Acupuncture with Rehabilitation in the Treatment of Ischemic Stroke Recovery: A Randomized Controlled Trial

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Research

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Abstract

Background: Acupuncture is a well known treatment for ischemic stroke recovery, but evidence of its effectiveness remains limited. Methods: Rehabilitation training was provided to a control group. In Arm 1 and Arm 2, acupoint schemes were determined by a consensus of acupuncture experts and previous clinical research. Arm 1 was based on an acupoint summary of ancient literature, and Arm 2 was based on the summary of effective acupuncture points from modern RCT literature. Acupuncture was given on the acupoint. After acupuncture, the needles were left in for 30 minutes, and checked every 10 minutes. The three groups received treatment once a day, 5 times a week, for 2 weeks. The primary outcome was the National Institute of Health stroke scale (NIHSS), and the secondary outcomes were the Barthel index (BI) and the modified Ashworth scale (MAS). Outcomes were observed in patients both before and after treatment. Results: A total of 497 patients with ischemic stroke were randomized into either Arm 1 (159 cases), Arm 2 (173 cases) or a control group (165 cases). After 2 weeks of treatment, the NIHSS scores for Arm 1 were lower than those of the control group (P=0.017); the BI scores were higher in Arm 2 than they were in the control group (P=0.020). Additionally, there was no significant difference between Arm 1 and the control group for either the BI scores or the modified Ashworth scale scores (P>0.05). Conclusion: The clinical efficacy of Arm 1 and Arm 2 (acupuncture groups) was superior to that of the control group.

Background

Stroke is widespread around the world. According to recent reports,[1-3] the incidence of stroke in China is 274-379/100,000, of which ischemic stroke accounts for 60-70%. The prevalence for individuals over 70 is 6.6 times that of those aged 40-49. Three-fourths of stroke survivors are left with varying degrees of disability, and about 40% are severely disabled. In China, the annual cost of stroke treatment imposes heavy burdens on both the state and many families.

Ischemic stroke is the common term for cerebral infarction in modern medicine. It disrupts cerebral artery blood flow through several pathways, causing hypoxia and ischemic necrosis in local brain tissue. This results in a corresponding neurologic deficit.[4] The clinical manifestations of ischemic stroke are focal neurological deficits such as hemiplegia, aphasia, dysphagia, visual impairment, and mental disturbance. Ultra-early thrombolysis has been used widely in the acute phase of stroke. However, due to its time-restricted application, the probability of thrombolysis is only 2.4%.[5] This leaves intravenous or oral medications, rehabilitation training, and prevention of complications as the primary treatment measures for most stroke patients.

There is a long history of acupuncture treatments for stroke. The earliest stroke symptoms and acupoints were recorded in the Huang Di Nei Jing, and staged syndrome differentiation and stroke treatment is recorded in Acupuncture Dacheng. This provides a theoretical basis for the treatment of Apoplexy by acupuncture. At present, new acupuncture theories and techniques are still being developed. These include body acupuncture, scalp acupuncture, electric acupuncture and eye acupuncture. Yet, acupuncture's efficacy needs further validation in clinical trials.
A prospective randomized-controlled trial was conducted to explore an optimal plan for acupuncture treatment of ischemic stroke, and to provide scientific evidence for the effectiveness of acupuncture as a stroke treatment.

**Methods**

**Settings and subjects**

The present study was a randomized controlled trial, conducted by the Guangzhou Hospital of Chinese Medicine, the First Affiliated Hospital of Guangzhou University of Chinese Medicine, and the Liwan District Hospital of Chinese Medicine. The study reporting complied with the requirements of the CONSORT 2010 statement.\[^{10}\]

Patients were randomly divided into either Arm 1, Arm 2 or the control group. The grouping was performed by personnel from the Key Research Laboratory of Clinical Research Methodology at the Guangdong Provincial Hospital of Chinese Medicine. SAS 9.2 was used to complete the procedure, and for randomization. The trials were single-blind so that the data analyst and evaluator were unaware of the groupings. Neither patients nor the clinical doctors performing the interventions were blinded. In order to avoid bias, individuals responsible for the evaluation of the efficacy were hired separately, and were unaware of patient groupings. Analysts were also chosen separately and did not participate in the clinical implementation, or the design of the project.

The trial was conducted between July 2016 and July 2017, and patients who met the following criteria were included in the study:

(1) diagnosed with ischemic cerebrovascular disease by either CT or MRI\[^{11}\]

(2) recovery period (2 weeks to 6 months after acute stroke), sequelae period (June to December)

(3) number of strokes $\leq 3$

(4) aged between 40 and 75, male or female

(5) clear cognitive faculties, stable vital signs, no obvious mental retardation, no obvious hearing impairment, and ability to cooperate with rehabilitation training

Exclusion criteria were:

(1) had already received other treatments that were not part of this research plan

(2) suffered from transient ischemic attack, or reversible neurological deficit (RIND)

(3) neurological deficit was not related to ischemic stroke
(4) suffering from mental disorders or other severe diseases

(5) patients with severe aphasia, sleep apnea, deafness, severe cognitive impairment, or communication barriers

**Treatment process**

The standards of the study met the requirements of the *Standards for Reporting Interventions in Clinical Trials of Acupuncture* (STRICTA) 2010.[12] Before the trial, the research team was authorized by the Ethics Committee of the Guangzhou Chinese Medicine Hospital, the First Affiliated Hospital of Guangzhou University of Chinese Medicine, and the Liwan District Chinese Medicine Hospital (Reference no. 2016NK001) to conduct the study. All included cases were treated with basic drugs, such as those to improve circulation, nourish nerves, prevent platelet aggregation, and control blood pressure, blood sugar, and blood lipids. Patients also received rehabilitation training.[11][13] Rehabilitation training followed the guidelines of the *Rehabilitation Treatment Guide 2011 of Stoke in China*[14] and *Practical Rehabilitation*. The members of the rehabilitation team examined the patient to determine the nature and extent of the disorder. The rehabilitation team also held review meetings to integrate patient care, formulate a rehabilitation plan and implement treatment. According to the specific conditions of the patients, they were trained to sit, balance, stand, shift their center of gravity, walk, feed themselves, change clothes, or go to the bathroom. They also received systemic coordination training which included balancing, practical walking, using a walking stick, and going up and down stairs.

**Acupoints**

The optimal acupoint scheme for this test was determined by a consensus of acupuncture experts and previous clinical research.[16] One group’s treatment was based on an acupoint summary from ancient literature,[17-18] and the other’s was based on a summary of effective acupuncture points from a consensus of acupuncture experts from modern RCT literature (Supplement 1). The most frequently used twelve acupoints in the ancient books and the modern RCT literature were determined by the consensus of acupuncture experts and previous clinical research. In treatment Arm 1, these included DU20 (*baihui*), DU26 (*shuigou*), PC9 (*zhongchong*), ST6 (*jiache*), ST4 (*dicang*), LI15 (*jianyu*), LI11 (*quchi*), LI4 (*hegu*), GB30 (*huantiao*), GB31 (*fengshi*), GB34 (*yanglingquan*) and GB39 (*xuanzhong*). In treatment Arm 2, they were DU20 (*baihui*), PC6 (*neiguan*), LI11 (*quchi*), LI10 (*shousanli*), SJ5 (*waiguan*), LI4 (*hegu*), GB30 (*huantiao*), ST36 (*zusanli*), GB34 (*yanglingquan*), SP6 (*sanyinjiao*), ST41 (*jiexi*) and LR3 (*taichong*). Other than PC9 and PC6, all acupoints were selected from the affected side.

**Acupuncture intervention**
The acupuncture treatment was performed by 16 different acupuncturists (with between 2 and 7 years’ experience) at 3 different hospitals. 7 of the acupuncturists had bachelor's level educations, 6 had master's degrees, and 3 had doctorates and were registered practitioners of Chinese medicine. All researchers and acupuncturists were required to undergo a four-day training session prior to the trial.

Appropriate positioning of the needles is crucial to obtaining good acupuncture results. The patients in the study lay in a lateral position with the affected side facing up, the hemiparalysis shoulder stretched forward, the shoulder joint flexed 90 degrees, and the paraplegic upper limb on a pillow at a 100° angle to the trunk. The elbow was straightened, with arm, wrist and fingers extended, and palm facing up. Next, the paraplegic side of the lower extremity was placed on the pillow, revealing a step-like shape (with hips and knees flexed). The disposable sterile acupuncture needles used had varying specifications (0.30 x 25 mm, 0.30 x 40 mm, 0.30 x 50 mm, or 0.30 x 75 mm). Conventional disinfection with 75% alcohol was employed after acupuncture point positioning, in accordance with Standard Acupuncture and Moxibustion Positioning by WHO[19]. During the acupuncture session, patients would feel soreness, numbness, distension or heaviness around the point, or an electric shock feeling during needling, demonstrating that needling had been effective. In order to stimulate needle sensation, the needles were inserted flat and backwards, 25 mm into DU20, and 8-15 mm obliquely and upward into DU26. Then, a reducing method was used for 30 s, rotating at small-amplitude and high-frequency. The other acupoints utilized the reinforcing-reducing method 2.5 mm deep into PC9; 15-20 mm vertically into ST6, ST4, GB39, ST41 and LR3; 15-25 mm perpendicularly into LI4, PC6, and SJ5; 25-40 mm obliquely and downward into LI15; 25-40 mm perpendicularly into LI11, GB34, GB31, LI10, ST36, and SP6; and 50-70 mm perpendicularly into GB30. After insertion, the needles were left in situ for 30 minutes. The course of treatment was 5 times a week, for 2 weeks. All necessary precautions were taken to prevent, record and treat any adverse events that occurred during treatment (e.g. fainting, broken needles).

Outcomes

The treatment effect of this trial was evaluated by three scales, at different time points (Baseline=T0, Week 1 = T1, Week 2 = T2 and Follow up = T4). The primary outcome was expressed using the National Institute of Health Stroke Scale (NIHSS). It ranged from 0 to 40, and included 11 items: consciousness, limb movement, eye movement, vision, facial paralysis, feeling, language, dysarthria and neglect. It also determined improvement in neurological function among the three groups (i.e. the lower the score, the lesser the patient's neurological deficit). The secondary outcomes were the Barthel Index Table (BI) and the Modified Ashworth Scale (MAS). The BI scale is typically used to assess patient self-care ability, and if the score is below 20, this means that the patient's self-care ability had been seriously impaired. A score of over 60 indicated patients had been able to care for themselves. The improvement and difference in muscle tension within the three groups was determined by the changes in the modified Ashworth scale, both before and after treatment—the higher the score, the higher the patient's muscle tone. Returning to the hospital after discharge is not an easy task for patients, and only BI data for these three observations.
could be obtained in a remote setting such as a telephone conversation. Thus, only BI was measured 4 times.

Sample size

According to Yang,\(^{[20]}\) the NIHSS score for simple stroke rehabilitation was \((12.78±2.99)\), and the NIHSS score for acupuncture combined with stroke rehabilitation was \((16.06±4.57)\). Setting \(\alpha\) to 0.05, \(\beta\) to 0.1, and substituting the sample size formulae of the two groups of means, the results showed that 30 patients were necessary for each group to complete the trial. Considering that the two treatment groups were compared with the control group, in order to control for type 1 error, the number of patients in each group was increased to \(30\times3=90\). Assuming a 10% dropout rate per group, each group was adjusted to 100, with a total of about 300 patients.

Statistical analysis

An intention-to-treat population was surveyed before the analyses, which included those patients undergoing baseline assessment and at least one evaluation after treatment. The NIHSS, BI and MAS scores, along with changes over time, were compared by using repeated measures designed for the three groups. We also employed Analysis of Variance (ANOVA) to define the among-group differences at each measure time point. A Chi-square or Fisher Exact test was used to analyze categorical variables, including categorical baseline variables and incidence of adverse events. Last observation carried forward (LOCF) was used in the ITT analysis to address missing data due to attrition and shedding. Statistical significance was defined as a two-tailed \(P < 0.05\). Statistical analysis was performed with PASW 20.0 (IBM SPSS Inc., Armonk, New York, USA).

Results

Baseline data

Between July 2016 and July 2017, a total of 2,369 patients were assessed for eligibility. 497 of them participated in the trial (Guangzhou Hospital of Chinese Medicine = 200, First Affiliated Hospital of Guangzhou University of Chinese Medicine = 247, Liwan District Hospital of Chinese Medicine = 50). They were randomly divided into 3 groups (Arm 1 = 159, Arm 2 = 173, control group = 165). Ten patients dropped out before the trial ended, six stopped because of sudden serious diseases such as heart failure or lung infection, and three could not comply with the researcher. One patient was lost due to a change in contact phone number (Fig. 1).

Table 1 lists the basic information for the patients involved in the study, totaling 311 males and 186 females, all aged around 65. Most of the patients were not college educated, and most lived in urban
areas. 74.2% of the patients had a history of smoking and 84.5% had a history of alcohol. There were no statistically significant relationships between the general variables (e.g. sex, age, education, career). There were also no statistically significant differences in ischemic stroke characteristics (disease course, number of strokes, infarct size and family history, see Table 2)

Mean scores and changes in NIHSS, BI and MAS at different time points in the three study arms are shown in Table 3. In the statistical analysis of the above three items, no difference was found between the three groups in the repeat measurement design.

The NIHSS scores of the three groups at each time point were analyzed, and the results showed no significant difference in NIHSS scores, at either T0 or T1 (P>0.05). However, the difference between the NIHSS scores at T2 was statistically significant (P = 0.014). Further between-group comparisons found that there was a statistically significant difference between Arm 1 and the control group (P = 0.017). As shown by Fig. 2 (A), the NIHSS score in Arm 1 had the largest decrease.

During the treatment and follow-up period, BI scores of the three groups trended upwards. Analysis of Variance showed that there were no significant differences either at T0 or T1 (P>0.05). While the difference between the BI scores at T2 and follow-up were statistically significant (P = 0.014 and P = 0.017). Between-group comparisons showed a statistically significant difference in the Arm 2 BI scores at T2 (P = 0.016) and follow-up (P = 0.020). However, we found no other apparent differences at other time points (see Fig. 2B).

Although there was an obvious decrease in MAS scores during the treatment period, no statistically significant difference across the three groups was found at any time point (see Fig. 2C).

**Safety assessment**

Over the course of treatment for the three groups, there were no obvious changes in blood counts, routine urine tests, liver function, renal function, or heart enzymes. There were 5 adverse events in Arm 1, 7 adverse events in Arm 2, and no adverse events in the control group. Of these adverse events, 9 were cases of bleeding and 3 were cases of delayed needles. We stopped the bleeding by applying pressure with a sterile swab for 10 seconds, and gently poking the needle handle, thus facilitating needle removal. No patients withdrew from the trial due to adverse events.

**Discussion**

Based on the above results, the following conclusions can be drawn: After comparison with the control group, Arm 1 and Arm 2 were determined to be clinically effective and safe. Research has shown that acupuncture treatment after ischemic stroke can generate neuroprotective and neuroregenerative effects that increase cerebral blood flow, regulate oxidative stress, maintain blood brain barrier integrity, inhibit apoptosis, and increase growth factor production. This may be the basis for acupuncture treatment of
ischemic stroke.\cite{21} At present, ischemic stroke treatment is mostly performed in the stroke unit, which is considered to be the most effective way to deal with the disease.\cite{22-24} In the stroke unit, various therapies and techniques are combined to provide patients with drugs and physical, language, and psychological rehabilitation, as well as health education.\cite{25} In the near future, acupuncture may also play an indispensable role in clinical rehabilitation.\cite{26-27}

Effective treatment is dependent on proper choice of acupuncture points. The acupoints in this study were selected based on both ancient and modern RCT literature. They were chosen because of their wide application, frequent usage and direct curative effect. These acupoints each possess the following characteristics: The first is that they connect to the **yangjing**. **Du Meridian**, **Large Intestine Meridian**, **Stomach Meridian** and **Gallbladder Meridian** are the most relevant **yangjing**. Because **DU20** is the meeting of Zhuyang, it is the most frequently selected acupoint, which has the effect of **Xingnaoanshen** and **Qufengkaiqiao**. The **Stomach Meridian** and the **Large Intestine Meridian** have the functions of **Harmonizing Qi and Blood** and relieving limbs and joints. The **Gallbladder Meridian** is related to tendons and has the function of stimulating the circulation of the blood and causing the muscles and joints to relax. In Chinese medicine, **yin** and **yang** are balanced. The acupoints on the **yangjing** have the effect of replenishing **yangqi**. This is in line with the **yin** symptoms for hemiplegia. The other feature of the acupoints in this study is that they each have a unique therapeutic effect and a specific name. The main ones are the **Jiaohui** and **He** acupoints, in which **Jiaohui** acupoint can make the **Qi and Blood** of meridians communicate with each other to treat the disease of intersecting meridians. The **He** acupoint is one of the **Wushuxue**, and it is the acupoint with the greatest **Qi and Blood**. Therefore, it is easier to mobilize **Qi and Blood** in the treatment of apoplexy by acupuncturing such acupoints. This provides a sound theoretical basis for effective stroke treatment.

NIHSS is an important scale for stroke. It comprehensively evaluates the consciousness, movement, sensation, and advanced neurological function of stroke patients. In this trial, Arm 1 was superior to the control group in treating neurological deficits, however there was no difference between Arm 2 and the control group. The reduction in the NIHSS score predicts that the degree of neurological impairment was better than before, and was beneficial to prognosis. Previous studies have shown that GV20-based acupoint combination combined with rehabilitation is more effective than simple rehabilitation in reducing NIHSS scores after 8 courses of treatment. This is because these acupoints can balance the body’s **yin** and **yang**, and dredge the **qi** and blood of the meridians.\cite{20} In terms of improving patient self-care ability, the effect of Arm 2 was better than that of the control group, but there was no difference between Arm 1 and the control group. Increased BI scores mean that patients have improved their lives in terms of eating, dressing, walking, and going to the bathroom. While a multi-center RCT revealed that the BI scores of patients with subacute stroke were significantly higher after 6 months of body and scalp acupuncture treatment, no obvious improvements were found when compared with the rehabilitation group.\cite{28} In the authors’ opinion, this negative result was due to the acupoints in the program deviating from the viewpoint of TCM syndrome differentiation. Thus, we should not only focus on the proximity to afferent nerve fibers, but also select points according to the specific conditions of the patients. The
acupoints in this study were derived from a combination of multiple clinical trials and the experience of several trained acupuncturists. The two treatment groups tested comparably to the control group in terms of improving muscle tension. However, many experiments have shown that acupuncture or electroacupuncture combined with rehabilitation can improve muscle tone and release spastic limbs.\textsuperscript{29-32} In our opinion, this is likely related to insufficient treatment or observation time. Confirming this would require further research.

**Limitations of this study**

Although this trial is one of the few random, multi-center, and large-sample trials of acupuncture treatment for stroke\textsuperscript{33}, there are some limitations that require attention. First, the course of treatment was short. However, the results reveal that with the passage of treatment time, positive effects emerged in the treatment group. Secondly, our study was not double-blinded. This may have led to treatment outcome bias.

**Conclusions**

The interventions with acupuncture showed better results than did the simple rehabilitation group, but there was no difference between the effects of the two acupuncture groups.

**Abbreviations**

NIHSS: National institutes of Health Stroke Scale; BI: Barthel index; MAS: Modified Ashworth Scale; STRICTA: Reporting Interventions in Clinical Trials of Acupuncture; WHO: World Health Organization.

**Declarations**

**Ethics approval and consent to participate**

The study protocol was approved, in writing, by the Ethics Committee at the Guangzhou Hospital of Chinese Medicine (Reference No. 2016NK001) before the study commenced. Informed consent to participate was obtained from all participants prior to their involvement.

**Consent for publication**

The consent form for the study participants was incorporated into the study protocol, and was approved by the Ethics Committee of the Guangzhou Hospital of Chinese Medicine. Study consent, including that for data publication, was obtained from each participant prior to joining the study.

**Availability of data and materials**
The datasets used and/or analysed during the current study are available from the corresponding author upon reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors’ contributions

L.X., C.Y. and L.H. designed and led the study. Z.F., T.H., W.R., L.L. and L.Y. analyzed and interpreted the patient data to generate the study results. L.L.H and X.Q. drafted the manuscript. All authors read and approved the final manuscript.

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References

[1] Sun HX, Wang WZ. A nationwide epidemiological sample survey on cerebrovascular disease in China. Chinese Journal of Contemporary Neurology and Neurosurgery. 2018; 18(2): 83-88.

[2] Wu YZ, Chen WW. Chinese stroke epidemics. Prevention and Treatment of Cardio-Cerebral-Vascular Disease. 2016, 16(6): 410-414.

[3] Yan YY, Wu B, Liu M. Advances on clinical researches of cerebrovascular diseases in 2017. West China Medical Journal. 2018, 33(6): 1-4.

[4] Yang QD. Neurology. Beijing: People's Medical Publishing House; 2002. p. 130.

[5] Chinese Medical Association Emergency Medicine Branch. Expert consensus of emergency green channel construction for acute cerebral infarction thrombolytic therapy. Chinese Journal of Emergency Medicine. 2017, 26(9): 995-998.
[6] Zhu B, Huang LX, Yang JS, et al. Analysis of the Nominations of acupuncture and moxibustion of traditional Chinese medicine for inscription on the Representative List of the Intangible Cultural Heritage of Humanity. Chinese Acupuncture & Moxibustion. 2011, 31(3): 193.

[7] Xu JF, Li J, Li Y, et al. Clinical Observation on Treatment of Different Degree of Apoplexy with Xingnao Kaiqiao Acupuncture. Liaoning Journal of Traditional Chinese Medicine. 2004, 31(4): 296.

[8] Lang JY, Zhuang LX, Jia C, et al. Therapeutic Effect of Jin's Three-needle Therapy Combined with Rehabilitation Therapy for Spastic Hemiplegia After Ischemic Stroke. Journal of Guangzhou University of Traditional Chinese Medicine. 2011, 28(4): 369-373.

[9] Xu XH, ZHeng P, Wang FC, et al. Comparison and Analysis of Three Kinds of Scalp System. Jilin Journal of Chinese Medicine. 2007, 27(4): 47-48.

[10] Schulz KF, Altman DG, Moher D; CONSORT Group. CONSORT 2010 statement: updated guidelines for reporting parallel group randomised trials. PLoS Med. 2010, 37(3): e1000251.

[11] Chinese Medical Association Neurology Branch. Diagnosis Guide of Acute Ischemic Stroke in China, Chinese Journal of Neurology. 2015, 48(4): 246-257.

[12] MacPherson H, Altman DG, Hammerschlag R, et al. Revised standards for reporting interventions in clinical trials of acupuncture (STRICTA): extending the CONSORT statement. PLoS Med. 2010, 7(6): e1000261.

[13] Ni JD, Liu X, Liu M, et al. Guidelines for the Prevention of Stroke in Patients with Stroke and Transient Ischemic Attack(2014AHA/ASA Edition). Chinese Journal of Clinical Neurosciences. 2015. 23(1): 65-73.

[14] Zhang T. Chinese stroke rehabilitation treatment guide. Chinese Journal of Rehabilitation Theory and Practice. 2012, 18(4): 301-317.

[15] Yan TB. Practical rehabilitation. Beijing: People's Medical Publishing House; 2010. p. 89-95.

[16] Chavez LM, Huang S-S, MacDonald I, et al. Mechanisms of Acupuncture Therapy in Ischemic Stroke Rehabilitation: A Literature Review of Basic Studies. International Journal of Molecular Sciences. 2017; 18(11): 2270.

[17] Lin YS, Chen CY, Li LX. Data Mining-based Analysis of Regularities in Acupoint Prescriptions for Stroke Hemiplegia in Ancient Books. Journal of Liaoning University of Traditional Chinese Medicine. 2018, 20(04): 151-153.

[18] Chen CY, Li LX, Li WL, et al. Data Mining-based Analysis of Regularities in Acupoint Prescriptions for Stroke Disorders in Ancient Books. Shanghai Journal of Acupuncture and Moxibustion. 2017, 36(12): 1494-1499.
Standard Acupuncture and Moxibustion Positioning by WHO. Beijing: People's Medical Publishing House; 2009.

Yang XH, Liu B, Ouyang B. Effect of acupuncture combined with rehabilitative training on neural functional recovery of stroke patients during recovery phase: a randomized controlled trial. World Journal of Acupuncture-Moxibusion. 2014; 24(4): 17-22.

Chang QY, Lin YW, Hsieh CL. Acupuncture and neuroregeneration in ischemic stroke. Neural Regen Res. 2018, 13(4): 573-583.

[22] He M, Wang G, Li MQ, et al. Clinical Study of Integrative Medicine in the Treatment of Acute Stroke Unit. Journal of Chengdu Medical College. 2018, 30(02): 1-5.

[23] Karl M, Leonhard S, Alexandra D, et al. Post-stroke pneumonia at the stroke unit-a registry based analysis of contributing and protective factors. BMC Neurology. 2016, 16 (1): 107.

[24] Daniel K. Y., Dennis C, Fintan R. Comprehensive stroke units: a review of comparative evidence and experience. International Journal of Stroke. 2013, 4: 260-264.

[25] Wang L, Wang CZ, Bian GR. Intervention Study of Stroke Unit Combined with Traditional Chinese and Western Medicine on Post stroke Fatigue. Liaoning Journal of Traditional Chinese Medicine. 2017, 44(11): 2356-2358.

[26] Wang Y. Study of Systematic Review and Meta Analysis of Effectiveness and Safety of Traditional Chinese Medicine in Treating Acute Ischemical Stroke. Guangzhou University of Chinese Medicine. 2015: 45-49.

[27] Lin GH, Lu LH, Chen CY. Effectiveness of Acupuncture and Rehabilitation for Treating Neurological Function Deficit Degree of Non-acute Stage Stroke: A Meta-analysis. Journal of Yunnan University of Traditional Chinese Medicine. 2016, 39(03): 44-47.

[28] Zhu Y, Zhang LX, Ouyang G, et al. Acupuncture in Subacute Stroke: No Benefits Detected. Physical Therapy. 2013, 93(11): 1447-1455.

[29] Tong S, Su L, Lv HB, et al. Observation on the efficacy of acupuncture at key acupoints combined with rehabilitation therapy for spasmodic hemiplegia after cerebral infarction. Chinese Acupuncture & Moxibustion. 2013, 33(05): 399-402.

[30] Sun YZ, Liu M, Shang LL. Efficacy of Electro-acupuncture Combined with rehabilitative Technology on Foot Drop after Stroke. Journal of Clinical Acupuncture and Moxibustion. 2014, 30(05): 24-25.

[31] Xing XM, Yang B, Li F, et al. Acupuncture and Moxibustion Combined with rehabilitation Treatment of 30 Case of Spastic Hemiplegia after Ischemic Stroke. Liaoning Journal of Traditional Chinese Medicine. 2015, 42(03): 595-597.
[32] Wang YZ, Xie H, Li GM. Clinical Observation of Nerve-trunk Stimulation plus Electroacupuncture at Antagonistic Points for Post-stroke Upper-limb Spasm. Shanghai Journal of Acupuncture and Moxibustion. 2015, 34(06): 518-520.

[33] Zhang SH, Wu B, Liu M. Acupuncture Efficacy on Ischemic Stroke Recovery Multicenter Randomized Controlled Trial in China. Stroke. 2015; 46: 1301-1306.

Tables

Table 1 Baseline characteristics of patients (n = 497)
| General information | Arm 1 (n=159) | Arm 2 (n=173) | Control group (n=165) | Total |
|---------------------|--------------|---------------|-----------------------|-------|
| **Sex**             |              |               |                       |       |
| Male                | 107(67.3)    | 107(61.8)     | 97(58.8)              | 311   |
| Female              | 52(32.7)     | 66(38.2)      | 68(41.2)              | 186   |
| **Age**             | 64.3±8.3     | 65.2±8.5      | 65.4±6.9              | 64.9±8.3 |
| **Education**       |              |               |                       |       |
| Primary school or illiterate | 31(19.5) | 31(18.0) | 36(22.0) | 98(19.8) |
| Secondary school    | 53(33.3)     | 68(39.5)      | 62(37.8)              | 183(37.0) |
| High school         | 61(38.4)     | 61(35.5)      | 61(35.5)              | 176(35.6) |
| University          | 14(8.8)      | 12(7.0)       | 54(32.9)              | 38(7.7) |
| Master's or above   | 0(0)         | 0(0)          | 0(0)                  | 0(0)  |
| **Career**          |              |               |                       |       |
| Desk worker         | 23(14.5)     | 23(13.3)      | 18(10.9)              | 64(12.9) |
| Manual worker       | 22(13.8)     | 27(15.6)      | 31(18.8)              | 80(16.1) |
| Student             | 0(0)         | 0(0)          | 0(0)                  | 0(0)  |
| Retired             | 84(52.8)     | 99(57.2)      | 87(52.7)              | 270(54.3) |
| Unemployed          | 11(6.9)      | 13(7.5)       | 12(7.3)               | 36(7.2) |
| Other               | 19(11.9)     | 11(6.4)       | 17(10.3)              | 47(9.5) |
| **Residence**       |              |               |                       |       |
| Town                | 132(83.0)    | 150(86.7)     | 137(83.0)             | 419(84.3) |
| Village             | 27(17.0)     | 23(13.3)      | 28(17.0)              | 78(15.7) |
| **Smoking**         |              |               |                       |       |
| None                | 114(71.7)    | 123(71.1)     | 132(80.0)             | 369(74.2) |
| Former smoker       | 31(19.5)     | 27(15.6)      | 20(12.1)              | 78(15.7) |
| Current smoker      | 14(8.8)      | 23(13.3)      | 13(7.9)               | 50(10.1) |
| **Alcohol**         |              |               |                       |       |
| None                | 130(81.8)    | 151(87.3)     | 139(84.2)             | 420(84.5) |
| Former user         | 19(11.9)     | 13(7.5)       | 17(10.3)              | 49(9.9) |
| Current user        | 10(6.3)      | 9(5.2)        | 9(5.5)                | 28(5.6) |
### Table 2 Ischemic stroke characteristics

| General information | Arm 1 (n=159) | Arm 2 (n=173) | Control group (n=165) | F/ | P |
|--------------------|---------------|---------------|-----------------------|----|----|
| **Disease course** |               |               |                       |    |    |
| Month              | 13.80±9.07    | 13.94±8.83    | 13.55±8.89            | 0.080 | 0.923 |
| Number of strokes  | 1.26±0.53     | 1.25±0.44     | 1.28±0.50             | 0.134 | 0.857 |
| **Infarct size**   |               |               |                       |    |    |
| Lacunar            | 28(17.7)      | 29(17.8)      | 45(27.4)              | 6.467 | 0.373 |
| Multiple           | 81(51.3)      | 87(53.4)      | 78(47.6)              |     |    |
| Large area         | 16(10.1)      | 15(9.2)       | 13(7.9)               |     |    |
| Other              | 33(20.9)      | 32(19.6)      | 28(17.1)              |     |    |
| **Family history of stroke** |         |               |                       |    |    |
| No                 | 129(81.1)     | 134(77.9)     | 123(74.5)             | 4.635 | 0.324 |
| Unknown            | 26(16.4)      | 36(20.9)      | 35(21.2)              |     |    |
| Yes                | 4(2.5)        | 2(1.2)        | 7(4.2)                |     |    |

### Table 3 Scores and changes for NIHSS, BI and MAS in the three study arms (x±SD)

| Group | T0=baseline | T1=1 week | T2=2 weeks | Follow up=4 weeks |
|-------|-------------|-----------|------------|-------------------|
| NIHSS | Arm 1       | 7.13±4.91 | 5.98±3.72  | 4.59±3.47ab       |
|       | Arm 2       | 6.88±4.08 | 6.11±4.01  | 4.88±4.11         |
|       | Control group | 6.98±3.93 | 6.62±4.03  | 5.81±4.11         |
| BI    | Arm 1       | 54.94±27.01 | 60.00±27.92 | 67.50±28.22a      |
|       | Arm 2       | 57.82±27.40 | 61.84±27.58 | 69.26±28.64c      |
|       | Control group | 54.34±27.52 | 56.62±28.31 | 60.52±28.69       |
| MAS   | Arm 1       | 2.17±1.32  | 2.03±1.18  | 1.78±0.99         |
|       | Arm 2       | 2.34±1.38  | 2.06±1.24  | 1.80±1.06         |
|       | Control group | 2.18±1.37  | 2.09±1.24  | 1.96±1.17         |

a There were significant differences between the three groups. b A comparison between Arm 1 and the control group was statistically significant. c A comparison between Arm 2 and the control group was also
statistically significant.

Figures

**CONSORT 2010 Flow Diagram**

**Figure 1**

Flow diagram.
Figure 2

Scores of NHISS, BI and MAS in three groups

Supplementary Files

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• supplement2.doc
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