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The Effectiveness of Acupuncture in Stroke Recovery: A Systematic Review and Meta-analysis

by

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Note

This systematic review and meta-analysis follows the guidelines set forth in the Cochrane guidelines for Systematic Reviews (SR) as specified in its Handbook (Higgins & Green, 2011). This handbook (and thus format) is the gold standard for systematic reviews. Additionally, this research paper is in APA 6 format as per the 7/5/2019 agreement. Although not a part of the Cochrane format, I have added a placeholder page for signatures and a copyright page as per the South Baylo University Clinical Research Manual document Clinical_Research_Manual_EN_2020, page 12. These pages still retain their APA 6 characteristics.

The Effectiveness of Acupuncture in Stroke Recovery: A Systematic Review and Meta-analysis

Leonard Joseph Hicks

SOUTH BAYLO UNIVERSITY at ANAHEIM, 2020

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Abstract

Background

Stroke and its concomitant effects are major causes of disability and financial hardship to people and their families. Acupuncture has long been used as an adjuvant treatment to standard care of patients with stroke. However, studies have shown different results regarding the effectiveness of the intervention.

Objectives

The aim of this meta-analysis is to investigate the effectiveness of acupuncture added to standard care of patients with stroke, compared with standard care alone or no acupuncture.

Materials and Methods

I searched EBSCO, PubMed, Cochrane CENTRAL, MEDLINE, EMBASE, WHO, clinicaltrials.gov, and Google Scholar databases from inception to February 10, 2020 for randomized controlled trials. The intended outcomes for analysis were the Fugl–Meyer

assessment (FMA) score, the National Institute of Health Stroke Scale (NIHSS), and the Barthel index scale (BIS). Data were pooled as mean differences and relative confidence intervals.

Results

Pooled analysis showed that acupuncture is not effective in improving motor disabilities assessed by the FMA score after four weeks of therapy (MD -3.41, 95% CI [-6.93, 0.11], p=0.06), and after eight weeks (MD = -3.12, 95% CI [-6.63, 0.39], p=0.08). The analysis of the results of the Barthel index scale was not significant as well (SMD = -0.10, 95% CI [-0.30, 0.10], p=0.32). NIHSS score showed no significant improvement as well (MD = 0.12, 95% CI [-0.27, 0.50], p=0.56). This is true even though the studies indicate that some subtests within these scores and other tests using different scores show significant improvement over standard treatment. For example, Chen et. al 2016 reports significant improvement with aspects of the FMA score (p=0.020); Wayne et. al 2005 reports significant benefit in the Nottingham Health Profile (NHP) (p=0.02); Du et. al 2018 reports significant improvement in the Lowenstein Occupational Therapy Cognitive Assessment (LOTCA) (p<0.05), and Zhang et. al 2015 reports significant improvement in the Scandinavian Stroke Scale (SSS) (p<0.03). Many of these example results could not be incorporated into the pooled data because they are taken from tests that are too dissimilar from the FMA, Barthel Index, or NIHSS scales to justify their inclusion. Thus, these examples offer a contrasting view of the pooled data's results and give a truer indication of the power of acupuncture and how to show it with meta-analysis.

Conclusion

Acupuncture is an effective adjuvant therapy to standard care for stroke patients even though this is not indicated by the pooled data analysis. The widespread use of standardized scores focused on specific functional areas can be instrumental for meta-analysis to show the power and effectiveness of acupuncture.

Background

Stroke is the fifth (5th) leading cause of death in the United States and is a major cause of serious disability. This high ranking as a cause of mortality/disability makes finding reliable therapeutic interventions for stroke a high priority (Scholte Op Reimer, De Haan, Rijnders, Limburg, & Van Den Bos, 1998; Xu, Murphy, Kochanek, & Arias, 2016). Both brain trauma and stroke are considered to be the commonest causes of injury of the current neural system. They both can cause serious body disorders affecting behavioral, cognitive, and motor functions. Post-stroke cognitive disorders are irreversible and often leave long-term complications on the patients (Twamley, Jak, Delis, Bondi, & Lohr, 2014). It has been reported that cognitive impairment occurs in about 50-90% of stroke patients. This high incidence rate served in including cognitive rehabilitation as a cornerstone and a standard component of stroke rehabilitation (Desmond et al., 2000; Hachinski et al., 2006; Hachinski & Munoz, 2000).

Different complications of stroke can be followed up by the distribution of cerebral blood flow. A positive correlation is present between blood flow and the glucose consumption rates by the tissues, and they both change in response to any changes of local activity of the brain (Sokoloff, 1981). Therefore, an adequate blood flow in a cerebral hemisphere indicates less damaged cells and subsequently relatively good rehabilitation outcomes (Treger, Aidinof, Lutsky, & Kalichman, 2010; Treger, Streifler, & Ring, 2005). There is strong evidence suggesting that 36% of patients with stroke have a cumulative risk of 5 years to develop a new major disability after the first-ever stroke (Hankey, Jamrozik, Broadhurst, Forbes, & Anderson, 2002).

Management and treatment of the cognitive disorders of stroke has become an interesting topic to focus on by the researchers (Jin, Di Legge, Ostbye, Feightner, & Hachinski, 2006). Acupuncture is an integral part of Traditional Chinese Medicine (TCM), which has been practiced for over 2000 years in China, where it has been traditionally considered as a relatively simple, cheap, and safe treatment for conditions associated with stroke (H. Liu et al., 2012).

It has been used to improve many neurological functions including motor, sensory, speech, and balance in stroke patients (Ivey, Hafer-Macko, & Macko, 2006). Acupuncture has been shown to have analgesic effects (Lee & Chan, 2006; Streitberger et al., 2010) and improves the motor function and limb balance (Kang, Sok, & Kang, 2009; S. Y. Liu et al., 2009). Animal trials demonstrated that acupuncture therapy protects from brain damage (Chuang, Hsieh, Li, & Lin, 2007; Gao, Guo, Zhao, & Cheng, 2002). In 1999, the National Institutes of Health stated that acupuncture may have some benefits as an adjunct therapy in rehabilitation of stroke patients ("Acupuncture Consensus Conference. Acupuncture," 1998).

Although there is an abundance of clinical studies regarding acupuncture, many clinicians still worry about its therapeutic effect and safety. The effectiveness of acupuncture as either primary or adjunctive treatment for stroke has raised considerable debate: there are published systematic reviews that conclude there is no compelling evidence that acupuncture is a useful adjunct for stroke rehabilitation (Kong, Lee, Shin, Song, & Ernst, 2010) contrasted with other reviews that support the use of acupuncture (Liu et al., 2019). Such conflicting reports lead one to question whether acupuncture is indeed a viable primary or adjunctive treatment for stroke recovery. This review aims to assess and appraise the effectiveness of acupuncture in patients with stroke.

Objectives

The goal of this study is to assess the effectiveness of acupuncture as an adjuvant therapy to standard care for patients with stroke This will be achieved through analysis of the reported scores used for assessment of the patients' motor conditions and analysis of ancillary scores that may influence motor conditions (e.g., cerebral blood flow measurements).

Methods

This systematic review and meta-analysis comply with the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) statement (Moher et al., 2009). I ensured that all steps follow Cochrane's handbook of systematic reviews of interventions (Higgins & Green, 2008).

Eligibility criteria

The decision of including or excluding studies was according to the following criteria: 1) studies designed as randomized, sham-controlled clinical trials, 2) participants: patients with stroke whose treatment therapy includes some form of acupuncture (e.g., scalp acupuncture, ipsilateral vs contralateral, traditional body points), 3) intervention: acupuncture as an adjuvant to standard care for stroke, and 4) comparator: acupuncture or sham acupuncture, or non-acupuncture groups. The following studies were excluded: 1) non-randomized controlled trials, 2) animal studies, non-clinical studies, non-randomized trials, systematic reviews and meta-analyses, 3) trials involving only Chinese Herbal medicine and 4) studies with no accessible data, conference abstracts, and studies for which I could not get an English language translation.

Literature search

From inception to February 10, 2020, I looked for relevant clinical controlled trials throughout the following databases: EBSCO, PubMed, Cochrane CENTRAL, MEDLINE, EMBASE, WHO, clinicaltrials.gov, and Google Scholar. No language restrictions were applied.

I developed a search strategy for conducting the literature search using a combination of the following keywords: 'stroke', 'acupuncture', and trial as follows: stroke AND acupuncture AND trial AND (controlled OR sham OR placebo).

Data collection and analysis

Screening of results

I performed the screening of retrieved studies through two main stages. The first stage involved the inclusion and exclusion of studies based on their title and abstract. Then, included studies by title and abstract were entered into the second stage, full-text screening to ensure that the study properly matches the inclusion and exclusion criteria. Studies that had a mismatch with a single inclusion criterion were excluded. I conducted another search through the references of the included trials to assure that I did not miss any controlled trial. Figure 1 shows a PRISMA flow chart of my literature search.

Data extraction

I mainly used Microsoft Excel for the extraction of data. Three main categories of data were extracted. The first category included baseline data about the study participants, such as patients' age, gender, baseline scores, sides affected, and time from stroke onset. The second category of data included different scores used for assessment of patients' general and motor functions, such as the Fugl–Meyer assessment (FMA) score, the National Institute of Health Stroke Scale (NIHSS), and the Barthel index scale (BIS). The third category of data involved data used to assess the risk of bias among the included studies.

Quality assessment

This systematic review and meta-analysis was evaluated using the Grading of Recommendations, Assessment, Development, and Evaluations (GRADE). I included randomized controlled trials only to ensure high-quality evidence. For assessment of the risk of bias, I used the Cochrane's risk of bias tool (Green et al., 2011) mentioned in chapter 8 of the Cochrane handbook. The tool assesses the risk of bias through the following domains: 1) proper patient randomization, 2) patients allocated into the intended groups through a blind method (Allocation concealment), 3) patient blinding only (termed single blinding), or both personnel and participants blinded (double-blinding), 4) Attrition bias, 5) are all mentioned protocol outcomes reported or not (Selection bias), 6) are outcome assessors blinded in order to prevent outcome value over- and/or under-estimation, and 7) other biases.

Data synthesis

The extracted data were restricted to continuous outcomes, as all the data for the analysis are scores with the relative mean and standard deviation (SD). Using the Review Manager Software version 5.3("RevMan 5 | Cochrane Community," n.d.), the intended scores were pooled as either mean differences (MD) or standardized mean differences (SMD) according to the measuring method of each study. I used the SMD for analysis of the Barthel index scale outcome, as one study (Bai et al., 2013) used a modified scale. Statistical analysis was performed using the inverse variance method, and heterogeneity was assessed using two main tests (Higgins, Thompson, Deeks, & Altman, 2003), the I-square test (I^2) and the P-value of the Chi-square test. The analysis is said to be heterogeneous if values of $I^2>50\%$ and $P<0.1$ are present, according to the Cochrane Handbook (Higgins & Green, 2008). I performed the analysis of homogeneous data under a fixed-effects model, while heterogeneous data were analyzed under the random-effects model.

The studies measured different scales across three main time points: 1) after application of the acupuncture, or week zero, 2) after four weeks, and 3) after eight weeks. A subgroup analysis was performed according to the aforementioned time points.

The included trials used various scores and methods for assessment of the patients' general and motor conditions. Therefore, I extracted the common scores from the studies and only five studies (Bai et al., 2013; Chen et al., 2016; Hsing, Imamura, Weaver, Fregni, & Azevedo Neto, 2012; Liao et al., 2017; Park, Jongbae et al., 2017) were eligible for meta-analysis. The remaining studies used different assessment methods that could not be combined under a single meta-analysis.

Results

Summary of included studies

A total of 1563 patients were included in this study, 778 patients received acupuncture as an adjuvant therapy to standard care for stroke, and 785 patients were control groups that received either a sham acupuncture intervention or no acupuncture intervention. Table 1 shows a summary of the included studies and demographic data of patients. The mean age of patients reached 62.54 years old for the acupuncture group, and 60.4 years old for the control group. Table 2 describes some baseline values of different reported scores used by different trials. Table 3 lists the acupuncture points used by each study.

Bai et al. (Bai et al., 2013) used three groups to assess the patients' motor condition. The groups were (1) body needle acupuncture alone, (2) body needle acupuncture and physiotherapy, and (3) physiotherapy alone. The FMA and Barthel index scales were used and found no significant difference between the acupuncture and non-acupuncture groups ($p=0.16$). This study indicates that all treatment groups showed improvement, but that there was no statistically significant improvement above the standard care (in this case, physiotherapy) for either of the acupuncture groups.

The results of Chen et al. (Chen et al., 2016) showed that acupuncture is effective ($p<0.001$) in improving some neurological conditions, swallowing disorders, cognitive impairment, and lower extremity function. However, no significant motor improvements in the upper extremity were noted. The study showed that FMA scores did not change from baseline values ($p=0.23$), in contrast to NIHSS which improved ($p<0.001$). This study used body needle points as listed in Table 3. While the FMA score did not change from baseline, the Lower FMA score (for the lower extremities – i.e., legs) did show significant motor improvement above standard care ($p=0.02$).

The study by Du et al. (Du, Yin, Liu, Chen, & He, 2018) used the Loewenstein Occupational Therapy Cognitive Assessment (LOTCA) score and found that the score is significantly higher in the acupuncture group than the control group ($p<0.05$). This study used scalp acupuncture as the primary acupuncture technique.

Hsing et al. (Hsing, Imamura, Weaver, Fregni, & Azevedo Neto, 2012) found significant improvements in the acupuncture group as measured by the NIHSS ($p=0.03$). However, Rankin and Barthel scores showed no significant results ($p=0.19$). This study used scalp electro-acupuncture as the intervention, and sham electro-acupuncture in the control group (see Table 3).

Liao et al. (Liao et al., 2017) found that acupuncture significantly reduces pain scores ($p=0.04$ for the Visual Analogue Scale (VAS) test). No statistically significant differences were noted regarding other scales, such as NIHSS ($p=0.97$) and the Barthel index ($p=0.6$). The study used a combination of body needles and scalp acupuncture with an emphasis on body needle points (see Table 3). Sham acupuncture was used in the control group. While there were no statistically significant differences reported in the major scales, both groups had improvements in the NIHSS and Barthel index scales ($p<0.05$). Interestingly enough, there was also a significant improvement in the Instrumental Activities of Daily Living (IADL) score for females in the sham acupuncture group only ($p<0.05$).

The study conducted by Park et al. (Park, Jongbae et al., 2017) used the Barthel index as its primary outcome and showed that acupuncture is not superior to sham acupuncture in the recovery of daily activities (Barthel index $p=0.38$). This study was conducted with a body needle acupuncture intervention (see Table 3) and used sham acupuncture as the control. While the Barthel index and NIHSS scored did not show a statistically significant difference between the two groups, the Barthel leg function subgroup showed a statistically significant difference on leg function ($p=0.02$). Interestingly, the sham group showed a statistically significant difference in “unsafe swallow” ($p=0.04$).

Ratmansky et al. (Ratmansky et al., 2016) showed that acupuncture significantly increases cerebral blood flow post-stroke, as measured by the mean flow velocity of the blood ($p<0.04$). This study used body needle acupuncture (see Table 3) as the intervention, and sham acupuncture as the control.

Wayne et al. (Wayne et al., 2005) used a combination of body electro-acupuncture and scalp acupuncture as the intervention, and used sham acupuncture on the control group (see Table 3). Although the study did not find any significant difference between acupuncture and control groups regarding quality of life scores ($p=0.7$), significant results were obtained regarding wrist spasticity, and both wrist and shoulder range of motion in the active acupuncture group ($p<0.01$).

Yan et al. (Yan & Hui-Chan, 2009) included three main arms in their trial: a transcutaneous electrical stimulation + standard care group, a placebo stimulation + standard care group, and a group with only standard care. Body acupuncture points were used (see Table 3). The results showed that patients in the acupuncture group showed increased ankle dorsiflexor strength, and decreased antagonist co-contraction ratio compared to control groups ($p<0.01$). Additionally, acupuncture helped patients to walk four days earlier than those in the control groups.

Zhang et al. (S. Zhang et al., 2015) measured the mortality rates in acupuncture and sham groups. Although no statistically significant difference was noted (95% CI [0.54, 1.05]), there was a tendency of lower mortality rates in the acupuncture group. Barthel index showed no difference as well. This study used body needle points as the intervention and standard care as the intervention.

Table 4 summarizes all statistically significant tests which were performed in the studies of this research paper (Bai et al., 2013; Chen et al., 2016; Du et al., 2018; Hsing et al., 2012; Liao et al., 2017; Park et al., 2005; Ratmansky et al., 2016; Wayne et al., 2005; Yan et al., 2009; Zhang et al., 2015) that used a body needling acupuncture technique and Table 5 summarizes all statistically significant tests which used a scalp acupuncture technique (Du et al., 2018; Hsing et al., 2012; Liao et al., 2017; Wayne et al., 2005). Two papers (Liao et al., 2017; Wayne et al., 2005) appear in both tables since they use a combination of scalp and body needle techniques.

Results of risk of bias assessment

Assessment of risk of bias among included trials revealed an overall low risk of bias. According to Cochrane's tool, all studies have been properly designed and adequately performed the randomization of patients. The studies ensured proper allocation concealment as well. However, regarding blinding of both patients and personnel, two studies (Yan & Hui-Chan, 2009; S. Zhang et al., 2015) were single-blinded studies. Only the patients were blinded to the intervention being performed. As for the blinding of the outcome assessment domain, all studies were at low risk of bias except Ratmansky et al. (Ratmansky et al., 2016), which reported that outcome assessors were not blinded. Therefore, the study was categorized as high risk of bias. Two studies (Yan & Hui-Chan, 2009; S. Zhang et al., 2015) did not provide enough evidence about the blinding of outcome assessors, therefore, they were categorized as 'unclear risk'. All studies were at low risk regarding ‘other’ risk of bias domains, such as attrition and reporting bias. I found no other bias in the studies as well. Figure 2 shows a risk of bias graph and a summary of the risk of bias assessment among included studies.

Analysis of efficacy endpoints

1. Analysis of FMA score

   Two studies reported the use of the FMA score (Bai et al., 2013; Chen et al., 2016). The studies measured the score on the same day after treatment (week 0), after four weeks, and after eight weeks. The combined analysis of the FMA score across all time points showed that acupuncture significantly reduces the FMA score, and therefore, is associated with more impairment of movement than the control group (MD = -3.27, 95% CI [-5.75, -0.78], p=0.01). Pooled data were homogeneous (I^2=0%, P=0.89). Single analysis according to each time point showed that there is no significant difference between acupuncture and control groups after four weeks (MD -3.41, 95% CI [-6.93, 0.11], p=0.06), and after eight weeks (MD = -3.12, 95% CI [-6.63, 0.39], p=0.08). Pooled analysis was homogeneous (I^2=0%). This is shown in Figure 3.

2. Analysis of the Barthel index scale

   The overall standardized mean difference (SMD) of the Barthel index scale across all time points showed that there is no statistically significant difference between acupuncture and control groups (SMD = -0.10, 95% CI [-0.30, 0.10], p=0.32). Results were homogeneous (I^2=0%, P=0.92). Three studies (Bai et al., 2013; Hsing et al., 2012; Liao et al., 2017) reported the use of the Barthel index scale to assess the patients' condition after acupuncture at 4 weeks, the results did not reveal any statistical difference (SMD = -0.06, 95% CI [-0.35, 0.22], p=0.67). Pooled analysis was homogeneous (I^2=0%, P>0.1). This is shown in Figure 4.

3. Analysis of NIHSS

Four studies (Chen et al., 2016; Hsing et al., 2012; Liao et al., 2017; Park, Jongbae et al., 2017) used the NIH stroke score for assessment of the patients' motor condition. The overall mean difference did not favor any of the two groups (MD = 0.12, 95% CI [-0.27, 0.50], p=0.56). The results were homogeneous (I^2=0%, P=0.41). This is shown in Figure 5.

Discussion

The analysis of this study suggests that applying acupuncture in addition to the standard care for stroke yields no clinically significant results. Results of the analysis of each score were non-significant when compared with the non-acupuncture group.

There is no dispute regarding the safety of the intervention, as a matter of fact, acupuncture is considered one of the safest invasive interventions with minimal or no side effects. However, the effectiveness of the procedure in patients with stroke is still controversial. Prior to acupuncture, other approaches have been introduced in an attempt to improve stroke symptoms such as constraint-induced movement therapy (Taub, Crago, & Uswatte, 1998; Wolf, Lecraw, Barton, & Jann, 1989), and computer-aided motion tracker measured by fMRI (Carey et al., 2004, 2002). More advanced techniques have been also tried, such as using robots for sensorimotor upper limb training (Ferraro et al., 2003; Volpe, Krebs, & Hogan, 2003). In a study by de Kroon et al., therapeutic electrical stimulation has been tried as well (de Kroon, van der Lee, Ijzerman, & Lankhorst, 2002). Although these techniques showed great promise in the past, their clinical effectiveness remained unconfirmed.

The first randomized controlled trial assessing the benefits of acupuncture in stroke surviving patients was conducted in the United States by Wayne and colleagues (Wayne et al., 2005). The study concluded that acupuncture has no effective role in the improvement of chronic stroke symptoms, as measured by the quality of life scale. Yan et al. (Yan & Hui-Chan, 2009) conducted a similar trial in China and concluded that three weeks of daily electric acupuncture leads to a significantly lower number of patients with spasticity. The effectiveness of treatment lasted for two weeks after the end of therapy sessions. Contrary to the previous results, Bai et al. (Bai et al., 2013) found that acupuncture leads to lower motor improvement rates as assessed by the FMA scale. Two years later, Zhang et al. (S. Zhang et al., 2015) performed a trial and measured the mortality rates of their included patients. The results did not support the use of acupuncture as an adjuvant to standard care of stroke. In the next year, two more clinical trials were published that further supported the role of acupuncture in improving the general and motor conditions of patients with stroke (Chen et al., 2016; Ratmansky et al., 2016). In 2017, two more trials were conducted with contradicting results. The first trial (Liao et al., 2017) found no significant effect of acupuncture in the activity of daily living score, while Park et al. (Park, Jongbae et al., 2017) reported that acupuncture improves patients' performance of daily life activities.

My results are consistent with previously published meta-analyses. Sze et al. (Sze, Wong, Or, Lau, & Woo, 2002) performed a meta-analysis of 14 trials and found that, in addition to stroke standard care, acupuncture has no additional effect on motor recovery. Another meta-analysis (Kong et al., 2010) found that acupuncture has no positive effects on functional recovery after stroke. Other studies have investigated the effectiveness of acupuncture on other neurological deficits. A meta-analysis by Tang et al. (Tang, Tang, Yang, Wu, & Shen, 2019) revealed that tongue acupuncture is effective in treating post-apoplectic aphasia. Zhang et al. (X. Y. Zhang, Li, Liu, Zhang, & Chen, 2019) proved that acupuncture has an effective role in reducing depression in patients with chronic stroke. A recently published meta-analysis also supported the role of acupuncture in relieving pain and improving daily activities (Liu et al., 2019). Adding acupuncture to routine swallowing training in patients with stroke was also found to be effective in treating dysphagia compared with routine swallowing training alone.

This meta-analysis included only randomized controlled trials, which adds a point of strength to the evidence provided. The included trials were at low risk of bias as assessed by the

Cochrane's risk of bias tool. Additionally, all scores that have been entered into the analysis are internationally standardized scales for assessment of stroke complications. The main limitation of this study is the lack of data. The diversity of the used scores came as a disadvantage, as meta-analysis cannot combine different scores. Three studies (Wayne et al., 2005; Yan & Hui-Chan, 2009; X. Y. Zhang et al., 2019) did not provide baseline characteristics of included participants. Also, although I included ten studies, only five provided eligible data for analysis. This lack of data might have affected the results of the analysis.

The majority of the tests/scores in Table 4 and Table 5 could not be included because they are basically single case tests and are different from the FMA, Barthel index, or NIHSS scales. For example, the LOTCA, the major measure from Du et al. (Du et al., 2018) could not be included because it is too different from either of the other three scores and there is no other study among the ten selected with which to perform a meta-analysis. Adding these to the meta-analysis would be like adding "apples" to "oranges" and still calling that total "apples". The data from Table 4 and Table 5 does indicate some trends.

- Cognitive and neurological tests appear to provide statistically significant results. Zhang et al. (Zhang et al., 2015) used the Scandinavian Stroke Score (SSS) as a measure of neurological deficits reported benefit from acupuncture ($p<0.03$). The LOTCA measurements taken in Du et al. (Du et al., 2018) reported benefit from acupuncture ($p<0.05$). The Montreal Cognitive Assessment (MoCA) measurement of Chen et al. (Chen et al., 2016) showed benefit from acupuncture ($p<0.001$).
- Swallowing tests appear to provide statistically significant results. The Chen et al. (Chen et al., 2016) study's Videofluoroscopic Swallowing Study (VFSS) and

Bedside Swallowing Assessment (BSA) both reported benefit from acupuncture ($p<0.001$ and $p=0.037$ respectively). Park et al. (Park et al., 2005) reported benefit from *sham* acupuncture with its “unsafe swallow” test ($p= 0.04$).

- Acupuncture helps in regaining wrist and shoulder motion. The study by Wayne et al. Wayne et al., 2005) reports that shoulder range of motion (ROM), wrist ROM, and the Ashworth wrist tests all showed statistically significant benefit (all p values $p<0.01$).
- Acupuncture can benefit lower leg muscles and movement. The study by Chen et al. (Chen et al., 2016) reports the FMA lower test (this is for the lower limbs) gave statistically significant results ($p=0.020$). Park et al. (Park et al., 2005) reports that the Barthel leg test provided statistically significant results ($p=0.02$) for those whose baseline score was below median (i.e., for the more severe deficits/injuries).
- Acupuncture provides pain relief. The Visual Analogue Scale (VAS) in the paper by Liao et al. (Liao et al., 2017) showed acupuncture provided a statistically significant benefit to pain ($p=0.04$).
- Acupuncture can enhance cerebral blood flow, a major building-block towards recovery from stroke. Ratmansky et al. (Ratmansky et al., 2016) reported acupuncture provided a statistically significant increase in the cerebral blood Mean Flow Velocity (MFV) ($p<0.04$).

If more studies performed these tests, then a proper meta-analysis could be done on them.

Liao et. al. 2017 reported that female members of the sham acupuncture group reported statistically significant improvement in the IADL score ($p<0.05$). This implies that the sham acupuncture in this study did have an effect. This study reported that acupuncture had no significant effect because the differences between the acupuncture measurements and the sham acupuncture measurements were not statistically significant. All trials showed improvement (as is the case for most of the other studies included in this research), in both the acupuncture and sham acupuncture groups. The implication here is that sham acupuncture cannot be used reliably as a control. Six of the ten studies in this research paper used some form of sham acupuncture (Hsing et al., 2012; Liao et al., 2017; Park et al., 2005; Ratmansky et al., 2016; Wayne et al., 2005; Yan et al., 2009). This could have significant implications for the results and conclusions of these studies.

Conclusion

To summarize, the pooled data in this study showed that adding acupuncture to the standard care for stroke does not yield clinically evident improvements among patients. This is contrary to my experience. Patients who have some kind of acupuncture intervention generally do recover better than those on traditional medications only – simple examples in this paper are the study by Du et al. (Du, Yin, Liu, Chen, & He, 2018) which found that the LOTCA score is significantly higher in the acupuncture group than the control group, and Ratmansky et al. (Ratmansky et al., 2016) that showed acupuncture significantly increases cerebral blood flow post-stroke. Both of these results indicate that acupuncture has beneficial results for stroke patients.

Stroke is a difficult condition to treat, and generally requires more time recover from than the typical two to three-month study covers. The short time period that these studies cover may be too short a time period- perhaps a year is a much better study timeframe.

Another factor is the number of studies available. So far, as mentioned above, the results of this study are consistent with other meta-analyses, indicating acupuncture has no (statistically) significant effect on recovery. As more studies are performed (and hopefully for longer periods of time) we should see that acupuncture can be shown to have an effective role in stroke treatment. The studies available for use in this research paper do not yield themselves to meta-analysis. The majority of the individual measurements are far too different to incorporate into a meta-analysis, and those that could be incorporated into the meta-analysis of this research paper are not strong enough (i.e., don't provide enough difference between study and control groups) to show favor towards acupuncture. Yes, indeed single trials show that acupuncture helps in stroke rehabilitation, however, the main power of meta-analysis lies in combining different trials into a single evidence that shows the "true" effect of the intervention. Acupuncture is known to positively affect stroke rehabilitation only because the controlled trials used different scores and various methods for assessment of the patients' motor conditions. If these scores were standardized among all studies, a meta-analysis would have been possible and the true effect would have shown (which is the case in the FMA, Barthel, and NIHSS scores).

The purpose of the meta-analysis is to combine similar small studies into one large study and show the combined result in an unbiased, mathematical way (which helps replace opinion with observed facts regarding efficacy). The standard interpretation of these results seems to be that a statistically significant difference means that “one is better than the other”. When there is not difference, then the possibility that the items are “as good as each other” exists. Declaring that acupuncture did not yield improvement over standard therapy is the incorrect way to interpret the results.

A note regarding the use of sham acupuncture as control in many of these studies. My opinion is that sham acupuncture is an unreliable control because it is an intervention and has the very real possibility of causing an effect. The case in Liao et al. (Liao et al.,2017) where the female IADL scores were better in the sham group than all other groups is a prime example. Since the six studies that used sham acupuncture indicated that generally there was no significant difference between the test and control groups, there is the very real possibility that the implementation of the control, no matter how well designed and executed, caused an effect similar to acupuncture, which in turn biases the result to statistical insignificance.

However, they don’t show failure either. Since the majority of the test results show no statistically significant difference, acupuncture generally did not reverse or diminish any treatment effect. Thus, the evidence is pointing toward the statement “acupuncture when combined with conventional therapy is at least as good as conventional therapy". Thus, acupuncture is an effective adjuvant therapy to standard care for stroke patients even though this is not indicated by the pooled data analysis. The widespread use of standardized scores focused on specific functional areas can be instrumental for meta-analysis to show the power and effectiveness of acupuncture.

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Appendix

Figures

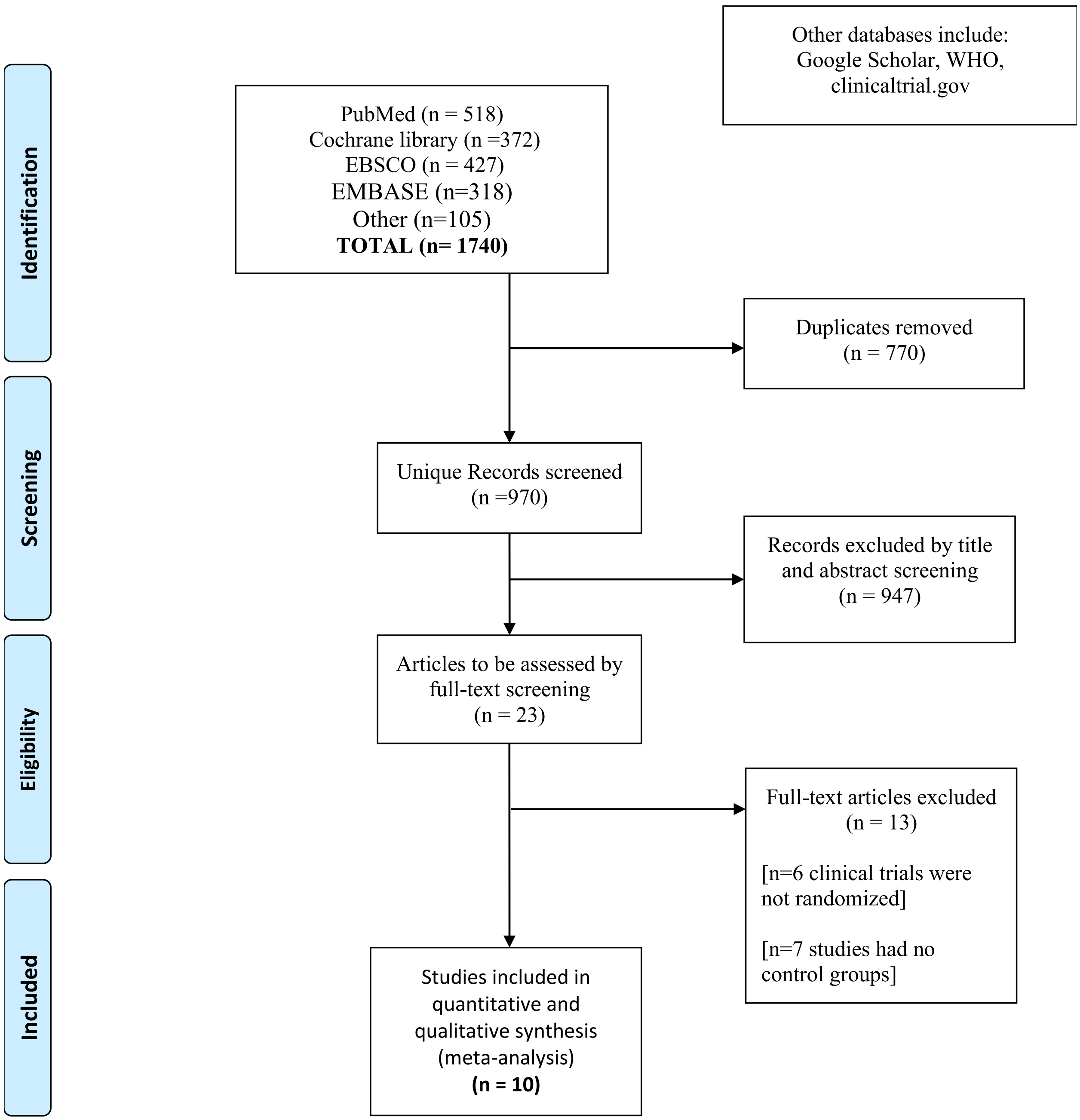

Figure 1. PRISMA flow chart depicting the literature search of included studies.

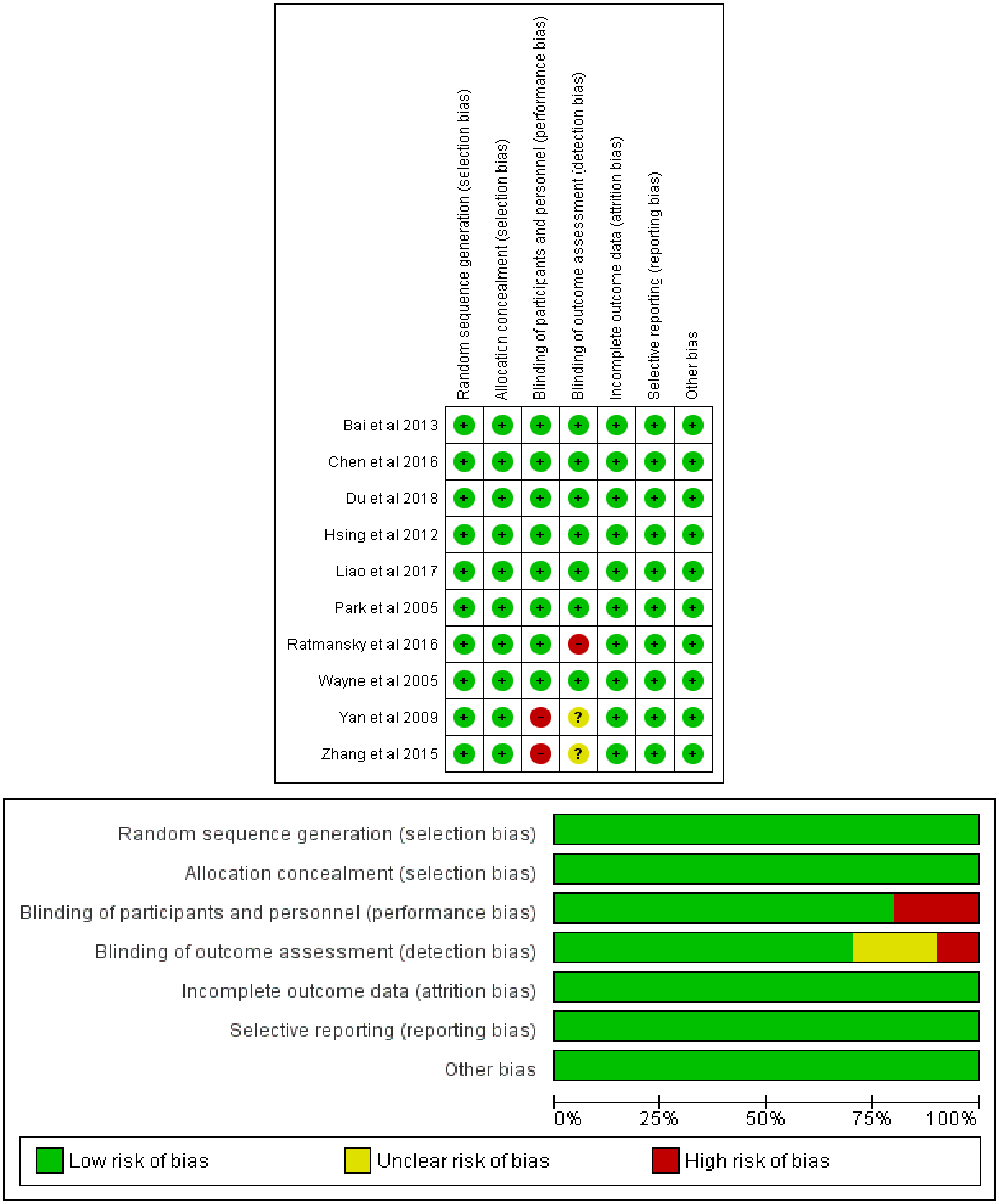

Figure 2. Detailed risk of bias assessment and risk of bias graph of included trials. Created with RevMan 5.3.

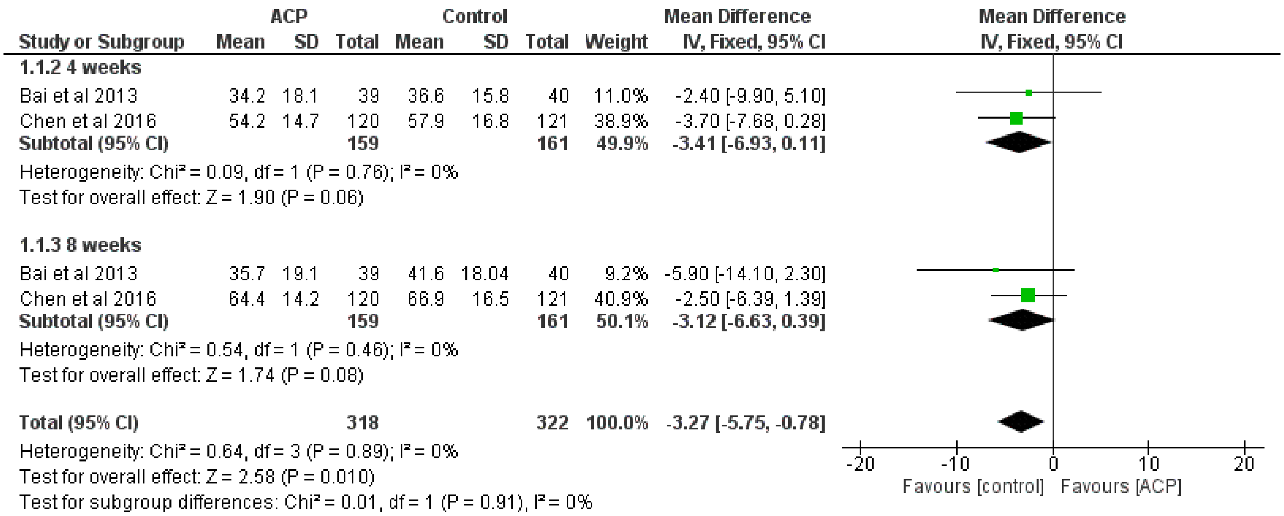

Figure 3. FMA score Forest plot. Created with RevMan 5.3.

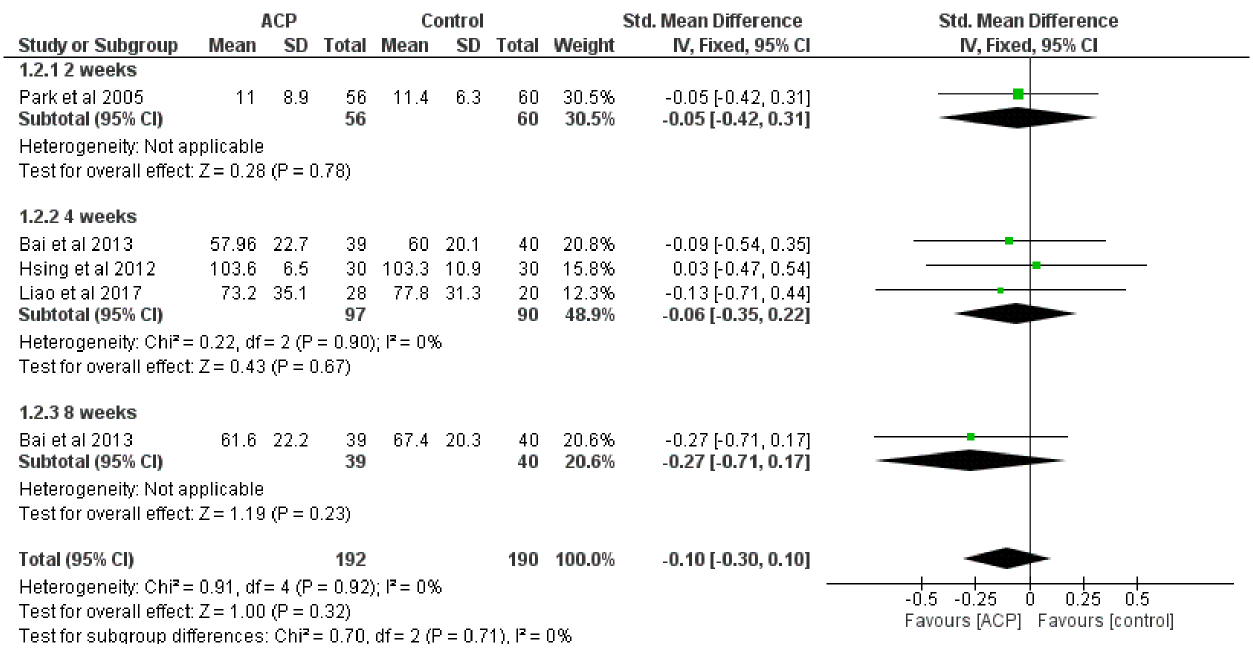

Figure 4. Barthel index scale Forest plot. Created with RevMan 5.3.

Study or Subgroup	ACP Mean	ACP SD	ACP Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Fixed, 95% CI
1.3.2 4 weeks								
Chen et al 2016	4.95	2.4	120	4.4	2.5	121	38.5%	0.55 [-0.07, 1.17]
Hsing et al 2012	3.8	2.3	30	4.27	2.39	30	10.5%	-0.47 [-1.66, 0.72]
Liao et al 2017	3.82	4.95	28	3.55	4.63	20	2.0%	0.27 [-2.46, 3.00]
Park et al 2005	5.9	6.1	56	5.3	5.2	60	3.4%	0.60 [-1.47, 2.67]
Subtotal (95% CI)			**234**			**231**	**54.4%**	**0.35 [-0.17, 0.87]**
Heterogeneity: Chi² = 2.29, df = 3 (P = 0.51); I² = 0%								
Test for overall effect: Z = 1.31 (P = 0.19)								
1.3.3 8 weeks								
Chen et al 2016	3.5	2.2	120	3.66	2.3	121	45.6%	-0.16 [-0.73, 0.41]
Subtotal (95% CI)			**120**			**121**	**45.6%**	**-0.16 [-0.73, 0.41]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.55 (P = 0.58)								
Total (95% CI)			**354**			**352**	**100.0%**	**0.12 [-0.27, 0.50]**
Heterogeneity: Chi² = 3.96, df = 4 (P = 0.41); I² = 0%								
Test for overall effect: Z = 0.59 (P = 0.56)								
Test for subgroup differences: Chi² = 1.66, df = 1 (P = 0.20), I² = 39.8%								

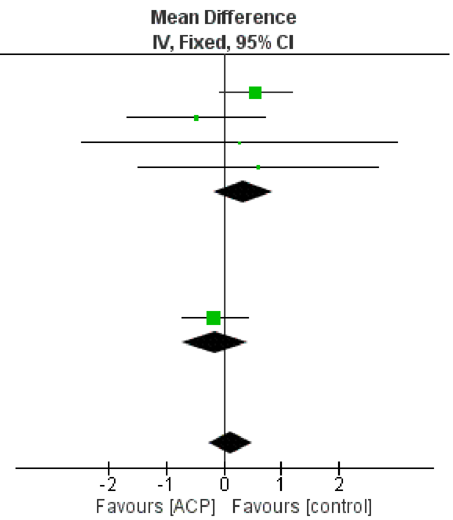

Figure 5. NIH stroke scale (NIHSS) Forest plot. Created with Revman 5.3.

Tables

Table 1

Participant Baseline Characteristic Summary

Study	Year	Sample size		Age, years		Males		Left side affection		Time from stroke onset, days		Comorbidities					
												HTN		DM		MI	
		ACP	Control	ACP	Control	ACP	Control	ACP	Control	ACP	Control	ACP	Control	ACP	Control	ACP	Control
Bai et al.	2013	39	40	63.7 ± 8.7	61.7 ± 11.1	29 (74.3)	25 (62.5)	18 (46.2)	19 (48.2)	37.1 ± 21.3	42.1 ± 20.1	23	22	5	8	7	6
Chen et al.	2016	125	125	62.5 ± 10.6	64.1 ± 10.5	74 (59.2)	75 (59.2)	83 (66.4)	79 (63.2)	NR	NR	NR	NR	NR	NR	NR	NR
Du et al.	2018	30	30	40.6 ± 5.7	37 ± 7.3	20 (66.6)	19 (63.3)	NR	NR	144 ± 39	141 ± 42	NR	NR	NR	NR	NR	NR
Hsing et al.	2012	30	30	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Liao et al.	2017	28	20	62.3 ± 12.3	55.45 ± 15.2	19 (67.9)	11 (55)	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Park et al.	2017	56	60	74.8 ± 10	74.1 ± 10.2	29 (51.7)	31 (51.6)	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Ratmansky et al.	2016	8	9	63.5 ± 11.9	60.2 ± 6.7	6 (75)	6 (66.6)	3 (37.5)	2 (22.2)	NR	NR	NR	NR	NR	NR	NR	NR
Wayne et al.	2005	16	17	63 ± 12.5	54 ± 9.6	12 (75)	12 (71)	NR	NR	66 ± 22.2	41 ± 16.7	NR	NR	NR	NR	NR	NR
Yan et al.	2009	19	19	68.4 ± 9.6	72.8 ± 7.4	9 (47.4)	10 (52.6)	11 (57.9)	12 (57.9)	NR	NR	NR	NR	NR	NR	NR	NR
Zhang et al.	2015	427	435	64.1 ± 11.1	64.6 ± 9.9	242 (56.7)	239 (54.9)	NR	NR	NR	NR	221	244	60	77	11	8

Values are mentioned as mean ± SD or n (%) unless otherwise specified, SD: standard deviation, ACP: acupuncture group, NR: Not Reported, HTN: hypertension, DM: diabetes mellitus, MI: myocardial infarction.

Table 2

Reported Trial Score Baseline Values

Study	**Baseline Barthel index**		**Baseline NIHSS**		**MMSE baseline**		**Baseline FMA score**	
	Acupuncture	Control	Acupuncture	Control	Acupuncture	Control	Acupuncture	Control
Bai et al.*	36.13±17.26	32.39±15.05	NR	NR	NR	NR	21.68±13.20	22.11±13.70
Chen et al.	NR	NR	8.3 ± 2.43	7.8 ± 2.7	20.9 ± 2.6	20.97 ± 2.7	46.1 ± 14.96	49.3 ± 15.9
Du et al.	NR	NR	NR	NR	14.6 ± 2.3	13.2 ± 2.8	NR	NR
Hsing et al.	102.8 ± 7.9	103.7 ± 10.5	4.36 ± 2.8	4.27 ± 2.2	NR	NR	NR	NR
Liao et al.	59.6 ± 41.9	65.8 ± 34.1	6 ± 5.8	6.9 ± 5.8	NR	NR	NR	NR
Park et al.	NR	NR	6.3 ± 3.9	6.4 ± 3.9	NR	NR	NR	NR
Ratmansky et al.	NR	NR	7 ± 3.5	7 ± 2	NR	NR	NR	NR

*Bai, et al. also had a combined physiotherapy and acupuncture group, baseline value of 18.65±11.97, Values are mentioned as mean ± SD, SD: standard deviation, NR: Not Reported NIHSS: National Institutes of Health Stroke Scale, MMSE: Mini-Mental State Examination, FMA: Fugl-Meyers Assessment

Table 3
Acupuncture Point Summary for each Trial

Study	Year	Selected acupoints
Bai et al.	2013	DU20, LI15, SI9, LI11, TE5, LI4, GB34, BL60, GB39, GB30, GB31, PC6, SP5, LR3, SP9, SP6, KI10, PC7, LI4, SI3, HT1, LU5, PC3.
Chen et al.	2016	Upper limbs:LI15, LI11, LI10, TE5, LI4 Lower limbs: ST34, ST36, GB34, SP6, ST40, ST41, LR3 Dysphagia: GB20, EX-HN14 (Yiming), BL10, DU16, Gongxue (1 cun below GB20), Ren23 Cognitive impairment: DU20, DU24, GB13, EX- HN1 (Sishencong).
Du et al.	2018	Acupuncture points were on the part of the scalp of the underlying diseased region.
Hsing et al.	2012	Scalp electrical acupuncture on the following points: (a) motor area of the face, upper limb, lower limb, (3 needles); (b) sensory correspondent areas, face, upper limb, lower limb (3 needles); (c) sensory-motor area of the lower limbs (bilateral) (2 needles); (d) supplementary motor area (3 needles); (e) area of language (only right hemiplegia) (+ 3 needles). Sham acupuncture performed through disconnected cables applied to the scalp.
Liao et al.	2017	Common points: DU20, EX-HN1 (Sishencong), temporal three- needle technique (Jin three-needle therapy, one side for the weakest limbs), LI11, LI4, PC6, TE5, GB34, ST36, SP6, LR3. According to each patient's specific complaint, other sites were added such as Speech II or Speech III areas (Jiao's Scalp Acupuncture) for aphasia, EX-HN12 (Jinjin) and EX-HN13 (Yuye) for dysarthria, and ST40 and LU5 for sputum. Sham acupuncture points were needled 1 cm away from the real acupoints, and no one in the sham group received scalp acupuncture.
Park et al.	2017	The study included ten points; six points determined by the patient's classification (BL66, LI1, HT3, HT4, GB43, GB44; LU8, SP3, HT8, HT9, KI3, KI7; ST36, LI5, LI11, HT7, HT8, SI5; and SP1, SP2, HT8, HT9, LR1, Ren4) and four points for all patients (ST40 [bilateral], Ren12, DU20, and DU26). Sham acupuncture was performed using blunt, telescopic nonpenetrating sham needles.
Ratmansky et al.	2016	LR3, LR4, TE5, and GB34. Sham acupoints were in a nonspecific location with no known acupuncture influence as follows: (1) above the biceps muscle, (2) above the deltoid muscle, (3) above the gastrocnemius muscle (medial aspect), and (4) forearm (above the ulna).

Study	Year	Selected acupoints
Wayne et al.	2005	Different combination of traditional acupuncture points on the body surface and a modern system of "scalp" acupuncture were used. Possible body points used are: Pool A: Points for treating upper and lower-extremity hemiparesis: LI15, LI14, LI11, LI10, LI4, TE14, TE5, TE3, Baxie, SI9, SI4, SI3, GB30, GB31, GB34, GB39, GB40, ST34, ST36, ST41, ST42, LR3, Bafeng. Pool B: Points for treating underlying TCM etiology: KD3, LU5, Ren4, LR3, UB18, UB23. Pool C: Points for treating associated symptoms including aphasia, facial paralysis, depression, and insomnia: Ren23, Extra Yinyuyue, HT5, HT7, ST5, ST6, ST7, LI4, Taiyang, TE17, TE5, Anmian, LR3, UB43, UB45, DU20, PC7. Scalp acupuncture was directed at sensory and motor components of the affected limb. Sham acupuncture needles placed at least 1 cm away from the acupuncture point were used for the sham group, and (sham) needles in the scalp were placed 2 cm away from active scalp lines. Electroacupuncture in the sham group was performed with non-conducting wires so no electricity was conducted.
Yan et al.	2009	ST36, LR3, GB34, BL60. Sham group had the circuit disconnected. All groups were told they may or may not feel the stimulation.
Zhang et al.	2015	DU26, PC6 (both sides) Ren6, SP6 (paretic side). Auxiliary acupoints include DU20, 4 acupoints on the paretic side (ST36, ST40, LR3, LU5), and GB20 on both sides.

Table 4

Body Needle Acupuncture Trial Significant Result Summary Table

Study	Year	Acupuncture group		Control group		Score	p-value	Comments
		Method	# Patients	Method	# Patients			
Chen, et al.	2016	Body needle	125	No ACP	125	NIHSS VFSS MoCA FMA Lower BSA	$p < 0.001$ $p < 0.001$ $p < 0.001$ $p = 0.020$ $p = 0.037$	 FMA upper = 0.707 for combined p = 0.228
Liao, et. al.*	2017	Body needle + scalp ACP as needed	18	Sham ACP (no scalp ACP)	15	VAS IADL	$p = 0.04$ $p < 0.05$	 Female sham group only
Park, et. al.	2005	Body needle ACP	56	Sham ACP	60	Barthel leg Unsafe swallow	$p = 0.02$ $p = 0.04$	Seen in those whose baseline score was below the median Sham group was better
Ratmansky, et. al.	2016	Body needle ACP		Sham ACP	9	MFV	$p < 0.04$	
Wayne, et. al.*	2005	Body EA + Scalp	16	Sham ACP	17	Ashworth wrist Shoulder ROM Wrist ROM	$p < 0.01$ $p < 0.01$ $p < 0.01$	 ROM through frontal plane ROM in the sagittal and frontal planes

Study	Year	Acupuncture group		Control group		Score	p-value	Comments
		Method	# Patients	Method	# Patients			
Yan, et. al.	2009	Body TENS + standard rehab	19	Standard rehab	18	MIVC	$p < 0.05$	Significant difference since week 2
		Placebo TENS standard rehab (Sham)	19	Standard rehab	18	Normal resistance	$p < 0.05$	Significant difference by week 1
						Electromyography co-contraction ratio	$p < 0.01$	By week 8; $p < 0.05$ by week 3
Zhang, et. al.	2015	Body needle ACP	427	Standard care	435	SSS	$p < 0.03$	Patients have greater reduction in neurological deficits

*Study appears in both body needle acupuncture and scalp acupuncture tables as it uses both techniques

Acronym Legend:
MIVC = Maximum Isometric Voluntary Contraction
VFSS = Videofluoroscopic Swallowing Study
NIHSS = National Institutes of Health Stroke Scale
IADL = Instrumental Activities of Daily Living
Barthel = Barthel Index for Activities of Daily Living
LOTCA = Lowenstein Occupational Therapy Cognitive Assessment
rehab = rehabilitation
MFV = Mean Flow Velocity
FMA = Fugl-Meyer Assessment
BSA = Bedside Swallowing Assessment
MoCA = Montreal Cognitive Assessment
SSS = Scandinavian Stroke Scale
NHP = Nottingham Health Profile
ROM = Range of Motion
VAS = Visual Analogue Scale
ACP = Acupuncture
EA = Electro-acupuncture
IADL = Instrumental Activities of Daily Living

Table 5

Scalp Acupuncture Trial Significant Result Summary Table

Study	**Year**	**Acupuncture Group**		**Control Group**		**Score**	**p Value**	**Comments**
		Method	**# Patients**	**Method**	**# Patients**			
Du, et. al.	2018	Scalp ACP + cognitive rehab	30	Cognitive rehab	30	LOCTA	$p < 0.05$	
Hsing, et. al.	2012	Scalp EA	35	Sham scalp EA	27	NIHSS	$p = 0.03$	
Liao, et. al.*	2017	Body needle + scalp ACP as needed	18	Sham ACP (no scalp ACP)	15	VAS	$p = 0.004$	
						IADL	$p < 0.05$	Female sham group only
Wayne, et. al.*	2005	Body EA + Scalp	16	Sham ACP	17	Ashworth wrist	$p < 0.01$	
						Shoulder ROM	$p < 0.01$	ROM through frontal plane
						Wrist ROM	$p < 0.01$	ROM in the sagittal and frontal planes

*Study appears in both body needle acupuncture and scalp acupuncture tables as it uses both techniques

Acronym Legend:

ACP = Acupuncture
FMA = Fugl-Meyer Assessment
NIHSS = National Institutes of Health Stroke Scale
LOTCA = Lowenstein Occupational Therapy Cognitive Assessment
IADL = Instrumental Activities of Daily Living

EA = Electro-acupuncture
NHP = Nottingham Health Profile
ROM = Range of Motion
VAS = Visual Analogue Scale
rehab = rehabilitation