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Efficacy of acupuncture in the treatment of limb dyskinesia after stroke: a systematic review and meta-analysis

Y.-X. TAO[1], Y.-H. WU[2], G.-Q. ZHU[2], M. WANG[3]

[1]Department of Cardiovascular Medicine, The First Affiliated Hospital of Guizhou University of Traditional Chinese Medicine, Guiyang, China
[2]Department of Neurology, The First Affiliated Hospital of Guizhou University of Traditional Chinese Medicine, Guiyang, China
[3]Department of Cosmetic Dermatology, Ximei Beauty Medical Clinic, Guiyang, China

Abstract. – OBJECTIVE: This meta-analysis was performed to investigate the effectiveness of acupuncture in post-stroke limb movement disorders.

MATERIALS AND METHODS: **An electronic search of databases including MEDLINE/PubMed, Web of Science, the Cochrane database, EMBASE, CBM, CNKI, WanFang, and VIP was performed to collect randomized controlled clinical studies on acupuncture administered for post-stroke dyskinesia from inception to April 2023. Data including baseline information, Fugl-Meyer Assessment (FMA) scores, and Barthel Index (BI) were included and analyzed using the meta package in R language.**

RESULTS: **After searching and screening, 17 pieces of literature involving 1,928 participants were included, with 962 participants in the control group and 966 in the study group. Results from the included studies suggested significant benefits provided by acupuncture to improve FMA scores and BI. In specific, incorporation of acupuncture in the treatment of post-stroke limb movement disorders significantly reduced the overall FMA scores of patients by 3.45 (95% CI: 0.22, 6.69) points, the upper extremity FMA scores by 3.63 (95% CI: 0.64, 6.62) points, the lower extremity FMA scores by 3.56 (95% CI: 1.78, 5.35) points, and BI by 7.75 (95% CI: 3.35, 12.16) points.**

CONCLUSIONS: **Acupuncture as an adjunct to the management of post-stroke limb movement disorders contributes significantly to enhancing the motor function and quality of life of patients. However, the evidence of this study is compromised by the limited quantity of the included randomized controlled trials (RCTs) and the mediocre methodological quality. Therefore, high-quality randomized controlled trials are required to validate the benefits of acupuncture on the motor function of patients with post-stroke limb movement disorders.**

Key Words:
Effectiveness, Acupuncture, Post-stroke, Limb movement disorders, Systematic review, Meta-analysis.

Introduction

Stroke is a common neurological disease and the leading cause of death across the world. Its prevalence and mortality have also been on the rise due to population aging[1]. Disabling symptoms of limb movement disorders, including limb muscle weakness, spasticity, twitching, and pain, are frequently observed after stroke, causing a heavy life and economic burden to society and families[2]. The prevalence of post-stroke spasticity in the first year ranges from 17% to 43%, with the involvement of both upper and lower extremities reported in approximately two-thirds of patients with spasticity[3]. Furthermore, comorbidity of spasticity and muscle weakness will lead to disabling motor deficits and complex complications such as muscle contractures, motor dysfunction, and spastic pain, which severely compromise the quality of life of patients[4].

Post-stroke rehabilitation aims to provide functional recovery and improve the quality of life of patients through physical therapy, muscle movement training, speech therapy, and stimulation therapy[5]. As a non-pharmacological treatment, acupuncture has been widely used as an important adjunctive treatment in post-stroke rehabilitation[6]. Moreover, previous research[7] has confirmed the effectiveness of novel acupuncture modalities such as electroacupuncture in memory and motor improvement of patients with stroke. Evidence[8] has suggested that acupuncture promotes regeneration and repair of nerve cells, increases blood flow and oxygen supply, and reduces symptoms such as pain and spasticity. Moreover, proactive acupuncture prior to muscle spasms in hemiplegic limbs has been shown to reduce the incidence of limb spasticity after stroke effectively[9].

Corresponding Authors: Yuanhua Wu, MD; e-mail: shishangwunanshi22@163.com; Guangqi Zhu, MD; e-mail: zhuguangqii@163.com

The main factors that determine the efficacy of acupuncture are acupoint selection and acupuncture technique. Most previous studies[10] have focused primarily on the selection of acupuncture points, striving to identify the most effective anti-spasticity acupoints or combinations of acupoints. Nonetheless, current research findings are inconsistent regarding the effectiveness of acupuncture in post-stroke rehabilitation. To this end, this meta-analysis was performed to investigate the effectiveness of acupuncture in post-stroke limb movement disorders.

Materials and Methods

Study Design

This meta-analysis follows the guidelines provided in the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) and proceeds based on the PICO principles for study design. P-Participants/population: participants were eligible for clinical diagnosis of stroke with movement disorders, without restriction of age, gender, and ethnicity. I- intervention(s): the study group was treated with acupuncture based on the treatment to the control group, without the restriction of acupuncture points; C- Comparator(s)/control: the control group, which did not receive acupuncture treatment, was not limited to rehabilitation treatment modalities; O- Outcome(s): the main outcome indicators included Fugl-Meyer Assessment (FMA) and Barthel Index (BI).

Literature Search Strategy

An electronic search of databases, including MEDLINE/PubMed, Web of Science, the Cochrane database, EMBASE, CBM, CNKI, WanFang, and VIP, was performed to collect randomized controlled clinical studies on acupuncture administered for post-stroke dyskinesia from inception to April 2023. Medical Subject Headings (MeSH) and non-MeSH phrases were used, including acupuncture, stroke, stroke, cerebrovascular accident, movement disorders, limb disorders, hemiplegia, Fugl-Meyer Assessment, and their corresponding English keywords, and the search language was limited to Chinese and English, where Chinese studies were enrolled only from Chinese core journals. Taking the Pubmed database as an example, the detailed search strategy is shown in Table I.

Inclusion and Exclusion Criteria

Inclusion criteria: 1) Patients presented with limb movement disorders after stroke, regardless of the stroke subtype. 2) Prospective randomized controlled study with comparable baseline information. 3) At least two treatment modalities were included, where acupuncture was only adopted in the study group, with treatment duration and other treatments being consistent between the two groups; there were no restrictions on acupuncture points, depth, or technique. 3) At least one of FMA and BI was used for outcome assessment, without restrictions on age, gender, duration of disease, and treatment site.

Exclusion criteria: 1) the number of patients in a single group was less than 10 or reported on a case-by-case basis. 2) Unspecified time of intervention and time of detection of outcome indicators; 3) Studies comparing the efficacy between different acupuncture modalities. (4) Some essential data were unavailable in the text and not obtained within 2 weeks after contacting the author.

Literature Screening and Quality Evaluation

Two investigators independently screened and extracted the study data. Data were extracted using standardized forms with data entries including baseline information, study characteristics, participants' characteristics, intervention characteristics, and outcomes. Discrepancies in data extraction were resolved through discussions with a third investigator. Should data be incomplete or other problems be encountered during data extraction, we contacted the authors by phone or email for additional information. Each eligible trial was assigned a study ID in the following

Table I. Literature search strategy for PubMed.

Search	Query
#1	("stroke" [Title/Abstract]) OR ("cerebral hemorrhage" [Title/Abstract]) OR ("Cerebral infarction" [Title/Abstract])
#2	("acupuncture" [Title/Abstract]) OR ("needle" [Title/Abstract])
#3	("motor" [Title/Abstract]) OR ("movement" [Title/Abstract]) OR ("hemiplegia" [Title/Abstract]) OR ("paralysis" [Title/Abstract])
#4	#1 and #2 and #3

format: first author's name + year of publication (e.g., Ying Shen 2022). This study used the FMA score as the primary endpoint and BI as a secondary endpoint, and the extracted data included baseline data, post-treatment data, and their difference values. The quality of the literature was evaluated using the Risk of Bias tool provided in the Cochrane Handbook for Systematic Reviews of Interventions[11]. This tool assesses the quality of the literature in terms of random sequence generation, concealment of random assignment, investigator-participant blinding, incompleteness and selective reporting of outcome data, relevance of the outcome data obtained, and other potential sources of bias. For each aspect, the study quality assessment can be classified as "low risk", "uncertain risk", and "high risk".

Statistical Analysis

In this study, the R language meta-package (The R Foundation for Statistical Computing, Vienna, Austria) was used to statistically analyze the data and plot the corresponding graphics. Mean difference (MD) and standardized mean difference (SMD) were employed to summarize the results, and the corresponding 95% confidence intervals (CI) were calculated. The I^2 test was used to analyze the heterogeneity of the included literature, where $I^2 \geq 50\%$ suggested the existence of significant heterogeneity between studies, and a random-effects model was used for analysis, and $I^2 < 50\%$ suggested the absence of significant heterogeneity between studies, and a fixed-effects model was used for analysis. Funnel plots were adopted to represent publication bias in the included literature, and publication bias was evaluated using a Linear regression test, where $p < 0.05$ indicates the presence of significant publication bias. If the number of included literature was less than 10, the evaluation of publication bias was considered unnecessary.

Results

Baseline Information

A total of 526 relevant pieces of literature were coarsely collected. After excluding 104 duplicate studies, 271 irrelevant studies, reviews, case reports, and nonclinical studies, and 122 pieces of literature without specified data or without specified intervention methods, the remaining 29 pieces of literature were further screened by reading the full text. Of the 29 publications, 4 pieces had no access to primary data, 3 showed significant flaws in the study methodology, and 5 were case reports, all of which were then excluded. Eventually, 17 pieces of literature[12-28] involving 1,928 participants were included, with 962 participants in the control group and 966 in the study group, as shown in Table II. The literature screening flowchart is shown in Figure 1.

Quality Assessment of the Included Literature

All 17 included RCTs[12-28] recorded the baseline profiles of patients. 7 studies[13,17,18,20,22,24,27] only mentioned "randomized grouping" without providing a specific method, 4[12,14,16,21] did not mention the grouping method, and 6[15,19,23,25,26,28] described the withdrawal of participants. None of the studies were blinded. The bar chart of literature quality evaluation is presented in Figure 2.

Results of Meta-Analysis

Analysis of FMA outcomes

Of the 17 included publications[12-28], 15[12-16,19-28] reported pre- and post-treatment FMA scores, of which 7[12,14,20,22,24-26] reported total FMA scores, 5[13,16,19,27,28] reported upper extremity FMA scores, and 6[15,16,19,23,27,28] reported lower extremity FMA scores. Subgroups were distinguished, and meta-analysis was performed separately according to different sites. Mean deviation (MD) was adopted in the meta-analysis to assess the effect of combined acupuncture treatment on FMA scores. With I^2 greater than 50% in all three subgroups, there was significant heterogeneity in the study, and random effects models were used for analysis. Results showed that the incorporation of acupuncture in the treatment of post-stroke limb movement disorders significantly reduced the overall FMA scores of patients by 3.45 (95% CI: 0.22, 6.69) points, the upper extremity FMA scores by 3.63 (95% CI: 0.64, 6.62) points, and the lower extremity FMA scores by 3.56 (95% CI: 1.78, 5.35) points. The MD forest plot of FMA scores is shown in Figure 3.

Considering the total upper extremity FMA score of 66 and the total lower extremity FMA score of 34, a greater benefit may exist for combined acupuncture in improving the lower extremity FMA score, and the results were further analyzed using the standardized mean difference (SMD). The results showed that the SMD was 0.32 (95% CI: 0, 0.65) in the overall FMA score, 0.63 (95% CI: 0.26, 1.00) in the

Table II. Baseline information of the included literature.

First author	Year	Treatment course	Control group n	Control group Male/Female	Control group Age	Study group n	Study group Male/Female	Study group Age	Outcome
Shen et al[12]	2022	4 weeks	55	31/24	68.75±6.14	55	38/17	70.22±5.23	a, d
Wang et al[13]	2022	6 weeks	102	72/30	61.90±10.50	102	77/25	60.6±12.5	b, d
Zhang et al[14]	2022	4 weeks	30	18/12	22/20	31	21/10	22/20	a, d
Huang et al[15]	2022	6 weeks	20	10/10	69±7	20	9/11	69±8	c
Bao et al[16]	2021	8 weeks	72	34/38	61.6±4.75	72	31/41	62.4± 3.93	b, c
Zhang et al[17]	2021	4 weeks	70	34/36	58±11	70	35/35	57±14	d
Wang et al[18]	2020	4 weeks	34	16/18	53±10	33	18/15	51±9	d
Wang et al[19]	2019	4 weeks	30	16/13	59±7.51	30	19/11	56.7±7.02	b, c
Chen et al[20]	2016	4 weeks	120	74/51	64.06±10.54	120	74/51	62.52±10.6	a, d
Jiao et al[21]	2016	2 weeks	48	26/22	56±6	48	28/20	56±6	d
Liu et al[22]	2016	12 weeks	20	10/10	68.1±9.16	18	14/4	65.6±12.40	a, d
Qiu et al[23]	2017	4 weeks	48	30/18	67±11	48	29/19	67±11	c
Wu et al[24]	2015	4 weeks	174	-	64.92±11.51	179	-	64.51±11.41	a
Tong et al[25]	2013	4 weeks	42	22/20	69±6	44	25/19	69±6	a
Bai et al[26]	2013	8 weeks	41	30/11	59.30±9.66	40	25/15	61.65±11.05	a, d
Zhang et al[27]	2010	3 weeks	40	24/16	69.2±9.7	40	26/14	65.9±11.1	b, c
Alexander et al[28]	2004	2 weeks	16	8/8	55.7±12	16	9/7	66.5±8.8	b, c

a, FMA total limbs, b, FMA of upper limbs, c, FMA of lower limbs, d, BI.

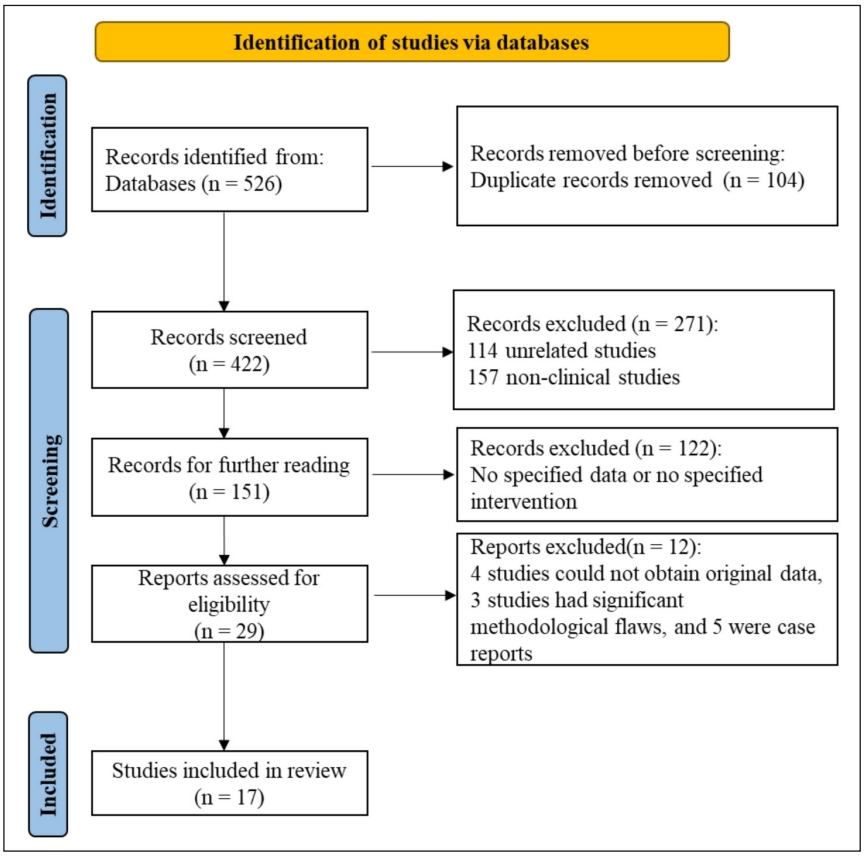

Figure 1. Literature screening flowchart.

upper extremity FMA score, and 1.87 (95% CI: 0.23, 3.51) in the lower extremity FMA score. This result indicates that the combined use of acupuncture provides more benefits in improving lower limb motor function. The SMD forest plot of FMA scores is shown in Figure 4.

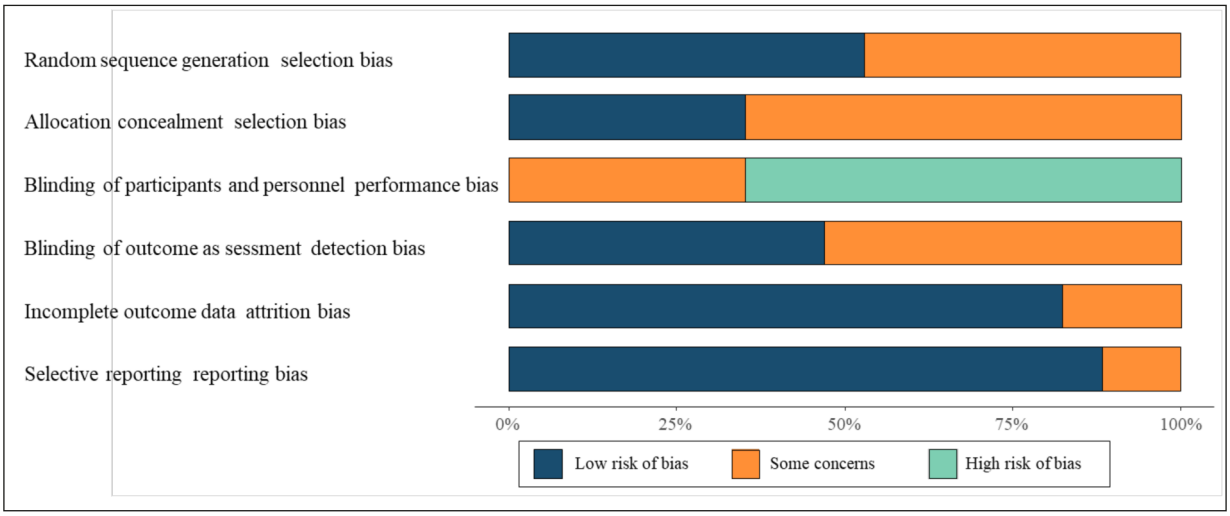

Figure 2. ROB figure of the enrolled pieces of literature.

Analysis of BI outcomes

Of the 17 included studies[12-28], 9[12-14,17,18,20-22,26] reported BI outcomes before and after treatment, and MD was used in the meta-analysis to compare the differences in BI results before and after treatment. With I^2 greater than 50% in all three subgroups, there was significant heterogeneity in the study, and random effects models were used for analysis. The results showed that incorporation of acupuncture therapy reduced the BI by 7.75 (95% CI: 3.35, 12.16) points. the MD forest plot of BI scores is shown in Figure 5.

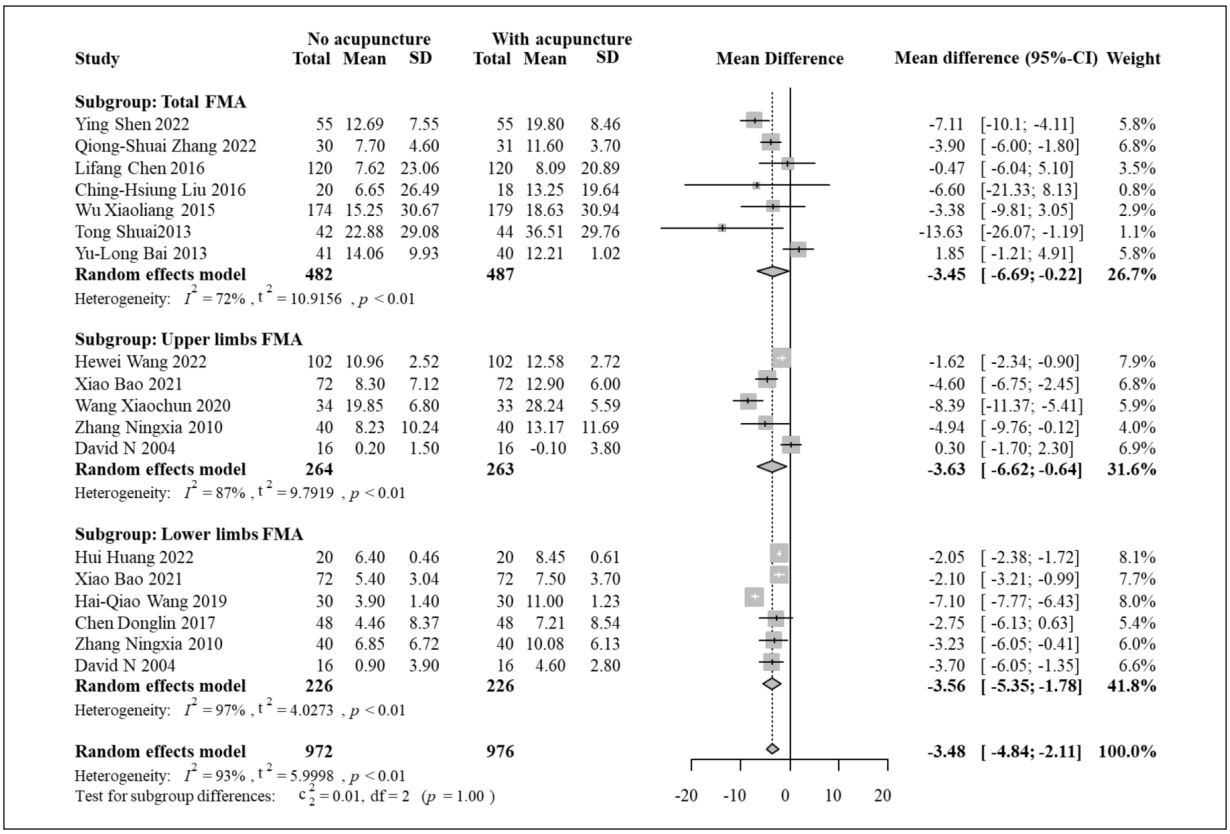

Figure 3. MD forest plot of FMA scores.

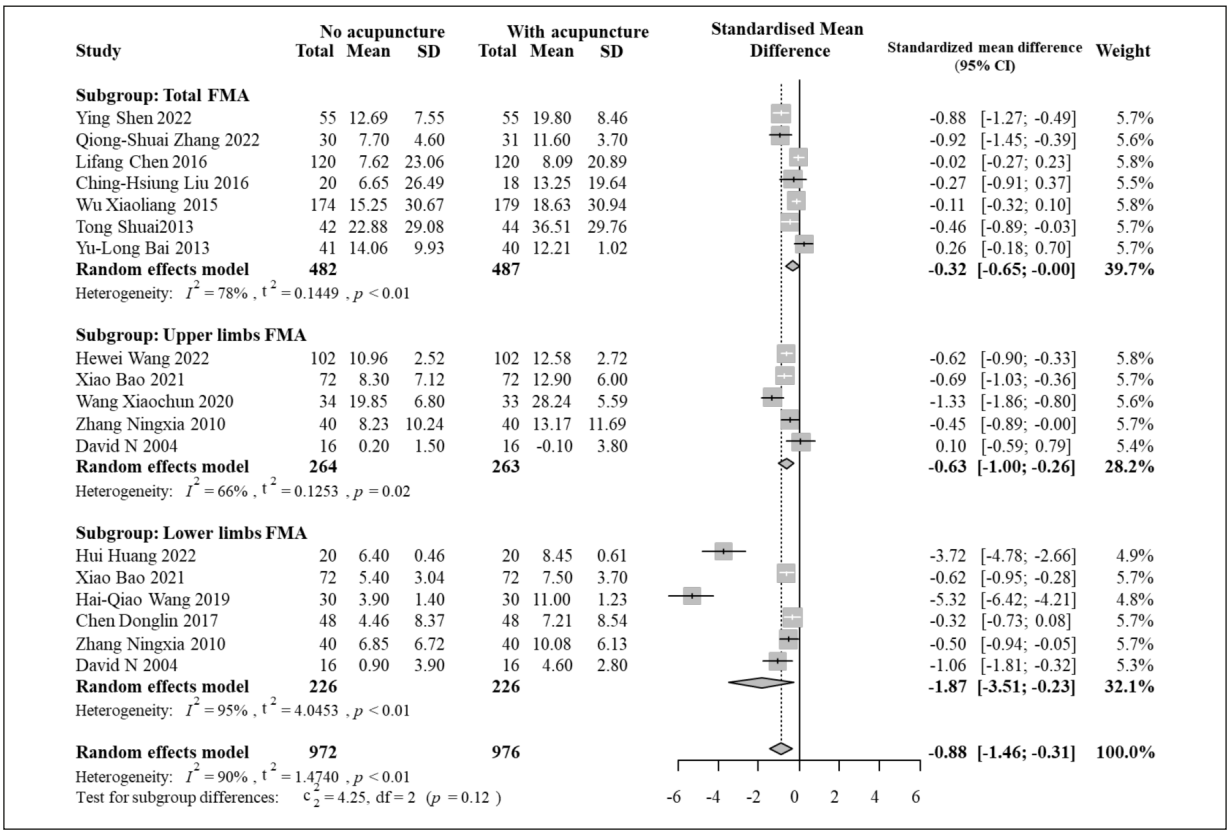

Figure 4. SMD forest plot of FMA scores.

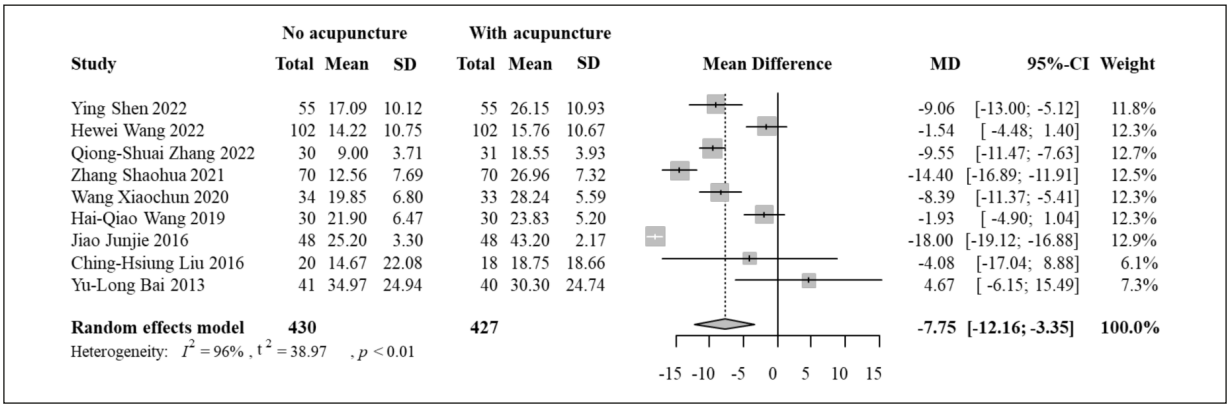

Figure 5. MD forest plot of BI scores.

Publication bias

Funnel plots were used to evaluate FMA and BI publication bias, and a Linear regression test was used to assess publication bias. Significant publication bias was absent for FMA (t=-0.75, p=0.4643) but was present for BI (t=2.62, p=0.0342), and this may be attributed to the small number of the included studies. The funnel plot of publication bias of the included literature is shown in Figure 6.

Discussion

Stroke is currently the leading cause of death and disability worldwide, posing a serious socioeconomic burden. Stroke may lead to irreversible sequelae such as motor dysfunction, sensory impairment, cognitive impairment, speech impairment, and swallowing disorders, resulting in lifelong disability. Motor dysfunction is one of the most common complications after stroke, and its

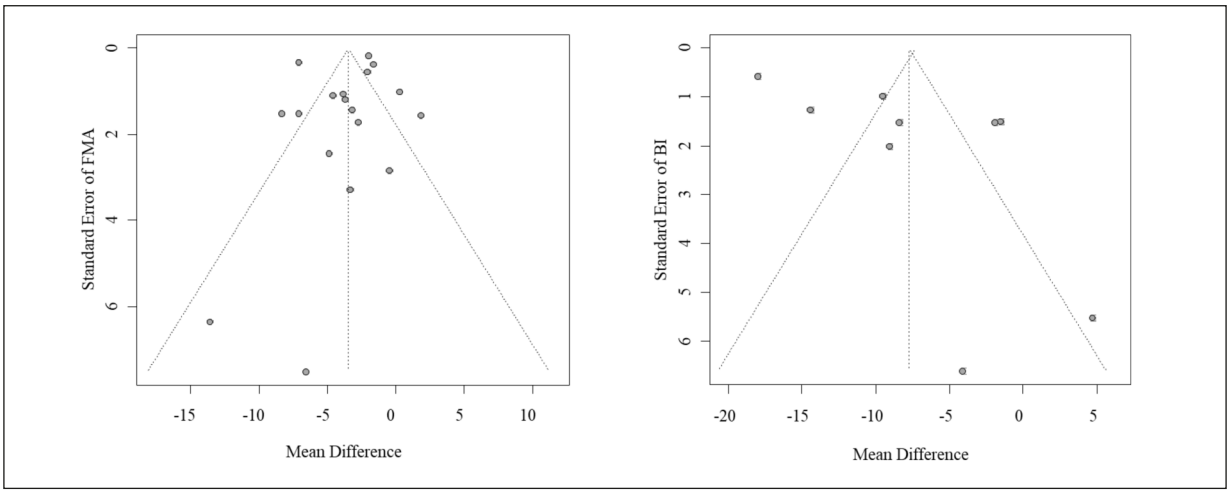

Figure 6. Funnel plot of publication bias.

management and prevention are closely associated with the prognosis of stroke patients[29]. Rehabilitation is the main treatment to improve motor impairment after stroke, and guidelines[30] recommend early rehabilitative intervention for patients with a stable disease condition for 72 hours after stroke.

As a non-invasive treatment modality, acupuncture plays an important role in the treatment of stroke and its sequelae[31]. At present, no meta-analysis comparing the difference in improving limb motor function after stroke with or without the combined use of acupuncture is available. In the present study, 17 eligible pieces of literature[12-28] were included, with FMA and BI as the main outcome indicators. Results from the included studies suggested significant benefits provided by acupuncture to improve FMA scores and BI. In specific, incorporation of acupuncture in the treatment of post-stroke limb movement disorders significantly reduced the overall FMA scores of patients by 3.45 (95% CI: 0.22, 6.69) points, the upper extremity FMA scores by 3.63 (95% CI: 0.64, 6.62) points, the lower extremity FMA scores by 3.56 (95% CI: 1.78, 5.35) points, and BI by 7.75 (95% CI: 3.35, 12.16) points. Clinical practice[32] has evidenced the effectiveness of acupuncture in the treatment of stroke. Early acupuncture can dilate blood vessels, promote blood circulation, reduce blood viscosity and platelet aggregation, improve blood microcirculation, enhance oxygen metabolic processes in brain cells, increase cerebral blood flow, and mitigate cerebral ischemia and hypoxia. A meta-analysis[33] that included 56 studies comparing the effects of different treatments on motor function after stroke showed that neuromodulatory interventions, such as acupuncture, may provide the best therapeutic effect in motor rehabilitation of upper limb injuries after stroke. Research[34] has shown that acupuncture stimulation at lesions or lesion-related acupoints improves local blood circulation, enhances local tissue metabolism, and relieves local tissue pathological changes such as edema, congestion, exudation, adhesions, calcification, contractures, and ischemia. Furthermore, functional magnetic resonance imaging findings[35] suggest that acupuncture treatment in patients with chronic hemiplegic stroke may moderately improve upper limb function (especially spasticity status and joint mobility) by increasing ipsilateral lesion motor cortex activity.

Significant heterogeneity existed in the literature included in the present study and remained unchanged by subgroup analysis. Such heterogeneity may lie in the differences in acupuncture point protocols. In these included studies, several acupoints have been frequently selected for treatment, such as Baihui, Quchi, Zusanli, Sanyinjiao, and Hegu. Research[36] has shown that acupuncture of the Hegu and Quchi acupoints affects local skin temperature and blood flow, while stimulation of the Zu Sanli and Quchi acupoints may activate brain regions (frontal, parietal, inferior lobe, cerebellar, and midbrain regions) and cause changes in ReHo values, thereby facilitating post-stroke recovery.

Limitations

The current study has some limitations. First, we searched only English and Chinese databases, risking the omission of some other potential studies that met the inclusion criteria. Second, the methodological quality of the evidence in this study was

poor, with some trials not reporting the implementation of allocation concealment. Due to the specificity of acupuncture, blind design is considered infeasible. In addition, acupuncture is "disease-specific and person-centered", and the acupuncture points and acupuncture modalities for different patients vary, resulting in a lack of standards for reference.

Conclusions

Acupuncture, as an adjunct to the management of post-stroke limb movement disorders, contributes significantly to enhancing the motor function and quality of life of patients.

Ethics Approval
Not applicable.

Informed Consent
Not applicable.

Conflicts of Interest
The authors declare that they have no competing interests.

Authors' Contributions
Yixi Tao designed the experiments. Yixi Tao and Yuanhua Wu performed the experiments. Guangqi Zhu and Mei Wang collected and analyzed the data. Yixi Tao and Mei Wang drafted manuscript. All authors read and approved the final manuscript.

Availability of Data and Materials
The data used for this study have been included in the manuscript.

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ORCID ID
Yuanhua Wu: 0009-0003-5364-6163.

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