Effect of acupuncture and Chinese herbal medicine on subacute stroke outcomes: a single-centre randomised controlled trial

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ABSTRACT

Objective To determine whether integrative medicine, combining acupuncture and Chinese herbal medicine with conventional rehabilitation during subacute stroke, is an effective comprehensive rehabilitation strategy for daily life activities, neurological deficits, motor dysfunction, cognitive impairment and depression.

Design Randomised controlled trial: patients were randomly assigned to a conventional rehabilitation (CR) group or an integrative medicine rehabilitation (IMR) group with CR plus acupuncture and Chinese herbal medicine.

Setting Single-centre inpatient teaching hospital, China

Participants 120 Patients aged 35–80 years, with a recent first incidence of subacute ischaemic stroke

Main outcome measures Measured at baseline (week 0), mid-point (week 4), week 8 and follow-up (week 20).

Primary outcome measurement Modified Barthel Index (MBI)

Secondary outcome measurements The National Institutes of Health Stroke Scale; Fugl-Meyer Assessment; the Mini-Mental State Examination; Montreal Cognitive Assessment; depression, Hamilton's Depression Scale; Self-Rating Depression Scale.

Results The primary outcome measurement, MBI, showed significant improvement in the IMR group compared with the CR group. The IMR group also showed significant improvement across all of the secondary outcome measures (repeated-measures analysis of variance group*time; independent Student's t test).

Limitations A small placebo bias may exist, but measures were undertaken to limit it. Sample sizes for cognitive impairment and depression in this study were small. Results cannot be generalised to one type of treatment only.

Conclusion This trial, evaluating a treatment protocol commonly used in clinical practice, demonstrates that comprehensive rehabilitation including acupuncture and Chinese herbal medicine may comprehensively improve subacute stroke outcomes.

Trial registration number ChiCTR-TRC-12001972.

INTRODUCTION

There are 1.5–2 million new strokes in China each year,[1] and 15 million worldwide.[2] Given that 63% of patients experience decreased function,[3] it is important to consider holistic rehabilitation strategies to improve post-stroke outcomes. Even though patients with stroke experience multiple symptoms simultaneously, many studies examining the impact of acupuncture on stroke often focus on a single dysfunction or on one type of standardised treatment. Acupuncture shows promise in randomised controlled trials (RCTs) assessing its impact on specific types of dysfunction, including post-stroke dysphagia,[4] hiccups,[5] depression,[6] activities of daily living (ADLs)[7] and disability.[8]

One recent meta-analysis concluded that acupuncture combined with rehabilitation may be more effective than rehabilitation alone, but called for greater consensus on treatment protocols and the duration of intervention.[9] The comprehensive implementation of traditional Chinese medicine (TCM) as it is commonly used in clinical settings is an interesting area for scientific inquiry and merits further study to help achieve greater consensus on treatment protocols for subacute stroke. Nearly all TCM clinical strategies use standardised pattern-differentiated protocols.[10 11]

Combining acupuncture and Chinese herbal medicine may more comprehensively improve post-stroke symptoms and may be more reflective of the clinical strategy most commonly applied in the field. Acupuncture has significant effects on cerebral vascular flow and flow velocity to both hemispheres of the brain,[12] and may reduce the volume of

injury between the hemispheres, according to PET studies.[13] Acupuncture and electroacupuncture may also reduce cognitive impairment in rats through the regulation of expression of apoptosis-related genes, Bcl-2 and Bax,[14] and has been shown to markedly suppress the generation of free radicals after just 2 weeks of treatment.[15] Overproduction of reactive oxygen species leads to increased brain damage after ischaemic stroke. Acupuncture has an antioxidant effect and significantly suppresses nicotinamide adenine dinucleotide phosphate (NADPH) oxidase activity through treatment at both classical acupuncture points and non-traditional acupuncture points, with longer-term positive effects. Documented neuroprotective effects include reductions in infarct size, neuronal cell loss and memory impairment by attenuation of stroke-induced NADPH oxidative stress in the hippocampus, demonstrating the potential for sustained improvement via the antioxidant pathway.[15]

Despite positive results demonstrating efficacy, well-designed trials testing TCM treatment protocols (with sufficient sample size, adequate treatment duration, standardised outcome measurements and skilled practitioners) are still warranted. The aim of this study was to investigate the effectiveness of a commonly used integrative rehabilitation strategy incorporating acupuncture and Chinese herbal medicine (as they are commonly combined clinically) on ADLs and a wide range of negative sequelae that are frequently experienced after a stroke, including neurological deficits, motor dysfunction, cognitive impairment and depression.

METHODS

Ethics

This trial was conducted according to the ethical principles of the Declaration of Helsinki and was prospectively registered in the Chinese Clinical Trial Register at www.chictr.org (registration No ChiCTR-TRC-12001972) on 1 March 2012. The trial lasted 20 weeks and is reported according to the CONSORT guidelines. It was approved by the ethics committees of the following three hospitals: Third Affiliated Hospital of Zhejiang TCM University, Hangzhou Hospital of TCM and Jiaxing Hospital of TCM.

Setting

Inpatient rehabilitation ward of a single-centre teaching hospital in China.

Design

RCT examining differences between conventional rehabilitation (CR, control group) and integrative medicine rehabilitation (IMR, intervention group). The IMR group received acupuncture once a day for 6 days a week and Chinese herbal medicine twice a day every day, for 8 weeks, in addition to CR, which was provided to both groups.

To assist recruitment, the trial was advertised in local newspapers, on health-related TV programmes, online, by fliers posted in hospitals and within communities. The treatment protocol was published prospectively[16]; however, the following alterations were made post hoc. First, patients with a swallowing disorder were excluded owing to the risk of aspiration on ingesting the liquid Chinese herbal decoction. Second, the follow-up time was extended from 12 weeks to 20 weeks before implementation of the trial to more accurately assess the longer-term effects of the intervention. Third, the trial was changed from multicentre to single-centre, although with the same methodology. The estimated sample size calculated with the following test statistic:

$$n = \frac{2\left(\frac{Z_\alpha}{2}+Z_\beta\right)^2\sigma^2}{\Delta^2}$$

A two sided 5% significance level and 80% power were used; n is needed sample size number, zx is the standard normal deviate, type I error rate is α, type II error rate is beta, delta is the expected value difference between two groups, variance σ^2.

It was estimated that, assuming a SD of 31, at a two-sided 5% significance level with 80% power, approximately 150 participants per group would be required to detect a difference of 10 between the CR and IMR groupsin the primary outcome, the Modified Barthel Index (MBI). However, the trial was reduced to 120 participants per group for cost-effectiveness.

Finally, there was a change in inclusion criteria from a National Institutes of Health Stroke Scale (NIHSS) score of between 4 and 24 to a score between 5 and 15 in order to eliminate patients with very minor stroke complications, who were typically discharged and therefore had poor compliance with an intervention for 6 days a week, and those patients with very serious complications.

Inclusion criteria

Eligible participants were aged 35–80 years with a recent incidence (within the past ~30–40 days) of subacute ischaemic stroke and a NIHSS score between 5 and 15. Patients needed to be having a first stroke or, for those with a prior history of stroke, have no residual disability from a previous stroke (determined by a modified Rankin Scale score ≤1).

Exclusion criteria

Patients with severe systemic diseases, such as heart, liver, kidney, or hematopoietic conditions, were excluded. Patients who were pregnant or breast feeding and those with swallowing disorders, congenital disabilities and serious psychiatric conditions, such as schizophrenia, dissociative disorders and bipolar affective disorder, were also excluded. Patients were not allowed to participate if they had been in any other clinical trials in the preceding 3 months or had already

received thrombolytic therapy or TCM treatment for the stroke.

Outcome measures

The primary outcome was the MBI for ADLs. Secondary outcomes included the NIHSS score for neurological deficits, the Fugl-Meyer Assessment (FMA) motor subscale for motor dysfunction of the upper and lower extremities,[17] the Mini-Mental State Examination (MMSE) and Montreal Cognitive Assessment (MoCA) for cognitive impairment,[18] and Hamilton's Depression Scale (HAMD)[19] and Self-Rating Depression Scale (SDS) for depression. All outcomes were evaluated at four time points: week 0 (baseline); week 4 (midway through treatment); week 8 (after completion of treatment); and week 20 (follow-up). Safety and tolerability were also assessed at each visit.

Randomisation and blinding

The randomisation sequence, created by a statistician, was placed into sequentially numbered, opaque, sealed envelopes, which were opened by dedicated screeners. All participants gave written informed consent before being randomly assigned to intervention or control groups in a 1:1 ratio (n=60 per group) by the screeners. All rehabilitation therapists, outcome assessors and analysts were blinded to group assignments.

Interventions and control group

Conventional therapy was consistent across both groups and given to every participant for 5 days a week for the entire 20 weeks. Conventional rehabilitation therapists were trained to conduct treatment consistently, according to stroke rehabilitation treatment guidelines in China,[20] and treatment included normal limb posturing, physical and occupational therapy, and cognitive training and psychological counselling (if criteria were met).

Intervention compliance was substantially increased by the investigator's recommendation that all study participants be hospitalised for the entire study. Participants were given a therapy card, which recorded their name, randomisation number in the trial and details of their rehabilitation programme. Therapists signed their names after every treatment, but were blinded to the group information.

The IMR group received acupuncture while lying supine on their hospital bed, once a day for 6 days a week for a total of 8 weeks, in addition to the CR programme described above. Interaction with the provider was kept to a minimum level. No additional attention, training or interaction with providers was given. Needles were inserted over the course of 5–7 min and the patient rested alone with needles left in situ for 30 min. Needles were removed over the course of 3–5 min. The IMR group also took 100 mL of a Chinese herbal decoction twice a day for 8 weeks.

Both acupuncture and Chinese herbal prescriptions were administered according to four types of patterns related to stroke (types 1 to 4; online supplementary table 1). Chinese medical doctors analysed the signs and symptoms and customised the acupuncture treatment and herbal decoctions accordingly.

Acupuncture treatment

All certified acupuncturists participating in the trial had more than 5 years' clinical experience. Huatuo brand filiform steel needles (size 0.25 mm x 40 mm) were used (Suzhou Medical Appliance Company, Suzhou, Jiangsu Province, China). Details of the acupuncture prescription are outlined in online supplementary table 1. Each patient received the same basic acupuncture prescription, including stimulation to achieve *de qi*, plus modification according to constitutional type/dysfunction. Electrical stimulation, with GB6805-2 Electro-Acu Stimulators (Huayi Medical Supply & Equipment Co, Ltd, Shanghai, China), was applied at the following acupuncture points using a 2 Hz intermittent wave: LI15 (*Jianyu*) and LI11 (*Quchi*), ST36 (*Zusanli*) and GB39 (*Xuanzhong*); intensity was adjusted within the patient's tolerance.

Chinese herbal medication

Patients received a total of 60 doses of herbal medicine. One dose of Chinese herbal medicine was divided across two packages (100 mL each). Patients took 100 mL at a time, twice a day, every day, for 8 weeks. Modifications were made to the herbal decoction if the participant met criteria for cognitive impairment or depression.

Statistical analysis

A statistician at the Clinical Research Institute of the Zhejiang Provincial Hospital of TCM, blinded to group allocation performed the data analysis using SPSS version 17.0 (SPSS Inc., Chicago, IL, USA). The predetermined level of statistical significance established before the study was a two-sided p value of <0.05. A full analysis according to the intention-to-treat principle was conducted for the MBI, NIHSS, FMA and safety parameters. A per protocol analysis was also performed to ensure that there were no substantial variations in the data due to protocol violations or missing data; no substantial differences were found between the full analysis set and per protocol analyses (latter therefore not presented). Analysis of the outcomes of cognitive impairment and depression was conducted only for cases that met the criteria of MMSE$\leq$24, MoCA$\leq$20 and HAMD$\geq$8 at baseline. A mixed model for repeated measurements was used for missing values. Normally distributed continuous variables are reported as mean and SD. Categorical data are presented as number and percentage. For all outcome variables, repeated-measures analysis of variance (ANOVA) was conducted by group and time

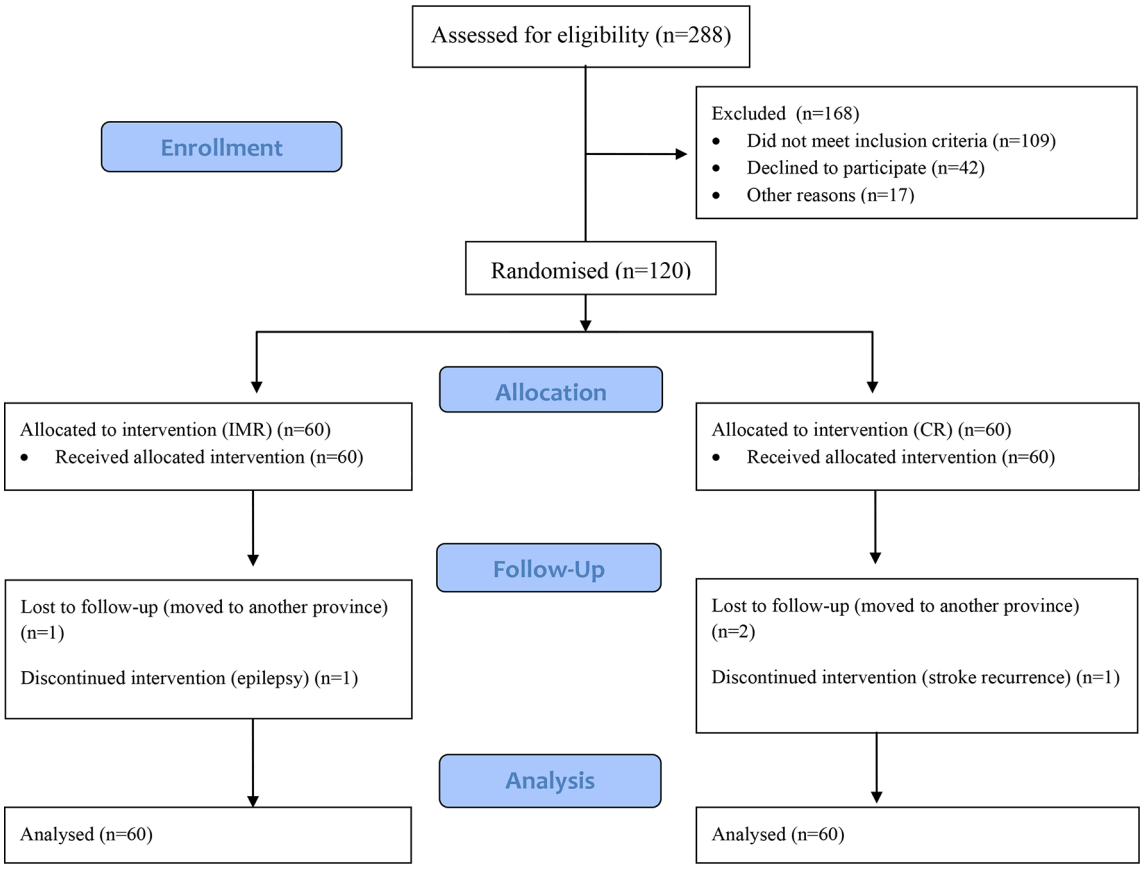

Figure 1 Flow chart of participants through the trial. CR, conventional rehabilitation; IMR, integrative medicine rehabilitation.

point to examine any differences between the intervention and control groups. Independent t tests were conducted.

RESULTS

A total of 120 participants were recruited between 1 March 2012 and 25 December 2014. Figure 1 shows the flow of participants through the trial. Of 288 individuals who were screened, 109 did not meet the inclusion criteria, 42 declined to participate and 17 were excluded for other reasons. Five cases were lost to follow-up (two in the intervention group and three in the control group). No patients died. The clinical trial ended on 30 May 2015.

The baseline characteristics of the participants in both groups were comparable for age, gender, education, history of stroke, laterality of stroke, vascular risk factors, syndrome differentiation (types 1 to 4) and outcome measurements (table 1).

The groups, which were relatively equivalent at baseline, began to diverge by weeks 4 to 8, depending on specific outcome measurement, but differences between the two groups were not significant for any outcome variable until week 20 (table 2).

Both groups demonstrated temporal improvements in the primary outcome measure of MBI between week 0 and week 20. Mean MBI increased from 40/100 to 74/100 in the IMR group and from 43/100 to 67/100 in the CR group. However, improvement among patients in the IMR group was significantly greater than for those in the CR group at week 20 (table 2, p=0.04).

Secondary outcomes also showed significant improvement. A lower score on the NIHSS indicates greater neurological function and improved recovery.[21] The IMR group (decreasing from 9.7 to 3.1) improved significantly from baseline to week 20 compared with the CR group (table 2, p=0.001).

The FMA motor subscale, measuring a total of 100 points for sensory motor stroke recovery and used to measure functional ability of upper and lower extremities, showed significant improvement for the IMR group compared with the CR group (table 2, p=0.035).

MoCA, HAMD and SDS also showed significant improvement in the IMR group by week 20. The MMSE between the two groups was not significant at a single time point (table 2, p=0.266). However, it was significant when comparing changes between two time points within the IMR group (table 3, p=0.03).

Independent Student's t tests (comparing changes before and after intervention by group) andtwo-way repeated-measures ANOVA (by group and time), showed significant differences for both the MMSE and the MoCA between groups (tables 3 and

Table 1 Baseline characteristics

Characteristics	IMR (n=60)	CR (n=60)	p Value
Male, gender, n (%)	31 (51.7%)	34 (56.7%)	0.583
Age, years, mean (SD)	66.3 (12.4)	65.7 (12.2)	0.802
History of stroke, mean (SD)	34.4 (2.7)	34.6 (2.9)	0.766
Education level (years)*			0.246
0–5, n (%)	10 (16.7%)	16 (26.7%)	
>5–8, n (%)	22 (36.7%)	24 (40.0%)	
>8, n (%)	28 (46.7%)	20 (33.3%)	
Laterality of hemiparesis			0.713
Left, n (%)	33 (55.0%)	35 (58.3%)	
Right, n (%)	27 (45.0%)	25 (41.7%)	
Vascular risk factors			
Hypercholesterolaemia, n (%)	36 (60.0%)	37 (61.7%)	0.852
Hypertension, n (%)	36 (60.0%)	39 (65.0%)	0.572
Diabetes mellitus, n (%)	21 (35.0%)	14 (23.3%)	0.160
Syndrome differentiation†			0.381
Type 1, n (%)	15 (25.0%)	15 (25.0%)	
Type 2, n (%)	12 (20.0%)	12 (20.0%)	
Type 3, n (%)	16 (26.7%)	23 (38.3%)	
Type 4, n (%)	17 (28.3%)	10 (16.7%)	
Cognitive impairment, n (%)	20 (33.3%)	19 (31.7%)	0.845
PSD, n (%)	22 (36.7%)	18 (30.0%)	0.439
MBI, mean (SD)	40.0 (14.7)	42.7 (19.9)	0.420
NIHSS, mean (SD)	9.7 (3.4)	10.3 (3.7)	0.400
FMA, mean (SD)	41.3 (14.9)	44.6 (18.1)	0.286
MMSE, mean (SD)	16.1 (2.0)	16.4 (4.3)	0.766
MoCA, mean (SD)	15.1 (3.01)	14.1 (2.8)	0.317
HAMD, mean (SD)	23.5 (6.6)	23.7 (6.6)	0.916
SDS, mean (SD)	63.1 (8.1)	64.6 (6.5)	0.528

*Education level; 0–5, elementary school; >5–8, middle school; >8, above middle school.
†See online supplementary table 1.
CR, conventional rehabilitation; FMA, Fugl-Meyer Assessment; HAMD, Hamilton's Depression Scale; IMR, integrative medicine rehabilitation; MBI, Modified Bathel Index; MMSE, the Mini-Mental State Examination; MoCA, Montreal Cognitive Assessment; NIHSS, the National Institutes of Health Stroke Scale; PSD, post-stroke depression; SDS, Self-Rating Depression Scale.

4). Finally, for both the HAMD and the SDS, the IMR group showed a significantly greater improvement by week 20 compared with the CR group (tables 2, 3 and 4). Two-way repeated-measures ANOVA showed significant group x time interactions for all outcome variables (table 4).

Safety results

All adverse events were monitored and recorded, together with routine tests of liver/kidney function, blood, urine and stool. No moderate or severe adverse events occurred. None of the participants had any renal dysfunction. Five per cent (three patients) began the study with mild hepatic dysfunction, which decreased to 3.3% (two patients) by the end of the study. There was a low incidence of mild adverse events only, including bleeding, local haematoma, unbearable prickling, dizziness and gastrointestinal discomfort. The scalp is highly vascular, which makes a small amount of bleeding from a mildly invasive procedure of needle insertion and manipulation highly likely. A small amount of bleeding from a drop to several drops occurred in 58.3% of cases.

DISCUSSION

Despite the rehabilitation strategy, the goal for patients with stroke is focused on improving ADLs and patients' functional independence.[22] This RCT demonstrated significant improvements in IMR versus CR groups for all post-stroke outcomes measured at week 20 (except the MMSE by Student's t test, measured at a single time point), although changes from baseline by t test and ANOVA showed significantly greater improvements in the MMSE in the IMR group. However, the sample size for this subset is too small to draw generalisable conclusions on cognitive impairment.

Even though the intervention stopped at week 8, the outcomes of the IMR group still continued improving at an increased rate compared with the

Table 2 Outcome measures by group and time point

Variables	Group	N	Week 0	Week 4	Week 8	Week 20	p Value (CR vs. IMR at week 20)
MBI	IMR	60	40.1 (14.7)	51.1 (16.2)	64.8 (16.8)	74.3 (17.8)*	0.04
	CR	60	42.7 (19.9)	50.6 (20.0)	60.6 (19.8)	67.1 (20.0)	
NIHSS	IMR	60	9.7 (3.4)	7.9 (3.4)	5.6 (3.2)	3.1 (2.3)**	0.001
	CR	60	10.3 (3.7)	8.3 (3.8)	6.4 (3.7)	5.0 (3.4)	
FMA	IMR	60	41.3 (14.9)	55.5 (17.9)	68.2 (18.4)	76.2 (17.5)*	0.035
	CR	60	44.6 (18.1)	52.7 (18.0)	62.3 (18.5)	69.1 (18.8)	
MMSE	IMR	20	16.1 (2.1)	18.3 (2.3)	20.0 (1.9)	22.3 (1.9)	0.266
	CR	19	16.4 (4.3)	17.6 (3.9)	19.6 (3.7)	21.2 (3.8)	
MoCA	IMR	20	15.1 (3.1)	16.3 (3.0)	19.1 (2.8)	21.6 (3.0)**	0.006
	CR	19	14.1 (2.8)	15.1 (2.9)	17.2 (3.3)	18.8 (3.1)	
HAMD	IMR	22	23.5 (6.6)	19.8 (6.7)	16.4 (6.1)	10.6 (5.1)*	0.014
	CR	18	23.7 (6.6)	20.6 (6.8)	17.9 (6.8)	14.9 (5.4)	
SDS	IMR	22	63.1 (8.1)	56.6 (10.9)	50.2 (9.1)	40.9 (8.7)**	0.007
	CR	18	64.6 (6.5)	60.1 (9.4)	55.7 (10.7)	48.9 (8.9)	

*p<0.05, **p<0.01 compared with the CR group. Groups were compared using Student's independent samples t test.
Results are shown as mean (SD).
CR, conventional rehabilitation; FMA, Fugl-Meyer Assessment; HAMD, Hamilton's Depression Scale; IMR, integrative medicine rehabilitation; MBI, Modified Bathel Index; MMSE, the Mini-Mental State Examination; MoCA, Montreal Cognitive Assessment; NIHSS, the National Institutes of Health Stroke Scale; SDS, Self-Rating Depression Scale.

CR group, indicating possible carry-over effects of IMR. The groups did not diverge significantly until week 20, even though they begin to separate by week 4 or 8. Several reasons for the delay in significance are possible. Firstly, the antioxidant effect seen in acupuncture studies may have a slower, longer-term effect. Secondly, the close relationship between the outcomes may contribute to a synergistic effect of treatment, which has previously been observed for cognitive impairment and depression.[23] Limb recovery is an important contributor to improved ability,[24] and our results suggested significant improvements in the IMR group for MBI and FMA at the same time point (week 20). When a patient with stroke gains improved use of their limbs they may intuitively feel less depressed. Thirdly, the length of time needed for successful rehabilitation after a stroke may need to be longer than 8 weeks in order to adequately reflect the

Table 3 Changes from baseline within each group (week 0 to week 20)

Variable	Group (N)	Changes week 0 to week 20 Mean (SD)	95% CI of the difference	T	p Value
MBI	IMR (60)	34.2 (13.0)	5.0 to 14.5	4.08	<0.001***
	CR (60)	24.4 (13.2)			
NIHSS	IMR (60)	−6.6 (1.8)	−2.1 to −0.4	−3.037	0.003**
	CR (60)	−5.3 (2.7)			
FMA	IMR (60)	34.9 (11.8)	5.9 to 14.7	4.625	<0.001***
	CR (60)	24.6 (12.6)			
MMSE	IMR (20)	6.2 (1.5)	0.1 to 2.7	2.25	0.030*
	CR (19)	4.7 (2.4)			
MoCA	IMR(20)	6.56 (1.7)	0.6 to 3.1	3.071	0.004**
	CR (19)	4.7 (2.1)			
HAMD	IMR (22)	−12.9 (4.5)	−6.7 to −1.4	−3.124	0.003**
	CR (18)	−8.83 (3.59)			
SDS	IMR (22)	−22.2 (7.2)	−10.8 to −2.3	−3.128	0.003**
	CR (18)	−15.7 (5.7)			

*p<0.05, **p<0.01, ***p<0.001.
CR, conventional rehabilitation; FMA, Fugl-Meyer Assessment; HAMD, Hamilton's Depression Scale; IMR, integrative medicine rehabilitation; MBI, Modified Bathel Index; MMSE, the Mini-Mental State Examination; MoCA, Montreal Cognitive Assessment; NIHSS, the National Institutes of Health Stroke Scale; SDS, Self-Rating Depression Scale.

Table 4 Results of two-way repeated measures analysis of variance (by group and time) for all variables

Variables	df Hypothesis	df Error	Effects	F	p Value	Partial eta squared
MBI	1	118	Group	0.552	0.459	0.005
	3	116	Time	201.880	<0.001	0.839
	3	116	Group by time	5.650	**0.001****	0.128
NIHSS	1	118	Group	2.353	0.128	0.020
	3	116	Time	268.350	<0.001	0.874
	3	116	Group by time	4.992	**0.003****	0.114
FMA	1	118	Group	1.040	0.310	0.009
	3	116	Time	257.110	<0.001	0.869
	3	116	Group by time	11.450	**<0.001*****	0.229
MMSE	1	37	Group	0.250	0.620	0.007
	3	35	Time	102.600	<0.001	0.898
	3	35	Group by time	3.619	**0.022***	0.237
MoCA	1	37	Group	3.476	0.070	0.086
	3	35	Time	118.160	<0.001	0.910
	3	35	Group by time	3.311	**0.031***	0.221
HAMD	1	38	Group	0.820	0.820	0.021
	3	36	Time	92.365	<0.001	0.885
	3	36	Group by time	4.709	**0.007****	0.282
SDS	1	38	Group	3.032	0.090	0.074
	3	36	Time	112.038	<0.001	0.903
	3	36	Group by time	3.256	**0.033***	0.213

*Significant p<0.05, **p<0.01, ***p<0.001.
FMA, Fugl-Meyer Assessment; HAMD, Hamilton's Depression Scale; MBI, Modified Bathel Index; MMSE, the Mini-Mental State Examination; MoCA, Montreal Cognitive Assessment; NIHSS, the National Institutes of Health Stroke Scale; SDS, Self-Rating Depression Scale.

progression of the disease. Finally, the sample sizes for cognitive impairment and depression were smaller than desired.

Overall, our results indicate that acupuncture and Chinese herbal medicine combined with conventional rehabilitation may improve stroke patients' ADLs, functional abilities, motor function, cognitive impairment (as measured by MoCA) and depression. NIHSS, which is a good early predictor of future functional abilities, was significantly improved after IMR group compared with CR alone, which may indicate a good chance of long-term improved functional ability in the IMR group. This result is important, considering the extent of disability that post-stroke survivors face. Having a positive effect on multiple sequelae simultaneously is important, because it indicates that comprehensive rehabilitation may contribute to overall function.

A recently published pilot study of 31 patients examined the effects of 2 weeks of daily acupuncture but found no persistent differences between the two groups at 12 weeks.[25] By contrast, our study examined an 8-week intervention and found significant results at 20 weeks. Several reasons for this may exist. Authors of the aforementioned pilot study considered that a sample size of 122 would be required for future studies; this is similar to the 120 participants included herein, which was associated significant results. Furthermore, acupuncture treatment in our trial included additional points not used in the pilot study including LI15, LI10 (*Shousanli*), ST31 (*Biguan*), GB34 (*Yanglingquan*), GB39 and BL60 (*Kunlun*) as well as electroacupuncture at certain points. In addition, this trial tailored the acupuncture treatment toward TCM patterns and added additional relevant points, while only using SP6 (*Sanyinjiao*) for type 3 (online supplementary table 1). This trial also used Chinese herbal decoction, which is designed to be used in conjunction with acupuncture for long-term efficacy.

Limitations

In China, post-stroke patients are commonly mangaged in an inpatient setting for their entire rehabilitation programme in order to facilitate compliance and improve health outcomes and functionality. Extrapolation to outpatient care may be limited, due to compliance and access to transportation.

Another limitation stems from a potential placebo bias through the use of acupuncture and Chinese herbal medicine without using sham acupuncture or placebo herbal medicine. Sham acupuncture literature is extremely heterogeneous with varied methods from design to implementation.[26] In addition, many Chinese patients have had previous exposure to acupuncture and Chinese herbal medicine. The prevalence of TCM within China would arguably make it easy for patients to know whether they had been assigned to a sham group or were receiving placebo herbal medicine.

The sample sizes of participants with cognitive impairment and depression were much smaller than the total sample size. Additional studies, screening for cognitive impairment and depression specifically, with a larger sample size would be useful.

CONCLUSION

The group receiving IMR showed significant improvement on all outcome measures compared with the CR group. Activities of daily living, functional independence, neurological function, motor function and coordination all improved, and depression was diminished, in the intervention group in comparison with conventional rehabilitation. This study provides support for the proposal that comprehensive rehabilitation with acupuncture and Chinese herbal medicine may improve overall post-stroke outcomes more than conventional therapy alone.

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Contributors JF and LC had full access to all the study data and had complete responsibility for the integrity of the data and the accuracy of the data analysis. JF, CLK and LC drafted the manuscript and revised it critically for important intellectual content. RM, CW and SX were responsible for the acquisition, analysis and interpretation of the data, and for conducting the trial in each centre, designating independent researchers as coordinators, therapists and evaluators. All authors made substantial contributions to the conception and design of the work, critically revised and approved the final manuscript.

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Competing interests None.

Ethics approval Third Affiliated Hospital of Zhejiang Traditional Chinese Medical University, Hangzhou Hospital of Traditional Chinese Medicine and Jiaxing Hospital of Traditional Chinese Medicine.

Provenance and peer review Not commissioned; externally peer reviewed.

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