

THE EFFECT OF 12-WEEK LIUZIJUE EXERCISE TRAINING ON PATIENTS WITH HYPERTENSION: A RANDOMIZED, CONTROLLED CLINICAL TRIAL

CAIPING ZHENG[#], XIN ZHANG[#], JUNYAO WANG[#], YUHAN WANG, LUMING QI, NANNAN LIU, LINA XIA*
College of Health Preservation and Rehabilitation, Chengdu University of Traditional Chinese Medicine, Chengdu, China
[#] Caiping Zheng, Xin Zhang and Junyao Wang have contributed equally to this work and share first authorship

ABSTRACT

Objective: The purpose of our study was to investigate the effect of 12 weeks Liuzijue exercise, a kind of traditional Chinese health exercise (TCHE), on middle-aged and elderly patients with hypertension.

Methods: The present program was a randomized, controlled clinical trial with Liuzijue exercise used as an intervention. 41 subjects with essential hypertension who met the inclusion criteria (mean age: 63.00±7.53 years) were randomly assigned to either the Liuzijue group (n=21) or the control group (n=20). The volunteers in the Liuzijue group were encouraged to take part in 12 weeks Liuzijue exercise training (60 minutes of Liuzijue exercise training, three times a week for a total of 12 weeks). While the subjects in the control group did not receive any exercise training and maintained their routine drug therapy regimens during the program period. 24-hour ABP, lipid profile (TC, TG, HDL-C, LDL-C), blood glucose, urea, and serum creatinine were measured within a week before and after the experiment.

Results: The 12 weeks Liuzijue exercise intervention led to a significant reduction of the nighttime SBP ($P=0.008$), pulse pressure ($P=0.024$), and a numerically, but had no significant effect on nighttime DBP ($P=0.095$). Conversely, SBP and DBP at other times did not significantly change. The nocturnal SBP fall rate improvements from pre- to post-treatment were from 1.77±0.10 to 6.75±7.77 ($P=0.037$) for the Liuzijue group and from 3.57±8.77 to 9.63±9.80 ($P=0.031$) for the control group. In addition, there was an upward trend in all of the blood pressure parameters in the control group. Liuzijue exercise did also influence lipid or glucose metabolism. The 12 weeks Liuzijue training had led to a significant increase in the concentration of HDL-C ($P=0.035$) and a greater reduction in LDL-C ($P=0.001$). The level of blood glucose in both groups had a marginally significantly increase within the normal range ($P<0.05$). No changes in urea were seen in the Liuzijue or the control group ($P>0.05$). The increase of serum creatinine was found in the Liuzijue group ($P=0.023$) but not in the control group.

Conclusion: This is the first report showing that 12 weeks of Liuzijue exercise training can reduce nighttime SBP, pulse pressure, and augmented nocturnal BP fall rate in hypertensive patients. Liuzijue exercise training can improve blood lipid metabolism and reduce risk factors for cardiovascular disease, which was an effective and safe alternative pharmacotherapy.

Keywords: Primary hypertension, Liuzijue exercise, blood pressure, circadian rhythms, ambulatory blood pressure.

DOI: 10.19193/0393-6384_2021_5_419

Received October 15, 2020; Accepted June 20, 2021

Introduction

Hypertension is one of the critical risk factors for cardiovascular diseases (CVD). Elevated blood pressure (BP) can result in target organs damage such as chronic kidney disease, heart failure, coronary heart disease, ischemic and hemorrhagic stroke, retinopathy, and so on⁽¹⁾. Hypertension ranks the first risk factor in the population attributable to CVD risk in the United States⁽²⁾. The number of patients

with hypertension increased from 594 million in 1975 to 1.13 billion in 2015, an increase of 90%⁽³⁾. Surprisingly, less than one-fifth of hypertension patients worldwide can be controlled because of lacking awareness and failure to treat in time⁽⁴⁻⁷⁾. Thereby, hypertension remains a major global health problem. Antihypertensive drugs, as the primary mean of treating hypertension, have many adverse reactions in the course of treatment, and also increase the economic burden for hypertension patients and

their families⁽⁸⁾. There is growing evidence indicating that exercise produces significant physiological and health benefits⁽⁹⁾. Various researches showed that regular exercise can decrease blood pressure levels, improve glucose and lipid metabolism disorders⁽¹⁰⁾. The guidelines for the prevention and treatment of hypertension unequivocally advocate that exercise should be used as adjuvant therapy for lowering blood pressure⁽¹¹⁾. Traditional Chinese Health Exercise (TCHE) has a history of 2,000 years. TCHE focuses on breathing and meditation, meditating on the nerve, which is soft and gentle. This strategy has played an important role in treating and preventing disease⁽¹²⁻¹³⁾. Like Taichi and Baduanjin⁽¹⁴⁻¹⁶⁾, Liuzijue exercise is also a kind of TCHE created by Tao Hongjing, who was an outstanding physician in Northern and Southern Dynasties. The Liuzijue exercise consists of six moves, which are Xu, He, Hu, Si, Chui and Xi. Because of its solid and flexible quality characteristics, Liuzijue exercise plays a vital role in promoting the relaxation of muscles and activating blood circulation and improving the quality of life.⁽¹⁷⁾

Previous studies have focused on the influence of Tai chi, Dongeui and Baduanjin exercise on hypertension⁽¹⁸⁻¹⁹⁾. Studies have shown that Liuzijue exercise can affect office or resting BP in patients with hypertension⁽²⁰⁾. However, by searching relevant research results that don't find the effect of Liuzijue exercise on ambulatory blood pressure (ABP), and blood pressure circadian rhythm (BPCR) in patients with hypertension. In the study, we analyzed and explored the effect of Liuzijue exercise on ABP, BPCR, and lipid metabolism of middle-aged and elderly essential hypertensive patients. This study could provide a new strategy for non-pharmacological treatment of clinical hypertension.

Materials and methods

Study design and ethics approval

This study was a randomized, controlled clinical trial that was designed to explore the effect of Liuzijue exercise on middle-aged and elderly patients with hypertension. In order to ensure the reliability of the results and avoid the interference of human factors on the test results, the researchers responsible for data collection were not informed the group allocations. SPSS software (version 23.0) was used to generate a random number table to determine the group of the included subjects, and relevant records were made in the Case Report Form (CRF).

Two groups of the Liuzijue group and the control group were performed in this study. The program had been approved by the Medical Ethics Committee of the Affiliated Hospital of Chengdu University of Traditional Chinese Medicine. All procedures of the experiment were carried out in accordance with the institutional guidelines.

Inclusion and exclusion criteria

Inclusion criteria:

- Patients with the age between 45 and 80 were included in this study. Their gender was not limited;
- According to the “Guidelines for Prevention and Treatment of Hypertension in China (2018 version)” and “the New Guidelines on Hypertension of the European Society of Cardiology (ESC) 2018”⁽²¹⁾, the hypertension of patients was 140mmHg \leq systolic blood pressure (SBP) <180 mmHg, and/or 90 mmHg \leq diastolic blood pressure (DBP) <110 mmHg without intaking antihypertensive drugs, or a previous diagnosis of hypertension, although the BP is less than 140/90 mmHg in the case of antihypertensive drugs, should still be diagnosed as hypertension;
- Candidates did not have the habit of overeating or regular exercise (exercise less than 2 times a week and <20 minutes each time) in the last four weeks prior to inclusion in the study.

Exclusion criteria:

- Volunteers who had secondary hypertension such as drug-induced hypertension or elevated blood pressure caused by primary aldosteronism, acromegaly, Cushing's syndrome, and other diseases were excluded;
- Patients with grade 3 hypertension (SBP \geq 180mmHg and (or) DBP \geq 110mmHg) were excluded;
- Participants complicated with other serious medical conditions, such as diabetes, heart failure, and so on; had long-term heavy smoking or drinking habits were excluded;
- Patients with a history of severe trauma or surgery within the last six months were excluded;
- People who had participated in clinical trials of exercise therapy such as Tai chi or Baduanjin exercise in the previous six months were excluded.

Research Methods

The subjects from two communities were recruited on a voluntary basis from March 2020 to August 2020. Recruitment was through on-site screening, propaganda posters, and patient databases. All volunteers were required to complete

a structured questionnaire of the basic information about name, age, gender, height, body mass, personal diet and exercise habits. Meanwhile, other measures including the history of hypertension, family history of hypertension, medication use, tobacco use, and alcohol consumption were also obtained at baseline. Body mass index (BMI) was calculated as body mass (kg) divided by height (m) squared. Then, all participants underwent the hospital physical examination. Finally, 52 hypertensive patients who met the criteria were randomly assigned to the Liuzijue exercise group ($n = 26$) and the control group ($n = 26$). All subjects were informed of the purpose of the trial and signed an informed consent voluntarily form prior to participating in the study.

The control group

The hypertensive patients in the control group did not take part in any exercise program and maintained their routine drug therapy regimens throughout the program period. Meanwhile, patients were given general health daily lifestyle intervention, including dietary guidance, life and daily living, psychological guidance, smoking cessation and alcohol restriction.

The Liuzijue group

On the basis of the general health daily lifestyle intervention, the participants in the Liuzijue group attended a 12 weeks Liuzijue exercise program. This program consisted of a warm-up period involving stretching (10 minutes), a main Liuzijue treatment (50 minutes: included six distinct movement routines, with each movement routine repeated six times, the bull's eye rate was used to determine individual exercise intensity), and a cool-down (10 minutes) portion, for three times a week session lasted 60 minutes. During the 12-week study period, neither group was allowed to change their original antihypertensive drugs therapy regimens except in exceptional circumstances.

Outcome measurements

Office BP measurement

The office BP was measured at sitting position after at least 5 minutes' rest without taking antihypertensive drugs using Omronan electronic sphygmomanometer. The patient was seated with the upper arm at heart level and kept quiet when the measurement was performed. BP was measured three times with intervals longer than 1 minute.

Then, the average values of BP measured in the three times taken as the final value.

ABP Monitoring

ABP was measured repeatedly every 30 minutes during daytime (8:00-20:00) and every 60 minutes during nighttime (20:00-8:00) using a non-invasive portable BioX dynamic ECG blood pressure recorder device and appropriate cuff, respectively. The patients were instructed by a professional to tie the cuff to the left upper arm. Patients were instructed to keep the left arm at the heart level, keep quiet and avoid strenuous exercise during the monitoring.

SBP and DBP Load was calculated as the percentage of blood pressure higher than normal readings, with normal readings for the 24-h period, daytime period and nighttime period defined as 130/80, 135/85 and 120/70 mmHg, respectively.

The nocturnal SBP/DBP fall rate was calculated as the percentage of nighttime BP lower daytime BP: $(\text{daytime BP} - \text{nighttime BP}) / \text{daytime BP} \times 100\%$.

A decrease of 10-20% in nocturnal systolic BP over daytime blood pressure was defined as "Dipper". It occurred as a normal physiological change. When the nocturnal BP fall rate was more than 20% or less than 10% was called "Non-dipper"⁽²²⁾.

Detection of biochemical indexes

Lipid profile include: triglyceride (TC), triglyceride (TG), high density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C), blood glucose, urea and serum creatinine were measured for patients in two groups prior to intervention and after the 12-week trial. All subjects were required to fasting for 12 hours. 5 mL of peripheral venous blood was extracted for the detection of lipid and other indicators. All biochemical analyses were performed in the clinical laboratory of Daying County Hospital of Traditional Chinese Medicine.

Statistical Analysis

To our knowledge, there were few studies related to the effect of Liuzijue exercise on hypertension. The sample size was estimated based on our previous experience. It was calculated based on a reduction of 4 mmHg in office DBP after 12-week TCHE training⁽²³⁾. The dropout rate was 10%. In order to achieve a power of 90% at a significant level of 5%, 32 participants each group with a total of 64 participants were needed in our study. The experimental data were analyzed using statistical

software (IBM SPSS version 23.0). Kolmogorov-Smirnov method was used to verify the normality of measurement data. The measurement data conforming to normal distribution were expressed in the form of means ± standard deviation (M±SD), while the measurement data conforming to non-normal distribution were expressed in the form of medians (interquartile ranges) and conducted with statistical disposal after normal transformation.

Independent-sample Test and Paired t-test were used to compare the differences between and within groups of the measurement data conforming to the normal distribution, respectively. When the assumption of normality was violated, the Wilcoxon rank-sum test and Wilcoxon signed-rank test were used. Dichotomous data were expressed by frequency or composition ratio, and the chi-square test was used. The control methods were intra-group before and after control and inter-group parallel comparison. The experimental data were tested by bilateral test, and the value of P<0.05, indicating a statistically significant difference.

Results

Basic information of subjects

A total of 52 hypertensive patients who met the criteria agreed to attend the study and were randomly divided into the Liuzijue group (n=26) and the control group (n=26). After 12-week Liuzijue exercise intervention, a total of 41 patients completed the program. Five subjects were dropout in the Liuzijue group because of failing to undergo hospital laboratory examination. Six subjects were dropout in the control group during the trial (one participant dropped out as a result of suffering from diabetes during the trial period and others did not undergo the final laboratory detection). In the final, there were 21 subjects in the Liuzijue group and 20 subjects in the control group. Data from all these subjects were used for the final statistical analysis.

Table 1 showed the basic characteristics of all subjects. There was no significant difference between two groups in baseline regarding demographic features including age, gender, height, body mass, body mass index (BMI), heart rate (HR), current smoking, current alcohol intake, and the conditions of hypertension including office SBP and DBP, the hypertension stage, hypertensive family history, and medication history (P>0.05) and the materials had good comparability.

Variables	Liuzijue group (N=21)	Control group (N=20)	P-value
Sex (male/female)	6/15	7/13	0.658
Age (years)	65.19±6.47	60.70±8.03	0.055
Height (cm)	153.86±7.94	156.80±8.51	0.259
Body mass (kg)	56.60±7.52	61.10±8.47	0.079
BMI (kg/m ²)	23.88±2.44	24.84±2.53	0.223
HR (beats/minute)	76.00±12.43	70.05±10.49	0.106
Hypertension duration (years)	8 (7)	7.5 (7)	0.570
Current smoking			
Yes	1	3	0.563
No	20	17	
Current alcohol intake			
Yes	2	6	0.208
No	19	14	
Hypertensive family history			
Yes	8	6	0.585
No	13	14	
Office SBP (mmHg)	153.81±16.57	144.85±18.20	0.107
Office DBP (mmHg)	85.19±12.15	88.90±10.33	0.300
Medication history (months)	1 (2)	1 (2)	0.084
Hypertension stage			
Grade 1	10	12	0.427
Grade 2	11	8	

Table 1: Baseline Characteristics of participants.

Note: BMI: body mass index; HR: heart rate; Office SBP: Office systolic blood pressure; Office DBP: diastolic blood pressure.

Treatment APP

The 12-week Liuzijue exercise intervention led to a significant reduction of the nighttime SBP from 140.67±18.47 to 132.62±12.02 mmHg (P=0.008) and pulse pressure from 62.71±12.46 to 57.38±10.10 mmHg (P=0.024) while had no changes in the control group. And there was a numerically, but no significant change in the nighttime SBP load compared to baseline (81.83±25.01 to 74.46±23.77%, P=0.095) in the Liuzijue group.

However, Liuzijue exercise did not significantly affect the SBP and DBP at daytime and over 24-hour (P>0.05). The results showed that there was an upward trend in all of the blood pressure parameters in the control group but was not statistically significant, except for SBP (P= 0.024), pulse pressure over 24-hour, and SBP (P=0.008), daytime pulse pressure (P=0.006), SBP load (P=0.043), pulse rate (P=0.027) during daytime. Changes of ABP meant

the differences (Δ) in ABP between the baseline and final values (final values minus the baseline).

Figure 1 showed the changes of ABP (Δ) in 24-hour, daytime, nighttime between the baseline and final values in two groups. As shown in Figure 1 that over the 24-hour period, SBP decreased in the Liuzijue group by 3.4 mmHg, while in the control group increased by 6.6 mmHg. There was a significant difference ($P=0.01$) in the magnitude of SBP changes between two groups. The changes of DBP in the two groups were similar. Daytime SBP and DBP increased in the control group while in the Liuzijue group did not change significantly. Nighttime SBP and DBP decreased in the Liuzijue group while SBP and DBP in the control group did not change significantly. The change of SBP and DBP in nighttime between the Liuzijue and the control group had no statistical significance. Examination of blood pressure dipping status revealed that two groups did not change significantly from baseline to post-intervention. While the nocturnal SBP fall rate in two groups improvements from pre- to post-treatment were from 1.77 ± 0.10 to 6.75 ± 7.77 ($P=0.037$) for the Liuzijue group and from 3.57 ± 8.77 to 9.63 ± 9.80 ($P=0.031$) for the control group (Table 2).

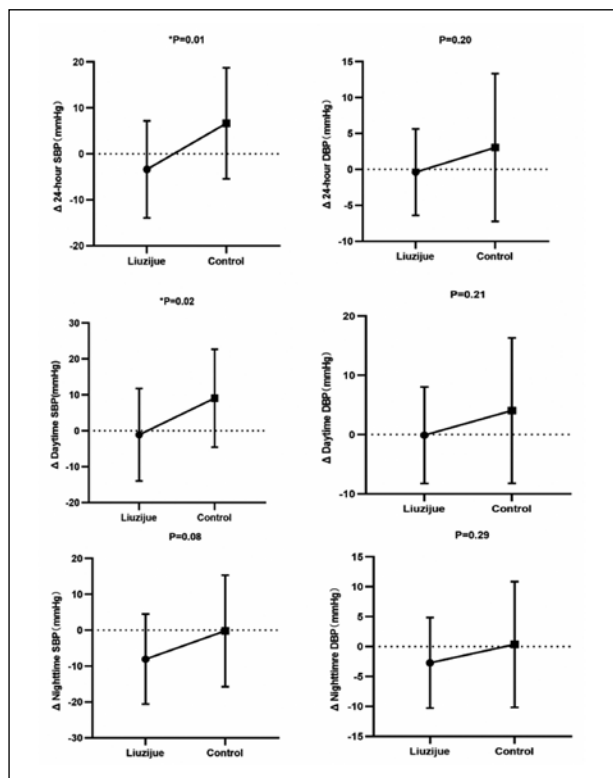


Figure 1: Change of ABP in 24-hour, Daytime, Nighttime periods in two groups.
 Note: Δ SBP/DBP=12 weeks final values - the baseline; Data were means \pm SD; * $p<0.05$; ** $p<0.01$.

Variables	Liuzijue group			Control group		
	Pre	Post	P	Pre	Post	P
24- hour ABP						
SBP, mmHg	142.57 ± 16.18	139.19 ± 10.72	0.158	130.60 ± 14.75	137.28 ± 11.68	0.024*
DBP, mmHg	82.52 ± 9.12	82.14 ± 8.19	0.775	84.55 ± 11.90	87.60 ± 10.52	0.201
Pulse pressure, mmHg	60.05 ± 11.24	57.05 ± 8.24	0.054	46.05 ± 8.00	49.65 ± 10.35	0.048*
Pulse rate, beats/min	71.05 ± 6.82	72.48 ± 6.38	0.234	74.10 ± 8.48	76.70 ± 5.94	0.174
SBP load, %	67.80 ± 24.04	66.03 ± 22.54	0.604	53.74 ± 29.08	54.94 ± 25.60	0.864
DBP load, %	52.03 ± 28.10	50.97 ± 26.10	0.779	53.65 ± 29.70	54.91 ± 29.74	0.827
Daytime ABP						
SBP, mmHg	143.71 ± 17.13	142.62 ± 12.34	0.701	132.15 ± 16.04	141.20 ± 15.45	0.008**
DBP, mmHg	85.76 ± 10.87	85.67 ± 9.54	0.958	87.05 ± 13.44	91.10 ± 12.81	0.156
Pulse pressure, mmHg	58.24 ± 12.34	56.95 ± 8.90	0.486	44.70 ± 9.37	50.10 ± 11.38	0.006*
Pulse rate, beats/min	75.38 ± 7.34	76.95 ± 6.79	0.304	78.25 ± 9.22	82.55 ± 6.68	0.027*
SBP load, %	60.63 ± 26.18	61.91 ± 28.43	0.770	41.00 ± 32.14	54.57 ± 25.80	0.043*
DBP load, %	47.27 ± 30.41	47.32 ± 28.80	0.989	45.10 ± 32.85	51.09 ± 30.35	0.371
Nighttime ABP						
SBP, mm Hg	140.67 ± 18.47	132.62 ± 12.02	0.008**	127.00 ± 16.14	126.80 ± 13.41	0.955
DBP, mm Hg	77.95 ± 8.88	75.24 ± 8.14	0.116	79.55 ± 11.51	79.90 ± 8.33	0.883
Pulse pressure, mmHg	62.71 ± 12.46	57.38 ± 10.10	0.024*	47.45 ± 8.05	46.90 ± 10.80	0.806
Pulse rate, beats/min	63.33 ± 6.80	65.57 ± 8.73	0.214	65.65 ± 8.43	66.00 ± 6.66	0.832
SBP load, %	81.83 ± 25.01	74.46 ± 23.77	0.095	58.73 ± 29.27	61.48 ± 31.75	0.684
DBP load, %	62.71 ± 32.25	62.71 ± 32.25	0.335	65.86 ± 27.37	63.91 ± 35.61	0.739
Circadian rhythm						
Nocturnal SBP fall rate, %	1.77 ± 0.10	6.75 ± 7.77	0.037*	3.57 ± 8.77	9.63 ± 9.80	0.031*
Nocturnal DBP fall rate, %	8.52 ± 9.06	11.67 ± 9.56	0.253	7.96 ± 10.03	11.22 ± 11.22	0.290
Dipper						
Dipper	4	6	0.469	7	6	0.736
Non-dipper	17	15		13	14	

Table 2: Ambulatory blood pressure (ABP) in two groups.
 Note: * $p<0.05$; ** $p<0.01$.

Lipids and biochemical indexes

As shown in Table 3, Figure 2 and Figure 3, the concentration of the TG and TC did not change significantly in the Liuzijue or the control group after the 12 weeks intervention.

The 12 weeks Liuzijue exercise training had led to a significant increase of the HDL-C from 1.47 ± 0.29 to 1.57 ± 0.40 mmol /L ($P=0.035$) with no significant change was found in the control group. The Liuzijue group shown greater reduction in LDL-C from 2.95 ± 0.67 to 2.47 ± 0.38 mmol/L ($P=0.001$) during 12weeks Liuzijue exercise. The level of blood

glucose in both groups had a marginally significantly increased within normal range from 5.40 (1.02) to 5.76 (0.51) mmol/L in the Liuzijue group (P=0.076) after the training period and from 5.10 (0.76) to 5.40 (2.19) mmol /L (P=0.042) in the control group. No significant change in urea was seen between the Liuzijue and the control group (Table 3).

The increase of serum creatinine from 67.07±35.10 to 71.59±43.25 umol/L (P=0.023) was found in the Liuzijue group but not in the control group, which remained at baseline levels (Table 3).

Variables	Pre	Post	P	Pre	Post	P
Blood glucose (mmol/L)	5.40 (1.02)	5.76 (0.51)	0.010*	5.10 (0.76)	5.40 (2.19)	0.042*
TC (mmol/L)	5.10 ±0.76	4.87 ±0.67	0.094	5.18 ±1.09	5.40 ±1.19	0.112
TG (mmol/L)	1.52 ±0.71	1.50 ±0.68	0.911	1.46 ±0.60	1.53 ±0.65	0.516
HDL-C (mmol/L)	1.47 ±0.29	1.57 ±0.40	0.035*	1.49 ±0.36	1.58 ±0.39	0.274
LDL-C (mmol/L)	2.95 ±0.67	2.47 ±0.38	0.001**	2.94 ±0.85	2.89 ±0.96	0.606
Serum creatinine (umol /L)	67.07 ±35.10	71.59 ±43.25	0.023*	65.70 ±14.02	66.73 ±15.65	0.526
Urea (mmol/L)	4.43 (1.21)	4.72 (1.53)	0.664	4.63 (1.56)	4.58 (2.12)	0.940

Table 3: Biochemical indexes under different interventions.

Note: TC: total cholesterol; TG: triglyceride; HDL-C: high density lipoprotein cholesterol; LDL-C: low density lipoprotein cholesterol; Values are expressed as mean ± SD or medians (interquartile ranges); *p<0.05; **p<0.01.

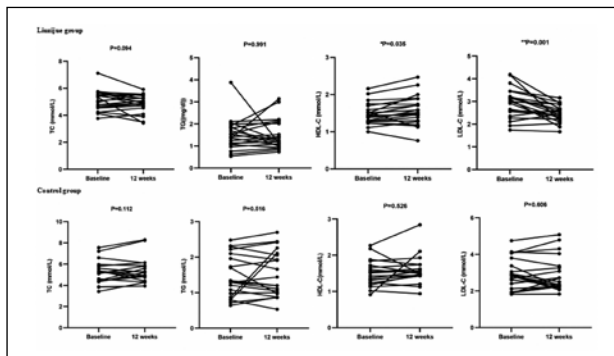


Figure 2: Change of TC, TG, HDL-C, LDL-C in two groups.

Note: between the baseline and 12 weeks final values (12 weeks final values minus the baseline).

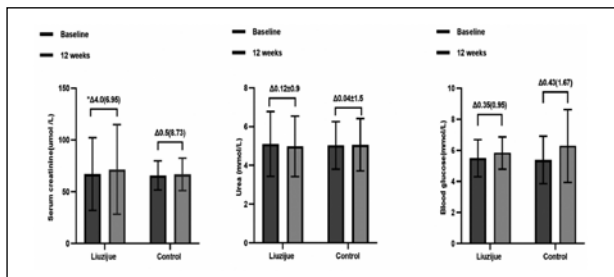


Figure 3: Change of Serum creatinine, Urea between the baseline and 12 weeks final values (12 weeks final values minus the baseline) in the Liuzijue and control group.

Discussion

Liuzijue exercise is a traditional Chinese health exercise that combines meditation and gentle movements. It is more compatible with middle-aged and old people to maintain function. However, the evidence on whether Liuzijue exercise is effective on patients with hypertension has not been evaluated to date. Our study aimed to investigate the effect of 12 weeks Liuzijue exercise intervention on ABP and related risk factors in middle-aged and elderly patients with hypertension.

As the results of our experiment shown, Liuzijue exercise was effective in reducing nighttime SBP level in patients with hypertension, however did not appear to be effective for lowering 24-hour ABP and daytime ABP. 12 weeks Liuzijue exercise intervention decreased the level of the nighttime SBP (from 140.67±18.47 to 132.62±12.02 mmHg) and nighttime pulse pressure (from 62.71±12.46 to 57.38±10.10 mmHg), augmented nocturnal SBP fall rate (from 1.77±0.10 to 6.75±7.77 %). While the subjects in the control group who did not take part in Liuzijue exercise training, the blood pressure showed an upward trend after 12 weeks. We suspected that the climate may have a great influence on the results of the experiment. Our clinical study was conducted between September and December at that time, temperature dropped and average temperatures of at most 10 degrees Celsius. Studies have reported that there is a significant negative correlation between indoor temperature and BP⁽²⁴⁾. Cooling increased left ventricular preload, index of myocardial oxygen demand, and arterial blood pressure in older adults⁽²⁵⁾. In a cross-sectional study involved 1897 patients indicated that daytime SBP was negatively related to personal-level environmental temperature (PET), daytime systolic BP fell by 0.14 mmHg for each °C increase in daytime PET, while average nighttime systolic BP was found to be significantly affected by seasonality rather than by temperature⁽²⁶⁾. Interestingly, there was no increase in blood pressure of patients in the Liuzijue group, which may be because the exercise compensated for the increase in blood pressure caused by the low temperature. Current Liuzijue exercise program was proven to be effective and resulted in blood pressure reductions.

Nocturnal hypertension (the average of nighttime values higher than 125/75 mmHg) and non-dipping blood pressure patterns are stronger risk predictors of future cardiovascular mortality and morbidity than either daytime or 24-hour BP⁽²⁷⁻²⁹⁾.

In recent years, chronomedicine gradually becomes an improved strategy in hypertension management⁽³⁰⁾. Taking antihypertensive drugs at night may be more effective than taking them in the morning in improving the dipping pattern of hypertensive patients⁽³¹⁾. Whether the time of day of exercise training also affects blood pressure is unknown. The results of the meta-analysis showed that aerobic endurance exercise significantly reduced daytime ABP, while evening exercise was not affected⁽³²⁾. While, the other study indicated that morning exercise increased ambulatory heart rate and morning exercise did not change ambulatory BP, while evening exercise decreased nighttime BP and cardiac work⁽³³⁾, which was consistent with our study. Our study was carried out at 15:00 to 16:00 afternoon. Liuzijue exercise may be a novel complementary or alternative approach to lowering nocturnal BP. The explanation for the failure of the Liuzijue exercise to change the ABP at other times maybe the trial period was short. This exercise training may need to be long enough to cause significant changes in blood pressure.

Hypertension and dyslipidemia are often reviewed as the independent risk factors for atherosclerosis⁽³⁴⁾. Arterial hypertension and hypercholesterolemia are frequently seen in clinical practice⁽³⁵⁾. The National Health and Nutrition Examination Survey from 2001 to 2002 showed that the overall prevalence of combined hypertension and hypercholesterolemia was 18%⁽³⁶⁾.

Hypertensive patients are often associated with abdominal obesity, decreased high density lipoprotein cholesterol (HDL-C), increased low density lipoprotein cholesterol (LDL-C), hyperglycemia, and hyperlipidemia⁽³⁷⁾. High density lipoprotein (HDL) is considered as good cholesterol because it can transport cholesterol from extrahepatic tissue to the liver for metabolism and excretion⁽³⁸⁾. Low density lipoprotein (LDL) is considered harmful because it can cause cholesterol to accumulate in arteries and form plaques. Therefore, higher Low-density lipoprotein (LDL), low-density lipoprotein (LDL), or both, which are beyond the normal systemic level, will increase the risk of cardiovascular disease⁽³⁹⁾. There is evidence suggesting that dyslipidemia is an important inductive factor for hypertension. The study founded that many newly diagnosed high blood pressure patients had at least one lipid abnormality⁽⁴⁰⁾. Global Cohort studies based on Chinese community indicated that increased TG and lower HDL-C will increase the risk of new-

onset hypertension⁽⁴¹⁾. Elevated serum levels of TC, LDL-C, and non-HDL-C increased the risk of hypertension in working-age Japanese men. The risk of hypertension increased regardless of low or high levels of HDL cholesterol⁽⁴²⁾. The risk of hypertension increased as the lever of LDL-C increased. One possible explanation is that dyslipidemia have some metabolites including fatty acids, glycerophospholipid metabolism, alanine, aspartate and glutamate metabolism and alanine implicated in insulin resistance, oxidized low-density lipoprotein formation, endothelial dysfunction and vascular remodeling and so on, which in turn leading patients with dyslipidemia develop to hypertension⁽⁴³⁾.

Therefore, it is crucial to reduce hypertension risk factors while lowering blood pressure. Six months of Liuzijue exercise lowered triglycerides and LDL-C and raised HDL-C in healthy middle-aged women⁽⁴⁴⁾. In our study, apart from its blood pressure-lowering effect, the Liuzijue exercise can also adjust the status of blood lipid metabolism that can decrease LDL-cholesterol while increasing HDL-cholesterol and to a certain extent, reduced the cardiovascular risk of patients with hypertension.

Conclusions

The novel results of our trial are important in several aspects. First, our study investigated the effect of Liuzijue exercise on ambulatory blood pressure and related risk factors on middle-aged and elderly patients with hypertension. The 12 weeks Liuzijue exercise intervention for stress obtained significant nighttime systolic blood pressure benefits for patients with hypertension. Second, Liuzijue exercise training can improve blood lipid metabolism and reduce risk factors for cardiovascular disease.

References

- 1) Roth G A, Mensah G A, Johnson C O, et al. Global Burden of Cardiovascular Diseases and Risk Factors, 1990-2019: Update From the GBD 2019 Study[J]. *J Am Coll Cardiol*, 2020, 76(25): 2982-3021.
- 2) Fuchs F D, Whelton P K. High Blood Pressure and Cardiovascular Disease[J]. *Hypertension*, 2020, 75(2): 285-292.
- 3) Worldwide trends in blood pressure from 1975 to 2015: a pooled analysis of 1479 population-based measurement studies with 19.1 million participants[J]. *Lancet*, 2017, 389(10064): 37-55.

- 4) Egan BM, Kjeldsen S E, Grassi G, et al. The global burden of hypertension exceeds 1.4 billion people: should a systolic blood pressure target below 130 become the universal standard[J]. *J Hypertens*, 2019, 37(6): 1148-1153.
- 5) Dzau V J, Balatbat C A. Future of Hypertension[J]. *Hypertension*, 2019, 74(3): 450-457.
- 6) Di Chiara T, Scaglione A, Corrao S, et al. Education and hypertension: impact on global cardiovascular risk[J]. *Acta Cardiol*, 2017, 72(5): 507-513.
- 7) Ortega Y, Dillon CF, Hughes JP, et al. Trends in hypertension prevalence, awareness, treatment, and control in older U.S. adults: data from the National Health and Nutrition Examination Survey 1988 to 2004[J]. *J Am Geriatr Soc*, 2007, 55(7): 1056-65.
- 8) Ferdinand K C, Nasser S A. Management of Essential Hypertension[J]. *Cardiol Clin*, 2017, 35(2): 231-246.
- 9) Bricca A, Harris L K, Jäger M, et al. Benefits and harms of exercise therapy in people with multimorbidity: A systematic review and meta-analysis of randomised controlled trials[J]. *Ageing Res Rev*, 2020, 63: 101166.
- 10) Press V, Freestone I, George C F. Physical activity: the evidence of benefit in the prevention of coronary heart disease[J]. *Qjm*, 2003, 96(4): 245-51.
- 11) Arnett D K, Blumenthal RS, Albert M A, et al. 2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease: Executive Summary[J]. *Journal of the American College of Cardiology*, 2019, 74(10): 1376-1414.
- 12) Wang XQ, Pi YL, Chen PJ, et al. Traditional Chinese Exercise for Cardiovascular Diseases: Systematic Review and Meta-Analysis of Randomized Controlled Trials[J]. *J Am Heart Assoc*. 2016, 5(3): e002562.
- 13) Fan B, Song W, Zhang J, Er Y, et al. The efficacy of mind-body (Baduanjin) exercise on self-reported sleep quality and quality of life in elderly subjects with sleep disturbances: a randomized controlled trial. *Sleep Breath*[J]. 2020, 24(2): 695-701.
- 14) Xiong X, Wang P, Li S, Zhang Y, Li X, et al. Effect of Baduanjin exercise for hypertension: a systematic review and meta-analysis of randomized controlled trials[J]. *Maturitas*. 2015, 80(4): 370-378.
- 15) Shao B Y, Zhang X T, Vernooij R W M, et al. The effectiveness of Baduanjin exercise for hypertension: a systematic review and meta-analysis of randomized controlled trials[J]. *BMC Complement Med Ther*, 2020, 20(1): 304.
- 16) Guan Y, Hao Y, Guan Y, Wang H, et al. Effects of Tai Chi on essential hypertension and related risk factors: A meta-analysis of randomized controlled trials[J]. *J Rehabil Med*. 2020, 52(5):jrm00057.
- 17) Li P, Liu J, Lu Y, Liu X, et al. Effects of long-term home-based Liuzijue exercise combined with clinical guidance in elderly patients with chronic obstructive pulmonary disease[J]. *Clin Interv Aging*. 2018, 3(13): 1391-1399.
- 18) Jiang Y, Zou J. Analysis of the TCM theory of traditional Chinese health exercise[J]. *Journal of Sport and Health Science*, 2013, 2(4): 204-208.
- 19) Song Y, Li J, István B, Xuan R, et al. Current Evidence on Traditional Chinese Exercises for Quality of Life in Patients With Essential Hypertension: A Systematic Review and Meta-Analysis[J]. *Front Cardiovasc Med*. 2021, 20(7): 627518.
- 20) Bergler-Klein J. What's new in the ESC 2018 guidelines for arterial hypertension: The ten most important messages[J]. *Wien Klin Wochenschr*, 2019, 131(7-8): 180-185.
- 21) Ishikawa J, Kario K, Shimada K. [Nocturnal blood pressure (dipper, non-dipper)][J]. *Nihon Rinsho*, 2004, 62 Suppl 3: 408-14.
- 22) Jin X, Pan B, Wu H, Xu D, et al. The effects of traditional Chinese exercise on hypertension: A systematic review and meta-analysis of randomized controlled trials[J]. *Medicine(Baltimore)*. 2019, 98(3): e14049.
- 23) Sherwood A, Smith P J, Hinderliter A L, et al. Effects of exercise and stress management training on nighttime blood pressure dipping in patients with coronary heart disease: A randomized, controlled trial[J]. *Am Heart J*, 2017, 183: 85-90.
- 24) Wilson T E, Gao Z, Hess K L, et al. Effect of aging on cardiac function during cold stress in humans[J]. *Am J Physiol Regul Integr Comp Physiol*, 2010, 298(6): R1627-33.
- 25) Modesty P A, Morabito M, Massetti L, et al. Seasonal blood pressure changes: an independent relationship with temperature and daylight hours[J]. *Hypertension*, 2013, 61(4): 908-14.
- 26) Cho M C. Clinical Significance and Therapeutic Implication of Nocturnal Hypertension: Relationship between Nighttime Blood Pressure and Quality of Sleep[J]. *Korean Circ J*, 2019, 49(9): 818-828.
- 27) Campbell PT, White W B. Utility of ambulatory blood pressure monitoring for the management of hypertension[J]. *Curr Opin Cardiol*, 2017, 32(4): 365-372.
- 28) Yano Y, Kario K. Nocturnal blood pressure and cardiovascular disease: a review of recent advances[J]. *Hypertens Res*, 2012, 35(7): 695-701.
- 29) Tsimakouridze E V, Alibhai F J, Martino T A. Therapeutic applications of circadian rhythms for the cardiovascular system[J]. *Front Pharmacol*, 2015, 6: 77.
- 30) Cappuccio F P. The Role of Nocturnal Blood Pressure and Sleep Quality in Hypertension Management[J]. *Eur Cardiol*, 2020, 15: e60.
- 31) Cornelissen V A, Buys R, Smart N A. Endurance exercise beneficially affects ambulatory blood pressure: a systematic review and meta-analysis[J]. *J Hypertens*, 2013, 31(4): 639-48.
- 32) Brito LC, Rezende R A, Mendes C, et al. Separate aftereffects of morning and evening exercise on ambulatory blood pressure in prehypertensive men[J]. *J Sports Med Phys Fitness*, 2018, 58(1-2): 157-163.
- 33) Hurtubise J, Mclellan K, Durr K, et al. The Different Facets of Dyslipidemia and Hypertension in Atherosclerosis[J]. *Curr Atheroscler Rep*, 2016, 18(12): 82.
- 34) Tadic M, Cuspidi C. Combination of hypertension and hypercholesterolemia: do we have an adequate response [J]. *Pol Arch Intern Med*, 2019, 129(12): 852-854.
- 35) Hu C, Kong H, Qu F, et al. Application of plasma lipidomics in studying the response of patients with essential hypertension to antihypertensive drug therapy[J]. *Mol Biosyst*, 2011, 7(12): 3271-9.
- 36) Wong N D, Lopez V, Tang S, et al. Prevalence, treatment, and control of combined hypertension and hypercholesterolemia in the United States[J]. *Am J Cardiol*, 2006, 98(2): 204-8.

- 37) Kulkarni H, Mamtani M, Blangero J, et al. Lipidomics in the Study of Hypertension in Metabolic Syndrome[J]. *Curr Hypertens Rep*, 2017, 19(1): 7.
- 38) Physical Exercise for Human Health[J]. *Med Sci Sports Exerc*, 2021, 53(4): 882.
- 39) Regev-Avraham Z, Halabi M, Israeli Z, et al. Lipid profile as a strong indicator of coronary plaques: noninvasive assessment by multislice computerized tomography[J]. *Coron Artery Dis*, 2020.
- 40) He D, Fan F, Jia J, et al. Lipid profiles and the risk of new-onset hypertension in a Chinese community-based cohort[J]. *Nutr Metab Cardiovasc Dis*, 2021, 31(3): 911-920.
- 41) Otsuka T, Takada H, Nishiyama Y, et al. Dyslipidemia and the Risk of Developing Hypertension in a Working-Age Male Population[J]. *J Am Heart Assoc*, 2016, 5(3): e003053.
- 42) Ke C, Zhu X, Zhang Y, et al. Metabolomic characterization of hypertension and dyslipidemia[J]. *Metabolomics*, 2018, 14(9): 117.

Acknowledgement

Fund Project: This work was supported by the Key research and development projects of Sichuan Province (Study on the thought of "preventive treatment of disease" of the Liuzijue exercise in the intervention of essential hypertension vascular disease, NO 2020YFS0302)

Corresponding Author:

LINA XIA
College of Health Preservation and Rehabilitation, Chengdu
University of Traditional Chinese Medicine, Chengdu, 610075,
China
Email: xialina@cdutcm.edu.cn
(China)