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Tuina for spasticity of poststroke: protocol of a systematic review and meta-analysis

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ABSTRACT

Introduction Spasticity is a common complication of poststroke, tuina is a widely used rehabilitation treatment, although there is a lack of supportive evidence on efficacy and safety for patients with poststroke spasticity. The aim of this systematic review is to assess and synthesis evidence of efficacy and safety of tuina for spasticity of poststroke.

Methods and analysis A comprehensive electronic search of EMBASE, MEDLINE, Cochrane Library, Web of Science, Wiley, Springer, PEDro, Chinese Science Citation Database, China National Knowledge Infrastructure, Chinese Biomedical Literature Database, Chinese Scientific and Journal Database (VIP), Wanfang Database (Wanfang), Japanese medical database (CiNii), Korean Robotics Institute Summer Scholars and Thailand Thai-Journal Citation Index Centre will be conducted to search literatures of randomised controlled trials of tuina for spasticity of poststroke survivors range from the establishment to 1 January 2020.

There is no time of publication limitations. The primary outcome will be measured with the Modified Ashworth Scale, and the second outcome will include Fugl-Meyer Assessment Scale, surface electromyogram RMS value, the Modified Barthel Index, Stroke Specific Quality of Life Scale, quality of life 36-Item Short-Form Health Survey and Visual Analogue Scale. Cochrane Handbook for Systematic Reviews of Interventions will be used to assess the risk of bias, and GRADE will be used to access the confidence in cumulative evidence. The protocol will be conducted according to approach and Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols 2015.

Ethics and dissemination Ethical approval will not be required, for no primary data of individual patients were collected. We will publish the findings in a peer-reviewed journal.

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Strengths and limitations of this study

► This is the first comprehensive systematic review focused on efficacy and safety of tuina for spasticity of poststroke.
► Only randomised controlled trials (RCTs) (not included quasi-RCTs) will be included in this study.
► We searched databases of English, Chinese, Japanese, Korean and Thailand, while other languages may be ignored.

times as much as poststroke patients without spasticity.[8 9] Limb spasticity not only severely restricts the ability of patients, reduces the quality of life, but also causes psychological impact on patients' rehabilitation, and brings a great burden to families and society.[10–14]

Physical therapy, oral or injection drug therapy and operation therapy are commonly used in Western medicine to treat poststroke spasticity at present. Oral drugs such as baclofen, eperisone, hydrochloride and diazepine have large side effects which hinder the recovery of motor function with long time taking.[15] Botulinum toxin treatment is difficult to achieve long-term results, and it is often injected for moderate or severe cases of poststroke spasticity.[16 17] Physical therapy often requires active exercise coordination of patients; however, patients with severe conditions are often unable to cooperate. Surgical treatment is traumatic and a large number of patients often find it difficult to accept. At present, much more of the patients with spasticity after stroke choose external treatment. In China, many external treatment methods of traditional Chinese medicine (TCM) are applied to the treat this disease.

Tuina is an ancient form of external treatment method, which was based on the meridian and acupoint theory of TCM, and uses specific operation skill acting on the surface or acupoints of the patient's body to

Stroke has been the first risk factor of death in China.[1] It is also one of the diseases with high mortality and disability rate in the world.[2] Limb spasticity is a common complication of poststroke patients.[3 4] Recent study shows that about 17%–43% of stroke patients had limb spasticity,[5–7] and the medical cost of patients with poststroke limb spasticity is about four

treat diseases.[18 19] Tuina has been widely used in China for hundreds of years and increasingly practiced in Western countries in recent years. Systematic evaluation[20] shows that acupuncture is efficacy and safety in the treatment of limb spasticity after stroke. Acupuncture and tuina belong to the external treatment of TCM, and both are based on the same theory of meridians and acupoints. However, it is still unclear whether the effectiveness of acupuncture is also applicable to tuina in the treatment of poststroke spasticity. We want to know the effect of tuina, which has the characteristics of intervention and low cost, for poststroke spasticity. At present, there is no systematic review of tuina in the treatment of poststroke limb spasticity, so this study will evaluate the efficacy and safety of tuina in the treatment of poststroke limb spasticity, and provide evidence for clinical decision-making of massage.

METHODS

The systematic review will be performed following the guideline of Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) 2015.[21]

Inclusion criteria
Types of studies

We will include randomised controlled trials (RCTs) (not included quasi-RCTs) of tuina for poststroke spasticity in the treatment groups. If multiarm RCTs comes, we will select the group which used tuina and another without tuina for analysis. We will select the first stage of cross over RCTs, in which tuina was first used in one group. RCTs' language of English, Chinese, Japanese, Korean and Thai will be included.

Types of participants

Patients suffering postacute phase of post-stroke spasticity (>18 years old) will be included. Stroke (cerebral infarction or cerebral haemorrhage) is diagnosed according to WHO criteria,[22] participants have the symptoms of limb muscle tension increase, and the Modified Ashworth Scale (MAS) score is grade 1–2. Participants of any sex and ethnicity will be enrolled.

Types of interventions

The treatment group using tuina while the control group receives treatment of oral medication, acupuncture, Chinese herbal medication, physical therapy, surgery, botox injections and so on or even with no treatment will be included.

Types of outcome measures
Primary outcome

Muscle tone will be evaluated by the MAS. MAS is a clinical instrument which is commonly used for measuring spasticity, and studies have proofed its reliability.[23–25]

Secondary outcome

Motor function was assessed with Fugl-Meyer Assessment Scale (FMA) or Simplified FMA Scale.

Muscle strength will be defined by surface electromyogram root mean square value (RMS).

Activities of daily living will be assessed by the Modified Barthel Index.

Quality of life will be measured by Stroke Specific Quality of Life Scale or quality of life 36-Item Short-Form Health Survey (SF-36).

Limb pain will be assessed by Visual Analogue Scale.

Safety outcome
Skin abrasions.

Exclusion criteria
► Repeatedly published studies.
► Experiences, letters, systematic reviews and animal experiments.
► Tuina was not only in the experimental group but also in the control group.
► Articles without full text or with data which are missed or cannot be used.

Search strategy
Electronic searches

The published electronic literature will be searched in EMBASE, MEDLINE (by PubMed), Cochrane Library, Web of Science, Wiley, Springer, PEDro, Chinese Science Citation Database, China National Knowledge Infrastructure, Chinese Biomedical Literature Database, Chinese Scientific and Journal Database (VIP), Wanfang Database, Japanese medical database (CiNii), Korean Robotics Institute Summer Scholars and Thailand Thai-Journal Citation Index Centre. We will also cheek reference lists, and the literature will be searched range from the establishment to 1 January 2020.

The search strategy is developed according to published reviews.[26 27] The detail search strategy of MEDLINE (by PubMed) is listed in table 1, while the search strategy will be modified according to other different databases.

Data collection and analysis
Selection of literature

Two authors (YL, JC) will identify studies according to the inclusion criteria independently. First, they will eliminate duplicate researches by using EndNote software (V.x9.0). Second, screening the title and abstract, if necessary, reading the full article to confirm if it should be included. They also use EndNote software to manage the included studies. The screening operation is performed as shown in figure 1. If there is disagreement during the screening process, discuss with the third experts (GJ) to make a decision.

Data extraction and management

Two authors (SS and YW) will extract data from the included studies independently. In multiarm RCTs, we will extract data from RCTs of two arms, while we will select one group which contains the treatment of tuina as the treatment group, we will also choose another group the treatment of which without tuina as the control group.

Table 1	MEDLINE (by PubMed) search strategy
Spasticity of post stroke	#1.Stroke[MeSH] OR Apoplexy [Tiab] OR post-stroke[tiab] OR poststroke[tiab] OR Apoplectic [Tiab] OR Apoplexia [Tiab] OR Cerebral hemorrhage [Tiab] OR Ich [Tiab] OR Cerebrovascular accident [Tiab] OR Cerebrovascular disorders [Tiab] OR Cerebral embolism [Tiab] OR Brain embolism [Tiab] OR Embolic stroke [Tiab] OR Cerebral infarct OR cva*[tiab]
	#2.spasm[Mesh] OR dystonia[tiab] OR paraparesis,spastic[tiab] OR muscle spasticity*[tiab] OR muscle hypertonia [tiab] OR muscle rigidity*[tiab] OR muscle tonus[tiab] OR spas*[tiab] OR high tone[tiab]
	#3. #1 AND #2
Tuina	#4.Tuina[tiab] or Massage[tiab] or Acupressure[tiab] or Rub[tiab] or Massageing[tiab] or Massotheraty[tiab] or manipulation[tiab]
Randomised controlled trial	#5. Randomised controlled trial [pt] OR controlled clinical trial [pt] OR randomized [tiab] OR placebo [tiab] OR drug therapy [sh] OR randomly [tiab] OR trial [tiab] OR groups [tiab]
Final search strategy	6.#3 AND #4 AND #5

The general information consists of title, publication year, authors, country, language and journal source; information of participants: gender, age, stroke type (cerebral infarction or cerebral haemorrhage), duration of onset and sample size; information of intervention characteristics: type, session, duration and follow-up time and outcome information about primary outcome, second outcome, observation time points and adverse effects.
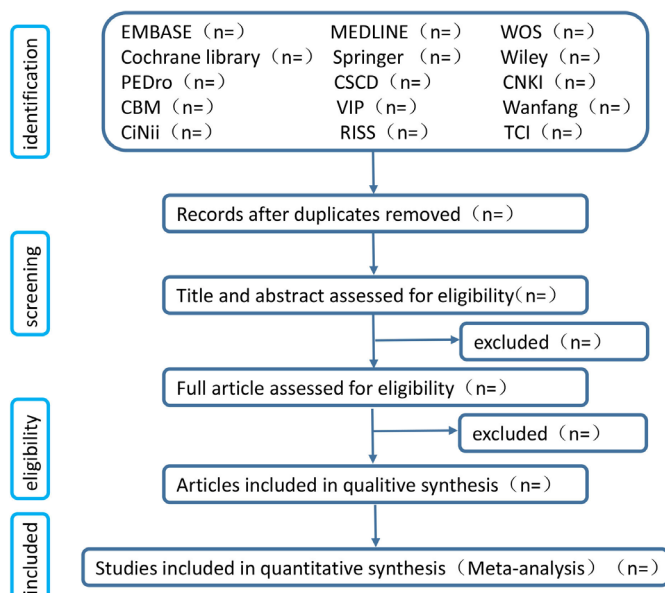
Figure 1 The screening process.

Assessment of risk of bias in included studies

Two independent authors (QZ and FC) will evaluate the risk of bias by using the Cochrane Collaboration bias risk assessment tool to assess the risk bias of the literature included in the systematic review. The two authors will assess the risk of bias of sequence generation, allocation concealment, blinding of participants personnel and outcome assessment, incomplete outcome data, selective outcome reporting and other bias. The evaluation grades are low, high and unclear risk of bias.

Measures of treatment effect

Two independent authors (YS and QZ) will use the mean difference (MD) or standard MD with 95% CI for continuous data of final measurements, the other binary data will be changed into relative risk (RR) form.

Dealing with missing data

When the included article lacks some important information, we will try to contact the correspondence author through e-mail, phone or other contacts. If we can't get the information through the ways above, we will turn to the following strategies to evaluate the potential influence of missing data:[28]

► Worst-case scenario analysis: all participants with missing data counted as failures.
► Extreme worst-case/best-case scenario analysis: participants with missing outcome data in the exercise arm counted as failures and in the control arm as success and vice versa.

Assessment of heterogeneity

We will use Q-test and I^2 statistic to assess the heterogeneity of the included studies, as the criteria: $I^2<50\%$ indicates low heterogeneity, while $I^2>50\%$ indicates high heterogeneity,

Assessment of reporting bias

We will construct funnel plots to assess asymmetry, only if at least 10 RCTs are included.

Data synthesis

The meta-analysis of intervention and outcome measures methods will be conducted by RevMan V.5.3.5 software (the Cochrane Collaboration, Oxford, England). If the statistical heterogeneity is low (P>0.1, or $I^2<50\%$), we will use the fixed-effect model to combine the data, while if the statistical heterogeneity is high (P<0.1, or $I^2>50\%$), we will use the random-effect model. However, if the heterogeneity level much significant, a descriptive analysis will be performed.

Subgroup analysis and investigation of heterogeneity

We will perform subgroup analysis to assess heterogeneity of the study according to the following potential factors from the available sufficient data:

► Age.
► Sex.

- ► Different types of stroke (Cerebral haemorrhage or cerebral infarction).
- ► Different types of tuina.
- ► Different time/course of treatment.
- ► Different parts of affected limbs (upper limb or lower limb).
- ► Different types of control group (acupuncture, placebo, oral/injection drug or no treatment).

We may make meta-regressions according to age and the different time/course of treatment if heterogeneity is obvious.

Sensitivity analysis

We will perform the sensitivity analysis to evaluate the robustness and reliability of the pooled results. If the results are not stable, we may turn to removing studies of high risk of bias, or cheek up processing method of missing data (worst-case scenario analysis: all participants with missing data counted as failures; extreme worst-case/best-case scenario analysis: participants with missing outcome data).

Grading of evidence quality

We will use the Grading of Recommendations Assessment, Development and Evaluation[29] to access the confidence in cumulative evidence. Risk of bias, heterogeneity, indirectness, imprecision and publication bias will be assessed, and the results will be divided into four levels: high, moderate, low and very low.

Amendments

We will show all the amendments with detailed description and rationale in the amendments of this study.

Ethics and dissemination

There is no need of ethical approval in this study, because there is nothing of the data which has a relationship with an individual patient. We will complete this systematic review according to the PRISMA guidelines. The review will provide an assessment of effect and safety of tuina for spasticity of poststroke. We will publish the findings in a peer-reviewed, open assess journal and the finished systematic review and meta-analysis will be disseminated online, which would be obtained freely for anyone. The results may contribute to improving the therapeutic strategy of patients with poststroke spasticity.

Patient and public involvement

No patient or public will be involved in our study directly. We only use data that existed in studies published.

DISCUSSION

This systematic review will focus on the efficacy and safety of tuina for spasticity of poststroke. Tuina is a traditional Chinese physical therapy, which is effective for 516 diseases in China,[30] of which spasticity is included. Clinical reports show tuina is well in treatment of spasticity of poststroke; however, high-quality study still did not

appear. We conducted this review with the aim to provide better evidence and guide for clinical decision-making. We plan to publish this review within 1 year since the protocol published, then we will update it every 3 years.

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