Original Article

Effect of acupuncture treatment on dysphagia caused by pseudobulbar paralysis after stroke: a systematic review and meta-analysis

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Background: The efficacy of acupuncture in the treatment of dysphagia caused by pseudobulbar paralysis after stroke is lack of evidence-based medicine. Our objective was to synthesize the efficacy of acupuncture in treating dysphagia caused by pseudobulbar paralysis after stroke.

Methods: A comprehensive literature search was performed in 9 databases [PubMed, Web of Science, Embase, Cochrane, Chinese BioMedical Literature Database (CBM), China National Knowledge Infrastructure (CNKI), WanFang Data, Chinese Science and Technology Periodicals database (VIP), and Open Grey online database] to screen eligible randomized controlled studies that evaluated the effect of acupuncture in dysphagia caused by pseudobulbar paralysis after stroke. The search time limit is from establishing the database to October 1, 2020. The random-effects model was used to calculate the significant effect size.

Results: A total of 7 studies comprising 637 participants were included in our meta-analysis. The results showed that compared with rehabilitation, acupuncture had a significant effect on improving dysphagia caused by pseudobulbar paralysis after stroke [the significant effective size: risk ratio $(RR)_{sig}$ =1.51; 95% confidence interval (CI): 1.30–1.75; I^2=0%]. In the subgroup analyses, the RR_{sig} of acupuncture + rehabilitation *vs.* rehabilitation was 1.56 (95% CI: 1.30–1.87; I^2=0%), and the RR_{sig} of acupuncture *vs.* rehabilitation was 1.38 (95% CI: 1.08–1.76; I^2=0.8%).

Discussion: Acupuncture can be used as an effective treatment for dysphagia caused by pseudobulbar paralysis after stroke. Acupuncture combined with rehabilitation therapy has better effects.

Keywords: Acupuncture; dysphagia; pseudobulbar paralysis; stroke; systematic review; meta-analysis; randomized controlled trials (RCTs)

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Introduction

Pseudobulbar paralysis is a common complication after stroke, with an incidence of more than 51% (1). It is caused by upper limb motor injury due to bilateral cortical tract disorders and is characterized by dysphagia, dysphonia, weakness of face and tongue, and emotional instability (2,3). Dysphagia caused by pseudobulbar paralysis affects daily eating and increases the risk of aspiration pneumonia as well as disability and mortality (4,5). Pseudobulbar paralysis lacks specific treatment, which is an urgent problem to be solved at present. Although there are some rehabilitation treatments for dysphagia caused by pseudobulbar paralysis, the efficacy varies greatly. Since dysphagia is multidimensional, a multidisciplinary and comprehensive approach is needed.

The research on acupuncture treatment of dysphagia caused by pseudobulbar paralysis has increased, but the results are not consistent. Moreover, there is a lack of conclusive evidence at present. Given the increasing number of randomized controlled trials (RCTs) of acupuncture for dysphagia caused by pseudobulbar paralysis, we conducted a systematic review and meta-analysis of the existing evidence to examine and explore the effect of acupuncture in dysphagia caused by pseudobulbar paralysis after stroke. We present the following article in accordance with the PRISMA reporting checklist (available at https://apm.amegroups.com/article/view/10.21037/apm-21-3551/rc).

Methods

The protocol has been registered on the PROSPERO platform (CRD42022306827).

Search strategy

We performed the literature search in PubMed, Web of Science, Embase, Cochrane, Chinese BioMedical Literature Database (CBM), China National Knowledge Infrastructure (CNKI), WanFang Data, Chinese Science and Technology Periodicals database (VIP), Open Grey online database, to identify relevant studies from the establishment of the database to October 1, 2020. The following terms individually or in combination were used to identify the potential articles: "pseudobulbar palsy", "pseudobulbar paralysis", "stroke", "stroke sequelae", "cerebral infarction", "hemorrhagic stroke", "cerebrovascular accident", "ischemic stroke", "acupuncture", "scalp acupuncture", "electroacupuncture", "tongue needle", "Jin's three needles", "pricking blood", "body acupuncture", and "rehabilitation training". The grey literature was searched using the Open Grey online database. The search was limited to English or Chinese. Besides, a manual search was carried out on included studies or conference abstracts to identify any ongoing studies or trial registries. All the studies have been rigorously evaluated.

Study selection

Studies were included if they met the following criteria: (I) study design: RCTs; (II) intervention: acupuncture with or without rehabilitation; (III) comparison: rehabilitation treatment without acupuncture; (IV) population: diagnosed as dysphagia caused by pseudobulbar paralysis after stroke, regardless of age, sex or race; (V) outcome: the number of patients who substantially recovered, markedly effective, effective and invalid in the intervention and control groups. We excluded non-RCTs, animal studies, prospective studies, case-control studies, cross-sectional studies, letters, reviews, commentaries, and studies that dysphagia not related to pseudobulbar paralysis after stroke or other unknown diseases. If the study was reported more than once, we would use the latest results. In the course of this work, any differences between the two authors need to be discussed with the third author (DHX) to reach a consensus.

Data extraction and quality management

Two groups of four investigators (PW and XMM, JH and JXL) independently reviewed and extracted relevant data from each included report. We extracted the following information: authors, publication year, number of patients, intervention duration, participant characteristics, intervention, acupoints, comparison, efficacy evaluation criteria, and drop-out rate. All results were displayed in the form of figures or tables. Adverse events were also collected from the included studies. The same investigators also assessed the risk of bias from each included study using the Cochrane risk of bias tool. Any differences were resolved by discussion and consensus.

Data synthesis and analysis

Meta-analysis of RCTs with available data was performed by calculating the effect size [risk ratio (RR)] and 95% confidence interval (CI) using the random-effect models

Table 1 The calculation method of RR_{sig} and RR_{total}

Group	N	Substantially recovered	Markedly effective	Effective	Invalid
Intervention	N2	A2	B2	C2	D2
Control	N1	A1	B1	C1	D1

N2: total number of intervention group; A2: substantially recovered number of intervention group; B2: markedly effective number of intervention group; C2: effective number of intervention group; D2: invalid number of intervention group; N1: total number of control group; A1: substantially recovered number of control group; B1: markedly effective number of control group; C1: effective number of control group; D1: invalid number of control group. RR, risk ratio.

and the Mantel-Haenszel (M-H) method.

The detailed calculation method is shown in *Table 1*.

The significant effective size: $RR_{sig} = \frac{(A2+B2)/N2}{(A1+B1)/N1}$.

The total effective size: $RR_{total} = \frac{(A2+B2+C2)/N2}{(A1+B1+C1)/N1}$.

Heterogeneity was considered statistically significant at I^2>50%. To explore the heterogeneity and stability of the results, we carried out sensitivity analyses. In addition, we conducted subgroup analyses to explore the effects of different interventions.

Publication bias was assessed by visual inspection of funnel plots and formal testing by Egger's and Begg's test if more than 10 studies were included.

Statistical analysis

StataSE 12.0 software (StataCorp, USA), and Review Manager 5.3 software (Cochrane collaboration network) were adopted to merge the statistics of the included articles.

Results

Search results

A total of 1,583 studies were identified by the initial database research. Six hundred studies were excluded because of duplication, and 873 studies were excluded based on the titles and or abstracts. The remaining 110 full-text reports were reviewed for more detailed evaluation. available online: https://cdn.amegroups.cn/static/public/apm-21-3551-01.pdf listed the reasons for excluded articles: the intervention of comparison is non-rehabilitation (n=58); the intervention of treatment group is non-acupuncture or non-acupuncture combined with rehabilitation (n=23); non-RCTs (n=11); reviews or meta-analysis (n=3); participants are not with pseudobulbar paralysis (n=6); duplicated (n=2). Finally, seven RCTs that met our eligibility criteria were included in the present meta-analysis (6-12). The selection process for RCTs included in the meta-analysis is shown in *Figure 1*.

Methodological quality assessment

We conducted a graphical summary of bias risk assessment for the 7 included studies (Figures S1,S2). Of these, patients were randomized using a random number table in 5 studies (8-12). The remaining 2 studies referred to"randomization" but did not describe specific randomization methods (6,7). None of the literature described allocation concealment. Due to the nature of acupuncture, blinding of participants and personnel was not attempted in any articles. Only one study clearly stated that results were assessed blindly by a third-party organization (12). All the included literature had complete data for analysis. Except for Yuan's study, 6 studies have not provided the protocol of its main and secondary outcomes, which were judged as an unknown risk of reporting bias. Other bias was assessed as low risk in all.

Characterization of included studies

Table 2 showed the characteristics of all included trials (7 studies with 637 participants) assessing the effect of acupuncture treatment in individuals with dysphagia caused by pseudobulbar paralysis after stroke. The average duration of symptoms for all trials was 48 days. The average sample size was 79. Most of the participants were older (the average age was 64 years). The average duration of intervention across all trials was 26 days.

The types of intervention used in all included studies were single acupuncture (8,10,12), or acupuncture combined with rehabilitation (6,7,9-11). Acupoints contain GB20, CV23, CV22, EX-HN12, etc., of which GB20 is mandatory (Table S1). The rehabilitation treatment methods included

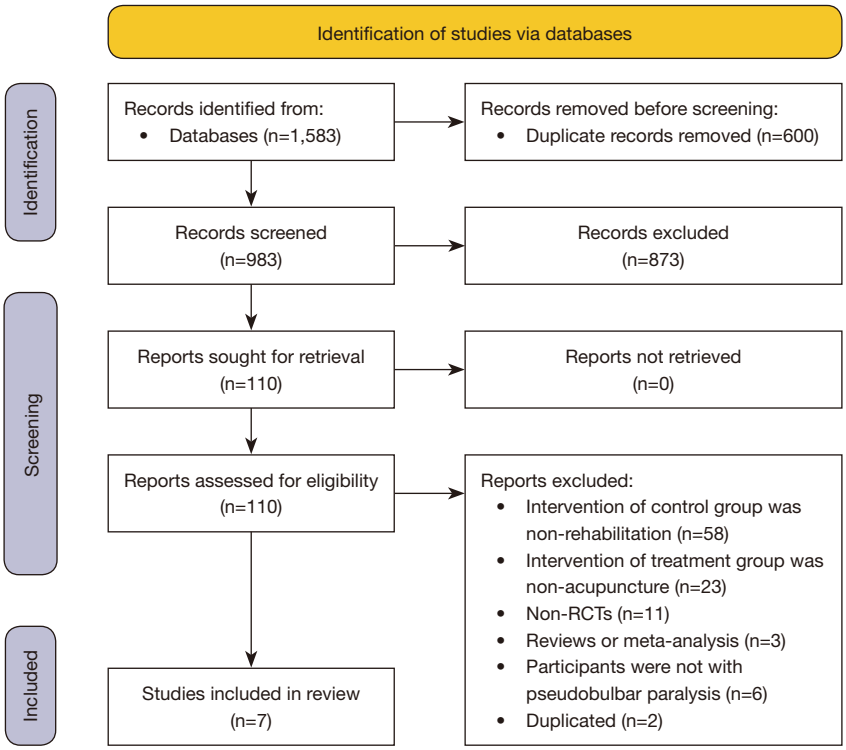

Figure 1 Summary of the search process. RCTs, randomized controlled trials.

could stimulation, vocalization training, swallowing training, tongue muscle training, ingestion training, soft palate lift training, masticatory muscle training, swallowing reflex training.

There were seven criteria for evaluating the curative effect, including Kubota Toshio Drinking Water Test (KTST), Swallow Quality-of-Lift Questionnaire (SWAL-QOL), Standard Swallowing Function Score (SSA), National Institute of Health Stroke Scale (NIHSS), Repeated Saliva Swallowing Test (RSST), Modified Water Swallowing Test (MWST), Fujishima Ichiro Swallowing Efficacy Score (FISES).

The drop-out rate of all studies was 0, except that Chu *et al.* (9) was 3% (2 cases in the intervention group and 1 case in the control group were caused by recurrence and aggravation of cerebrovascular accident).

Efficacy of acupuncture

Seven studies reported the effective rate of acupuncture for dysphagia caused by pseudobulbar palsy after stroke. As shown in Figure S3, acupuncture had a significant effect on improving the total effective rate of dysphagia with substantial heterogeneity (RR_{total} =1.13; 95% CI: 1.02–1.25; I^2=64.4%). Surprisingly, acupuncture markedly increased the significant effective rate of dysphagia without heterogeneity (*Figure 2*; RR_{sig} =1.51; 95% CI: 1.30–1.75; I^2=0%). In the following, we focus on the research of RR_{sig}.

Subgroup analyses

According to whether the intervention group was combined with rehabilitation, we conducted subgroup analyses. In the subgroup of acupuncture + rehabilitation *vs.* rehabilitation, the RR_{sig} was 1.56 (95% CI: 1.30–1.87; I^2=0%) using the random-effects model (Figure S4); in the subgroup of acupuncture *vs.* rehabilitation, the RR_{sig} was 1.38 (95% CI: 1.08–1.76; I^2=0.8%) using the random-effects model (Figure S4). Therefore, acupuncture combined with rehabilitation shows a better effect on dysphagia.

Sensitivity analyses

As shown in Figure S5, we implemented sensitivity analyses by systematically omitting a single study step by step, and the result did not change, indicating that our result was stable.

Table 2 Trial characteristics

Study	Age (years)	Duration of symptoms (days)	No. of patients (T/C)	Intervention (whether combined with R)	Control (rehabilitation)	Duration of intervention (days)	Drop-out rate (%)	Efficacy evaluation criteria
Liu, 2009 (6)	T: 59.2; C: 57.4	T: 63; C: 66	82 (42/40)	Y	3, 4	30	0	I
Liu & Zhao, 2014 (7)	T: 70.22±6.60; C: 69.75±6.85	T: 19.75±6.12; C: 20.50±5.88	64 (32/32)	Y	4, 6, 7	21	0	I, II
Wang, 2017 (8)	T: 65.04; C: 65.73	T: 27.01; C: 26.12	135 (90/45)	N	2, 3, 4, 5, 8	24	0	III, IV
Chu, 2017 (9)	T: 67±11; C: 67±10	T: 41.1±38.6; C: 40.5±30.8	97 (48/49)	Y	1, 2, 3, 4, 5	40	3	II, III, V
Cao-1, 2019 (10)	T: 60.30±8.75; C: 57.25±10.38	T: 85.5±49.5; C: 110.7±44.7	58 (30/28)	Y	1, 2	20	0	I
Cao-2, 2019 (10)	T: 62.66±8.54; C: 57.25±10.38	T: 96.3±46.8; C: 110.7±44.7	60 (32/28)	N	1, 2	20	0	I
Liu & Chen, 2019 (11)	T: 66.2±11.3; C: 65.9±10.9	T: 42; C: 32	94 (47/47)	Y	1, 2, 3, 4, 5	40	0	II, III, V, VI
Yuan, 2020 (12)	T: 63.29±8.91; C: 62.84±7.54	T: 16.5; C: 15.0	75 (38/37)	N	2, 3, 5	14	0	II, VII

1: cold stimulation; 2: vocalization training; 3: swallowing training; 4: tongue muscle training; 5: ingestion training; 6: soft palate lift training; 7: masticatory muscle training; 8: swallowing reflex training. I: KTST; II: SWAL-QOL; III: SSA; IV: NIHSS; V: RSST; VI: MWST; VII: Fujishima Ichiro Swallowing Efficacy Score. T, Treatment; C, Control; R, Rehabilitation; Y, Yes; N, No; KTST, Kubota Toshio Drinking Water Test; SWAL-QOL, Swallow Quality-of-Life Questionnaire; SSA, Standard Swallowing Function Score; NIHSS, National Institute of Health Stroke Scale; RSST, Repeated Saliva Swallowing Test; MWST, Modified Water Swallowing Test.

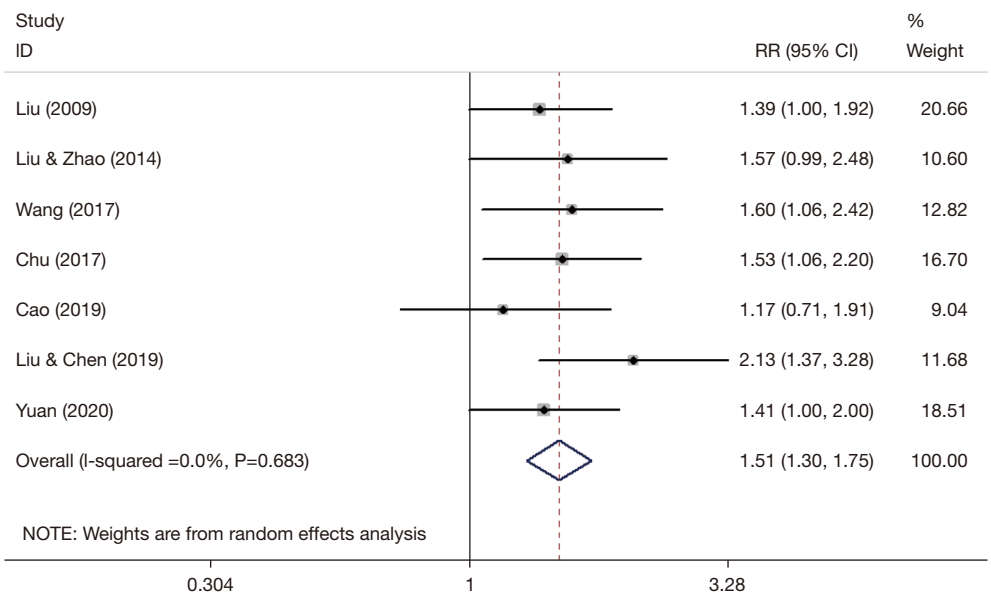

Figure 2 Forest plot of the estimated RR_{sig} in dysphagia caused by pseudobulbar paralysis poststroke with acupuncture compared with rehabilitation. RR, risk ratio.

Publication bias analyses

Publication bias was not assessed for outcome since fewer than 10 articles were included.

Adverse events

All of the included trials provided information on adverse events, and only two of them had adverse events. Wang *et al.* (8) reported that pneumonia (control group 7/45; intervention group: 7/90), asphyxia (control group 6/45; intervention group: 2/90), dehydration (control group 7/45; intervention group: 11/90), and malnutrition occurred (control group 5/45; intervention group: 8/90). Yuan *et al.* (12) reported that 10 participants (control group 4/37; intervention group: 6/38) had mild pain during treatment but did not affect follow-up treatment. Other adverse events were not reported.

Discussion

This is a systematic review and meta-analysis of seven RCTs to evaluate the efficacy of acupuncture compared with rehabilitation in patients with dysphagia caused by pseudobulbar paralysis after stroke. The present meta-analysis demonstrates that acupuncture can significantly improve the dysphagia caused by pseudobulbar paralysis after stroke, and acupuncture combined with rehabilitation shows a better effect.

Bulbar paralysis is a kind of low motor neuron paralysis that affects the nuclei of IX, X, XI, and XII of cerebral nerves. In contrast, pseudobulbar paralysis is upper motor neuron paralysis that affects the cortical bulbar bundles of the V, VII, IX, X, XI, and XII. Any injury to the nucleus or cortical tract can lead to medulla oblongata or pseudobulbar paralysis (e.g., stroke, multiple sclerosis, infection, brainstem tumor) (13-15). Bulbar paralysis and pseudobulbar paralysis are mainly seen in men over 75 years old, characterized by dysarthria and dysphagia (16,17). Acupuncture has been the primary medical intervention for stroke and stroke-related complications in China and other parts of East Asia, and the effect is significant (18). There have been numerous meta-analyses on acupuncture in treating dysphagia after stroke, which has proved that acupuncture was an effective method for treating dysphagia after stroke (19-23). However, these meta-analyses did not separate pseudobulbar paralysis from true bulbar paralysis. Our meta-analysis is the first to identify pseudobulbar palsy, demonstrating the superiority of acupuncture in this condition and providing evidence-based evidence for precise clinical treatment.

Expectedly, our subgroup analyses shows that acupuncture combined with rehabilitation is more effective than that acupuncture without rehabilitation. The clinical application of this result can reasonably explain that if the hospital does not have enough rehabilitation measures, acupuncture can improve dysphagia. What is more, if there is adequate rehabilitation treatment, the addition of acupuncture is more effective.

The mechanism of acupuncture stimulation is considered to be closely related to the nervous system and is expected to improve neurological function after stroke (24). Acupuncture treatment of dysphagia caused by pseudobulbar paralysis after stroke may be related to the swallowing cortex's excitement (25). Also, acupuncture can promote the establishment of collateral circulation and angiogenesis, improve nerve function, regulate inflammatory factors, regulate the production of inflammatory factors, growth factors, and transcription factors, and effectively reduce nerve injury (26,27). In addition, some animal experiments and clinical trials show that acupuncture mainly regulates the release of neurotransmitters, improves cerebral microcirculation, protects neurons, inhibits inflammation, and so on (28-31).

GB20 and CV23 have become the most frequently used acupoints in the included studies. Therefore, acupuncture in these two acupoints may help to improve dysphagia caused by pseudobulbar paralysis after stroke. According to the standard acupoints of the World Health Organization (WHO Western Pacific Regional Office, 2008), GB20 is located at the back of the neck, suboccipital depression, between the origin of the sternocleidomastoid muscle and the trapezius muscle, and the surrounding anatomical tissue includes the sternocleidomastoid muscle, trapezius muscle, head clamp muscle and branches of the lesser occipital nerve. Another important acupoint CV23 was located in the anterior part of the cervical midline, above Adam's tubercle, and in the depression of the superior margin of the hyoid bone. The surrounding anatomical tissues include the suprahyoid muscle, facial nerve, glossopharyngeal nerve, hypoglossal nerve branch, and vagus nerve branch. Studies have shown that electroacupuncture stimulation of CV23 activated the swallowing-related neurons of (VLM) in the ventrolateral medulla of rats, and promoted swallowing activity in rats, 5-hydroxytryptamine (5-HT1A) in the nucleus of the solitary tract (NTS) may play an essential role in this excitatory effect (32,33).

Overall, this meta-analysis demonstrates the efficacy of acupuncture in treating dysphagia caused by pseudobulbar paralysis after stroke, although more high-quality RCTs are needed. In terms of treatment, we have also found that acupuncture combined with rehabilitation has a better effect, which may have some implications for clinical practice.

Limitations

This study has several limitations. Firstly, we paid attention to the efficacy of acupuncture in the treatment of dysphagia caused by pseudobulbar paralysis, but there was no comparison and research on true bulbar paralysis. Then, due to the small number of studies included, the design of RCTs was not strict, which may have an impact on the accuracy of the results. Besides, all studies were conducted in China, and it was impossible to evaluate the efficacy of acupuncture in different regions and different ethnic groups.

Conclusions

At present, there is no unified standard for the treatment of dysphagia caused by pseudobulbar paralysis after stroke. This meta-analysis fully confirmed that acupuncture could effectively improve dysphagia caused by pseudobulbar paralysis after stroke, and acupuncture combined with rehabilitation has a better effect. However, because the included studies' quality was not high enough, the findings should be interpreted with caution. Also, further high-quality RCTs are needed.

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Footnote

Reporting Checklist: The authors have completed the PRISMA reporting checklist. Available at https://apm.amegroups.com/article/view/10.21037/apm-21-3551/rc

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://apm.amegroups.com/article/view/10.21037/apm-21-3551/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Supplementary

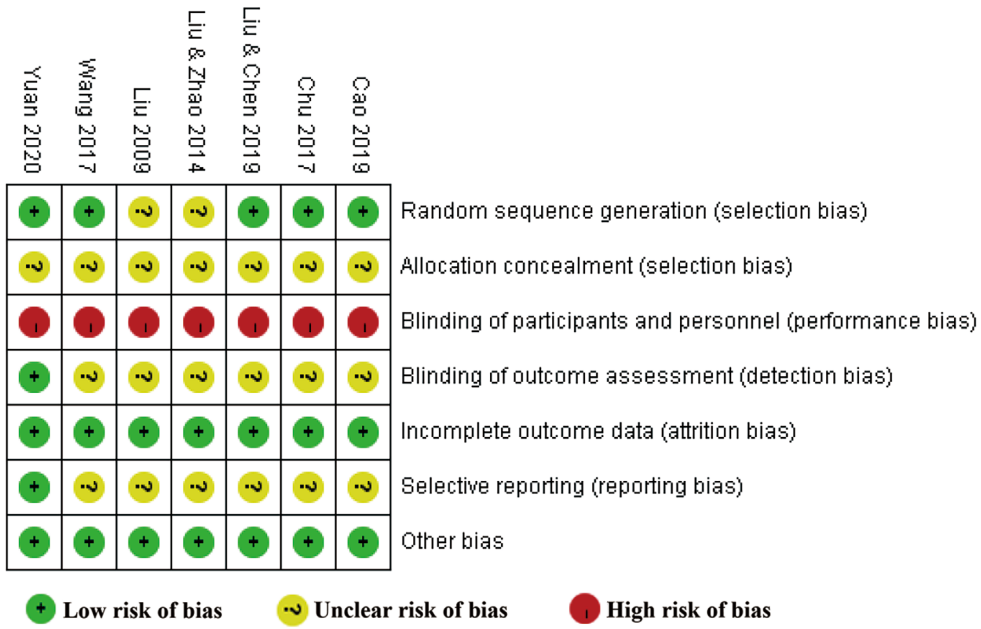

Figure S1 Cochrane risk of bias summary for all included trials.

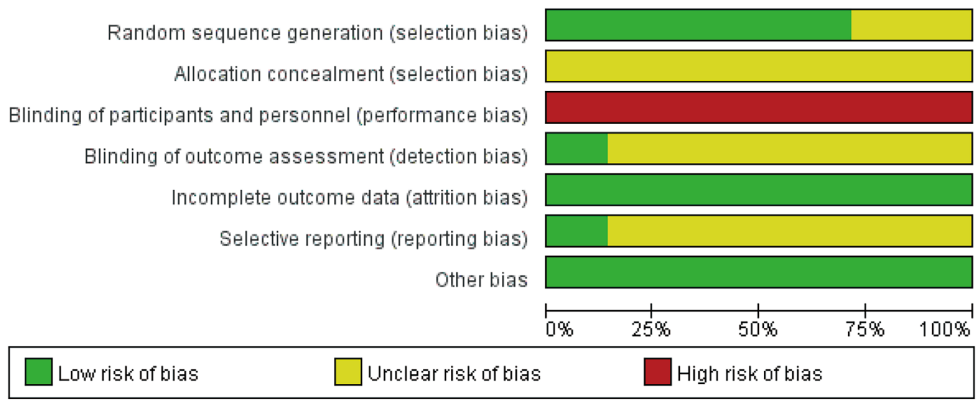

Figure S2 Risk of bias proportion for all included trials.

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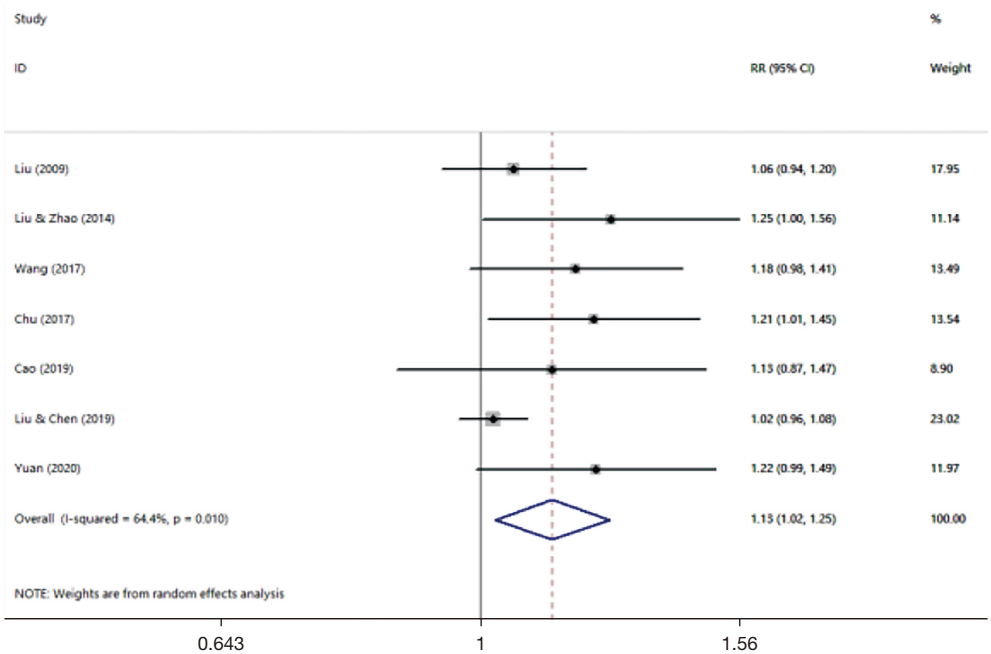

Figure S3 Forest plot of the estimated RRtotal in dysphagia caused by pseudobulbar paralysis poststroke with acupuncture compared with rehabilitation. RR, risk ratio; CI, confidence interval.

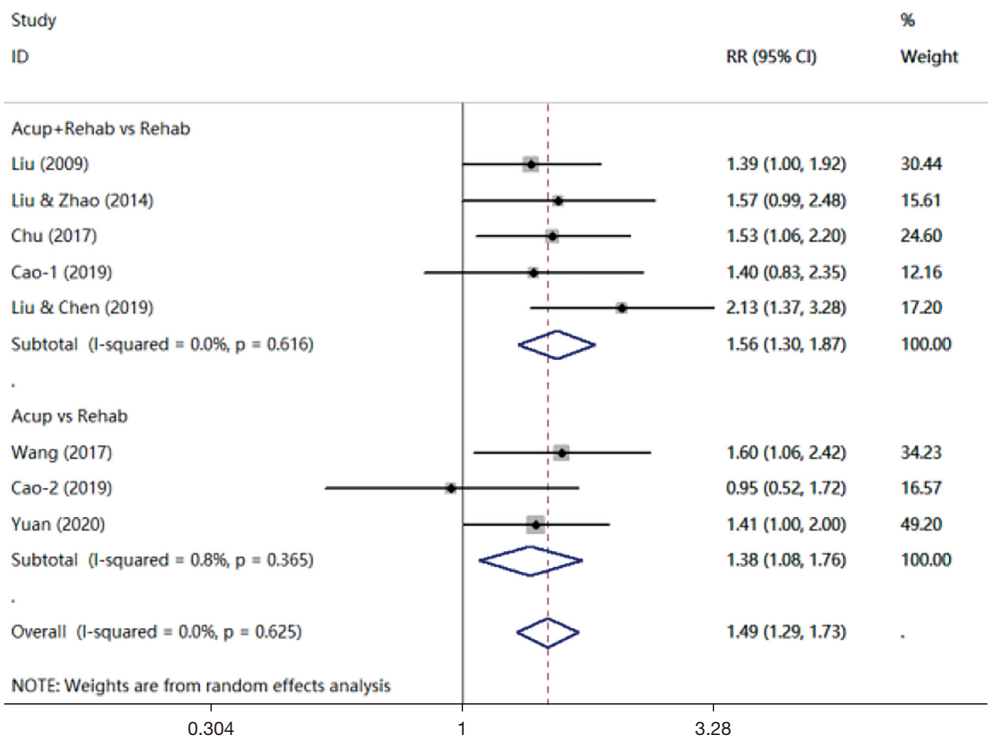

Figure S4 Subgroup analyses. RR, risk ratio; CI, confidence interval.

https://dx.doi.org/10.21037/apm-21-3551

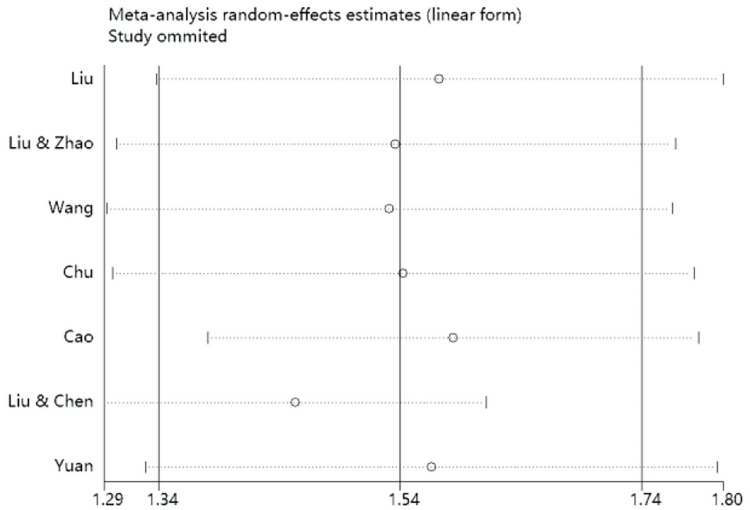

Figure S5 Sensitivity analyses.

Table S1 Acupoint summary

Study	Acupoints
Liu, 2009	GB20, LR3, KI3, ST40, LI4, RN6, SP10
Liu & Zhao, 2014	GB20, CV23, SJ17, Shanglianquan, EX-HN12
Wang, 2017	GB20, Aqiang, Zhiqiang, Tunyan, Tiyan, PC6, EX-HN12
Chu, 2017	GB20, CV23, EX-HN14, Gongxue, Zhiqiang, Tunyan, Fayin, Waijinjinyuye GB20
Cao, 2019	GB20, Shanglianquan, Ashi, GV15, DU20, CV22
Liu & Chen, 2019	GB20, CV23, EX-HN14, Gongxue, Zhiqiang, Tunyan, Fayin, Waijinjinyuye GB20
Yuan, 2020	CV23, GB12, GV26, PC6, ST36

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