plus RT, EA plus CD, and EA plus both CD and RT because none of included trials reported adverse events. Considering the pooled effects on FMA and FMA-L with significant heterogeneity, meta-regression analysis was conducted to explain the impact of treatment duration as a covariable. The result showed that the treatment duration was not significant in the meta-regression model. This means the heterogeneity could not be explained by the trial-level's treatment duration.

Some limitations should be cautious. In this review, most of included trials had small sample sizes. 63% of included trials used a high risk of bias method or did not describe the generation of a random sequence. 89% of the trials did not report allocation concealment and had inadequate blinding of outcome assessments. 58% of the trials used inadequately designed statistical methods or did not fully describe the statistical methods. Only two trials [32, 34] were well-designed so as to assess the effect of EA combined with RT for PSMD. Additionally, all trials included in this review were conducted in China and most were published in Chinese, which likely lead to a selection bias, and therefore limits their representativeness.

Although two previous systematic reviews were reported to assess the effects of EA for the treatment of ischemic stroke [17, 18], but both reviews did not focus on evaluating EA as an adjunctive therapy for PSMD of acute stage within 14 days of onset. We still need to gain a clear evidence for PSMD in this important stage which will influence the prognosis of stroke.

Most of the included trials had methodological defects and the funnel plots of FMA and ADL suggested a potential publication bias. These issues potentially lead to low quality of evidence, overreporting of positive results, and underreporting of adverse events. Also, the use of diverse RT as an add-on basis in the included trials makes it difficult to pool data by using a fixed effect model to interpret the clinical significance of EA. Therefore, the potential benefits of EA as an adjunctive therapy for PSMD evident in this review need to be further appraised through well-designed, large-scale, multi-centre RCTs.

Conclusions

EA as a complementary therapy that appears to have clinical benefits in terms of improving the function of extremities, ADL and balance function. However, these

apparent benefits require further evaluation through well-designed multi-centre trials with large sample sizes. The safety of EA combined with RT and/or CD is still uncertain.

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Contributors

J Zhan and Z Wen are responsible for conception and design of this systematic review. The manuscript of this article was drafted by J Zhan, and revised by Z Wen and F Tan. The search strategies were designed by Z Wen and J Zhan. The electronic search was conducted by J Zhan, M Zhou and J Dong. Z Huang manually searched key journals. J Zhan and M Zhou extracted data. The risk of bias was assessed by J Zhan and R Pan, independently. J Zhan and Z Wen analyzed and interpreted the data. Z Wen arbitrated any disagreements in the process of systematic review. All authors approved this manuscript.

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Competing interests: None.

Data sharing statement: No additional data are available.

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Figure Legends

Figure 1 Study flow diagram

Figure 2 Risk of bias assessments of included studies

Figure 3 Forest plot and meta-analysis of FMA (CD, conventional drugs; EA, electroacupuncture; FMA, Fugl-Meyer Assessment Scale; RT, rehabilitation therapy)

Figure 4 Forest plot and meta-analysis of ADL (ADL, activities of daily living; CD, conventional drugs; EA, electroacupuncture; RT, rehabilitation therapy)

Figure 5 Funnel plots illustrating meta-analysis of FMA (CD, conventional drugs; EA, electroacupuncture; FMA, Fugl-Meyer Assessment Scale; RT, rehabilitation therapy; SE, standard error; MD, mean difference)

Figure 6 Funnel plots illustrating meta-analysis of ADL (ADL, activities of daily living; CD, conventional drugs; EA, electroacupuncture; RT, rehabilitation therapy; SE, standard error; MD, mean difference)

Table 1 Characteristics of included trials (BI, Barthel Index; BBS, Berg Balance Scale; C, control group; CD, conventional drugs; d, day; EA, electroacupuncture; ER, effective rate; FMA, Fugl-Meyer Assessment Scale; FMA-U, Fugl-Meyer Assessment Scale for upper extremity; FMA-L, Fugl-Meyer Assessment Scale for lower extremity; FIM, Functional Independence Measure; MCS, muscles contract slightly; NR, not referred; PCT, patient can tolerate; RT, rehabilitation therapy; T, treatment group; w, week)

Table 2 Results of sensitivity analysis (CD, conventional drugs; CI, confidence interval; df, degrees of freedom; EA, electroacupuncture; RT, rehabilitation therapy; WMD, weighted mean difference; # Presented as relative risk; * Presented as standardized mean difference; + Represents the meta-analysis results was not shown in the figures)

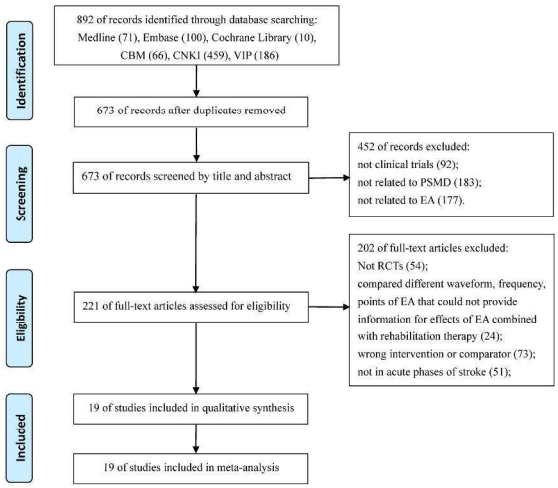

Figure 1 Study flow diagram

312x297mm (300 x 300 DPI)

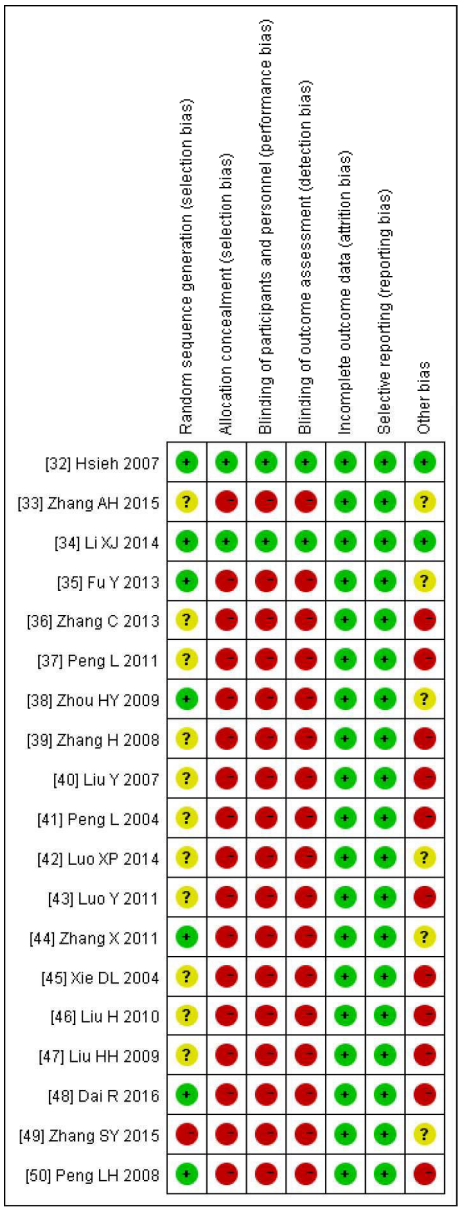

Figure 2 Risk of bias assessments of included studies

121x321mm (300 x 300 DPI)

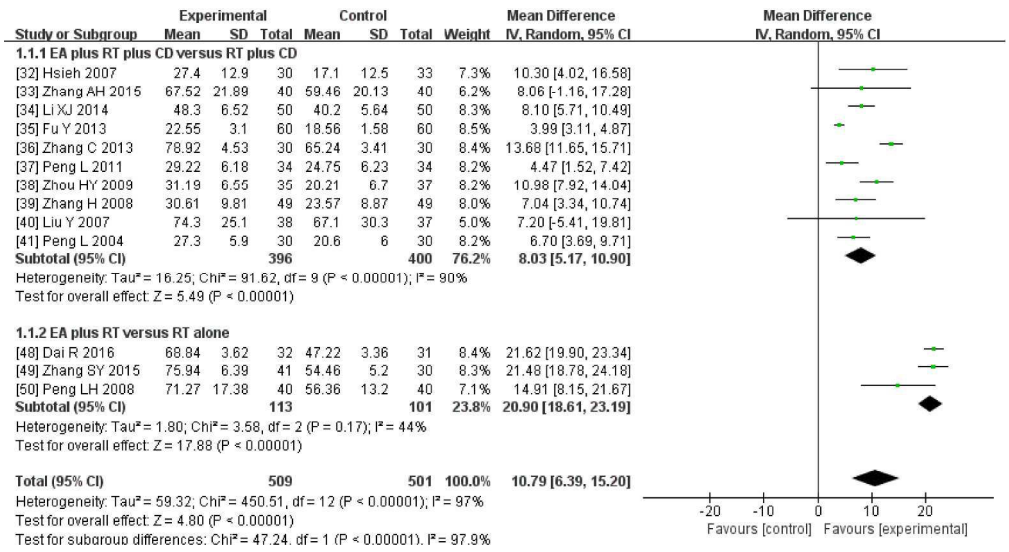

Figure 3 Forest plot and meta-analysis of FMA (CD, conventional drugs; EA, electroacupuncture; FMA, Fugl-Meyer Assessment Scale; RT, rehabilitation therapy)

303x163mm (300 x 300 DPI)

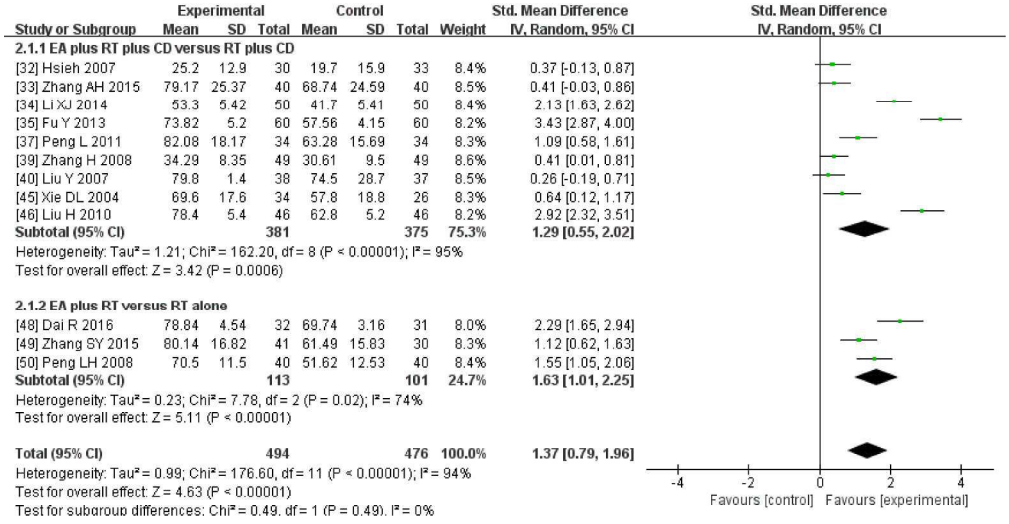

Figure 4 Forest plot and meta-analysis of ADL (ADL, activities of daily living; CD, conventional drugs; EA, electroacupuncture; RT, rehabilitation therapy)

305x158mm (300 x 300 DPI)

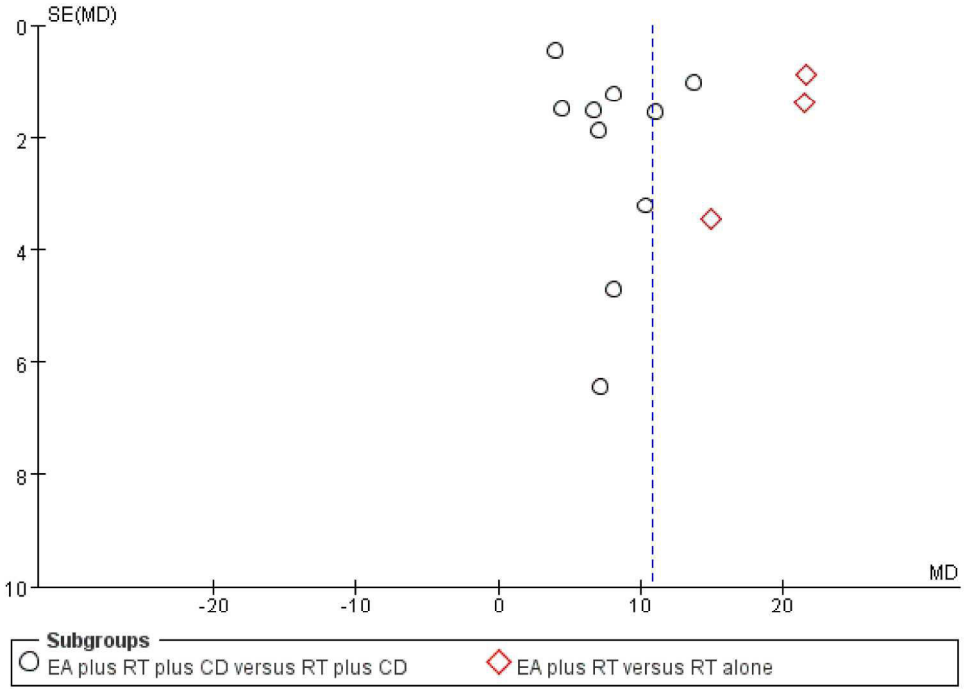

Figure 5 Funnel plots illustrating meta-analysis of FMA (CD, conventional drugs; EA, electroacupuncture; FMA, Fugl-Meyer Assessment Scale; RT, rehabilitation therapy; SE, standard error; MD, mean difference)

211x151mm (300 x 300 DPI)

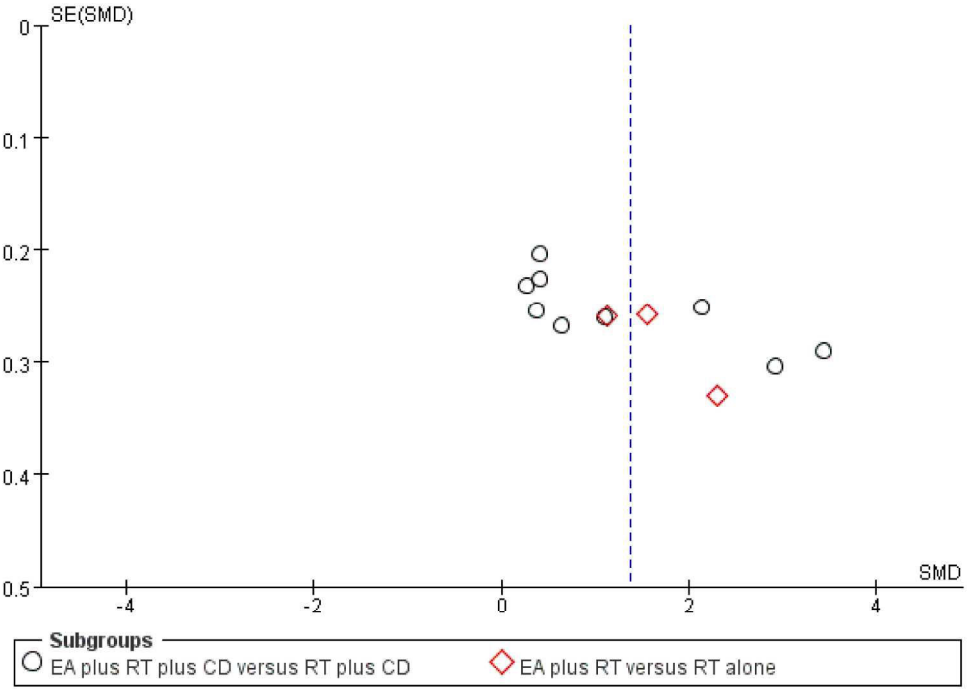

Figure 6 Funnel plots illustrating meta-analysis of ADL (ADL, activities of daily living; CD, conventional drugs; EA, electroacupuncture; RT, rehabilitation therapy; SE, standard error; MD, mean difference)

211x151mm (300 x 300 DPI)

Appendix 1：search in different databases

Embase (Ovid)

1 exp basal ganglia cerebrovascular disease/ (589)
2 cerebrovascular disorders/ (28457)
3 exp intracranial arterial diseases/ (4033)
4 exp intracranial arteriovenous malformations/ (7627)
5 exp intracranial embolism/ and thrombosis/ (341)
6 exp intracranial hemorrhages/ (112672)
7 stroke/ (142289)
8 exp brain infarction/ (63904)
9 exp brain ischemia/ (146312)
10 exp carotid artery diseases/ (58463)
11 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 (435950)
12 (stroke$ or cva or poststroke or post-stroke tw).af. (377113)
13 (cerebrovasc$ or cerebral vascular tw).af. (258529)
14 (cerebral or cerebellar or brain$ or vertebrobasilar tw).af. (2073620)
15 (infarct$ or ish?emi$ or thrombo$ or emboli$ or apoplexy tw).af. (1331966)
16 14 and 15 (190335)
17 (cerebral or brain tw).af. (427090)
18 (haemorrhage or hemorrhage or haematoma or hematoma or bleed$ tw).af. (419811)
19 17 and 18 (51165)
20 exp hemiplegia/ or exp paresis/ (25724)
21 (hempar$ or paretic or paresis or hemipleg$).tw. (27554)
22 Gait Disorders, Neurologic/ (186)
23 11 or 12 or 13 or 16 or 19 or 20 or 21 or 22 (736569)
24 exp Upper Extremity/ (298321)
25 (upper limb$ or upper extremit$ or arm or shoulder or hand or axilla or elbow$ or forearm$ or finger$ or wrist$).tw. (815222)
26 exp Lower Extremity/ (340988)
27 (lower lib$ or lower extremit$ or buttock$ or foot or feet or hip or hips or knee or knees or leg or legs or thigh$ or ankle$ or heel$ or toe or toes).tw. (587073)
28 24 or 25 or 26 or 27 (1454564)
29 acupuncture.mp. or acupuncture/ or auricular acupuncture/ or acupuncture needle/ (39351)
30 electroacupuncture.mp. or electroacupuncture/ (5962)
31 29 or 30 (41050)
32 23 and 28 and 31 (352)
33 controlled clinical trial/ or randomized control.mp. (463239）
34 human/ (18118592)
35 32 and 33 and 34 (100)

Medline (Ovid)

1 ((cerebrovascular disorders/ or exp basal ganglia cerebrovascular disease/ or exp brain ischemia/ or exp carotid artery diseases/ or exp intracranial arterial diseases/ or exp intracranial arteriovenous malformations/ or exp intracranial

embolism/) and thrombosis/) or exp intracranial hemorrhages/ or stroke/ or exp brain infarction/ (174619)
2 (stroke$ or cva or poststroke or post-stroke).tw. (184045)
3 (cerebrovasc$ or cerebral vascular).tw. (48126)
4 (cerebral or cerebellar or brain$ or vertebrobasilar).tw. (1080871)
5 (infarct$ or isch?emi$ or thrombo$ or emboli$ or apoplexy).tw. (802321)
6 4 and 5 (112916)
7 (cerebral or brain).tw. (1000104)
8 (haemorrhage or hemorrhage or haematoma or hematoma or bleed$).tw. (299810)
9 7 and 8 (38074)
10 exp hemiplegia/ or exp paresis/ (18750)
11 (hempar$ or paretic or paresis or hemipleg$).tw. (19881)
12 Gait Disorders, Neurologic/ (5535)
13 1 or 2 or 3 or 6 or 9 or 10 or 11 or 12 (394414)
14 exp Upper Extremity/ (155762)
15 (upper limb$ or upper extremit$ or arm or shoulder or hand or axilla or elbow$ or forearm$ or finger$ or wrist$).tw. (603271)
16 exp Lower Extremity/ (156126)
17 (lower limb$ or lower extremit$ or buttock$ or foot or feet or hip or hips or knee or knees or leg or legs or thigh$ or ankle$ or heel$ or toe or toes).tw. (459027)
18 14 or 15 or 16 or 17 (1120852)
19 Acupuncture Therapy/ or Acupuncture/ or Acupuncture Points/ or Acupuncture, Ear/ or acupuncture.mp. (25001)
20 electroacupuncture.mp. or Electroacupuncture/ (4748)
21 19 or 20 (26152)
22 13 and 18 and 21 (183)
23 Random Allocation/ or Treatment Outcome/ or randomized control.mp. or Clinical Trials as Topic/ (1070629)
24 Humans/ (17431024)
25 22 and 23 and 24 (71)

Cochrane Library

1 "Cerebrovascular Disorders" or "Brain Ischemia" or "Cerebral Hemorrhage" or "Stroke" "Cerebrovascular" or "Cerebrovascular Disorder" or "cva"
2 MeSH descriptor: [Cerebrovascular Disorders] this term only
3 MeSH descriptor: [Brain Ischemia] this term only
4 MeSH descriptor: [Cerebral Hemorrhage] explode all trees
5 MeSH descriptor: [Stroke] explode all trees
6 1 or 2 or 3 or 4 or 5
7 "acupuncture" or "electroacupuncture" or "electroacupuncture":ti,ab,kw (Word variations have been searched)
8 MeSH descriptor: [Acupuncture] explode all trees
9 MeSH descriptor: [Acupuncture Therapy] this term only
10 MeSH descriptor: [Electroacupuncture] explode all trees
11 7 or 8 or 9 or 10
12 6 and 11
13 Upper Extremity:ti,ab,kw (Word variations have been searched)
14 Lower Extremity:ti,ab,kw (Word variations have been searched)
15 MeSH descriptor: [Motor Activity] explode all trees

16 13 or 14 or 15
17 12 and 16
18 human
19 17 and 18
20 randomized control
21 19 and 20

CNKI

主题=脑卒中 or 主题=中风 or 主题=脑梗死 or 主题=脑出血 or 主题=脑血管病 or 主题=脑血管障碍 and 主题=运动障碍 or 主题=运动功能 or 主题=偏瘫 and 主题=电针 and 主题=随机 or 主题=对照 and (模糊匹配)

VIP

(K=卒中 OR K=中风 OR K=脑梗死 OR K=脑出血 OR K=脑血管病 OR K=脑血管障碍) AND K=电针 AND (K=运动功能 OR K=运动障碍 OR K=偏瘫)

CBM

(((((((("卒中"[不加权:扩展]) OR "中风"[不加权:扩展]) OR "脑梗死"[不加权:扩展]) OR "脑出血"[不加权:扩展]) OR "脑血管障碍"[不加权:扩展]) AND "运动障碍"[不加权:扩展]) OR "偏瘫"[不加权:扩展]) AND "电针"[不加权:扩展] AND "随机对照试验"[不加权:扩展]

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	1-2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	4
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	5
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	5
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	5-6
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	6-7
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	7
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	7
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	7
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	7
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	7
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	8

PRISMA 2009 Checklist

Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	8

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	8
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	8
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	8
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	8-11
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	12
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	12
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	12-16
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	12
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	16-17
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	17-18
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	18
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	18-19
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	19

BMJ Open

Electroacupuncture as an adjunctive therapy for motor dysfunction in acute stroke survivors: a systematic review and meta-analyses

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Electroacupuncture as an adjunctive therapy for motor dysfunction in acute stroke survivors: a systematic review and meta-analyses

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ABSTRACT

Objectives: To assess the effectiveness and safety of electroacupuncture (EA) combined with rehabilitation therapy (RT) and/or conventional drugs (CD) for improving post-stroke motor dysfunction (PSMD).

Design: Systematic review and meta-analysis.

Methods: The China National Knowledge Infrastructure, Chinese Biological Medicine Database, Chinese Scientific Journal Database, Cochrane Library, Medline, and Embase were electronically searched from inception to December 2016. The methodological quality of the included trials was assessed using the Cochrane risk of bias assessment tool. Statistical analyses were performed by RevMan Version 5.3 and Stata SE 11.0.

Results: Nineteen trials with 1,434 participants were included for qualitative synthesis and meta-analysis. The methodological quality of the included trials was generally poor. The meta-analysis indicated that the EA group might be benefitting more than the non-EA group in terms of the changes in the Fugl-Meyer Assessment

Scale (FMA) (weighted mean difference [WMD]: 10.79, 95% confidence interval [CI]: 6.39 to 15.20, P < 0.001), FMA for lower extremity (WMD: 5.16, 95% CI: 3.78 to 6.54, P < 0.001), and activities of daily living (standardized mean difference [SMD]: 1.37, 95% CI: 0.79 to 1.96, P < 0.001), respectively. However, there was no difference between EA and non-EA groups in the effective rate (relative risk [RR]: 1.13, 95% CI: 1.00 to 1.27, P = 0.050). Moreover, there were not any reports of side effects due to EA combined with RT and/or CD in the included trials.

Conclusions: This review provides new evidence for the effectiveness of EA combined with RT and/or CD for PSMD. However, its effectiveness and safety should be accompanied by caution owing to methodological weakness and publication bias. Further rigorously designed trials with multicentre and large sample sizes are warranted.

Keywords: motor function; post-stroke; electroacupuncture; RCT; systematic review

PROSPERO registration number: CRD42016037597

Strengths and limitations of this study:

- This systematic review with a comprehensive searching of 3 English and 3 Chinese databases and up to December 2016 was focused especially on assessing the adjunctive effects of EA for motor dysfunction in acute stroke survivors within 14 days.
- Although the included trials in this review have methodological weakness, meta-regression analyses used to explain the potential influence of the duration of treatment was performed and sensitivity analyses with different risk of bias showed that the results were robust.
- Build on the low quality of included trials, we anticipate considerable difficulties in identifying the effectiveness of EA for motor dysfunction in acute stroke.

INTRODUCTION

Stroke is a part of the world's leading causes of death and disability, [1-2] causing heavy burdens to patients' families, communities and healthcare systems. [3] Motor dysfunction is a frequent and widely recognised complication that often follows strokes. Approximately 85% of stroke patients suffer from hemiparesis immediately after their stroke, and between 55% and 75% of stroke survivors may experience incomplete recovery with lingering motor dysfunction. [4] Post-stroke motor dysfunction (PSMD), which has a negative impact on the independence of functional activities, can reduce quality of life (QoL) and limit activities of daily living (ADL). Therefore, effective treatment of PSMD is necessary in order to promote neurological function recovery and to alleviate the social and familial burdens of stroke.

Motor function recovery after stroke not only requires multi-disciplinary treatment team, but also involves various approaches such as conventional drugs (CD), rehabilitation therapy (RT), and nursing care. RT play an important role in comprehensive stroke rehabilitation programs aimed at recovering the function so as to reduce disabilities. Previous studies have demonstrated that the rehabilitation of neurological deficits due to stroke can benefit from RT. [5] However, the effects of current RT for motor dysfunction caused by stroke are not a lotted. [6] Over the last decade, an increasing number of researchers have focused on alternative therapies for stroke rehabilitation such as acupuncture.

In recent years, acupuncture, as one of the best known complementary and alternative medicines, has also been increasingly applied in China and other regions of the world. [7] Electroacupuncture (EA), derived from the integration of traditional acupuncture and modern electrical stimulation, is another kind of acupuncture. EA is generally accepted because it is a relatively straightforward, safe and cheap therapy, compared with other conventional therapies. [8] Additionally, EA has become more and more widely used in clinical practice because of its repeatability and standardization of frequency, intensity and duration. [9,10] After the needles inserting into the acupuncture points, the electrodes are attached to the pairs of needles, then a small electric current, usually pulse frequency of 1-100 Hz and pulse amplitude of 2-3 mA, is passed through the needles into the subject for 15 - 60 min. [11,12] The efficacy of EA with strongly continued stimulation to treat peripheral facial paralysis is preferable to manual acupuncture. [12] Furthermore, EA has been commonly

recommended for use in clinic and research on acupuncture in China and the other countries. [10,13] EA may improve functional recovery after stroke by inhibiting cell apoptosis, regulating miR-9-mediated nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB) downstream pathway and miR-181b / paired-immuno-globulin-like receptor B (PirB) / ras homolog family member A (RhoA) / growth associated protein 43 (GAP43) axis, and dynamically maintaining the balance of matrix metallopeptidase-9 (MMP-9) and tissue inhibitor of metalloproteinase-1 (TIMP-1). [14-16]

A systematic review had suggested that EA was helpful for the treatment of acute ischemic stroke, but its search time was up to June 2013 and not focus on PSMD. [17] Another newly published systematic review had revealed that EA had the potential of reducing spasticity within 180 days poststroke. [18] However, these systematic reviews did not focus specifically on the effects of EA as an adjunctive therapy for motor dysfunction of acute stroke (within 14 days of onset [19]). Up to now, no clear evidence has been found that EA is more effective than non-EA in improving motor dysfunction within 14 days after stroke. Therefore, this study was conducted to assess the effectiveness and safety of EA combined with RT for PSMD in acute period, and to provide the best available evidence of clinical practice. The systematic review was registered on PROSPERO (https://www.crd.york.ac.uk/PROSPERO/) (No. CRD42016037597).

METHODS

Types of studies

We included all randomized controlled trials (RCTs) evaluating the effectiveness and safety of EA combined with RT for PSMD. The comparators or controls in the trials were any other therapy modalities. Also, we only included trials with outcomes measuring changes in motor function. All eligible trials published in Chinese or English were included, regardless of publication status.

Types of participants

We considered trials that included patients in the acute stage being the onset of their first stroke, with motor dysfunction measured by validated instruments or by a decrease in the level of movement activity. Patients were to be more than 18 years old,

and from any ethnicity. Stroke diagnosis had to meet the WHO criteria or the corresponding diagnostic criteria adopted in China, [20-23] and had to be confirmed by computerized tomography or magnetic resonance imaging. Trials involving participants with subarachnoid hemorrhages or cerebrovascular tumors, as well as those in which patients were not acute stroke (within 14 days of onset [19]), were excluded.

Types of interventions

Patients in the experimental groups of the included trials had been treated with EA combined with RT and/or CD, at any frequency, intensity or duration. Patients in the control group of the trials had been treated by other therapies such as CD, RT, sham acupuncture, or no treatments. However, trials which did not provide a detailed description or explanation of intervention, or those that compared different acupoint prescriptions or acupuncture types, were excluded.

Primary outcome assessments

The primary outcome for the system review was motor function. There are many types of motor function scales including but not limited to: the Fugl-Meyer Motor Assessment Scale (FMA); [24] the modified Rankin Scale (mRS); [25] the Motor Assessment Scale (MAS); [26] and Brunnstrom Stages. [27]

Secondary outcome assessments

Secondary outcomes included measures of ADL, such as the Barthel Index (BI)**,** [28] the Functional Independence Measure (FIM)**,** [29] and the response or effective rate (ER). The ER was a standard of therapeutic effect recommended by the Fourth National Cerebrovascular Diseases Conference in China. The ER classified disability of stroke into five grades: cure (the scores of functional deficit were decreased up to 91-100%), significant improvement (the scores of functional deficit were decreased at 46-90%), improvement (the scores of functional deficit were decreased at 18-45%), no improvement (the scores of functional deficit were decreased less than 18%), and deterioration (the scores of functional deficit were increased over 18%). [30] Safety assessments involved adverse events reporting and evaluation of causality. Adverse events as reported in the included trials were also recorded. The time of the outcome assessments was at the end of the intervention phase.

Electronic searches

We electronically searched databases from their respective inceptions up to December 2016. Databases included China National Knowledge Infrastructure (CNKI), Chinese

Biological Medicine Database (CBM), Chinese Scientific Journal Database (VIP), Cochrane Library, Medline and Embase. We combined the PubMed search with the Cochrane highly sensitive search strategy for identifying randomized trials, and adapted the search strategy for searching the other databases.

We also searched other resources in order to identify potentially relevant trials. For example, we screened reference lists of included trials, and contacted trial authors. The detailed search steps are illustrated in supplementary *appendix 1*.

Data extraction and quality assessment

Two review authors (J Zhan and M Zhou) independently scanned the titles and abstracts of articles derived from the search and kept all potentially relevant articles. Then, they retrieved the full texts of these articles, and another two authors (Z Huang and R Pan) independently examined them to confirm that the trials met the inclusion criteria. We also recorded the reasons for exclusion of trials. If the same trial had more than one report, we only kept one originally published version. If necessary, we acquired additional information from trial authors by e-mail or telephone. Moreover, we discussed any disagreements to decide whether a trial should be included or excluded, and if necessary, we consulted with another author (Z Wen).

Two authors (J Zhan and M Zhou) independently extracted information from the included trials. The information was entered into an Excel formatted table (J Zhan) and the accuracy of the information entered was also checked (R Pan). The information extracted was as follows: trial design (e.g. sample size, randomization method, blinding method); participants (e.g. gender, age); the details of intervention; outcomes (primary and secondary outcomes); adverse events; the name of the author, publication year, and so on. Trial selection details are shown in a PRISMA-complied flow chart (*Figure 1*).

Risk of bias assessment in the included studies

Two review authors (J Zhan and R Pan) independently used the risk of bias assessment tool in the *Cochrane Handbook for Systematic Reviews of Interventions* [31] to assess the methodological quality of each included trial. The specific domains were assessed as follows: random sequence generation, allocation sequence concealment, blinding, incomplete outcome data, selective outcome reporting, and other sources of bias. We graded the risk of bias for each domain as is low risk of bias, high risk of bias, or unclear. We settled quality assessment disagreements by discussion with a third reviewer (Z Wen).

Data analysis

We performed all statistical analyses by using RevMan version 5.3 (The Nordic Cochrane Centre, the Cochrane Collaboration 2014) and Stata SE 11.0 (StataCorp LP, College Station, TX, USA). For continuous data, we calculated weighted mean difference (WMD) with corresponding 95% confidence interval (CI). If the outcomes were measured by different scales in the included trials, we calculated standardized mean difference (SMD) with 95% CI instead of WMD. For dichotomous data, we calculated the relative risk (RR) with 95% CI. We tested clinical and statistical heterogeneity among trials by comparing the characteristics of the trials, and used the I-squared statistic to test heterogeneity. If heterogeneity was not significant, we chose a fixed effects model to pool the data; otherwise, we used a random effects model after considering clinical homogeneity. When heterogeneity was substantial, we examined trials for potential explanations, or else conducted a qualitative summary rather than a meta-analysis.

A meta-regression analysis was used to explain the potential trial-level covariates such as the duration of treatment. Subgroup analyses were carried out as follows: EA and RT plus CD compared to RT plus CD; and EA plus RT compared to RT alone. Sensitivity analysis was performed to explore the robustness of our analysis, excluding studies from the overall analysis of high risk of bias due to lack of allocation concealment and blinding of assessors for the primary outcome. If the number of included trials was greater than ten, funnel plots and Egger's test were employed for publication bias analysis.

RESULTS

Trial description

We initially identified 892 relevant articles according to the search strategy while 219 were excluded due to being duplicates from different databases. In total, nineteen trials met the eligibility criteria after being screened by title, abstract or full-text, and were included in meta-analysis (*Figure 1*). We did not find additional trials for this review by examining the reference lists of included trials. All trials were published between 2004 and 2016. One trial [32] was published in English, while the others were all published in Chinese. A total of 1,434 participants were enrolled in these trials. All trials were conducted in China. Sixteen trials [32-47] compared EA plus CD

and RT with CD plus RT. Three trials [48-50] gave EA and RT to the experimental groups, while the control groups only received RT. CD was used according to the Chinese national guidelines, including general supportive care and specialized care such as antiplatelet agents, anticoagulants, fibrinogen-depleting agents, volume expansion and vasodilators. Because the patients enrolled in the trials were all within 14 days after stroke, CD was used similarly in each included trial. Trial characteristics included in this review are shown in *Table 1*.

Table 1 Characteristics of included trials

Study	Sample size	Age (year)	Sex (male/female)	T regimen vs C regimen	Electrical stimulation frequency	Power	Needle retention duration	Treatment duration	Main outcomes
[48] Dai R 2016	T:32 C:31	T:66.4 ± 3.2 C:65.7 ± 4.1	T:18/14 C:17/14	EA+RT vs RT	NR	2 mA	30 min	4 w	FMA, BI
[33] Zhang AH 2015	T:40 C:40	T:60.50 (51 - 69) C:58.75 (47 - 72)	T:22/18 C:24/16	EA+RT+CD vs RT+CD	NR	PCT	30 min	4 - 12 w	FMA ,BI
[49] Zhang SY 2015	T:41 C:30	T:58.5 ± 12.27 C:52.43 ± 12.24	T:24/17 C:17/13	EA+RT vs RT	NR	PCT	20 min	4 w	FMA, BI, ER
[34] Li XJ 2014	T:50 C:50	T:64 ± 5 C:65 ± 4	T:27/23 C:29/21	EA+RT+CD vs RT+CD	15 - 30 Hz	1 - 2 mA	30 min	4 w	FMA, BI , ER
[42] Luo XP 2014	T:30 C:26	T:60.83 ± 9.58 C:62.47 ± 8.72	T:21/9 C:19/7	EA+RT+CD vs RT+CD	NR	PCT	30 min	4 w	FMA-L
[35] Fu Y 2013	T:60 C:60	T:62.05 ± 6.25 C:63.07 ± 5.10	T:37/23 C:36/24	EA+RT+CD vs RT+CD	NR	PCT	30 min	4 w	FMA, BI, BBS
[36] Zhang C 2013	T:30 C:30	60.7 ± 8.6	36/24	EA+RT+CD vs RT+CD	NR	MSC	20 min	20 d	FMA
[37] Peng L 2011	T:34 C:34	55 (37 - 77)	41/27	EA+RT+CD vs RT+CD	NR	PCT	30 min	8 w	FMA, BI
[43] Luo Y 2011	T:30 C:30	55 (37 - 78)	39/21	EA+RT+CD vs RT+CD	NR	PCT	25 min	8 w	FMA-L
[44] Zhang X 2011	T:29 C:29	T:67.14 ± 10.17 C:68.14 ± 10.93	T:16/13 C:14/15	EA+RT+CD vs RT+CD	20 Hz	PCT	30 min	2 w	FMA-L

Table 1 Characteristics of included trials (Continued)

Study	Sample size	Age (year)	Sex (male/female)	T regimen vs C regimen	Electrical stimulation frequency	Power	Needle retention duration	Treatment duration	Main outcomes
[46] Liu H 2010	T:46 C:46	T:65 C:62	T:29/17 C:30/16	EA+RT+CD vs RT+CD	100 Hz	PCT	30 min	4 w	BI
[38] Zhou HY 2009	T:35 C:37	T:63.7 ± 10.5 C:64.5 ± 10.6	T:17/18 C:20/17	EA+RT+CD vs RT+CD	2.7 Hz	PCT	30 min	4 w	FMA
[47] Liu HH 2009	T:49 C:49	55 ± 0.24	T:26/23 C:24/25	EA+RT+CD vs RT+CD	10 - 15Hz	PCT	20 min	8 w	FMA-U
[50] Peng LH 2008	T:40 C:40	58.5 (35 - 78)	48/32	EA+RT vs RT	1.0 - 2.0 Hz	PCT	30 min	6 w	FMA, BI
[39] Zhang H 2008	T:49 C:49	T:51.49 ± 8.35 C:54.73 ± 6.75	T:26/23 C:24/25	EA+RT+CD vs RT+CD	10 - 15 Hz	PCT	20 min	8 w	FMA, BI
[32] Hsieh 2007	T:30 C:33	T:68.8 C:70.7	T:12/18 C:23/10	EA+RT+CD vs RT+CD	3 - 15 Hz	1 - 10 mA	20 min	4 w	FMA, FIM
[40] Liu Y 2007	T:38 C:37	T:59.4 ± 10.2 C:56.4 ± 10.5	T:25/13 C:14/23	EA+RT+CD vs RT+CD	3.3 Hz,	PCT	30 min	20 d	FMA, BI
[41] Peng L 2004	T:30 C:30	55 (37 - 78)	39/21	EA+RT+CD vs RT+CD	NR	PCT	25 min	8 w	FMA
[45] Xie DL 2004	T:34 C:26	T:53.0 ± 9.3 C:56.5 ± 6.4	T:22/12 C:17/9	EA+RT+CD vs RT+CD	2.7 Hz	MCS	20 min	30 - 40 d	FMA-L, BI

Notes. BI, Barthel Index; BBS, Berg Balance Scale; C, control group; CD, conventional drugs; d, day; EA, electroacupuncture; ER, effective rate; FMA, Fugl-Meyer Assessment Scale; FMA-U, Fugl-Meyer Assessment Scale for upper extremity; FMA-L, Fugl-Meyer Assessment Scale for lower extremity; FIM, Functional Independence Measure; MCS, muscles contract slightly; NR, not referred; PCT, patient can tolerate; RT, rehabilitation therapy; T, treatment group; w, week.

Assessing risk of bias in the included trials

In general, the methodological quality of the included trials was poor. In random sequence generation, seven trials [32, 34, 35, 38, 44, 48, 50] used proper generation methods with a low risk of bias, and the random number sequences were produced by either a random number table, computer software or drawing lots. One trial used an incorrect sequence generation method. [49] Eleven trials [33, 36, 37, 39-43, 45-47] did not describe the randomization procedure clearly. Two trials [32, 34] used concealed envelopes, and the other trials did not report allocation concealment. Two trials [32, 34] reported that outcome assessors were blind to group allocation. Two trials [32, 34] mentioned that investigators were unknown for allocation. One trial [32] reported drop-outs and conducted intention-to-treat analyses. In other sources of bias, eleven trials [36, 37, 39-41, 43, 45-48, 50] had a high risk because of inadequate statistical methods. These trials had not described the specific steps and methods of statistical analysis. The results of the assessments are presented in *Figure 2*.

Primary outcomes

1. Fugl-Meyer Assessment Scale (FMA)

The primary outcome, FMA score, was mentioned in thirteen trials with 1,010 patients. [32-41, 48-50] The effect of EA on FMA between the EA and non-EA groups was evaluated by a random effects model, owing to significant heterogeneity. A meta-regression analysis was used to explain the potential covariates. The treatment duration was included as a potential covariable in the meta-regression model because the duration was from 2 to 12 weeks. However, there was no significant differences for the treatment duration in the meta-regression model (adjusted R^2: 0.124, t = -1.57, P = 0.144). FMA score in the EA group increased more than those in the non-EA group, and there was a significant difference (WMD 10.79, 95% CI 6.39 to 15.20, P < 0.001) (*Figure 3*).

2. FMA for upper extremity (FMA-U)

One trial [47] with 98 participants used FMA-U to evaluate the function of upper extremity, and the difference between the EA group and the non-EA group was obvious (P < 0.050).

3. FMA for lower extremity (FMA-L)

The function of the lower extremity was assessed by FMA-L in four trials [42-45] with 234 participants. The effect on FMA-L was analyzed by using a fixed effects model, and there was a significant difference between the EA group and the non-EA

group in the FMA-L (WMD 5.16, 95% CI 3.78 to 6.54, P < 0.001) (*Table 2*). A meta-regression analysis was also carried out to explain the potential impact of the treatment duration. And there was no significance for the treatment duration in the meta-regression model (adjusted R^2: -0.198, t = -0.86, P = 0.482).

Table 2 Results of sensitivity analysis

Study type	Studies, no.	Participants, no		Study heterogeneity				Analysis model	WMD (95% CI)	*p* value
		Experiment group	Control group	Chi^2	df	I^2, %	*p* value			
Fugl-Meyer Assessment scale (FMA)										
EA versus non EA	13	509	501	450.51	12	97	<0.001	random	10.79 (6.39, 15.20)	<0.001
								fixed[+]	8.97 (8.35, 9.58)	<0.001
EA plus RT plus CD versus RT plus CD	10	396	400	91.62	9	90	<0.001	random	8.03 (5.17, 10.90)	<0.001
								fixed[+]	6.13 (5.45, 6.82)	<0.001
EA plus RT versus RT alone	3	113	101	3.58	2	44	0.170	random	20.90 (18.61, 23.19)	<0.001
								fixed[+]	21.29 (19.86, 22.71)	<0.001
FMA for lower extremity (FMA-L)										
EA versus non EA	4	123	111	1.76	3	0	0.620	random[+]	5.16 (3.78, 6.54)	<0.001
								fixed	5.16 (3.78, 6.54)	<0.001
Activities of daily living (ADL)										
EA versus non EA	12	494	476	176.60	11	94	<0.001	random	1.37 (0.79, 1.96)[*]	<0.001
								fixed[+]	1.20 (1.06, 1.35)[*]	<0.001
EA plus RT plus CD versus RT plus CD	9	381	375	162.20	8	95	<0.001	random	1.29 (0.55, 2.02)[*]	<0.001
								fixed[+]	1.10 (0.94, 1.27)[*]	<0.001
EA plus RT versus RT alone	3	113	101	7.78	2	74	0.020	random	1.63 (1.01, 2.25)[*]	<0.001
								fixed[+]	1.57 (1.25, 1.88)[*]	<0.001

Table 2 Results of sensitivity analysis (Continued)

Study type	Studies, no.	Participants, no		Study heterogeneity				Analysis model	WMD (95% CI)	*p* value
		Experiment group	Control group	Chi^2	df	I^2, %	*p* value			
Response or effective rate (ER)										
EA versus non EA	2	91	80	2.80	1	64	0.090	random+	1.13 (0.90, 1.42)#	0.290
								fixed+	1.13 (1.00, 1.27)#	0.050
Trials with adequate sequence generation: FMA										
EA versus non EA	6	247	251	327.63	5	98	<0.001	random+	11.61 (4.17, 19.04)	0.002
								fixed+	7.98 (7.26, 8.69)	<0.001
Trials with adequate concealed allocation and blinding of assessors: FMA										
EA versus non EA	2	80	83	0.41	1	0	0.520	random+	8.38 (6.14, 10.61)	<0.001
								fixed+	8.38 (6.14, 10.61)	<0.001

Notes. CD, conventional drugs; CI, confidence interval; df, degrees of freedom; EA, electroacupuncture; RT, rehabilitation therapy; WMD, weighted mean difference.

Presented as relative risk (RR); * Presented as standardized mean difference (SMD); + Represents the meta-analysis results was not shown in the figures.

Secondary outcomes

1. Activities of daily living (ADL)

The effect of EA on the ADL was analyzed by using a random effects model, due to significant heterogeneity in twelve trials [32-35, 37, 39, 40, 45, 46, 48-50] with 970 participants. We calculated SMD with 95% CI as the outcomes were measured by different scales (FIM and BI) in the included trials. The improvement of ADL in the EA group was better than that in the non-EA group (SMD 1.37, 95% CI 0.79 to 1.96, P < 0.001) (*Figure 4*).

2. Response or effective rate (ER)

Two trials [34, 49] with a total of 171 participants showed that there was no significant difference between EA and non-EA groups on the ER (RR 1.13, 95% CI 1.00 to 1.27, P = 0.050; fixed effects model) (*Table 2*).

3. Berg Balance Scale (BBS)

BBS was assessed in one trial [35] with 120 participants. The improvement of BBS in the EA group was preferable to that in the non-EA group (P < 0.050).

Safety assessment

None of included trials mentioned adverse events reporting owing to both EA combined with RT and/or CD and RT and/or CD alone.

Subgroup analysis

1. EA plus RT and CD versus RT plus CD

Ten trials [32-41] used FMA to measure the motor function of 796 participants with PSMD. A random effects model was used to analyze the effect on FMA and ADL in this subgroup analysis due to significant heterogeneity. There was a significant difference between EA combined with RT and CD versus RT plus CD (WMD 8.03, 95% CI 5.17 to 10.90, P < 0.001) (*Figure 3*). Nine trials [32-35, 37, 39-40, 45-46] used BI or FIM to measure the ADL of 756 patients following PSMD. EA plus RT and CD for the improvement of ADL was better than that of RT plus CD (SMD 1.29, 95% CI 0.55 to 2.02, P < 0.001) (*Figure 4*).

2. EA plus RT versus RT alone

Three trials [48-50] with 214 participants applied FMA to compare the effectiveness of EA plus RT against RT alone. Meta-analyses with a random effects model were performed to evaluate the effect on FMA and ADL in this subgroup analysis owing to statistical heterogeneity. There was a significant difference in these three trials (WMD 20.90, 95% CI 18.61 to 23.19, P < 0.001) (*Figure 3*). In comparison of EA plus RT

versus RT alone in the three trials, the difference in ADL was obvious (SMD 1.63, 95% CI 1.01 to 2.25, P < 0.001) (*Figure 4*).

Sensitivity analysis

We used the method of removing item-by-item to test the stability of meta-analysis, and the results showed that there had been no noticeable change of any of the outcomes. The difference between the random and fixed effects models may have influenced the outcomes. Therefore, we used different statistical models to pool the data for the FMA, FMA-L, ADL and ER. No observable change in any of the outcomes was found (*Table 2*).

Furthermore, sensitivity analysis was carried out to explore the robustness of our analysis, excluding trials from the overall analysis of high risk of bias due to lack of adequate sequence generation, allocation concealment and blinding of assessors for primary outcomes (*Table 2*). The effects on FMA, ADL and ER were robust, with random and fixed effects models with adequate sequence generation, with the exception of the comparison of EA plus RT versus RT alone and the trial subgroups (*Table 2*).

Publication bias

Thirteen trials [32-41, 48-50] and twelve trials [32-35, 37, 39, 40, 45, 46, 48-50] respectively showed a difference in FMA and ADL between the EA and the non-EA groups. Egger's tests showed that there were publication biases for included trials of FMA (t = 5.21, P < 0.001) or ADL (t = 3.61, P= 0.005). The funnel plots showed that some trials did not lie inside the 95% CI and the distribution was placed in unbalance. This may indicate potential publication bias (*Figure 5* and *Figure 6)*.

DISCUSSION

This systematic review included nineteen RCTs with 1,434 participants comparing the effectiveness and safety of EA therapy and non-EA therapy. The meta-analysis of 4 RCTs with 234 patients showed that adjunctive EA was better for improving the motor function of the lower extremity. One RCT with 98 patients demonstrated that added EA was benefit for upper extremity motor control. The meta-analysis of 13 RCTs with 1010 patients indicated that adjunctive EA had more advantage in the recovery of overall motor function. And the pooled results of 12 RCTs with 970 patients revealed that adjunctive EA was benefit for the improvement of ADL. There was no any difference between EA and non-EA for the ER. However, it should be

noted that the review included add-on designed trials of EA plus RT and/or CD, which suggests that EA is a complementary therapy for PSMD. Meanwhile, there was insufficient data to assess the safety for EA plus RT, EA plus CD, and EA plus both CD and RT because none of included trials reported adverse events. Considering the pooled effects on FMA and FMA-L with significant heterogeneity, meta-regression analysis was conducted to explain the impact of treatment duration as a covariable. The result showed that the treatment duration was not significant in the meta-regression model. This means the heterogeneity could not be explained by the trial-level's treatment duration.

Some limitations should be cautious. In this review, most of included trials had small sample sizes. 63% of included trials used a high risk of bias method or did not describe the generation of a random sequence. 89% of the trials did not report allocation concealment and had inadequate blinding of outcome assessments. 58% of the trials used inadequately designed statistical methods or did not fully describe the statistical methods. Only two trials [32, 34] were well-designed so as to assess the effect of EA combined with RT for PSMD. Additionally, all trials included in this review were conducted in China and most were published in Chinese, which likely lead to a selection bias, and therefore limits their representativeness.

Two previous systematic reviews were reported to assess the effects of EA for the treatment of ischemic stroke [17, 18]. However, there were noticeable differences in the study characteristics of participants, comparison and outcomes, and both two reviews did not focus on evaluating EA as an adjunctive therapy for PSMD of acute stage within 14 days of onset. We still need to gain a clear evidence for PSMD in this critical stage which will influence the prognosis of stroke.

Most of the included trials had methodological defects and the funnel plots of FMA and ADL suggested a potential publication bias. These issues potentially lead to low quality of evidence, overreporting of positive results, and underreporting of adverse events. Also, the use of diverse RT as an add-on basis in the included trials makes it difficult to pool data by using a fixed effect model to interpret the clinical significance of EA. Therefore, the potential benefits of EA as an adjunctive therapy for PSMD evident in this review need to be further appraised through well-designed, large-scale, multicentre RCTs.

Conclusions

EA as a complementary therapy that seems to have clinical benefits in terms of

improving the function of extremities, ADL and balance function. However, these apparent benefits require further evaluation through well-designed multicentre trials with large sample sizes. The safety of EA combined with RT and/or CD is still uncertain.

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Contributors

J Zhan and Z Wen are responsible for conception and design of this systematic review. The manuscript of this article was drafted by J Zhan, and revised by Z Wen and F Tan. The search strategies were designed by Z Wen and J Zhan. The electronic search was conducted by J Zhan, M Zhou and J Dong. Z Huang manually searched key journals. J Zhan and M Zhou extracted data. The risk of bias was assessed by J Zhan and R Pan, independently. J Zhan and Z Wen analyzed and interpreted the data. Z Wen arbitrated any disagreements in the process of systematic review. All authors approved this manuscript.

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Competing interests: None.

Data sharing statement: No additional data are available.

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Figure Legends

Figure 1 Study flow diagram

Figure 2 Risk of bias assessments of included studies

Figure 3 Forest plot and meta-analysis of FMA (CD, conventional drugs; EA, electroacupuncture; FMA, Fugl-Meyer Assessment Scale; RT, rehabilitation therapy)

Figure 4 Forest plot and meta-analysis of ADL (ADL, activities of daily living; CD, conventional drugs; EA, electroacupuncture; RT, rehabilitation therapy)

Figure 5 Funnel plots illustrating meta-analysis of FMA (CD, conventional drugs; EA, electroacupuncture; FMA, Fugl-Meyer Assessment Scale; RT, rehabilitation therapy; SE, standard error; MD, mean difference)

Figure 6 Funnel plots illustrating meta-analysis of ADL (ADL, activities of daily living; CD, conventional drugs; EA, electroacupuncture; RT, rehabilitation therapy; SE, standard error; MD, mean difference)

Table 1 Characteristics of included trials (BI, Barthel Index; BBS, Berg Balance Scale; C, control group; CD, conventional drugs; d, day; EA, electroacupuncture; ER, effective rate; FMA, Fugl-Meyer Assessment Scale; FMA-U, Fugl-Meyer Assessment Scale for upper extremity; FMA-L, Fugl-Meyer Assessment Scale for lower extremity; FIM, Functional Independence Measure; MCS, muscles contract slightly; NR, not referred; PCT, patient can tolerate; RT, rehabilitation therapy; T, treatment group; w, week)

Table 2 Results of sensitivity analysis (CD, conventional drugs; CI, confidence interval; df, degrees of freedom; EA, electroacupuncture; RT, rehabilitation therapy; WMD, weighted mean difference; # Presented as relative risk; * Presented as standardized mean difference; + Represents the meta-analysis results was not shown in the figures)

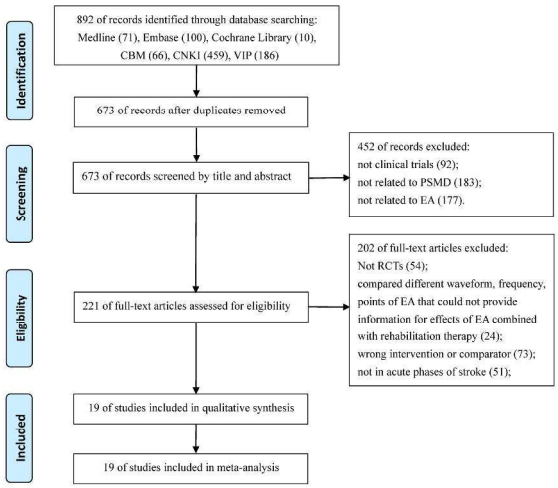

Figure 1 Study flow diagram

312x297mm (300 x 300 DPI)

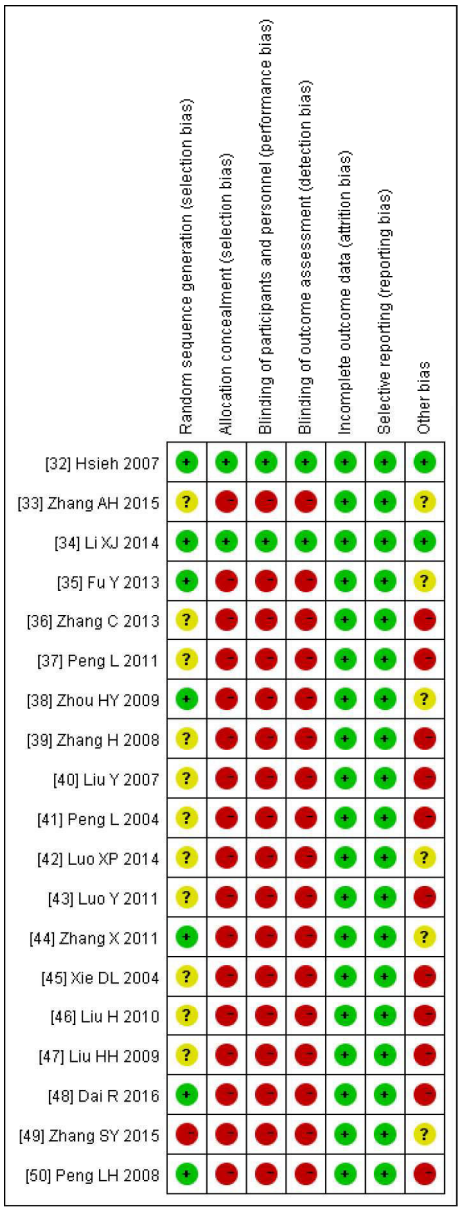

Figure 2 Risk of bias assessments of included studies

121x321mm (300 x 300 DPI)

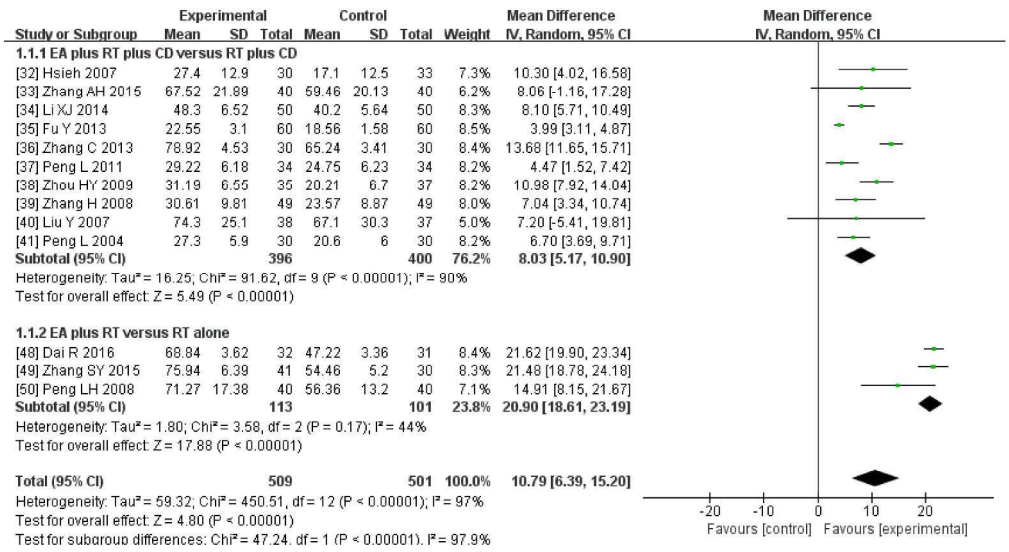

Figure 3 Forest plot and meta-analysis of FMA (CD, conventional drugs; EA, electroacupuncture; FMA, Fugl-Meyer Assessment Scale; RT, rehabilitation therapy)

303x163mm (300 x 300 DPI)

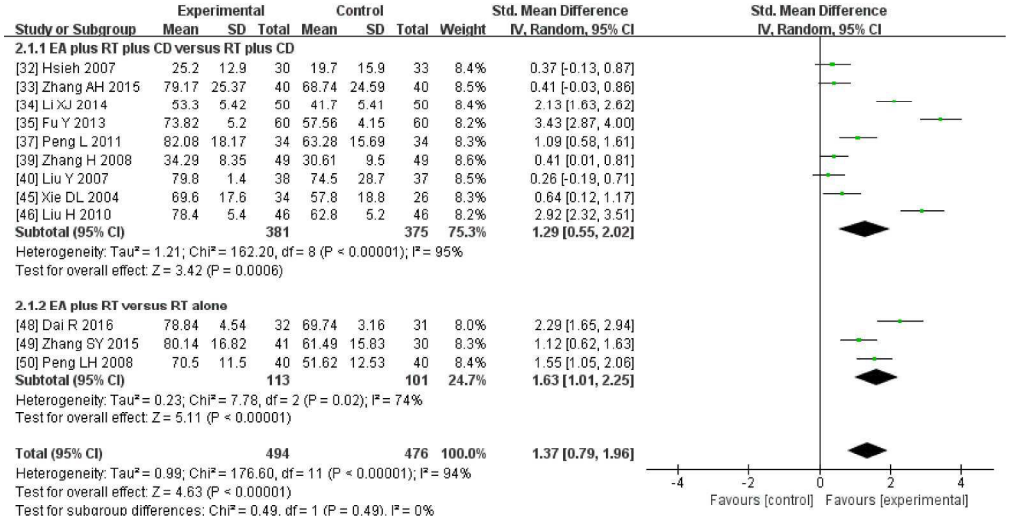

Figure 4 Forest plot and meta-analysis of ADL (ADL, activities of daily living; CD, conventional drugs; EA, electroacupuncture; RT, rehabilitation therapy)

305x158mm (300 x 300 DPI)

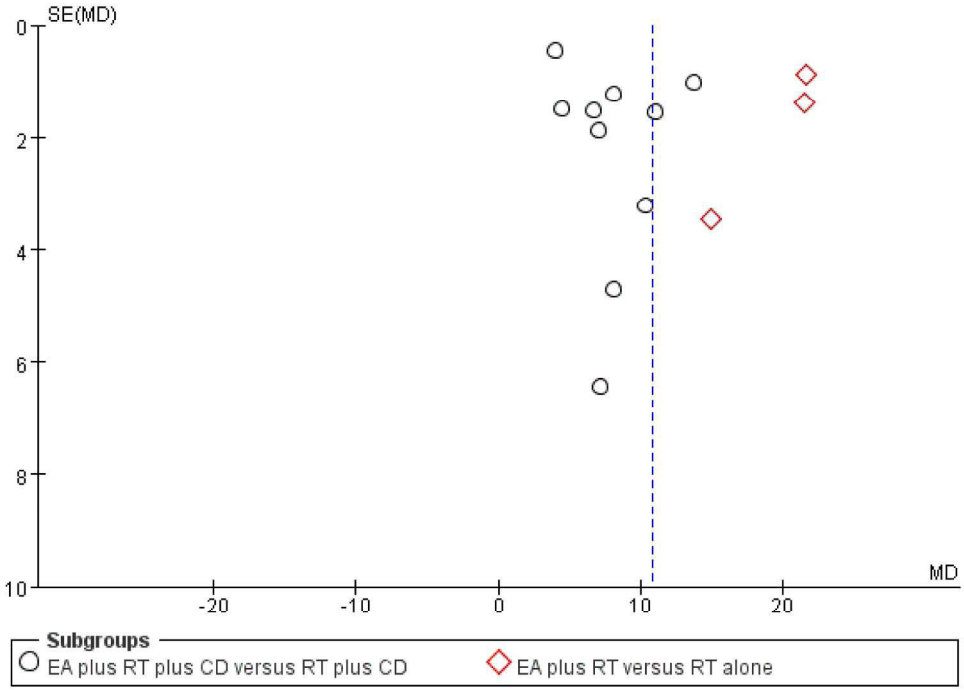

Figure 5 Funnel plots illustrating meta-analysis of FMA (CD, conventional drugs; EA, electroacupuncture; FMA, Fugl-Meyer Assessment Scale; RT, rehabilitation therapy; SE, standard error; MD, mean difference)

211x151mm (300 x 300 DPI)

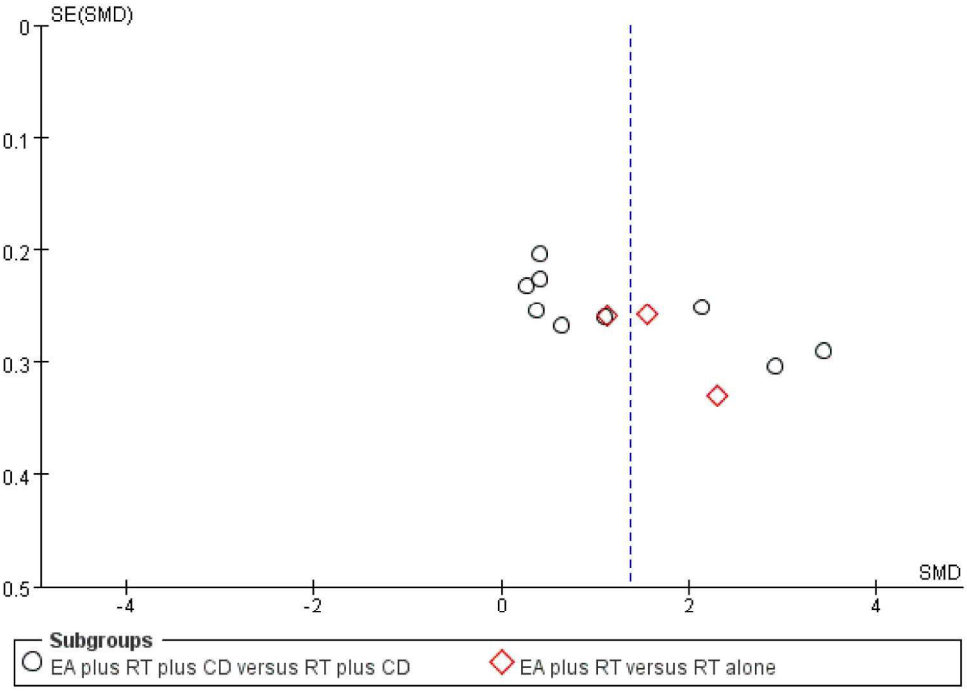

Figure 6 Funnel plots illustrating meta-analysis of ADL (ADL, activities of daily living; CD, conventional drugs; EA, electroacupuncture; RT, rehabilitation therapy; SE, standard error; MD, mean difference)

211x151mm (300 x 300 DPI)

Appendix 1：search in different databases

Embase (Ovid)

1 exp basal ganglia cerebrovascular disease/ (589)
2 cerebrovascular disorders/ (28457)
3 exp intracranial arterial diseases/ (4033)
4 exp intracranial arteriovenous malformations/ (7627)
5 exp intracranial embolism/ and thrombosis/ (341)
6 exp intracranial hemorrhages/ (112672)
7 stroke/ (142289)
8 exp brain infarction/ (63904)
9 exp brain ischemia/ (146312)
10 exp carotid artery diseases/ (58463)
11 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 (435950)
12 (stroke$ or cva or poststroke or post-stroke tw).af. (377113)
13 (cerebrovasc$ or cerebral vascular tw).af. (258529)
14 (cerebral or cerebellar or brain$ or vertebrobasilar tw).af. (2073620)
15 (infarct$ or ish?emi$ or thrombo$ or emboli$ or apoplexy tw).af. (1331966)
16 14 and 15 (190335)
17 (cerebral or brain tw).af. (427090)
18 (haemorrhage or hemorrhage or haematoma or hematoma or bleed$ tw).af. (419811)
19 17 and 18 (51165)
20 exp hemiplegia/ or exp paresis/ (25724)
21 (hempar$ or paretic or paresis or hemipleg$).tw. (27554)
22 Gait Disorders, Neurologic/ (186)
23 11 or 12 or 13 or 16 or 19 or 20 or 21 or 22 (736569)
24 exp Upper Extremity/ (298321)
25 (upper limb$ or upper extremit$ or arm or shoulder or hand or axilla or elbow$ or forearm$ or finger$ or wrist$).tw. (815222)
26 exp Lower Extremity/ (340988)
27 (lower lib$ or lower extremit$ or buttock$ or foot or feet or hip or hips or knee or knees or leg or legs or thigh$ or ankle$ or heel$ or toe or toes).tw. (587073)
28 24 or 25 or 26 or 27 (1454564)
29 acupuncture.mp. or acupuncture/ or auricular acupuncture/ or acupuncture needle/ (39351)
30 electroacupuncture.mp. or electroacupuncture/ (5962)
31 29 or 30 (41050)
32 23 and 28 and 31 (352)
33 controlled clinical trial/ or randomized control.mp. (463239）
34 human/ (18118592)
35 32 and 33 and 34 (100)

Medline (Ovid)

1 ((cerebrovascular disorders/ or exp basal ganglia cerebrovascular disease/ or exp brain ischemia/ or exp carotid artery diseases/ or exp intracranial arterial diseases/ or exp intracranial arteriovenous malformations/ or exp intracranial

embolism/) and thrombosis/) or exp intracranial hemorrhages/ or stroke/ or exp brain infarction/ (174619)
2 (stroke$ or cva or poststroke or post-stroke).tw. (184045)
3 (cerebrovasc$ or cerebral vascular).tw. (48126)
4 (cerebral or cerebellar or brain$ or vertebrobasilar).tw. (1080871)
5 (infarct$ or isch?emi$ or thrombo$ or emboli$ or apoplexy).tw. (802321)
6 4 and 5 (112916)
7 (cerebral or brain).tw. (1000104)
8 (haemorrhage or hemorrhage or haematoma or hematoma or bleed$).tw. (299810)
9 7 and 8 (38074)
10 exp hemiplegia/ or exp paresis/ (18750)
11 (hempar$ or paretic or paresis or hemipleg$).tw. (19881)
12 Gait Disorders, Neurologic/ (5535)
13 1 or 2 or 3 or 6 or 9 or 10 or 11 or 12 (394414)
14 exp Upper Extremity/ (155762)
15 (upper limb$ or upper extremit$ or arm or shoulder or hand or axilla or elbow$ or forearm$ or finger$ or wrist$).tw. (603271)
16 exp Lower Extremity/ (156126)
17 (lower limb$ or lower extremit$ or buttock$ or foot or feet or hip or hips or knee or knees or leg or legs or thigh$ or ankle$ or heel$ or toe or toes).tw. (459027)
18 14 or 15 or 16 or 17 (1120852)
19 Acupuncture Therapy/ or Acupuncture/ or Acupuncture Points/ or Acupuncture, Ear/ or acupuncture.mp. (25001)
20 electroacupuncture.mp. or Electroacupuncture/ (4748)
21 19 or 20 (26152)
22 13 and 18 and 21 (183)
23 Random Allocation/ or Treatment Outcome/ or randomized control.mp. or Clinical Trials as Topic/ (1070629)
24 Humans/ (17431024)
25 22 and 23 and 24 (71)

Cochrane Library

1 "Cerebrovascular Disorders" or "Brain Ischemia" or "Cerebral Hemorrhage" or "Stroke" "Cerebrovascular" or "Cerebrovascular Disorder" or "cva"
2 MeSH descriptor: [Cerebrovascular Disorders] this term only
3 MeSH descriptor: [Brain Ischemia] this term only
4 MeSH descriptor: [Cerebral Hemorrhage] explode all trees
5 MeSH descriptor: [Stroke] explode all trees
6 1 or 2 or 3 or 4 or 5
7 "acupuncture" or "electroacupuncture" or "electroacupuncture":ti,ab,kw (Word variations have been searched)
8 MeSH descriptor: [Acupuncture] explode all trees
9 MeSH descriptor: [Acupuncture Therapy] this term only
10 MeSH descriptor: [Electroacupuncture] explode all trees
11 7 or 8 or 9 or 10
12 6 and 11
13 Upper Extremity:ti,ab,kw (Word variations have been searched)
14 Lower Extremity:ti,ab,kw (Word variations have been searched)
15 MeSH descriptor: [Motor Activity] explode all trees

16 13 or 14 or 15
17 12 and 16
18 human
19 17 and 18
20 randomized control
21 19 and 20

CNKI

主题=脑卒中 or 主题=中风 or 主题=脑梗死 or 主题=脑出血 or 主题=脑血管病 or 主题=脑血管障碍 and 主题=运动障碍 or 主题=运动功能 or 主题=偏瘫 and 主题=电针 and 主题=随机 or 主题=对照 and (模糊匹配)

VIP

(K=卒中 OR K=中风 OR K=脑梗死 OR K=脑出血 OR K=脑血管病 OR K=脑血管障碍) AND K=电针 AND (K=运动功能 OR K=运动障碍 OR K=偏瘫)

CBM

(((((((("卒中"[不加权:扩展]) OR "中风"[不加权:扩展]) OR "脑梗死"[不加权:扩展]) OR "脑出血"[不加权:扩展]) OR "脑血管障碍"[不加权:扩展]) AND "运动障碍"[不加权:扩展]) OR "偏瘫"[不加权:扩展]) AND "电针"[不加权:扩展] AND "随机对照试验"[不加权:扩展]

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	1-2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	4
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	5
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	5
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	5-6
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	6-7
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	7
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	7
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	7
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	7
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	7
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	8

PRISMA 2009 Checklist

Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	8

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	8
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	8
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	8
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	8-11
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	12
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	12
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	12-16
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	12
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	16-17
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	17-18
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	18
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	18-19
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	19