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Acupuncture for patients with mild hypertension: A randomized controlled trial

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Acupuncture may be beneficial for patients with mild hypertension, but the evidence is not convincing. We aimed to examine the effect of acupuncture on blood pressure (BP) reduction in patients with mild hypertension. We conducted a multicenter, single-blind, sham-controlled, randomized trial in eleven hospitals in China. The trial included 428 patients with systolic blood pressure (SBP) from 140 to 159 mm Hg and/or with diastolic blood pressure (DBP) from 90 to 99 mm Hg. The patients were randomly assigned to receive 18 sessions of affected meridian acupuncture (n = 107) or non-affected meridian acupuncture (n = 107) or sham acupuncture (n = 107) during 6 weeks, or to stay in a waiting-list control (n = 107). All patients received 24-hour ambulatory blood pressure monitoring at weeks 6, 9, and 12. We included 415 participants in the intention-to-treat analysis. The two acupuncture groups were pooled in the analysis, since they had no difference in all outcomes. SBP decreased at week 6 in acupuncture group vs sham acupuncture vs waiting-list group (7.2 ± 11.0 mm Hg vs 4.1 ± 11.5 mm Hg vs 4.1 ± 13.2 mm Hg); acupuncture was not superior to sham acupuncture (mean difference 2.7 mm Hg, 95% CI 0.4 to 5.9, adjusted $P = 0.103$) or waiting-list control (2.9 mm Hg, 95% CI −0.2 to 6.0, adjusted $P = 0.078$). However, acupuncture was superior to sham acupuncture (3.3 mm Hg, 95% CI 0.2 to 6.3, adjusted $P = 0.035$) and waiting-list control (4.8 mm Hg, 95% CI 1.8 to 7.8, $P < 0.001$) at week 9. Acupuncture had a small effect size on the reduction of BP in patients with mild hypertension.

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1 | INTRODUCTION

Hypertension is an independent risk factor for stroke and cardiovascular diseases, and it affects 26.4% of the adult population.[1] Mild hypertension, also called stage I hypertension, refers to systolic blood pressure (SBP) increasing to a range of 140-159 mm Hg and/or diastolic blood pressure (DBP) increasing to a level of 90-99 mm Hg. Recent systematic reviews showed that reducing blood pressure (BP) in patients with mild hypertension significantly reduced the mortality rate in stroke and cardiovascular diseases,[2,3] and a recent guideline suggested controlling SBP to a level lower than 130 mm Hg[4]; reducing BP in patients with mild hypertension is therefore necessary.

About 9% of the hypertensive individuals discontinue pharmacological treatments due to the adverse effects of the treatments, and their effectiveness is still under investigation.[5] Nonpharmacological treatments prevail among hypertensive patients. They had advantage in patient compliance and caused fewer adverse events when compared with conventional medication.[6] However, most of the nonpharmacological treatments are questioned for their effectiveness in treating hypertension[7]; trials with rigorous design are therefore warranted. Acupuncture was proposed to be used for decreasing BP in hypertensive patients. Several systematic reviews found the promising effect of acupuncture on BP reduction; the magnitude of BP reduction ranges from 3 to 40 mm Hg.[8-12] However, these reviews have inconclusive results because of the lack of high-quality randomized controlled trials, and the two randomized controlled trials with adequate power in testing the efficacy of acupuncture in treating hypertensive patients showed conflict results.[13,14] In addition, the efficacy of acupuncture in treating patients with mild hypertension has never been examined in previous studies. Given the facts above, we conducted a randomized controlled trial to test the effect of acupuncture on BP reduction in patients with mild hypertension.

2 | METHODS

2.1 | Study overview

We designed a multicenter, sham-controlled, randomized trial comparing acupuncture with sham acupuncture or waiting-list control in reducing BP in 428 patients with mild hypertension. The trial was carried out from July 2012 to April 2016 in 11 hospitals in China. The patients were randomly assigned to one of the two active acupuncture treatments, sham acupuncture, or waiting-list group in a 1:1:1:1 ratio. The study period of the trial consisted of 1-week run-in, 6-week treatment, and 6-week follow-up. Patients in the two acupuncture groups or sham acupuncture group received 18 sessions of acupuncture in the 6-week treatment period with a treatment frequency of three sessions per week. Patients in the waiting-list control group received no treatment during the study period, but they were given an option to receive 18 sessions of free acupuncture treatment after they finished the 13-week study period or to receive treatment advice from cardiologists. The BP of the patients was measured by using 24-hour ambulatory blood pressure monitoring (ABPM) at the end of the run-in period (week 0), the end of acupuncture treatment (week 6), 3 weeks after treatment (week 9), and 6 weeks after treatment (week 12).

The trial was conducted in the following 11 hospitals: the Teaching Hospital of Chengdu University of Traditional Chinese Medicine (TCM), the Third Affiliated Hospital of Chengdu University of TCM, the Affiliated Hospital of Ningxia Medicine University, the First Affiliated Hospital of Hunan University of TCM, the Second Affiliated Hospital of Hunan University of TCM, the Affiliated Hospital of Hunan University of TCM, the Chenzhou No. 1 People's Hospital, the First Affiliated Hospital of Guiyang University of Chinese Medicine, the Second Affiliated Hospital of Guiyang University of Chinese Medicine, the Yunnan Provincial Hospital of TCM, and the Second Affiliated Hospital of Shaanxi University of Chinese Medicine. The conduction of the trial conformed to the Declaration of Helsinki[15] and was granted ethical approval in the 11 hospitals (clinical registry: clinicaltrials.gov, NCT01701726).

2.2 | Patients

Patients were recruited from the outpatient clinics in the participating hospitals and the nearby communities, and we posed advertisement in local media to recruit patients who were potentially interested in participating in the trial. The recruitment was started on July 1, 2012, and finished at February 20, 2016. The patients were noticed that they would be compensated for entering the trial. Patients were considered eligible when they met all the following conditions: aged between 40 and 75 years; diagnosed by JNC-7 and 2010 Chinese guidelines for management of hypertension; having SBP from 140 to 159 mm Hg and/or DBP from 90 to 99 mm Hg; and providing written informed consents. Patients were excluded for having one of the following conditions: secondary hypertension; taking antihypertensive drugs; having stroke or myocardial infarction; undergoing severe depression or anxiety (had a Self-Rating Anxiety Scale[16] score or a Self-Rating Repression Scale score[16] larger than 70); undergoing pregnancy or lactation; and having received acupuncture treatment in the recent 3 months.

2.3 | Randomization and masking

Randomization sequence was generated and concealed by the Brightech-Magnsoft Data Services Company. The sequence was stratified by the duration of hypertension with a block of 12. Patients, outcome assessors, and statisticians were blinded to group assignment.

2.4 | Interventions

Eligible patients were randomly assigned to receive one of the two active acupuncture treatments or sham acupuncture, or to stay in waiting-list group. The two treatments of active acupuncture

were different in the selection of acupuncture points. Patients in the affected meridian acupuncture group received acupuncture at points in the Jueyin and Yangming meridian; patients in the non-affected meridian acupuncture group received acupuncture at points in the Shaoyang and Taiyin meridian (these points were also selected for the treatment of hypertension). We provided the location of the acupuncture points in Appendix S1; and the rationale for selecting these points was described in the trial protocol published elsewhere.[17] The acupuncture points were bilaterally needled, with each point being punctured by two needles: one main needle (25 to 40 mm in length and 0.25 mm in diameter) and one auxiliary needle (13 mm in length and 0.18 mm in diameter). The main needle and the auxiliary needle were connected in pairs to an electrical stimulator (HAN's acupoint nerve stimulator 200; Nanjing, China), and each point was electrically stimulated (frequency, 2 Hz; intensity, 2 mA). The depth of insertion (usually 0.3-1.5 cm in depth) was determined by the arrival of *deqi* sensation that is a sense of distension, soreness, numbness, or dull pain in the needled sites. The acupuncture needles were retained for 30 minutes in each session.

Patients in the sham acupuncture group received the same procedure as those in the acupuncture group, except that they were needled at four sham acupuncture points. The sham points were selected on the basis of our previous studies proving their inertia.[18-20]

2.5 | Outcomes

Every participant took blood pressure measurements through 24-hour ABPM (A&D Co. Ltd., Japan TM-2430) at weeks 0, 6, 9, and 12; a total of 76 measurements were taken in 24 hours. Daytime measurements were taken every 15 minutes from 08:00 to 22:00; nighttime measurements were taken every 30 minutes from 22:00 to 08:00. The following parameters were calculated on the basis of the 24-hour ABPM: average SBP and DBP, average daytime SBP and DBP, and 24-hour blood pressure variability (BPV) of SBP and DBP.

The primary outcome was the change from baseline in SBP at week 6. Secondary outcomes included change in DBP, average daytime and nighttime BP, 24-hour BPV, visit-to-visit BPV, responder rate, and adverse events.

Twenty-four-hour ABPM device automatically provided the standard deviation of daytime and nighttime BP mean, respectively; and 24-hour BPV was calculated from the average of the daytime and nighttime BP SD (weighted by the period of daytime vs nighttime as 7 vs 5).[21]

Visit-to-visit BPV was calculated according to the reports of previous studies.[22,23] We asked each participant to take 4 visits during 12 weeks (weeks 0, 6, 9, and 12) and take 24-hour ABPM at each visit. The visit-to-visit BPV was calculated as the variance of the four average BPs. To make visit-to-visit BPV independent of mean BP, we used the following algorithm: $SD/mean^{x}$; SD referred to the standard deviation of the four average BPs, and x was derived from curve fitting.[22,23]

2.6 | Statistical analysis

Systematic reviews showed that the reduction in BP after acupuncture varied between 3 and 40 mm Hg.[8-11] We anticipated a 12-mm Hg reduction in SBP after affected meridian acupuncture, a 10-mm Hg reduction after non-affected meridian acupuncture, a 3-mm Hg reduction after sham acupuncture, and no improvement after waiting-list control. We determined these effect-size parameters on the basis of group discussion. We needed 372 patients in total to test the hypothesis that acupuncture treatments were superior to sham acupuncture and waiting-list control at a significance level of 0.05 and with a power of 0.9. Accounting for a possible attrition bias of 15%, we needed at least 428 patients.

All analyses were based on the intention-to-treat (ITT) population that was defined as participants who received at least one session of acupuncture treatment and took at least one measurement of 24-hour ABPM. Additional analyses were performed on the basis of the per-protocol (PP) population that was defined as participants who received at least 12 sessions of acupuncture treatment and had taken outcome measures at baseline and week 6. Missing values were imputed by using the last-observation-carried-forward (LOCF) method. The data from the two active acupuncture treatments were pooled in the analyses, since they were both effective treatments in clinical practice and they showed similar effects in BP reduction in this trial.

The primary outcome was analyzed by using an analysis-of-covariance (ANCOVA) model. The model included age, baseline BP, study site, duration of hypertension, and family history of hypertension as covariates. Change from baseline in 24-hour BPV, visit-to-visit BPV, and DBP were also analyzed by using the same ANCOVA model. Responder rate was analyzed with a random-intercept logistic regression model, in which the outcome of response is included as the dependent variable, whereas the study group, visit time points, age, baseline BP, study site, duration of hypertension, and family history of hypertension were included as the independent variables. Difference between the groups was calculated as mean differences or odds ratios alongside with their 95% confidence intervals (95% CIs). Multiple comparisons between the groups were adjusted by the Bonferroni method. The statistical analyses were performed by using R 3.10.

3 | RESULTS

3.1 | Baseline characteristics

From September 2012 to April 2016, we screened 1218 patients with mild hypertension, and 428 of them were included and randomly assigned (Figure 1). We included 415 participants in the ITT population (five participants did not receive treatment that they were assigned to; four participants declined participation; and four participants had no assessment record at baseline evaluation) and 357 participants in the PP population (10 participants did not finish treatment, 21 participants did not finish follow-up

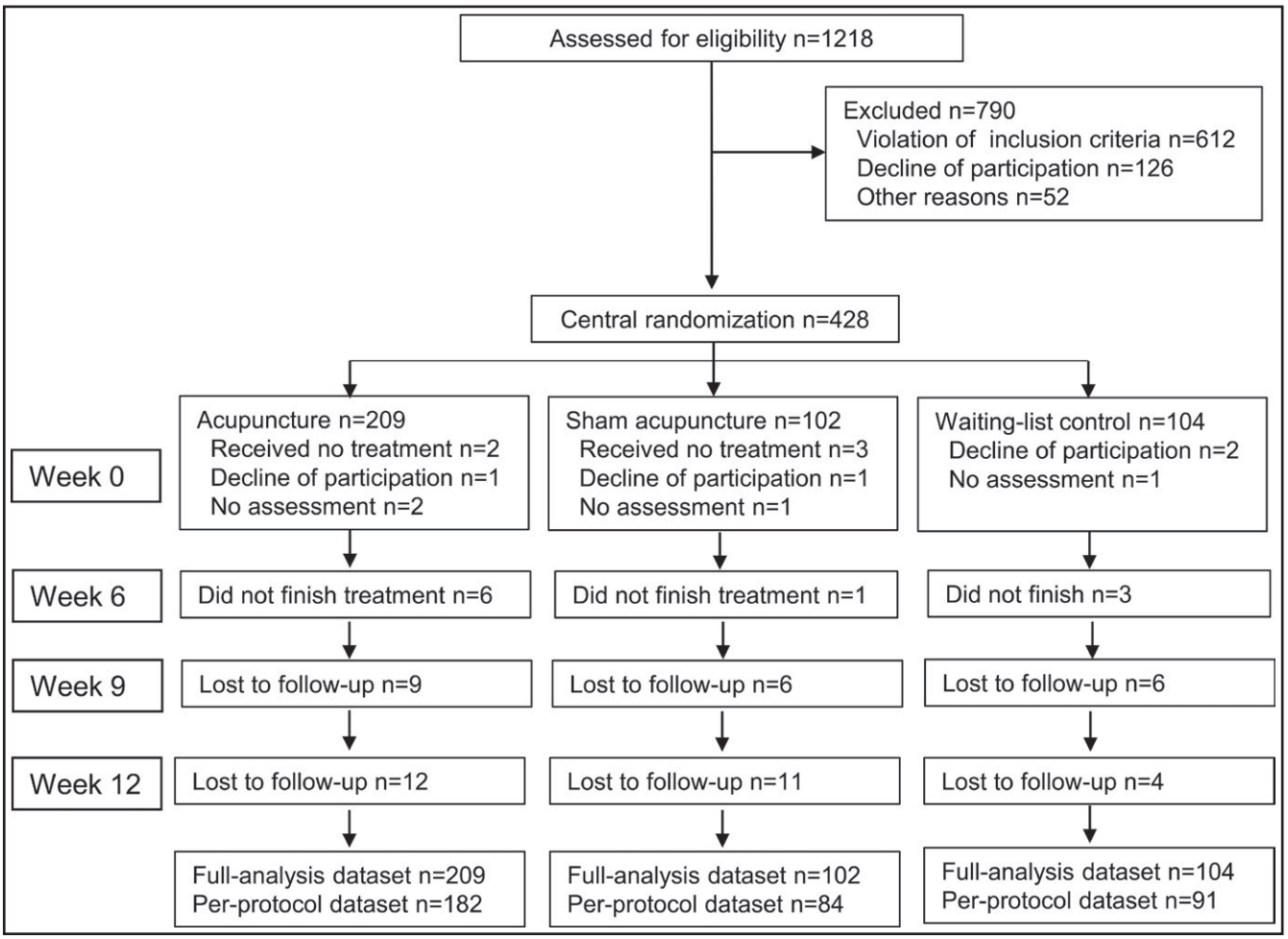

FIGURE 1 Study flowchart. Full-analysis dataset (based on ITT population) included participants who received at least one session of acupuncture treatment and at least one assessment of 24-hour ambulatory blood pressure monitoring (ABPM). Per-protocol analysis included participants who received at least 12 sessions of acupuncture and 24-hour ABPM at weeks 0 and 6. The two active acupuncture groups (affected meridian acupuncture n = 107 and non-affected meridian acupuncture n = 107) were pooled in statistical analysis

visits at week 9, and 27 participants were lost to follow-up at week 12).

Baseline characteristics were comparable among the four groups (Table 1). The participants had mean SBP of 147.6 mm Hg and mean DBP of 89.6 mm Hg. All participants had elevated SBP at baseline, and 259 (62.4%) of them had elevated DBP. The mean values of 24-hour BPV of SBP and DBP were 16.0 and 11.9, respectively. Fourteen (3.4%) participants had used antihypertensive drugs, and all of them were willing to withdraw.

3.2 | BP reduction

Participants receiving active acupuncture had reduction in SBP at week 6 (7.2 mm Hg), week 9 (8.9 mm Hg), and week 12 (7.8 mm Hg). Compared with participants in the waiting-list group, those in the active acupuncture group had more reduction in SBP at week 6 (adjusted mean difference 2.9 mm Hg, 95% CI −0.2 to 6.0, $P = 0.078$), week 9 (4.8 mm Hg, 95% CI 1.8 to 7.8, $P < 0.001$), and week 12 (4.6 mm Hg; 95% CI 1.2 to 8.0, $P = 0.004$). Compared with participants receiving sham acupuncture, those receiving active acupuncture had better improvement in SBP at week 6 (2.7 mm Hg, 95% CI, 0.4 to 5.9; $P = 0.103$), week 9 (3.3 mm Hg; 95% CI, 0.2 to 6.3; adjusted $P = 0.035$), and week 12 (3.0 mm Hg; 95% CI, −0.5 to 6.4; $P = 0.104$). Similar results were found in the improvement of daytime SBP and nighttime SBP (Table 2). The effect size of active acupuncture on SBP reduction was generally small (Figure 2). The analysis of DBP showed significant improvement after acupuncture at weeks 9 and 12 (Table 2 and Figure 2).

3.3 | Changes of visit-to-visit and 24-hour BPV

Both acupuncture (difference 0.00, 95% CI, −0.009 to 0.009, $P = 0.992$) and sham acupuncture (−0.003, 95% CI, −0.013 to 0.007, $P = 0.768$) had no effect on the visit-to-visit BPV of SBP as compared with waiting-list group. Acupuncture had no effect on visit-to-visit BPV of DBP (−0.001, 95% CI −0.003 to 0.001, $P = 0.5331$), but sham acupuncture had slight but significant effect (−0.025 95% CI −0.051 to 0.000, $P = 0.045$). For 24-hour BPV, no significant difference was found between groups (Appendix S1).

TABLE 1 Baseline characteristics

	Acupuncture (n = 209)	Sham acupuncture (n = 102)	Waiting-list control (n = 104)
Age, year, mean (SD)	58.2 (9.9)	60.4 (9.3)	59.4 (10.5)
Female, n (%)	105 (50.2)	53 (52.0)	54 (51.9)
Study sites, n (%)			
Sichuan	46 (22.0)	21 (20.6)	21 (20.2)
Hunan	43 (20.5)	22 (21.6)	24 (23.1)
Guizhou	42 (20.2)	24 (23.5)	20 (19.2)
Yunnan	34 (16.3)	14 (13.7)	17 (16.3)
Shaanxi	44 (21.0)	21 (20.6)	22 (21.2)
Body mass index, kg/m^2, mean (SD)	25.0 (4.2)	24.4 (3.5)	24.7 (3.1)
Abdominal girth, mean (SD)	87.2 (10.3)	86.1 (9.5)	86.0 (11.2)
Hipline, mean (SD)	98.5 (10.7)	95.4 (9.3)	97.4 (10.2)
Diabetes, n (%)	2 (1)	0 (0)	2 (2)
Coronary heart disease, n (%)	2 (0.9)	4 (4)	1 (1)
Disease duration, year median (range)	2 (0-40)	2 (0-25)	2 (0-30)
History of acupuncture use, n (%)	2 (0.9)	1 (0.9)	2 (1.9)
History of TCM use, n (%)	3 (1.4)	0 (0)	1 (0.9)
History of antihypertensive drug use, n (%)	9 (4)	5 (5)	0 (0)
SBP, mm Hg, mean (SD)	147.8 (5.8)	147.4 (5.2)	147.6 (5.6)
DBP, mm Hg, mean (SD)	89.8 (7.7)	88.7 (7.0)	90.2 (7.6)
24-h BPV of SBP, mean (SD)	15.9 (6.2)	15.5 (5.3)	16.6 (5.9)
24-h BPV of DBP, mean (SD)	11.8 (4.6)	11.7 (4.0)	12.1 (4.6)

DBP, diastolic blood pressure; SBP, systolic blood pressure; SD, standard deviation.
The SBP and DBP were measured by using 24-h ambulatory blood pressure monitor (ABPM).

3.4 | Responder rate and adverse events

At week 6, 88 participants (42.1%) were responders in active acupuncture groups vs 36 (35.3%) in sham acupuncture group and 39 (37.5%) in waiting-list control group. There was no significant difference between the three groups ($P = 0.468$). At week 9, responder rate increased in active acupuncture groups (47.3%) and sham acupuncture group (44.1%); we found that active acupuncture was superior to waiting-list control (active acupuncture vs waiting-list control: 47.3% vs 34.6%, $P = 0.029$) but was not superior to sham acupuncture (acupuncture vs sham acupuncture: 47.3% vs 44.1%, $P = 0.502$). At week 12, the results were similar to week 9 (acupuncture vs waiting-list control: 47.8% vs 34.6%, $P = 0.024$; acupuncture vs sham acupuncture: 47.8% vs 40.1%, $P = 0.181$).

Five participants (2.4%) receiving active acupuncture reported five adverse events; four events were hematoma after acupuncture, and one was nausea during acupuncture. Four participants (3.9%) receiving sham acupuncture reported four adverse events, all of which were hematoma. The rate of adverse events was comparable between the three groups ($\chi^2 = 3.832$, $P = 0.147$).

4 | DISCUSSION

We found that acupuncture decreased SBP in patients with stage I hypertension by nearly 8 mm Hg after the patients received 18 sessions of acupuncture in a 6-week treatment, and the effect of SBP reduction sustained for another 6 weeks. However, the effect on BP reduction may largely be the consequence of regression to the mean. In addition, acupuncture had no effect on 24-hour BPV or visit-to-visit BPV.

A reduction in SBP by at least 5 mm Hg in the general population was corresponding to a 14% overall reduction in mortality caused by stroke, a 9% reduction in mortality caused by coronary heart disease, and a 7% reduction in all-cause mortality.[24] Systematic reviews showed a wide range in the effect of acupuncture on BP

TABLE 2 Reduction of blood pressure after acupuncture

	Acupuncture group	Sham acupuncture group	Waiting-list control group	Acupuncture vs sham (mean difference, 95% CI)	*P* value	Acupuncture vs waiting-list (mean difference, 95% CI)	*P* value	Sham acupuncture vs waiting-list (mean difference, 95% CI)	*P* value
Mean SBP (mm Hg)									
Week 6	7.2 (11.0)	4.1 (11.5)	4.1 (13.2)	2.7 (−0.4 to 5.9)	0.103	2.9 (−0.2 to 6.0)	0.078	−0.1 (−3.4 to 3.7)	0.995
Week 9	8.9 (9.9)	5.4 (11.8)	3.9 (13.6)	3.3 (0.2 to 6.3)	0.035	4.8 (1.8 to 7.8)	<0.001	1.6 (−2.0 to 5.1)	0.552
Week 12	7.8 (11.4)	4.6 (12.5)	3.0 (14.3)	3.0 (−0.5 to 6.4)	0.104	4.6 (1.2 to 8.0)	0.004	1.7 (−2.3 to 5.6)	0.582
Mean DBP (mm Hg)									
Week 6	3.7 (9.1)	0.8 (8.6)	3.3 (10.2)	2.9 (0.3 to 5.5)	0.026	0.4 (−2.2 to 3.1)	0.915	−2.5 (−5.5 to 0.6)	0.137
Week 9	4.3 (9.2)	1.8 (8.8)	3.9 (9.5)	2.5 (−0.1 to 5.2)	0.057	0.4 (−2.2 to 3.0)	0.934	−2.2 (−5.2 to 0.8)	0.210
Week 12	3.5 (9.4)	2.1 (7.9)	2.4 (10.2)	1.4 (−1.2 to 4.1)	0.412	1.1 (−1.5 to 3.7)	0.564	−0.3 (−3.3 to 2.7)	0.973
Day SBP (mm Hg)									
Week 6	5.8 (12.2)	3.8 (11.2)	2.9 (12.2)	2.0 (−1.4 to 5.4)	0.355	2.9 (−0.5 to 6.3)	0.105	0.9 (−3.0 to 4.8)	0.839
Week 9	6.6 (11.8)	5.1 (11.5)	3.3 (12.6)	1.6 (−1.7 to 4.9)	0.508	3.3 (0.1 to 6.6)	0.045	1.8 (−2.0 to 5.6)	0.514
Week 12	6.5 (11.3)	4.5 (12.3)	2.1 (14.4)	2.0 (−1.6 to 5.5)	0.388	4.4 (0.9 to 7.9)	0.009	2.4 (−1.6 to 6.5)	0.336
Night SBP (mm Hg)									
Week 6	2.7 (14.1)	1.6 (13.1)	0.8 (22.6)	1.9 (−1.2 to 5.0)	0.877	1.0 (−3.7 to 5.6)	0.501	0.8 (−3.2 to 4.8)	0.348
Week 9	4.8 (13.5)	5.8 (24.2)	1.6 (21.3)	−1.0 (−6.3 to 4.3)	0.905	3.3 (−2.0 to 8.5)	0.315	4.2 (−1.9 to 10.3)	0.238
Week 12	4.9 (17.6)	2.1 (14.9)	0.3 (16.4)	2.9 (−1.9 to 7.6)	0.327	4.6 (−0.1 to 9.3)	0.058	1.7 (−3.8 to 7.1)	0.744
Day DBP (mm Hg)									
Week 6	2.2 (8.7)	0.9 (8.9)	−0.4 (9.0)	2.9 (0.3 to 5.5)	0.026	0.4 (−2.2 to 3.1)	0.915	−2.5 (−5.5 to 0.6)	0.137
Week 9	2.6 (9.3)	2.1 (10.0)	0.7 (9.1)	2.5 (−0.1 to 5.2)	0.057	0.4 (−2.2 to 3.0)	0.934	−2.2 (−5.2 to 0.8)	0.210
Week 12	1.8 (9.0)	2.3 (9.2)	−1.3 (10.0)	1.4 (−1.2 to 4.1)	0.412	1.1 (−1.5 to 3.7)	0.564	−0.3 (−3.3 to 2.7)	0.973
Night DBP (mm Hg)									
Week 6	2.0 (10.2)	1.2 (9.4)	2.0 (12.4)	0.8 (−2.2 to 3.8)	0.823	0.0 (−3.0 to 3.0)	1.000	−0.8 (−4.2 to 2.7)	0.863
Week 9	3.4 (10.1)	3.6 (15.8)	0.7 (13.6)	−0.2 (−3.8 to 3.4)	0.989	2.7 (−0.9 to 6.2)	0.185	2.9 (−1.3 to 7.0)	0.232
Week 12	2.9 (11.6)	2.0 (9.2)	0.3 (10.5)	0.9 (−2.1 to 4.0)	0.750	2.6 (−0.4 to 5.6)	0.108	1.7 (−1.9 to 5.2)	0.503

95% CI, 95% confidence interval; DBP, diastolic blood pressure; SBP, systolic blood pressure.

Regarding the effect on SBP reduction, no statistical difference between the three groups was found at week 6; acupuncture was significantly better than both sham acupuncture ($P = 0.035$) and waiting-list control ($P < 0.001$) at week 9; difference between acupuncture and sham acupuncture was not statistically significant at week 12, but it was between acupuncture and waiting-list control ($P = 0.004$). Regarding the effect on DBP reduction, acupuncture was significantly better than sham acupuncture ($P = 0.027$) at week 6; no significant difference was found between the three groups at weeks 9 and 12.

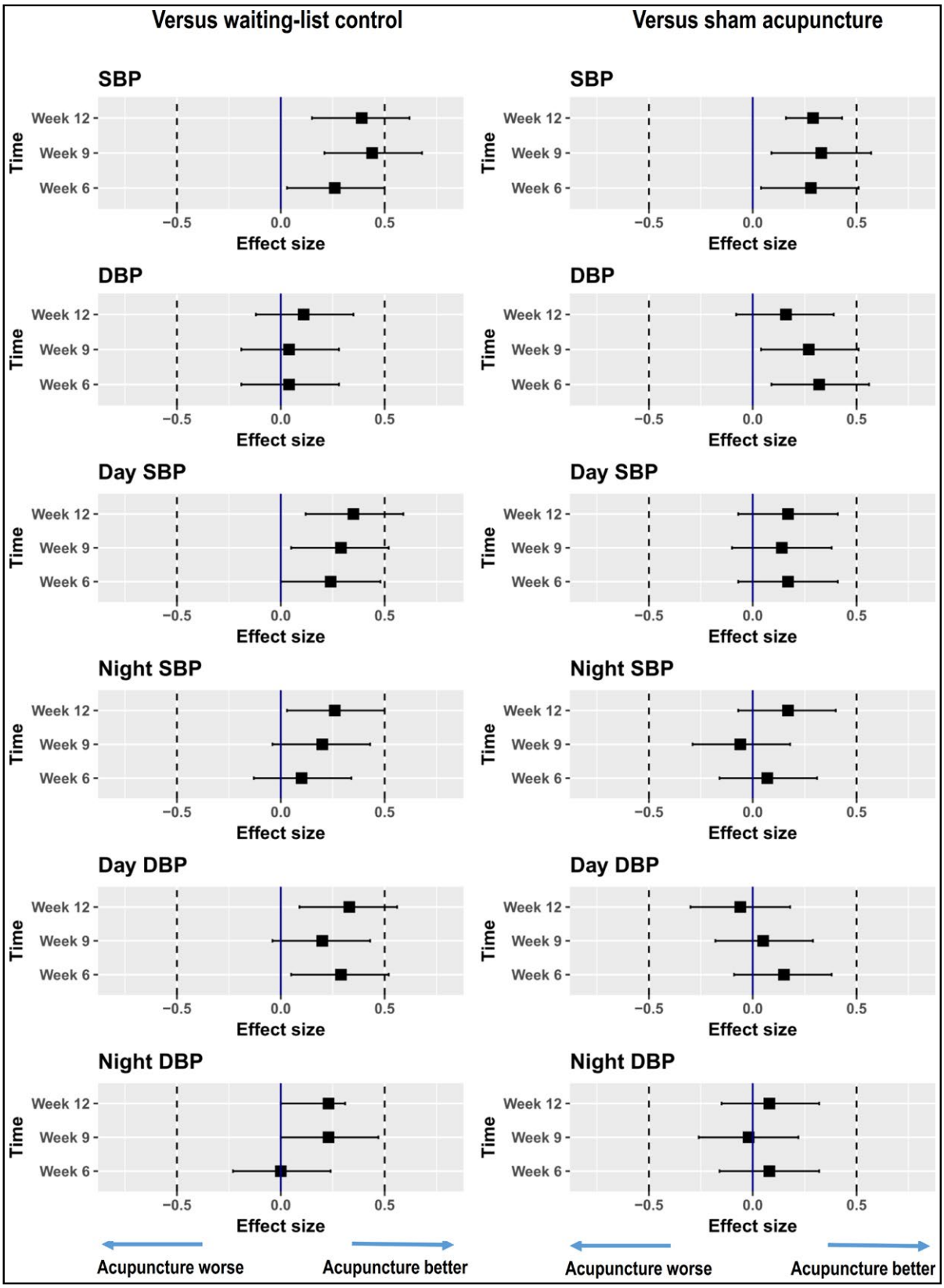

FIGURE 2 The effect sizes of acupuncture on BP control. Compared with waiting-list control and sham acupuncture, active acupuncture had small effect size in the improvement of SBP and DBP

reduction. The level of BP reduction fluctuated between 3 and 40 mm Hg; however, the generally low quality of the trials included in these systematic reviews limits the credibility of these results.[8-12] The American Heart Association (AHA) reviewed the evidence for using acupuncture for patients with hypertension and concluded that three trials were with relatively high quality.[7] One study from Germany and China showed that acupuncture induced a reduction in SBP by 5.4 mm Hg[13]; one from the United States demonstrated a reduction in SBP by 3.6 mm Hg[14]; and another one showed a reduction of 14 mm Hg in SBP.[25] The three studies also found a reduction in DBP by 3-7 mm Hg. In our trial, we found that acupuncture caused an 8-mm Hg reduction in SBP. Therefore, we may assert that acupuncture has clinical meaningful effect on SBP reduction, since it had at least 5-mm Hg reduction of SBP after 12-18 sessions of treatment. We noticed an interesting phenomenon that 24-hour BPV increased after acupuncture treatment. An increase in 24-hour BPV is correlated to cardiac, vascular, and renal damage.[26] Both positive (reduction in BP) and negative (increase in 24-hour BPV) aspects were observed in our trial. Although the harm of the increase in BPV was gradually recognized, the majority of the evidence confirms the superior prognostic value of mean BP over BPV.[26] Additionally, the 24-hour BPV also increased in the waiting-list control group. These facts indicate the positive aspect of acupuncture in hypertension treatment.

The acupuncture effect is assumed to be the composite of the regression-to-the-mean effect, the placebo effect, and specific effect of acupuncture. Whether acupuncture should be recommended for the treatment of hypertension was doubted owing to the small to moderate effect size of acupuncture compared with sham acupuncture. No study has investigated the role of the regression-to-the-mean effect in treating hypertension with acupuncture, although the effect is a common phenomenon in hypertensive patients.[27,28] The results of our study showed that the participants in the waiting-list group had SBP decreased by 4 mm Hg, and it constituted half of the acupuncture effect in BP reduction; and we also found that the participants in the waiting-list group had DBP reduced by 3 mm Hg, and this effect size was the same as active acupuncture. Based on these grounds, we assumed that the effect of regression to the mean may contribute a large part in the acupuncture effect.

A recent study showed that electroacupuncture reduced SBP by 30 mm Hg,[29] which provokes thinking on whether electrostimulation adds additional benefit on BP reduction. Our study adopted electrostimulation. However, we only found a mean reduction of 8 mm Hg in SBP. This phenomenon indicates that we may not have used the best protocol of acupuncture treatment or that the large effect size on BP reduction may be a chance finding. Therefore, we need more trials with improved acupuncture protocol and larger sample size to clarify the true effect of acupuncture.

Our study founded that acupuncture had no effect on 24-hour or visit-to-visit BPV, and we had several assumptions. First, the study subjects were patients with mild hypertension. The magnitude of BP fluctuation was smaller in patients with mild hypertension than those with stage II or III hypertension. Smaller magnitude of fluctuation leads to smaller change in BPV. Second, acupuncture exerted a sustained effect. The change from baseline in SBP was 7.2 mm Hg at week 6, 8.9 mm Hg at week 9, and 7.8 mm Hg at week 12, respectively. This sustained effect reduced the magnitude of fluctuation in BP and therefore showed no improvement in visit-to-visit BPV. Third, the follow-up period was short for the assessment of visit-to-visit BPV. With a longer follow-up period, we may be able to observe the actual BP fluctuation as the acupuncture effect gradually washed off.

Although the result of our trial confirmed that acupuncture had beneficial effect on mild hypertension, there are several questions needed to be addressed before it could be translated into clinical practice. First, performing acupuncture needs special training. We need to find out an effective and easy-to-perform protocol of acupuncture. Ideally, it should be a protocol that could be managed by hypertensive patients, like self-managed acupressure.[30,31] Second, electrostimulation on the basis of acupuncture seems to provide additional benefit,[29] so it is reasonable to conduct a trial testing the effect of transcutaneous electric stimulation on hypertension. Third, lowering BP is a long-term treatment. The role of acupuncture in the management of hypertension should be further clarified. We need to clarify the comparative effectiveness of acupuncture vs conventional medication or the add-on benefit of acupuncture when it is used on the basis of conventional medication.

The study had limitations. First, a 12-week duration is short for monitoring the effect of acupuncture on the reduction of BP and BPV. Second, unblinding the acupuncturists from group assignment may induce performance bias. Third, we did not assess the outcomes related to hypertension, like cardiovascular events or cerebrovascular events.

In conclusion, we found that 18 sessions of acupuncture had a small effect size on BP reduction but not BPV reduction, and the effect on SBP reduction lasted for another 6 weeks after acupuncture treatment was stopped. However, studies are still needed before acupuncture could be translated into clinical practice.

CONFLICT OF INTEREST

The authors declared no conflict of interest.

AUTHOR CONTRIBUTION

FRL had full access to all the data in the study and took responsibility for the integrity of the data and the accuracy of the data analysis. HZ and JL contributed equally to the manuscript. FRL, YL, and XW contributed to the study concept and design. JL, JC, XL, YLH, XRC, ML, RHW, XD, JS, and TPG collected the data. LZ and HZ supervised the performance of the study. XS performed statistical analysis. XW, XRC, RHW, and JS gave administrative, technical, or material support. HZ and JL drafted the first manuscript, and all the authors read and revised the manuscript and approved it for publication.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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