Original Article

The effectiveness and safety of cupping therapy for stroke survivors: A systematic review and meta-analysis of randomized controlled trials

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Objectives: Including stroke. The aim of this study was to systematically review the clinical evidence of CT for stroke.

Methods: To identify randomized controlled trials (RCTs) reporting the effectiveness and/or safety of CT, seven databases including PubMed, EMBASE, and Cochrane Library were searched for articles published from January 2000 to February 2021 without language restrictions. Meta-analysis was performed using Review Manager 5.4 software and the results were presented as mean difference (MD) or standard mean difference (SMD) for continuous variables and odds ratio (OR) for diverse variables with 95% confidence intervals (CIs). Assessment of the methodological quality of the eligible trials was conducted using the Cochrane Collaboration tool for risk of bias in RCTs.

Results: Twenty-two RCTs with 1653 participants were included in the final analysis. CT provided additional benefit in improving upper limb motor function (Fugl-Meyer assessment for upper limb motor function, MD 6.91, 95% CI 4.64 to 1.67, $P < 0.00001$) and spasticity (response rate, OR 3.28, 95% CI 1.31 to 8.22, $P = 0.08$) in stroke survivors receiving conventional medical treatment. These findings were supported with a moderate level of evidence. CT did not significantly increase the occurrence of adverse events.

Conclusions: This study demonstrated the potential of CT to be beneficial in managing a variety of complications in stroke survivors. However, to compensate for the shortcomings of the existing evidence, rigorously designed large-scale RCTs are warranted in the future.

Key Words : Cerebrovascular diseases; Cupping; Meta-Analysis, Stroke; Systematic review

Introduction

Stroke is one of the leading causes of death worldwide, accounting for 10% of the world's mortality¹⁾. Although stroke mortality is on the decline¹⁾, many stroke survivors still suffer from residual disability²⁾. The aging of the population and the reduction in stroke deaths are expected to

lead to further increases in the prevalence of stroke and socioeconomic burden in the future³⁾. Therefore, now is the time to pay attention not only to current stroke strategies mainly focused on emergent and intensive care in the acute stage but also to continuous monitoring and medical support for stroke survivors³⁾. Interest in complementary and alternative medicine, represented

• Received : 16 July 2021

• Revised : 3 August 2021

• Accepted : 5 November 2021

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by traditional or folk medicine, has been increasing as one of the methods to satisfy the unmet needs of stroke survivors⁴⁾.

Cupping therapy is a form of intervention that provides negative pressure on the skin by suctioning the air inside a cup and has been widely used in multiple cultures throughout the world^{5,6)}. In particular, it has one of the most commonly used interventions in modern East Asian traditional medicine to date⁵⁾. Indications of cupping therapy covered almost all systems of the human body and mind in traditional medicine¹⁾, including various complications experienced by stroke survivors⁶⁾.

In 2010, Lee et al⁶⁾ published the results of a systematic review of the clinical literature on the effect of cupping therapy for stroke rehabilitation. However, at the time, only two uncontrolled observational studies and three randomized controlled trials (RCTs) comparing the effects of cupping therapy with different unproven techniques were identified in the search, so only a narrative review of the clinical evidence available at the time for this topic was possible.

Therefore, this study aimed to update the findings of the previous study⁶⁾ by systematically reviewing currently available RCTs, performing a meta-analysis and providing evidence-based information for those considering the application of cupping therapy for stroke patients.

Methods

1. Data sources and search strategy

1) Data sources

Considering that the primary studies included

in the previous systematic review on this topic⁶⁾ have been published since 2000, we searched the following databases from 1 January 2000 to 16 February 2021: English (PubMed, EMBASE, and Cochrane Library), Chinese (China Academic Journals Full-text Database), and Korean databases (Science On, Korean Studies Information Service System, and Oriental Medicine Advanced Searching Integrated System). Twelve major Korean traditional medicine journals were also manually searched for relevant articles.

2) Search strategy

The search terms were used in the form of a combination of (“stroke” OR “cerebral infarction” OR “cerebral hemorrhage” OR “cerebrovascular disorder” OR “cerebrovascular accident” OR “apoplexy” OR “brain ischemia”) AND (“cupping”), but modified to suit the condition of the search platform of each database in Korean, Chinese, and English (Supplement 1). There were no language restrictions. In addition to articles published in academic journals, thesis and conference abstracts were also included. Hand searches were also conducted for related references. This study was conducted according to the Preferred Reporting Items for Systematic reviews and Meta-Analyses 2020 (Supplement 2 & 3).

2. Study selection and eligibility criteria

1) Study selection

MK and CH screened the retrieved records. The selection of potentially relevant articles for this study was decided after reading the abstract or full text of the articles. The two authors

worked independently and any disagreement was resolved by discussion.

2) Types of studies

Parallel-design RCTs that investigated the effectiveness and safety of cupping therapy in stroke patients were selected. Observational studies, qualitative studies, animal studies, and literature reviews were not included. Clinical studies that were nonrandomized studies, crossover-design studies, before-and-after studies, or studies without a control group in comparison to the cupping therapy group were also excluded.

3) Types of participants

Studies that recruited patients who were confirmed to have stroke by clinical signs and symptoms supported by brain imaging were included. There were no other restrictions, such as age, sex, stroke type, or stroke stage. Studies including nonstroke patients were excluded. When more than one study used duplicated data were obviously from the same population, only the one study that provided more information was selected.

4) Types of interventions

We defined cupping therapy as an intervention that provides negative pressure on the skin by suctioning air inside a cup-shaped device (mainly made of plastic, glass, or bamboo).⁴⁾ Generally, cupping therapy is classified as wet cupping or dry cupping^{5,6)}. Wet cupping refers to cupping with bloodletting puncture. In other words, it involves pricking the skin of the cupping site before suction and subsequently drawing blood in

addition to cupping. Dry cupping involves only cupping without bleeding. This study included both types of cupping.

5) Types of control interventions

All types of control interventions other than cupping therapy were allowed as control interventions, including active control, sham or placebo control, and no cupping therapy. Therefore, both A versus B and A+B versus B type studies were included.

6) Types of outcome measures

All types of clinical outcomes that evaluated the therapeutic effect and safety of cupping therapy for stroke patients were allowed. Reporting of the response rate based on predefined criteria was also allowed.

Outcomes showing the add-on effect of cupping therapy were also allowed. However, cases that provided only the combined effects of cupping plus other interventions in which the effects of cupping therapy could not be identified were excluded (e.g. cupping + acupuncture, cupping + herbal medicine, and cupping + bloodletting of noncupping sites).

When the outcomes were measured multiple times after the completion of planned treatment, the first measured value was preferentially adopted.

2. Data extraction

One of the authors (MK) extracted data, and another one (CH) cross-checked the data. Disagreements were resolved by discussion between the two reviewers. The extracted data

were as follows: number of participants in the final analysis, time-to-onset of stroke, stroke conditions, types and details of intervention, types of control intervention, outcome measures, and findings of each study.

3. Data synthesis

Meta-analysis was conducted when two or more studies provided quantifiable values. In the case of A versus B designs, data were combined when there were two or more studies using the same endpoints and control interventions. In the case of A+B versus B designs, data were combined when there were two or more studies using the same endpoints. Cochrane Collaboration software (Review Manager (RevMan) Version 5.4 for Windows. The Cochrane Collaboration, 2020) was used for data synthesis and constructing forest plots. For continuous variables, the mean difference (MD) and its 95% confidence interval (CI) were calculated using the inverse variance method. However, when the measurement tools were not identical across studies, the standard mean difference (SMD) was calculated. For binomial variables, odds ratios (ORs) and 95% CIs were calculated using the Mantel-Haenszel method. Heterogeneity among trials was evaluated using Higgins' I^2 test⁷⁾. The fixed effect model was preferentially adopted, but a random effect model was selected when the stroke conditions of the participants were not homogeneous or the statistical heterogeneity between studies was considerable (I^2 value $\geq 75\%$)⁸⁾. When heterogeneity was substantial, subgroup analysis was considered. Subgroup analysis was also performed based on the type of cupping therapy (dry or wet cupping).

When data from 10 or more studies were combined, the possibility of publication bias was assessed using a funnel plot.

4. Risk of bias (RoB) assessment

The Cochrane Collaboration tool for RoB in RCTs (RoB 2) was used to assess the methodological quality of the studies included in the meta-analysis. The RoB 2 consists of five domains: randomization process, deviations from intended interventions, missing outcome data, measurement of the outcome, and selection of the reported results⁹⁾. Based on the evaluation results for each domain, the overall RoB for each study was judged to be one of the three levels including low, high, or some concerns. The two authors independently evaluated the RoB of individual studies, and any disagreements were resolved through discussion.

5. Level of evidence

The certainty in evidence from the meta-analysis was assessed by the methodology of the grading of recommendations, assessment, development, and evaluation (GRADE)¹⁰⁾. Meta-analysis data were imported into GRADEpro, web-based software, and the quality of evidence was rated based on the following criteria: study design, RoB, inconsistency, indirectness, imprecision, and other considerations including publication bias. Synthesizing the ratings of each criterion, the final level of evidence was decided to be high, moderate, low, or very low¹⁰⁾.

Results

1. Study selection

Fig. 1. Flowchart of the study selection

A total of 374 articles were identified through the database search, and 3 articles were identified through hand searching, and of these, 50 were excluded due to duplication. The titles and abstracts of the remaining 327 articles were screened, and 271 articles not suitable for this study were excluded. Full texts of the remaining 56 articles were read and 24 articles that did not meet the eligibility criteria of this study were excluded.

Out of the remaining 32 articles, 22 articles providing data suitable for quantitative synthesis were finally selected for meta-analysis and methodological quality assessment. The study selection process is summarized in Fig. 1, and a list of articles excluded during the process from full text reading to the final selection is presented in Supplement 4.

1. Characteristics of the included studies

1) Study design and sample size

A total of 22 studies¹¹⁻³²⁾ with 1653 participants published in China from 2001 to 2020 were included in the final analysis. Most of them were studies with a 2-arm design with the exception of three studies^{14,19,31)} with 3 arms. The number of participants included in the posttreatment evaluation ranged from 40 to 135 (Table 1).

2) Participants

The participants of all included studies were patients with stroke, and none of the studies limited the stroke subtype of the patients. There was no study that recruited only patients in the acute stage within one week of stroke onset, but most of the participants were patients within 6 months of stroke onset. Of the exceptions, 4 studies included patients with more than 6 months since stroke onset,^{15,18,30,31)} and 3 studies did not provide any information regarding the time from onset (Table 1)^{22,23,32)}.

The most commonly treated stroke condition was spasticity, which was reported in 9 studies^{12-14,16,17,20,23,24,31)}. Six^{12-14,16,17,24)} of these studies targeted patients with upper limb spasticity, of which 4^{12,14,16,17)} were about elbow spasticity. There were three studies each on spasticity in lower limbs²³⁾, four limbs,³¹⁾ and nonspecified parts²⁰⁾. The most commonly studied stroke conditions after spasticity were hemiplegic shoulder pain (5 studies)^{19,22,25,26,28)} and poststroke shoulder-hand syndrome (4 studies).^{21,27,29,30)} The remaining studies targeted sensory dysfunction^{18,32)}, upper limb dysfunction¹⁵⁾, and neglect syndrome (Table 1)¹¹⁾.

Two studies considered the type of syndrome

differentiation based on traditional Chinese medicine.^{15,20)} One enrolled patients with spasticity and qi deficiency with blood stasis type¹⁵⁾ and the other enrolled patients with upper limb dysfunction with phlegm and blood stasis obstructing collaterals type (Table 1)²⁰⁾.

3) Intervention, control and outcome measures

① A versus B type studies

Two studies^{17,24)} compared the effects of wet cupping and Western medication (baclofen, a muscle relaxant) in patients with upper limb spasticity. In both studies, the treatment period was 4 weeks, the treatment group received wet cupping on the center of the biceps brachii belly twice a week, and the control group was orally administered 10 mg of baclofen three times a day. These two studies evaluated changes in upper limb motor function and spasticity. In terms of the safety of the cupping therapy, one study²⁴⁾ described the plan for adverse event monitoring in the methods session but did not report the results. Another study¹⁷⁾ did not provide any information on the safety of cupping therapy (Table 1 & 2).

② A+B versus B type studies

Twenty studies^{11-16,18-23,25-32)} were designed as an A+B versus B form, comparing the add-on effect of cupping therapy with the noncupping control in patients receiving standard treatment for stroke. Three of them^{14,19,23)} were 3-arm studies, and the other 18 were 2-arm studies. No studies used sham devices or placebo controls (Table 1).

Of the 20 studies, 5^{11,19,21,25,31)} used dry cupping and 15^{12-16,18,20,22,23,26-30,32)} used wet cupping. The

retention time for cupping was between 5 and 15 minutes in both dry and wet cupping studies. The amount of blood drawn by wet cupping therapy ranged from a few drops to 10 ml. Ten^{13,15,18-20,22,25-27,32)} of the included studies performed cupping therapy once every other day. The next most common protocols were once a day^{14,28,30,31)} and twice a week^{12,16,23)}. The treatment period was most frequently 4 weeks^{11,12,16,18,21)} and ranged between at least 2 weeks and at most 6 months. The most common sites for cupping were the pain site of the affected shoulder for patients with hemiplegic shoulder pain or shoulder-hand syndrome and the center of the biceps brachii belly for patients with upper limb spasticity (Table 1).

The therapeutic effects of cupping therapy for stroke patients was evaluated on various scales. Most of the studies presented the response rates for the main outcomes in stroke survivors. In addition, many other studies measured upper limb motor function using the Fugl-Meyer assessment (FMA) scale, and there were also studies that evaluated overall motor function or sensory function. Some studies assessed the intensity of shoulder pain using a visual analog scale (VAS) or numeric rating scale. There were also studies that assessed the activities of daily living using the Barthel or modified Barthel index. There was only one study¹⁵⁾ that assessed neurological deficits using an internationally accepted stroke scale, such as the National Institute Health stroke scale, and no study reported mortality, disability, or recurrence of stroke (Table 1 & 2).

Most studies did not mention safety. One study on dry cupping²¹⁾ reported that any serious

adverse events were observed, and three studies on wet cupping^{13,15,25)} described the adverse events identified during the study period (Table 1 & 2).

2. RoB of the included studies

Only two studies^{15,24)}, which provided enough information to confirm that both the random sequence generation and allocation concealment process were properly performed, met the first domain of the RoB 2 (randomization process). The remaining included studies did not provide enough information to judge relevant procedures and were judged to be at the level of raising some concerns in this domain.

In the second domain, deviations from the intended interventions, all studies were judged to be at low RoB. Although patient blinding and performer blinding were not performed, it was judged that this situation was due to the unique nature of the cupping therapy and would not have affected the intended intervention.

In the third domain, missing outcome data, most studies were judged to be at high RoB. This was because they did not mention anything about loss to follow-up or dropout and we could not rule out the possibility that any missingness led to biased results. Only 3 studies^{15,18,24)} reported dropout, and we could confirm that the missingness did not bias the results, these studies were judged to be at low RoB.

In the fourth domain, measurement of the outcome, all the included studies were judged to be at high RoB. This was because no studies mentioned anything about the achievement or impact of assessor blinding.

Table 1. Characteristics of included studies (Participants, interventions and control interventions)

Study ID	Participants		Conditions	Interv	Con. interv
	No	TFO			
[11] JIPB2020	30/30	74-106 d	neglect syndrome	DC+RH DC: 1-2/d, 5/wk, total 20 times for 4 wks, LI11 LI13 LI10 L14 ST32 ST34 ST36 ST40 LR3	RH
[12] ZhangP2020	40/40	2-6 mo	spasticity, U/E (elb)	WC+RH WC: 10 ml, 2/wk, total 8 times for 4 wks, center of belly of biceps brachii	RH
[13] LiYY2019	48/48	22-135 d	spasticity, U/E	WC+ST WC: 5-10 min, 1-2 ml, EOD, total 15 times for 40 min, center of belly of biceps brachii	ST
[14] ShanYL2019	30, 30/30	50 d-6 mo	spasticity, U/E (elb)	WC+EA, WC WC: 5 min, 2 ml, 5/wk, total 10 times for 2 wks, tense points of affected site	EA
[15] JiangL2018	36/36	1-12 mo	U/E dysf + spasticity (SD: psoc)	WC+Ac WC: 10 min, EOD, total 45 times for 3 mns, LI15 LI11 LI10 (affected site)	Ac
[16] HuangZQ2018	30/30	24-165 d	spasticity, U/E (elb)	WC+ST WC: 10 ml, 2/wk, total 8 times for 4 wks, center of belly of biceps brachii	ST
[17] ChenJY2017	43/43	1-6 mo	spasticity, U/E (elb)	WC: 10 ml, 2/wk, total 8 times for 4 wks, center of belly of biceps brachii	MED
[18] ChenYP2017	43/43	1 d - 7 mo	sensory disturbance	WC+ST WC: 8-10 min, 1-2 ml, EOD, total 14 times for 4 wks, PC3 BL40 (affected site)	ST
[19] LiuHY2016	45, 45/45	Avr 2.1-2.3 mo	HSP	DC+Aelnj, DC DC: EOD, total 9 times for 3 wks, SI9 GB21 LI15 Ex-UE13Ashi-point (affected site)	AcInj
[20] ZhangBB2016	30/30	Avr 67-68 d	spasticity (SD: qdbs)	WC+Ac WC: 5 min, 1-3 ml, EOD-3/wk, total 9 times for 3 wks, LU5 BL40 BL17 (bilateral)	Ac
[21] ChengXL2014	20/20	NA	SHS	DC+ST DC: 10 min, 6/wk, total 24 times for 4 wks, SI9 LI15 TE14 SI11	ST
[22] ZhangQF2014	31/31	NA	HSP	WC+ST WC: 10 min, EOD, 30 times for 3 mns, total 30 times for 3 mns, LI15 TE14 LI11 Ashi-point (affected site)	ST

Table 1. Characteristics of included studies (Participants, interventions and control interventions) (Continued)

Study ID	Participants		Interv	Con. interv
	No	Conditions		
[23] MiaoT2014	30/30/30	Avr 67-68 d spasticity, L/E	WC+RH, WC WC: 15 min, 2/wk, total 8 times for 1 mm, most painful points among ST31 ST32 SP10 ST34 GB31 BL56 BL57 SP6	RH
[24] HuangZQ2014	30/30	25-165 d spasticity, U/E	WC WC: 10 ml, 2/wk, total 8 times for 4 wks, center of belly of biceps brachii	MED
[25] YangMY2013	34/30	18-112 d HSP	DC+RH DC: 5-10 min, EOD, total 10 times for 20 days, pain site	RH
[26] GaoLA2015	46/42	< 6 mo HSP	WC+RH WC: 5 min, 5-10 ml, EOD, total 10 times for 20 d	RH
[27] PengL2012	37/37	1-3 mo SHS	WC+RH WC: 10 min, 3-5 drops, EOD, total 10 times for 20 d, pain site	RH
[28] WuZY2011	23/23	18-113 d HSP	WC+RH WC: 5-7 min, ED, total 15 times for 3 wks, pain site	RH
[29] FuL2009	40/40	30-128 d SHS	WC+Ac WC: 2-5 ml, total 30 times for 36 d, LI15 TE14 LI14 LI11 LI10 LI4 EX-UE9 Ah-point	Ac
[30] ZouC2006	30/30	11-202 d SHS	WC+Ac WC: 2 ml, total 20 times for 22 d, Ex-UE & TE14 or S19 & LI15	Ac
[31] DingBY2003	52/30	3 mo - 2 yrs Spasticity, F/E	DC+Ac DC: 15 min, ED, total 36 times for 45 d, Yangming meridian points of flexor muscles of U/E or extensor	Ac
[32] CuiSZ2001	44/38	NA Sensory disturbance	WC+EA WC: 5 min, EOD, total 20 times for 40 d, affected site	EA

Ac, acupuncture; AcInj, acupoint injection; Avr, average; con, control; d, day; DC, dry cupping; dysf, dysfunction; EA, electroacupuncture; elb, elbow; EOD, every other day; F/E, four extremity; HSP, hemiplegic shoulder pain; Interv, intervention; MED, medication; min, minute; mo, month; NA, not available; No, number; psoc, phlegm and blood stasis obstructing collaterals; qdbs, qi-deficiency with blood stasis type; RH, rehabilitation therapy; SD, syndrome differentiation; SHS, shoulder-hand syndrome; ST, standard therapy; TFQ, time from onset; U/E, upper extremity; WC, wet cupping; wk, week

Table 2. Characteristics of included studies (Outcome measures and findings)

Study ID	Conditions	Interv	Con Interv	Outcome measures		Findings	
				Effectiveness	Safety		
[11] JiPB2020	neglect syndrome	DC+RH	RH	1. CBS, 2. MMSE, 3. FMA (motor), 4. MBI, 5. PPCT, 6. CDT, 7. LCT, 8. BLT, 9. Patients satisfaction	NA	1. 13.2±2.1 vs 15.6±2.0, 2. 27.5±1.4 vs 25.6±1.9, 3. 45.2±5.5 vs 41.7±4.9, 4. 67.0±13.3 vs 59.0±10.9, 5. 1.00±0.64 vs 1.50±0.75, 6. 1.10±0.541 vs 1.50±0.60, 7. 1.04±0.60 vs 1.44±0.60, 8. 1.20±0.70 vs 1.70±0.80, 9. 82.1±10.0 vs 62.1±9.3	
[12] ZhangP2020	spasticity, U/E (elb)	WC+RH	RH	1. IEMG (biceps), 2. FMA (U/E)	NA	1. 33.25±6.84 vs 38.63±7.79, 2. 45.36±12.27 vs 40.46±10.93	
[13] LiYY2019	spasticity, U/E	WC+ST	ST	1. RR (no subjects MAS 0-1), 2. MAS, 3. FMA (U/E), 4. BI	AE	1. 25 vs 13, 2. 1.1875±0.76231 vs 1.77083±0.91068, 3. 52.22±11.28 vs 41.97±10.35, 4. 82.87±18.59 vs 74.90±17.53	
[14] ShanYL2019	spasticity, U/E (elb)	WC+EA, WC	EA	1. FMA (U/E), 2. RR, 3. Hmax/Mmax (3-1, Median nerve, 3-2, Ulnar nerve, 3-3, Radial nerve)	NA	1. 34.76±16.01 vs 26.00±17.15 vs 17.50±11.22, 2. 30 vs 30 vs 18, 3-1. 0.07±0.10 vs 0.08±0.09 vs 0.13±0.10, 3-2. 0.08±0.05 vs 0.07±0.03 vs 0.12±0.09, 3-3. 0.08±0.10 vs 0.07±0.09 vs 0.14±0.13	
[15] JiangL2018	U/E dysf + spasticity (SD: psoc)	WC+Ac	Ac	1. FMA (U/E), 2. NIHSS, 3. MBI, 4. RR, 5. VAS	AE	1. 34.61±7.613 vs 31.36±6.257, 2. 13.06±4.296 vs 16.50±2.104, 3. 67.36±9.296 vs 62.78±7.507, 4. 31 vs 24, 5. no of participants per categories	
[16] HuangZQ2018	spasticity, U/E (elb)	WC+ST	ST	1. MAS, 2. FMA (U/E), 3. IEMG (bicep), 4. IEMG (triceps), 5. ROM, 6. RR	NA	1. 1.57±0.50 vs 2.23±0.43, 2. 46.07±10.28 vs 40.27±10.32, 3. 33.59±6.67 vs 37.08±6.21, 4. 30.30±6.43 vs 27.27±4.53, 5. 48.4±13.3 vs 41.4±10.6, 6. 25 vs 28	
[17] ChenJY2017	spasticity, U/E (elb)	WC	MED	1. RR, 2. MAS, 3. FMA (U/E), 4. IEMG (biceps), 5. IEMG (triceps)	NA	1. 39 vs 31, 2. 1.48±0.31 vs 2.21±0.52, 3. 45.2±12.1 vs 40.3±10.8, 4. 33.1±6.7 vs 38.5±7.6, 5. 29.8±6.6 vs 25.7±5.2	
[18] ChenYP2017	sensory disturbance	WC+ST	ST	1. RR, 2. FMA (motor), 3. FMA (sensory)	NA	1. 39 vs 32, 2. 68.12 ± 14.79 vs 69.37 ± 13.96, 3. 13.47 ± 2.95 vs 12.09 ± 3.93	
[19] LiuHY2016	HSP	DC+AcInjDC	AcInj	1. VAS, 2. MBI	NA	1. 1.96±1.05 vs 3.71±1.39 vs 3.58±1.43, 2. 68.7±5.22 vs 45.6±4.92 vs 46.6±5.06	
[20] ZhangBB2016	spasticity (SD: qdbs)	WC+Ac	Ac	1. RR, 2. CSI	NA	1. 29 vs 22	
[21] ChengXL2014	SHS	DC+ST	ST	1. RR, 2. CSI, 3. Brunnstrom stage	AE	1. 17 vs 16, 2&3, No of participants per categories	
[22] ZhangQF2014	HSP	WC+ST	ST	1. RR, 2. VAS, 3. FMA (U/E)	NA	1. 30 vs 21, 2. 2.58 ± 1.93 vs 4.74 ± 1.53, 3. 43.97 ± 7.29 vs 36.90 ± 8.49	

Table 2. Characteristics of included studies (Outcome measures and findings) (Continued)

Study ID	Conditions	Interv	Con Interv	Outcome measures		Findings
				Effectiveness	Safety	
[23] MiaoT2014	spasticity, U/E	WC+RH, WC	RH	RR	NA	29 vs 27 vs 28
[24] HuangZQ2014	spasticity, U/E	WC	MED	1. MAS, 2. FMA (U/E), 3. IEMG (biceps), 4. IEMG (triceps), 5. RR vs 21	NR	1. 1.53±0.23 vs 2.18±0.44, 2. 45.83±11.77 vs 40.23±10.65, 3. 34.94±6.68 vs 37.12±7.42, 4. 29.73±7.46 vs 26.96±4.13, 5. 27
[25] YangMY2013	HSP	DC+RH	RH	1. NRS, 2. FMA (U/E)	NA	1. 2.25±1.40 vs 4.26±1.51, 2. 23.18±3.26 vs 19.20±2.67
[26] GaoLA2015	HSP	WC+RH	RH	1. RR, 2. VAS, 3. BI, 4. FMA (U/E)	AE	1. 41 vs 27, 2. 2.57±1.797 vs 3.60±1.849, 3. 61.20±22.365 vs 50.83±21.411, 4. 36.89±12.946 vs 28.40±14.244
[27] PengL2012	SHS	WC+RH	RH	1. VAS, 2. RR (hand edema), 3. RR (ROM), 4. RR (FMA, U/E)	NA	1. 36 vs 31, 2. 35 vs 34, 3. 34 vs 25, 4. 31 vs 32
[28] WuZY2011	HSP	WC+RH	RH	VAS	NA	2.3±0.7 vs 4.1±0.8
[29] Ful.2009	SHS	WC+Ac	Ac	1. VAS, 2. frequency, 3. RR, 4. ROM	NA	1. 1.37±1.18 vs 2.54±1.69, 2. 2.73±1.74 vs 4.55±1.21, 3. 37 vs 28, 4-1. Ant flx: 153.6±5.3 vs 102.6±10.8, post ext: 38.8±4.6 vs 21.2±4.1, abd: 145.5±9.7 vs 96.3±11.6, add: 40.1±4.7 vs 27.6±4.6, pron: 42.6±9.5 vs 31.2±6.4, supin: 74.8±11.6 vs 56.6±12.2
[30] ZouCJ2006	SHS	WC+Ac	Ac	RR	NA	24 vs 16
[31] DingBY2003	spasticity, F/E	DC+Ac	Ac	RR	NA	52 vs 28
[32] CuiSZ2001	sensory disturbance	WC+EA	EA	RR	NA	44 vs 34

abd, abduction; Ac, acupuncture; add, adduction; AE, adverse event; Ant, anterior; BLT, bisection line task; CBS, Catherine Bergego scale; CDT, clock drawing test; Con, control; CSI, clinical spasticity index; DC, dry cupping; dysf, dysfunction; elb, elbow; ext, extension; F/E, four extremities; Hmax/Mmax, ratio between the maximum H reflex and the maximum M responses; flx, flexion; FMA, Fugl-Meyer assessment; HSP, hemiplegic shoulder pain; IEMG, integrated electromyography; Interv, intervention; LCT, line cancellation test; MAS, modified Ashworth scale; MBI, modified Barthel ind; MED, medication; MMSE, Mini-Mental status examination; NA, not available; NIHSS, national institute of health stroke scale; post, posterior; PPCT, planar pattern copying test; pron, pronation; psoc, phlegm and blood stasis obstructing collaterals; qdbs, qi-deficiency with blood stasis; RH, rehabilitation therapy; ROM, range of motion; RR, response rate; SD, syndrome differentiation; SHS, shoulder-hand syndrome; ST, standard therapy; supin, supination; U/E, upper extremity; VAS, visual analogue scale; WC, wet cupping

Fig. 2. Forest plot of the effect of cupping therapy versus medication on upper limb motor function Assessed by upper limb motor function subdomain of the Fugl-Meyer assessment scale

In the fifth domain, selection of the reported result, we judged that some concerns were raised in the RoB of all included studies. No studies involved previously published study protocol papers prior to initiation of trial. Therefore, we reviewed whether the results session was described in accordance with the plans mentioned in the Methods section of the paper. No significant biases were identified in the Methods and Result sections. However, no studies provided information that could confirm whether the reported outcome was selected from among multiple outcome measurements, and therefore, this issue raised some concerns for all included studies.

The overall RoB of all included studies derived by synthesizing the evaluations in the above domains was judged to be high. The results of the RoB assessment for each domain of the included studies are schematically shown in Supplements 5 and 6.

3. Meta-analysis and evidence level

1) Effectiveness of cupping therapy compared to Western medication

Two studies^{17,24)} compared the effect of wet cupping therapy with Western medication (baclofen 10 mg tid pc [P.O.]) in patients with upper limb spasticity after stroke. The meta-analysis of these

two studies showed that cupping therapy was significantly more advantageous in improving upper limb dysfunction assessed by the subdomain score of the FMA scale (MD 5.20, 95% CI 1.51 to 8.88, $P=0.006$) (Fig. 2). The degree of spasticity assessed by the modified Ashworth scale (MAS) was also significantly improved in the cupping therapy group compared to the Western medication group (MD -0.69, 95% CI -0.82 to -0.56, $P<0.00001$) (Fig. 3(A)). The proportion of patients who responded positively regarding the clinical aspects of spasticity was also significantly higher in the cupping group (MD 3.81, 95% CI 1.50 to 9.65, $P=0.005$) (Fig. 3(B)). Changes in the biceps and triceps muscles detected by integrated electromyography were also more favorable with cupping therapy (MD -4.05, 95% CI -6.36 to -1.74, $P=0.0006$; MD=3.56, 95% CI 1.62 to 5.50, $P=0.0003$) (Fig. 3(C, D)). The certainty of the evidence assessed by the GRADE approach was low in all cases. This was because of the high RoB and small sample size of the included studies (Supplement 7).

2) Effectiveness of cupping therapy as an add-on to conventional treatment

① Activities of daily living (ADL)

Five studies^{11,13,15,19,26)} assessed the additive

(A) Modified Ashworth scale

(B) Response rate

(C) Integrated electromyography (biceps brachii)

(D) Integrated electromyography (triceps brachii)

Fig. 3. Forest plot of the effect of cupping therapy versus medication on spasticity

effect of cupping therapy using the Barthel index (BI) or modified Barthel index (MBI). Combining the data, the additional implementation of cupping therapy for patients who were receiving conventional treatment was significantly more advantageous than the noncupping condition (SMD 1.23, 95% CI 0.21 to 2.25, $P=0.02$) (Fig. 4), and the level

of evidence supporting this result was low (Supplement 8). The subgroup analysis including only wet cupping studies^{13,15,26} showed similar results (SMD 0.48, 95% CI 0.23 to 0.72, $P=0.0002$) (Fig. 4). The heterogeneity detected in the whole synthesis ($I^2=95\%$) was resolved in the wet cupping subgroup analysis ($I^2=0\%$) (Fig. 4).

Fig. 4. Forest plot of the effect of additional cupping therapy on activities of daily living Assessed by Barthel index

However, when pooling the two studies involving only dry cupping^{11,19)}, the significant benefit of cupping therapy disappeared (SMD 2.44, 95% CI -1.10 to 5.99, $P=0.18$) (Fig. 4), and the level of evidence was also downgraded (Supplement 8).

② Motor function

i. General motor function

Only wet cupping study¹⁸⁾ and one dry cupping study¹¹⁾ evaluated the change in the motor function subdomain score on the FMA scale. Only the dry cupping study showed a significant benefit of cupping therapy (MD 3.50, 95% CI 0.86 to 6.14, $P=0.009$) (Fig. 5(A)). However, when combining the two studies, the additional benefits of cupping therapy were not confirmed (MD 1.95, 95% CI -2.42 to 6.31, $P=0.38$) (Fig. 5(A)), and the level of evidence was still very low (Supplement 8).

ii. Upper limb motor function

Seven studies using wet cupping^{12-16,22,26)} and one study using dry cupping²⁵⁾ reported changes in the upper limb motor function subdomain score

of the FMA scale. All studies showed significantly beneficial effects of additive cupping therapy (Fig. 5(B)). Meta-analysis also showed positive results of cupping therapy (MD 6.91, 95% CI 4.36 to 9.46, $P<0.00001$) (Fig. 5(B)), which was supported by a moderate level of evidence (Supplement 6). The subgroup analysis including only wet cupping studies showed similar results (MD 7.66, 95% CI 4.64 to 10.67, $P=0.01$) (Fig. 5(B)) (Supplement 8).

iii. Sensory function

Two studies^{18,32)} compared the response rates with and without additional wet cupping therapy in patients with sensory impairment after stroke. Meta-analysis of these studies showed that the benefit of wet cupping therapy was significant and the level of evidence supporting the result was low (OR 4.35, 95% CI 1.42 to 13.32, $P=0.010$) (Fig. 6) (Supplement 8).

iv. Spasticity

Two studies^{13,16)} assessed the level of spasticity using the MAS before and after wet cupping

(A) General motor function (motor function subdomain of Fugl-Meyer assessment scale)

(B) Upper limb motor function (upper limb motor function subdomain of Fugl-Meyer assessment scale)

Fig. 5. Forest plot of the effect of additional cupping therapy on motor function

Fig. 6. Forest plot of the effect of additional cupping therapy on sensory function Assessed by sensory domain of Fugl-Meyer assessment scale

therapy in patients with upper arm spasticity. The meta-analysis of these two studies showed that the additional effect of wet cupping was significant with a low level of evidence (MD

-0.63, 95% CI -0.83 to -0.44, $P < 0.00001$) (Fig. 7(A)) (Supplement 8).

Seven studies^[13-15,20,23,31] investigated the proportion of participants who responded positively in terms

(A) Modified Ashworth scale

(B) Response rate

(C) Integrated electromyography (biceps brachii)

Fig. 7. Forest plot of the effect of additional cupping therapy on spasticity

of spasticity after cupping therapy. The meta-analysis of these studies showed the significant benefit of cupping therapy (OR 3.28, 95% CI 1.31 to 8.22, $P=0.01$) (Fig. 7(B)), and a moderate level of evidence supported this result (Supplement 8). The subgroup analysis of the wet cupping studies showed similar results (OR 3.06, 95% CI 1.13 to 8.26, $P=0.03$), whereas the dry cupping

subgroup did not (OR 9.21, 95% CI 0.43 to 198.49, $P=0.16$) (Fig. 7(B)) (Supplement 8).

Changes in biceps brachii muscle detected by integrated electromyography in patients with upper limb spasticity were also more favorable for wet cupping (MD -4.45, 95% CI -6.74 to -2.16, $P=0.0001$) (Fig. 7(C))^{12,16}. However, the level of evidence supporting this benefit was very

(A) Visual analog scale

(B) Response rate

Fig. 8. Forest plot of the effect of additional cupping therapy on shoulder pain

low (Supplement 8).

v. Shoulder pain

Four studies^{19,22,26,28} reported changes in shoulder pain measured by a VAS after additive cupping therapy for patients with hemiplegic shoulder pain. The meta-analysis of these studies showed that adjuvant cupping therapy had significant benefits in reducing VAS scores (MD -1.67, 95% CI -1.96 to -1.39, $P < 0.00001$) (Fig. 8(A)), although the level of evidence supporting this effect was very low (Supplement 6). Similar results were reproduced in the subgroup analysis including only the wet cupping studies (MD -1.70, 95% CI -2.05 to -1.35) (Fig. 8(A)) (Supplement 8).

Two studies^{22,26} investigated the proportion of hemiplegic shoulder pain patients who responded positively to wet cupping therapy. Combining these studies showed that additive wet cupping therapy had significant benefits in improving shoulder pain, although the level of evidence was very low (OR 4.28, 95% CI 1.91 to 9.60, $P = 0.0004$) (Fig. 8(B)) (Supplement 8).

vi. Shoulder-hand syndrome

Four studies^{21,27,29,30} assessed the response rates to cupping therapy for patients with poststroke shoulder-hand syndrome. The meta-analysis of these studies showed that cupping therapy had significant benefits in increasing the response rate

Fig. 9. Forest plot of the effect of additional cupping therapy on shoulder-hand syndrome Assessed by response rate

in patients with poststroke shoulder-hand syndrome (OR 2.73, 95% CI 1.35 to 5.53, $P=0.005$) (Fig. 9). The results of the subgroup analysis of studies involving only wet cupping therapy also reproduced similar results (OR 3.15, 95% CI 1.43 to 6.94, $P=0.004$) (Fig. 9). However, the level of evidence supporting these findings was very low in all cases (Supplement 8).

vii. Safety

Five studies^{13,15,21,24,26} mentioned plans for collecting adverse events (AEs) during the study period. All of them were designed to compare the additional effectiveness of cupping therapy with the noncupping control. One²⁴ of the five studies mentioned the AE collection plan in the Methods section of the article but did not provide any information on the safety profile in the Result section. Out of the 4 studies describing the intervention-related AEs in the Results section, one study²¹ was about dry cupping, and the others^{13,15,26} were about wet cupping. The dry

cupping study²¹ reported that they did not identify any serious AEs in either cupping or noncupping groups. One of the wet cupping studies reported the occurrence of blistering with pain after cupping therapy, but did not disclose how many cases were identified²⁶. Therefore, we could secure data available for meta-analysis from only two wet cupping studies^{13,15}.

One study provided wet cupping therapy every other day for 30 days to patients with upper arm spasticity and reported two cases of subcutaneous bleeding at the cupping site¹³. These AEs spontaneously disappeared after 1 week, and no AEs were identified in the control group¹³. Another study provided wet cupping therapy every other day for 3 months to patients with upper arm dysfunction and identified two cases of AEs, including either bleeding or pain¹⁵. Combining the AEs identified in these two studies, no significant difference was found in the occurrence of AEs between the additional cupping group and the noncupping control group (OR 6.33, 95% CI

Fig. 10. Forest plot of the safety of additional cupping therapy Assessed by incidence of adverse events

0.74 to 53.99, $P=0.09$) (Fig. 10), and the level of evidence supporting this result was very low (Supplement 8).

Discussion

To confirm the therapeutic effect of cupping therapy, one of the oldest interventions used across the world in multiple cultures⁵, scientific explorations have been attempted in modern times. Clinical trials have shown the potential of cupping therapy to be effective in a variety of diseases, including herpes zoster, facial palsy, acne, and cervical spondylosis, as well as pain^{33, 34}.

Nevertheless, the mechanism of action of cupping remains unclear^{35,36}. However, the hypotheses that this intervention has local effects, including improving capillary and lymphatic circulation and extension of the underlying tissue, as well as systemic effects through activation of the neuroendocrine immune system resulting from the signaling molecules released from the blood vessels or tissues damaged by the cupping procedure^{35,36}, support the reason why cupping therapy can be applied to a variety of conditions across multiple systems of the whole body.

Among the wide range of indications for

cupping therapy, this study mainly presented the effects related to improving various complications in stroke survivors. This topic had already been addressed by a previous systematic review published in 2010⁶. However, at the time, sufficient data for meta-analysis were not obtained, so only narrative reviews of five clinical studies were possible⁶. Since that previous review⁶, more RCTs exploring the effect of cupping therapy in patients with stroke have been published. Therefore, we updated the findings of the previous study⁶ by performing quantitative synthesis and qualitative evaluation of the currently available evidence. To the best of our knowledge, this study is the first to systematically review and meta-analyze RCTs on the effectiveness and safety of cupping therapy in stroke survivors.

The findings of this study showed the potential of cupping therapy as an add-on intervention for stroke survivors receiving conventional treatment. Among the various clinical outcomes, the additional benefits of wet cupping therapy for improving motor function of the upper limb were identified. Cupping therapy may have directly influenced upper limb motor function. However, considering that the original studies supporting this result were derived from patients with upper limb spasticity or hemiplegic shoulder pain and

that the main findings of this systematic review also showed the advantage of cupping therapy for improving upper limb spasticity and reducing shoulder pain, we speculate that the effect of wet cupping for improving upper limb motor function may have been the result of muscle tone control and pain relief effects. However, this study could not find evidence supporting the effect of cupping therapy on lower limb motor function.

Another finding of this study, supported by a moderate level of evidence, was that additional wet cupping therapy increased the positive response rate for poststroke spasticity. This effect of wet cupping therapy, although at a very low evidence level, was also confirmed by improvements in MAS scores and decreases in muscle tone of the affected biceps brachii, a flexor muscle that is generally overhypertensive in poststroke elbow spasticity. These findings seem to reflect the possibility that muscle relaxation, one of the known actions of cupping therapy³⁷⁾, could also work on upper limb spasticity in stroke patients.

Other studies have shown the positive potential of adjuvant cupping therapy in a wider range of indications. This study identified additional benefits of cupping therapy for improving ADLs, sensory dysfunction, shoulder pain, and shoulder-hand syndrome in stroke survivors, although the level of supportive evidence was low or very low. The effect of additional cupping to reduce pain and improve functions was confirmed in previous studies targeting patients with pain in various underlying diseases^{4,5)}, and this study confirmed that this therapeutic action of cupping therapy could also work in stroke survivors.

This study also identified head-to-head studies comparing the effects of wet cupping therapy with active control interventions. The meta-analysis of these studies showed the possibility of wet cupping therapy being more beneficial than oral administration of baclofen in improving muscle tone and motor function in patients with poststroke upper arm spasticity. However, since there were only two small-sized studies supporting the findings and the level of evidence was low, it is necessary to be careful in interpreting this result.

The findings of this study mainly supported the additional benefits of cupping therapy, especially wet cupping therapy, in upper limb motor function, upper limb spasticity, shoulder pain and shoulder-hand syndrome in stroke survivors. Although the level of evidence was often low or very low, with rare studies with moderate levels of evidence, these findings may be helpful in determining priorities when considering application of cupping therapy for stroke survivors.

Subgroup analysis of wet cupping or dry cupping studies showed that the number of wet cupping studies was higher, and the treatment effect and evidence level were also higher than those of dry cupping studies. The fact that there were more studies on wet cupping than on dry cupping is consistent with the results of previous studies^{6,33)}. We found that not only was the number of studies on dry cupping therapy small, but the heterogeneity between those studies was also great. Therefore, it is difficult to draw conclusions about the effectiveness of dry cupping therapy on stroke based on the findings of this study. More clinical evidence needs to be collected.

Further consideration is also required on the effects of wet cupping therapy on stroke survivors, considering that wet cupping is a complex form of at least two kinds of interventions, namely, cupping and bloodletting puncture. In traditional Chinese medicine, bloodletting puncture without cupping is often performed, especially in stroke patients in the acute stage or with impaired consciousness, and a recent clinical trial has recently been published showing that bloodletting puncture could provide clinical benefits to stroke patients with disturbance of consciousness³⁸⁾. Further studies to compare and classify the effects of dry cupping, bloodletting puncture, and their combined form, wet cupping are required.

Generally, cupping therapy has been considered safe³³⁾, but AEs including anemia, infection, and scar formation have been reported^{39,40)}. There have also been concerns that it might actually cause stroke⁴¹⁾. However, this study detected no serious AEs related to cupping therapy and demonstrated that the incidence of AEs in the additional cupping group was not significantly higher than that in the noncupping control group. This is consistent with the suggestions in previous studies that cupping therapy is a relatively safe intervention under the condition that it is carefully performed by experienced practitioners⁴⁰⁾. However, considering that the meta-analysis on the occurrence of AEs in this study was based on only two small trials and that most of the reviewed studies did not consider the safety profile of cupping therapy in the process of study design, or omitted the reporting of AEs in the articles, we are hesitant to draw definitive conclusions about the safety of cupping therapy

here. In particular, considering that there have been concerns⁴¹⁻⁴³⁾ that cupping therapy performed on the neck area might cause arterial dissection by excessively raising the blood pressure of the carotid artery or vertebral artery that supplies cerebral circulation and eventually causes stroke, practitioners need to be careful not to induce excessive stress on the inside of the neck when performing cupping therapy in the neck area for stroke survivors.

This study has several limitations. First, despite our best efforts to secure as many relevant articles as possible, there may have been related trials that were not discovered by the search strategy in this study. We searched some databases based in Korea and China in addition to globally used core databases. This approach may have resulted in not identifying local publications in other regions, such as the Middle East or Africa, where cupping therapy has been used as a traditional intervention.

Second, there was a problem regarding the quantitative limitations of the included studies. Since there was no case in which the meta-analysis included more than 10 original trials, we could not construct a funnel plot to explore the existence of publication bias. Moreover, the scale of individual trials was too small. None of the trials had more than 100 participants per group. Crucially, no studies had previously calculated the optimal sample size for adequate power.

Third, the reporting quality of the included studies was low. Most studies did not clearly disclose how they corrected for the biases related to the random sequence generation, allocation concealment, dropout, and data selection. Most of

them also omitted the reporting of AEs, as mentioned above. These omissions in reporting deteriorated the overall quality of the methodology of each trial and consequently lowered the certainty of the evidence derived from this systematic review and meta-analysis.

Fourth, none of the included studies considered blinding. Some researchers have attempted to develop a sham or minimal cupping device as a control intervention for cupping therapy⁴⁴⁻⁴⁶. However, no sham/minimal cupping device has been confirmed to be perfectly suitable for blinding patients or practitioners⁴⁴⁻⁴⁶. Nevertheless, at least assessor blinding should have been ensured as a minimum measure to reduce detection bias. However, none of the included studies mentioned assessor blinding.

Fifth, the underlying mechanisms of the therapeutic effects of cupping therapy in the context of stroke has not been clearly determined. A previous systematic review⁶) speculated that the benefit of cupping therapy for stroke rehabilitation may be due to the excretion of excess fluid and toxins and improvements in subcutaneous blood flow. To date, however, all of the hypotheses remain unclear.

Sixth, no conclusion was drawn about the influence of cupping therapy on critical outcomes directly related to stroke itself. In particular, as there are no long-term follow-up outcomes, the effects of cupping therapy on mortality, severe disability, and recurrence of stroke is still unexplored.

Finally, a large number of studies have adopted response rates as the main outcome measure instead of the internationally accepted standardized

endpoints. This issue is one of the well-known chronic problems of RCTs dealing with cupping therapy³³). It can be a factor that prevents readers worldwide from trusting and adequately understanding the study results.

Conclusion

The findings of this study demonstrated the potential of cupping therapy to be beneficial in managing a variety of complications in stroke survivors. In particular, wet cupping therapy as an add-on for stroke survivors receiving conventional treatment provided significant benefits in improving upper limb motor function and spasticity, and these findings were supported by a moderate level of evidence. It was also found that cupping therapy did not significantly increase the occurrence of AEs, although the level of supporting evidence was very low. However, considering that the overall quality of the methodology of the included studies was low, further large-scale RCTs with rigorous designs are warranted to draw definite conclusions on the effectiveness and safety of cupping therapy for stroke survivors.

Conflicts of interest

The authors declare that they have no competing interests.

Acknowledgments

This study was undertaken as part of the KHIDI, funded by the Ministry of Health & Welfare, Republic of Korea. The funders did not

play any role in the design and conduct of this study.

Author contributions

Conceptualization: CH. Methodology: MK and CH. Formal Analysis: MK and CH. Wiring – Original Draft: MK. Writing – Reviewing & Editing: MK and CH. Supervision: CH. Project Acquisition: CH

Funding

This research was supported by a grant from the Korean Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (HB16C00001).

Ethical statement

This study did not involve any human or animal experiment.

Data availability

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

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Supplement 1. Electronic database and search term

1. PubMed (<https://www.ncbi.nlm.nih.gov/>)
(((((((stroke[Title/Abstract]) OR (cerebral infarction[Title/Abstract])) OR (cerebral hemorrhage[Title/Abstract])) OR (cerebrovascular disorder*[Title/Abstract])) OR (cerebrovascular accident*[Title/Abstract])) OR (apoplexy[Title/Abstract])) OR (brain ischemia[Title/Abstract])) OR ((((((cerebral infarction[MeSH Terms]) OR (cerebral hemorrhage[MeSH Terms])) OR (cerebrovascular accident[MeSH Terms])) OR (cerebrovascular disorder[MeSH Terms])) OR (apoplexy, cerebrovascular[MeSH Terms])) OR (apoplexy[MeSH Terms])) AND ((cupping [MeSH Terms]) OR (cupping [Title/Abstract]))
2. Embase (<https://www.embase.com/>)
(stroke:ti,ab,kw OR 'cerebral infarction':ti,ab,kw OR 'cerebral hemorrhage':ti,ab,kw OR 'cerebrovascular disorder':ti,ab,kw OR 'cerebrovascular disease':ti,ab,kw OR 'cerebrovascular accident':ti,ab,kw OR apoplexy:ti,ab,kw OR 'cerebrovascular accident'/exp OR 'stroke patient'/exp OR 'brain infarction'/exp OR 'brain hemorrhage'/exp OR 'cerebrovascular disease'/exp) AND (cupping:ti,ab,kw OR 'cupping therapy'/exp)
3. Cochrane Library (<https://www.cochranelibrary.com/>)
[TiAbKw] (stroke OR 'cerebral infarction' OR 'cerebral hemorrhage' OR 'cerebrovascular disorder' OR 'cerebrovascular accident' OR apoplexy OR 'brain ischemia') AND (cupping)
4. China Academic Journals (<https://oversea.cnki.net/index/>)
[TiKwAb] [Precise] (中风 OR 卒中 OR 脑卒中 OR 脑梗死 OR 脑栓塞 OR 脑溢血 OR 脑出血 OR 缺血性脑卒中 OR 出血性脑卒中 OR 脑血管) AND (拔罐)
5. Science On (<https://scienceon.kisti.re.kr/>)
6. Korean Studies Information Service System (<http://kiss.kstudy.com/>)
7. OASIS (<https://oasis.kiom.re.kr/>)
[TiAbKw] (뇌졸중 OR 뇌경색 OR 뇌출혈 OR 중풍 OR 뇌혈관질환) AND (부항)

Supplement 2. PRISMA 2020 abstract checklist

Section and Topic	Item #	Checklist item	Reported (Yes/No)
TITLE			
Title	1	Identify the report as a systematic review.	Y
BACKGROUND			
Objectives	2	Provide an explicit statement of the main objective(s) or question(s) the review addresses.	Y
METHODS			
Eligibility criteria	3	Specify the inclusion and exclusion criteria for the review.	Y
Information sources	4	Specify the information sources (e.g. databases, registers) used to identify studies and the date when each was last searched.	Y
Risk of bias	5	Specify the methods used to assess risk of bias in the included studies.	Y
Synthesis of results	6	Specify the methods used to present and synthesise results.	Y
RESULTS			
Included studies	7	Give the total number of included studies and participants and summarise relevant characteristics of studies.	Y
Synthesis of results	8	Present results for main outcomes, preferably indicating the number of included studies and participants for each. If meta-analysis was done, report the summary estimate and confidence/credible interval. If comparing groups, indicate the direction of the effect (i.e. which group is favoured).	Y
DISCUSSION			
Limitations of evidence	9	Provide a brief summary of the limitations of the evidence included in the review (e.g. study risk of bias, inconsistency and imprecision).	Y (conclusion)
Interpretation	10	Provide a general interpretation of the results and important implications.	Y (conclusion)
OTHER			
Funding	11	Specify the primary source of funding for the review.	NA
Registration	12	Provide the register name and registration number.	NA

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ* 2021;372:n71. doi: 10.1136/bmj.n71

Supplement 3. PRISMA 2020 checklist

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	P1. title
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	P2 & Supple 2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	P3, line 2-19
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	P3, line 20-22
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	P4. Chapter 2.2
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	P4. Chapter 2.1
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Supple 3 & P4. Chapter 2.1.2
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	P4. Chapter 2.2.1
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	P5. Chapter 2.3.
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	P5. Chapter 2.2.6
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	P5, line 2-4 (Chapter 2.3.)
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	P5. Chapter 2.5
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	P5. Chapter 2.4
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	P5. Chapter 2.4
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	Not done (The data presented in a form that could be quantitatively synthesized were chosen)

Section and Topic	Item #	Checklist item	Location where item is reported
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	Not done (The results were presented in the most widely used methods; Tables for individual studies and forest plots for synthesized data)
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	P5. Chapter 2.4
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	P5. Chapter 2.4
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	Not done
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	P5. Chapter 2.4 Followed the methods of RoB 2. Its third domain is about the missing outcome data. (Fig 2)
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	P6. Chapter 2.6
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	P7. Chapter 3.1 & Fig. 1
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	P7. Chapter 3.1 & Fig.1 & Supple 4
Study characteristics	17	Cite each included study and present its characteristics.	P7. Chapter 3.1., reference no. 11-32
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	P8. Chapter 3.3 & Fig 2&3
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	Table 2, Fig.4-12
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	P9. Chapter 3.4 & Supple 5&6
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	P9. Chapter 3.4 & Fig.4-12 & Supple 5&6
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	P9. subgroup analysis in Chapter 3.4) & Fig.4-12
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	Not done
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	Fig 2 – RoB2, Domain 3. missing outcome data
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	P9. Chapter 3.4) & Supple 5&6

Section and Topic	Item #	Checklist item	Location where item is reported
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	P12. 3rd paragraph-P13. 4th paragraph
	23b	Discuss any limitations of the evidence included in the review.	P14
	23c	Discuss any limitations of the review processes used.	P13. last paragraph
	23d	Discuss implications of the results for practice, policy, and future research.	P15. Chapter 5
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	P14 line 15-16
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	P14 line 15-16
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	P14 line 15-16
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	P14 line 7-10
Competing interests	26	Declare any competing interests of review authors.	P14 line 12-13
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	P14 line 18-21

Supplement 4. List of the articles excluded from the final analysis

No	Author	Year	Title	Bibliographic information	Reason for exclusion
1	YS Huang	2012	Observation on Therapeutic Effect of Zhuang Medicine Lotus Needle Cupping and Removing Blood Stasis on Post-Stroke Shoulder-Hand Syndrome	China Health Care & Nutrition 22(6) 591-2	NRCT
2	GT Guo, et al.	2017	Clinical Observation of Puncturing and Cupping Combined with Rehabilitation Training for Elbow Spasm after Stroke	Journal of Fuyang Institute of Technology 28(2) 51-3	NRCT
3	DD Zhang, et al.	2009	Puncture and Cupping Combined with Acupuncture for the Treatment of Shoulder-Hand Syndrome after Stroke	Jilin Journal of Traditional Chinese Medicine 29(9) 796-7	NRCT
4	GC Kim, et al.	2009	A Comparative Study on The Effect of Cupping and Moxibustion Therapy on Treating Constipation of Stroke Patients	Journal of Society of Preventive Korean Medicine 13(3) 101-12	NRCT
5	LJ Dong, et al.	2014	Efficacy Observation on the Treatment of 30 Cases of Shoulder-Hand Syndrome after Stroke by Yi Cup Therapy	Hebei Journal of Traditional Chinese Medicine 36(9) 1353-4	NRCT
6	RM Lee, et al.	2008	Effect of Moving Cupping Therapy on the Post-stroke Hand Edema: Single Subject Design	Journal of Korean Acupuncture & Moxibustion Society	NRCT
7	LT Xi	2016	Clinical Observation of Quanjing Acupuncture Therapy Combined with Blood-letting Puncture and Cupping Therapy for Upper Limb-spasticity after Cerebral Stroke in The Recovery Phase	[Thesis/Master] Hunan University of Traditional Chinese Medicine	Duplicated data
8	HY Liu, et al.	2016	Acupoint injection with cupping therapy effect of post-stroke shoulder pain	Jilin Journal of Traditional Chinese Medicine 36(10) 1056-8	Duplicated data
9	BY Ding, et al.	2000	Combination of Acupuncture and Cupping in Treating 52 Cases of Joint Contracture of Apoplexy Hemiplegia	Shanghai Journal of Acupuncture 19(3) 28	Duplicated data
10	FL Chen, et al.	2020	Application of Moxibustion and Cupping in Nursing Care of Stroke Hemiplegia	Yunnan Journal of Traditional Chinese Medicine 41(6) 89-90	Data not available for MA
11	N Li	2018	Curative Effect of Pricking and Cupping Combined with Rehabilitation Training in Stroke Patients with Upper Limb Elbow Flexion Spasm	Electronic Journal of Integrated Traditional Chinese and Western Medicine Cardiovascular Diseases 6(30) 163-6	Data not available for MA
12	HY Liu, et al.	2016	Acupuncture Point Injection Combined Cupping Therapy in Patients with Post-Stroke Shoulder Pain of Shoulder Joint Mobility	Journal of Changchun University of Chinese Medicine 32(6) 1211-3	Data not available for MA
13	XM Sun, et al.	2014	Acupuncture and Cupping Therapy combined with Western Aspiration Pneumonia	Journal of Practical Traditional Chinese Internal Medicine 28(3) 176-7	Data not available for MA
14	LY Li, et al.	2013	Clinical Observation on Hand Cupping Treatment of Hand Swelling after Stroke	Journal of Liaoning University of TCM 15(7) 157-8	Data not available for MA
15	FL Ni, et al.	2013	Observation on 31 Cases of Hyperhidrosis of Acute Cerebral Infarction Treated by Acupoint Cupping	Zhejiang Journal of Traditional Chinese Medicine 48(9) 633-4	Data not available for MA
16	YC Yang	2008	Blood Punching and Cupping in Treating 30 Cases of Hemiplegia and Shoulder Pain after Apoplexy	Traditional Chinese Medicinal Research 21(4) 54-6	Data not available for MA
17	HY Niu, et al.	2000	Discussion on the effect of cupping therapy in the treatment of cerebrovascular disease with pulmonary infection	Proceedings of the 8th Academic Conference of China Association of Acupuncture-Moxibustion (clinical branch). Part 2 (clinical study). 38-9	Data not available for MA

Supplement 4. List of the articles excluded from the final analysis (Continued)

No	Author	Year	Title	Bibliographic information	Reason for exclusion
18	SY Zhang	2002	Warm needle treatment for stroke hemiplegic of high limb end of the edema in 150 cases	Journal of Emergency in Traditional Chinese Medicine 11(6):489-90	Data not available for MA
19	XY Tao	2013	Observation on the curative effect of cupping therapy in preventing stroke patients with shoulder-hand syndrome in recovery period	Zhejiang Journal of Traditional Chinese Medicine	Data not available for MA
20	D Yang, et al.	2015	Observation on Curative Effect of Bloodletting at Jing Points on Post-stroke Depression	Liaoning Journal of Traditional Chinese Medicine 42(1) 157-8	Non cupping study
21	WM Ni, et al.	2004	Clinical Study on the Reduction of High Upper-limb Myodynamia by Blood-letting Puncture and Cupping in Cerebrovascular Accident Patients	Shanghai Journal of Acupuncture and Moxibustion 23(7) 10-1	Comparison btw cupping Tx's
22	HY Liu, et al.	2018	Effect of acupoint injection combined with cupping treatment on the daily life ability of patients with shoulder pain after stroke	Chinese Community Doctors 32(27) 169-70	Mixed effect of cupping + others
23	Y Liu	2013	Clinical Study on Combination Therapy for Treatment of Post-stroke Depression	Modern Journal of Integrated Traditional Chinese and Western Medicine 22(27) 3006-7	Mixed effect of cupping + others
24	HB Zhu, et al.	2019	Effects of Blood-Letting Puncturing and Cupping Assisted with Intelligent Motion Control Training on Balance and Lower Limb Function in Patients with Hemiplegia after Stroke	Guiding Journal of Traditional Chinese Medicine and Pharmacy 25(9) 123-6	Mixed effect of cupping + others
25	J Liu	2019	Clinical Observation on the Treatment of Upper Limb Spasticity in the Recovery Period of Stroke	Journal of Practical Traditional Chinese Medicine 35(9) 1105-6	Mixed effect of cupping + others
26	Z Li, et al.	2018	Observation on Curative Effect of Acupuncture Combined with Cupping Treating Post – Stroke Unilateral Hypermyotonia by Using DONG's Unique Extra – Ordinary Points	Journal of Clinical Acupuncture and Moxibustion 34(12) 14-7	Mixed effect of cupping + others
27	AL Zhan, et al.	2018	Effect Observation on Qianjing Acupuncture combined with Blood-letting Cupping Therapy on Upper Extremity Spasticity in Recovery Stage of Stroke	Rehabilitation Medicine 28(6) 52-5	Mixed effect of cupping + others
28	ML Xi, et al	2018	Blood-Letting and Cupping Therapy for Upper Limb Spasticity in Recovery Phase of Stroke	Chinese Acupuncture & Moxibustion 38(11) 1145-9	Mixed effect of cupping + others
29	YS Huang, et al.	2017	Clinical Study on Zhuang Medicine Lotus Needle Cupping and Removing Blood Stasis Method in Treating Hemisensory Disturbance in Stroke	Journal of Clinical Medical Literature 4(55) 10714-5	Mixed effect of cupping + others
30	JY Zheng	2016	The Clinical Research of "The Pricking Method of Removing Blood Stasis for Promoting Tissue Regeneration" Combined Xiaoyaosan for Post-stroke Depression	[Thesis/Master] Guangzhou University of Chinese Medicine	Mixed effect of cupping + others
31	Z Jiang	2015	The Clinical Research of "The Pricking Method of Removing Blood Stasis for promoting Tissue Regeneration" for Acute Cerebral Infarction	[Thesis/Master] Guangzhou University of Chinese Medicine	Mixed effect of cupping + others
32	XD Feng, et al.	2015	Effect of Blood-letting Puncture and Cupping Therapy on Hemianesthesia after Stroke	Chinese Journal of Rehabilitation Theory and Practice 21(10) 1206-8	Mixed effect of cupping + others
33	HC Liu, et al.	2013	MOTomed IA Exercise System Combined with Blood Pricking Cupping for Treatment of Increased Muscle Tone of Lower Limbs in Stroke Patients	Journal of Practical Traditional Chinese Medicine 29(3) 199-200	Mixed effect of cupping + others
34	X Li	2009	Clinical Observation and Nursing of Patients with Shoulder Pain after Apoplexy Treated by Cupping	Conference Proceeding of Chinese Nursing Association 246-7	Nonparallel study

NRCT: nonrandomized controlled trial, MA: meta-analysis, btw: between, Tx's: therapies

Supplement 5. Risk of bias summary of individual studies

Study ID	D1	D2	D3	D4	D5	Overall
JiPB2020	!	+	-	-	!	-
ZhangP2020	!	+	-	-	!	-
LiYY2019	!	+	-	-	!	-
ShanYL2019	!	+	-	-	!	-
JiangL2018	+	+	+	-	!	-
HuangZQ2018	!	+	-	-	!	-
ChenJY2017	!	+	-	-	!	-
ChenYP2017	!	+	+	-	!	-
LiuHY2016	!	+	-	-	!	-
ZhangBB2016	!	+	-	-	!	-
ChengXL2014	!	+	-	-	!	-
ZhangQF2014	!	+	-	-	!	-
MiaoT2014	!	+	-	-	!	-
HuangZQ2014	+	+	+	-	!	-
YangMY2013	!	+	-	-	!	-
GaoLA2015	!	+	-	-	!	-
PengL2012	!	+	-	-	!	-
WuZY2011	!	+	-	-	!	-
FuL2009	!	+	-	-	!	-
ZouC2006	!	+	-	-	!	-
DingBY2003	!	+	-	-	!	-
CuiSZ2001	!	+	-	-	!	-

+	Low risk
!	Some concerns
-	High risk

D1	Randomisation process
D2	Deviations from the intended interventions
D3	Missing outcome data
D4	Measurement of the outcome
D5	Selection of the reported result

Supplement 6. Overall risk of bias of included studies

Supplement 7. GRADE evidence profile for cupping versus medication

Question: Cupping compared to baclofen for stroke

Certainty assessment										No. of patients		Effect		Certainty	Importance
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	cupping	baclofen	Relative (95% CI)	Absolute (95% CI)					
FMA(U/E)															
2	randomised trials	serious ^a	not serious	not serious	serious ^b	none	73	73	-	MD 5.2 higher (1.51 higher to 8.88 higher)	⊕⊕○○ LOW	important			
MAS															
2	randomised trials	serious ^a	not serious	not serious	serious ^b	none	73	73	-	MD 0.69 lower (0.82 lower to 0.56 lower)	⊕⊕○○ LOW	important			
IEMG(biceps)															
2	randomised trials	serious ^a	not serious	not serious	serious ^b	none	73	73	-	MD 4.05 lower (6.36 lower to 1.74 lower)	⊕⊕○○ LOW	important			
IEMG(triceps)															
2	randomised trials	serious ^a	not serious	not serious	serious ^b	none	73	73	-	MD 3.56 higher (1.62 higher to 5.5 higher)	⊕⊕○○ LOW	important			
response rate (spasticity)															
2	randomised trials	serious ^a	not serious	not serious	serious ^b	none	66/73 (90.4%)	52/73 (71.2%)	OR 3.81 (1.50 to 9.65)	192 more per 1,000 (from 76 more to 248 more)	⊕⊕○○ LOW	important			

FMA: Fugh-Meyer assessment scale; **U/E:** upper extremity; **MAS:** modified Ashworth scale; **IEMG:** integrated electromyography; **Ci:** Confidence interval; **MD:** Mean difference; **OR:** Odds ratio

Explanations

a. All studies had high risk of bias in one or two domains of the Cochrane risk-of-bias tool for randomized trials (version 2).

b. N < 400

Supplement 8. GRADE evidence profile for additional cupping versus no cupping control

Question: Additional cupping compared to no cupping for stroke

Certainty assessment										No. of patients		Effect		Certainty	Importance
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	additional cupping	no cupping	Relative (95% CI)	Absolute (95% CI)					
Barthel index															
5	randomised trials	serious ^a	serious ^c	not serious	not serious	none	205	201	-	SMD 1.23 higher (0.21 higher to 2.25 higher)	⊖⊖⊖ LOW	Important			
Barthel index – Wet cupping															
3	randomised trials	serious ^a	not serious	not serious	serious ^d	none	130	126	-	SMD 0.48 higher (0.23 higher to 0.72 higher)	⊖⊖⊖ LOW	important			
Barthel index – Dry cupping															
2	randomised trials	very serious ^b	serious ^c	not serious	very serious ^{de}	none	75	75	-	SMD 2.44 higher (1.1 lower to 5.99 higher)	⊖⊖⊖ VERY LOW	important			
FMA(motor)															
2	randomised trials	serious ^a	not serious	not serious	very serious ^{de}	none	73	73	-	MD 1.95 higher (2.42 lower to 6.31 higher)	⊖⊖⊖ VERY LOW	important			
FMA(motor) – Wet cupping															
1	randomised trials	serious ^a	not serious	not serious	very serious ^{de}	none	43	43	-	MD 1.25 lower (7.33 lower to 4.83 higher)	⊖⊖⊖ VERY LOW	important			
FMA(motor) – Dry cupping															
1	randomised trials	very serious ^b	not serious	not serious	serious ^d	none	30	30	-	MD 3.5 higher (0.86 higher to 6.14 higher)	⊖⊖⊖ VERY LOW	important			
FMA(U/E)															
8	randomised trials	serious ^a	not serious	not serious	not serious	none	285	277	-	MD 6.91 higher (4.36 higher to 9.46 higher)	⊖⊖⊖ MODERATE	important			

FMA(U/E) – Wet cupping

7	randomised trials	serious ^a	not serious	not serious	not serious	none	251	247	-	MD 7.66 higher (4.64 higher to 10.67 higher)	○○○○ MODERATE	important
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FMA(U/E) – Dry cupping

1	randomised trials	very serious ^b	not serious	not serious	serious ^d	none	34	30	-	MD 3.98 higher (2.53 higher to 5.43 higher)	○○○○ VERY LOW	important
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response rate (sensory)

2	randomised trials	serious ^a	not serious	not serious	serious ^d	none	83/87 (95.4%)	66/81 (81.5%)	OR 4.35 (1.42 to 13.32)	136 more per 1,000 (from 47 more to 168 more)	○○○○ LOW	important
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MAS

2	randomised trials	very serious ^b	not serious	not serious	serious ^d	none	78	78	-	MD 0.63 lower (0.83 lower to 0.44 lower)	○○○○ VERY LOW	important
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IEMG (biceps)

2	randomised trials	very serious ^b	not serious	not serious	serious ^d	none	70	70	-	MD 4.45 lower (6.74 lower to 2.16 lower)	○○○○ VERY LOW	important
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response rate (spasticity)

7	randomised trials	serious ^a	not serious	not serious	not serious	none	225/259 (86.9%)	165/237 (69.6%)	OR 3.28 (1.31 to 8.22)	186 more per 1,000 (from 54 more to 253 more)	○○○○ MODERATE	important
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response rate (spasticity) – Wet cupping

6	randomised trials	serious ^a	not serious	not serious	not serious	none	173/207 (83.6%)	137/207 (66.2%)	OR 3.06 (1.13 to 8.26)	195 more per 1,000 (from 27 more to 280 more)	○○○○ MODERATE	important
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response rate (spasticity) – Dry cupping

1	randomised trials	very serious ^b	not serious	not serious	very serious _{de}	none	52/52 (100.0%)	28/30 (93.3%)	OR 9.21 (0.43 to 198.49)	59 more per 1,000 (from 76 fewer to 66 more)	○○○○ VERY LOW	important
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VAS

4	randomised trials	very serious ^b	serious ^c	not serious	serious ^d	none	145	141	-	MD 1.67 lower (1.96 lower to 1.39 lower)	○○○○ VERY LOW	important
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VAS – Wet cupping

3	randomised trials	very serious ^b	serious ^c	not serious	serious ^d	none	100	96	-	MD 1.70 lower (2.05 lower to 1.35 lower)	○○○○ VERY LOW	important
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VAS – Dry cupping

1	randomised trials	very serious ^b	not serious	not serious	serious ^d	none	45	45	-	MD 1.62 lower (2.14 lower to 1.10 lower)	○○○○ VERY LOW	important
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response rate (pain)

2	randomised trials	very serious ^b	not serious	not serious	serious ^d	none	71/81 (87.7%)	48/77 (62.3%)	OR 4.28 (1.91 to 9.60)	253 more per 1,000 (from 136 more to 317 more)	○○○○ VERY LOW	important
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response rate (SHS)

4	randomised trials	very serious ^b	not serious	not serious	serious ^d	none	119/133 (89.5%)	102/133 (76.7%)	OR 2.73 (1.35 to 5.53)	133 more per 1,000 (from 49 more to 181 more)	○○○○ VERY LOW	important
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response rate (SHS) – Wet cupping

3	randomised trials	very serious ^b	not serious	not serious	serious ^d	none	102/113 (90.3%)	86/113 (76.1%)	OR 3.15 (1.43 to 6.94)	148 more per 1,000 (from 59 more to 196 more)	○○○○ VERY LOW	important
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response rate (SHS) – Dry cupping

1	randomised trials	very serious ^b	not serious	not serious	very serious ^{d,e}	none	17/20 (85.0%)	16/20 (80.0%)	OR 1.42 (0.27 to 7.34)	50 more per 1,000 (from 281 fewer to 167 more)	○○○○ VERY LOW	important
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AE

2	randomised trials	serious ^a	not serious	not serious	very serious ^{d,e}	none	5/84 (6.0%)	0/84 (0.0%)	OR 6.39 (0.75 to 54.25)	0 fewer per 1,000 (from 0 fewer to 0 fewer)	○○○○ VERY LOW	important
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CI: Confidence interval; **SMD:** Standardised mean difference; **MD:** Mean difference; **OR:** odds ratio; **FMA:** Fugl-Meyer assessment scale; **UIE:** upper extremity; **MAS:** modified Ashworth scale; **IEMG:** integrated electromyography; **VAS:** visual analogue scale; **SHS:** shoulder-hand syndrome; **AE:** adverse event

Explanations

- a. All studies had high risk of bias in one or two domains of the Cochrane risk-of-bias tool for randomized trials (version 2).
- b. All studies had high risk of bias in two domains of the Cochrane risk-of-bias tool for randomized trials (version 2).
- c. I25 ≥ 75%
- d. N < 400
- e. The 95% CI includes the null value.